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Clinical and basic cardiovascular features of patients with COVID-19 admitted to a tertiary care center in Turkey

Türkiye'de bir üçüncü basamak sağlık merkezine başvuran COVID-19'lu hastaların klinik ve temel kardiyovasküler özellikleri

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Abstract

Aim: COVID-19 is a new zoonotic infectious disease that can cause acute respiratory failure, which first occurred in Wuhan, China in December 2019. The aim of study was to analyze cases with COVID-19 admitted to a tertiary care center in Turkey.

Methods: We evaluated demographic characteristics, clinical symptoms or signs, comorbidities, laboratory results, chest computed tomography (CT) findings and outcomes including hospitalization, intensive care unit (ICU) admission and survival of 49 patients (20 females, 29 males) diagnosed with COVID-19 disease.

Results: Twenty (40.9%) of the cases were female and 29 (59.1%) were male. The mean age of the patients was 56.20 (17.65) years. The most common symptom was cough (75.5%). Hypertension (26.5%) was the most prevalent comorbid disease. Troponin I result of 42 (85.7%) patients were negative (reference value <0.1 ng/mL). Ten patients (18.4%) were admitted to the ICU and overall mortality rate was 4.1% (n=2). The important characteristics of two non-survivors were as follows: 1) A 67-year-old-man, high fever (38.5^{0}C), current smoker, diabetes mellitus (+), chronic obstructive pulmonary disease (COPD) (+), congestive heart failure (+), first admission to ICU, bilateral infiltration on chest CT, troponin I: 4.01 ng/L. 2) A 38-year-old-man, current smoker, COPD (+), first admission to ICU and high CRP (120.86 m/L).

Conclusion: The clinical parameters that determine the prognosis of COVID-19 are currently acute respiratory tract exacerbation and accompanying cardiovascular diseases such as hypertension and coronary artery disease. Cardiac enzyme monitoring is important in patients with cardiovascular risk factors.

Keywords: COVID-19, Clinical profile, Tertiary care center

Öz

Amaç: COVID-19 akut solunum yetmezliğine neden olabilen, ilk kez Aralık 2019'da Çin'in Wuhan şehrinde ortaya çıkan yeni zoonotik bir enfeksiyöz hastalıktır. Bu çalışmanın amacı Türkiye'de bir üçüncü basamak hastaneye başvuran COVID-19'lu hastaları analiz etmektir.

Yöntemler: Çalışmada, COVID-19 hastalık tanısı almış 49 hastanın (20 kadın, 29 erkek) demografik özellikleri, klinik semptom ve bulguları, komorbiditeleri, laboratuvar sonuçları, toraks bilgisayarlı tomografi (BT) bulguları ve sağkalım, yoğun bakım ünitesine (YBÜ) ve servis yatışlarını değerlendirdik.

Bulgular: Vakaların 20'si (%40,9) kadın ve 29'u (%59,1) erkekti. Hastaların ortalama yaşı 56,20 (17,65) idi. En sık görülen semptom öksürüktü (%75,5). Hipertansiyon en sık eşlik eden hastalıktı (%26,5). 42 hastanın (%85,7) troponin I değeri negatifti (referans değer <0,1 ng/mL). 10 hasta YBÜ'ye başvurmuştu ve genel mortalite oranı %4,1 idi (n=2). Ölen iki hastanın önemli karakteristik özellikleri şöyleydi: i) 67 yaş erkek hasta, yüksek ateş (38,5^{0}C), sigara içici, diabetes mellitus (+), kronik obstrüktif akciğer hastalığı (KOAH) (+), konjestif kalp yetmezliği (+), ilk başvuru YBÜ'ye, toraks BT'de bilateral infiltrasyon ve troponin I (4,01 ng/L). ii) 38 yaş erkek hasta, sigara içici, KOAH (+), ilk başvuru YBÜ'ye ve yüksek c-reaktif protein (120,86 m/L).

Sonuç: Mevcut bilgilerimize göre COVID-19'da prognozu belirleyen klinik parametreler akut solunum yolu alevlenmesi ve hipertansiyon veya koroner arter hastalığı gibi kardiyovasküler hastalıkların eşlik etmesidir. Kardiyovasküler risk faktörleri olan hastalarda kardiyak enzim takibi önemlidir.

Anahtar kelimeler: COVID-19, Klinik profil, Üçüncü basamak merkez

Introduction

An infectious new zoonotic coronavirus disease (COVID-19), which first occurred in Wuhan, China in December 2019, was declared as a pandemic in March 2020 and since April 2020, thousands of people have been affected by the disease and died in more than a hundred countries [1-3]. COVID-19 has become a serious public health problem causing socio-economic collapse all over the world. The first positive case in Turkey had contact with Europe and was announced on 11 March 2020 [4-6]. New positive cases and deaths due to this highly contagious disease continue in many countries, including ours. The numbers of COVID-19 patients in Turkey are as follows: Total number of tests: 889,742, number of positive cases: 110,130, number of deaths: 2,805, number of cases admitted to intensive care unit (ICU): 1,776, number of intubated patients: 883, number of cases recovered from the disease 29,140 [7].

Vaccine and drug studies have been conducted in several countries of the world, including our country, to no avail [5]. In the literature, there are studies reporting the clinical progress and outcomes of patients with COVID-19 and it is reported that the disease is directly and indirectly associated with cardiovascular complications [2,3,5,8].

In the study, we aimed to evaluate the clinical and basic-simple cardiovascular features of patients with COVID-19 infection admitted to a tertiary care center in Turkey.

Materials and methods

Study design and population

We performed a retrospective cohort study with 49 COVID-19 cases from a tertiary hospital in Turkey. The study was conducted in accordance with the Declaration of Helsinki guidelines. An official study permit was obtained from Amasya University Medical Faculty Sabuncuoglu Serefeddin Research and Training Hospital with issue number 62949364-929. In addition, a system registration was created with the number 2020-05-05T14-08-05 in the Ministry of Health. The study included patients with laboratory-confirmed COVID-19 infection who were hospitalized and treated in Amasya University Sabuncuoglu Serefeddin Research and Training Hospital in Turkey from March 14 to April 13, 2020. Nasopharyngeal swab samples were obtained, and patients with laboratory-confirmed positive test results of reverse-transcriptase-polymerase-chain-reaction (RT-PCR) were considered to have definitive diagnoses of COVID-19 infection. We summarized the epidemiological characteristics and examined the prognosis of the disease. Hospital archive records and computer database were reviewed and demographic characteristics, clinical symptoms, comorbidities (smoking, hypertension, chronic obstructive pulmonary disease, diabetes mellitus, coronary artery disease, congestive heart failure, malignancy), vital signs, laboratory test results, chest computed tomography (CT) imaging findings and outcomes (hospitalization, ICU admission and survival) of patients were recorded.

Computed tomography and nasopharyngeal swab were obtained for the definitive diagnosis of COVID-19 from suspected patients. A suspected patient was defined as any of the followings: i) exhibiting any one of fever, cough or sputum complaints, ii) the clinical status cannot be explained by another disease except COVID-19, iii) a history of travel to other countries in his/her relatives or himself/herself within 14 days before the beginning of symptoms, iv) contact history with COVID-19 with an accurate diagnosis within 14 days before the beginning of symptoms [3].

Patients who required hospitalization or ICU admission due to definitive diagnosis of COVID-19 were included in the study in the presence of at least one of following findings: i) any lesion on the radiological imaging (chest x-ray or CT), ii) severity of the symptoms and findings (temperature 38^0C, dyspnea, cough, sputum, malaise, altered mental status, increased respiratory rate ($\geq$30 per minute), shortness of breath, peripheral cyanosis, oxygen saturation below 93%, arterial blood oxygen partial pressure (PaO_2)/oxygen concentration (FiO_2) $\leq$300 mmHg), iii) critically ill patients (acute respiratory failure, requiring endotracheal intubation, sepsis or shock, admission to ICU and organ failure), iv) coexisting diseases (hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, coronary artery disease, neoplastic disease, chronic renal-liver disease, congestive heart failure, cerebrovascular diseases, nursing home resident), v) patients who cannot provide their own isolation (soldiers, crowded family, elderly patients, lack of space in the house, nursing home resident, dormitory-dwellers) [3].

Patients who had pneumonia agents or clinical findings other than COVID-19, positive patients to which home isolation is recommended according to the guideline of the Scientific Committee of Turkish Ministry of Health and those diagnosed with COVID-19 but not requiring hospitalization per the decision of an infectious disease specialist or pulmonologist (based on severity of the symptoms, radiological imaging, physical examination) were excluded from the study [3].

Recovery discharge criteria included regression of respiratory symptoms, decreased fever, regression of pulmonary findings on chest CT, and a negative RT-PCR result [9].

Statistical analysis

All statistical analyses were performed with SPSS 23.0 (SPSS for Windows, Chicago, IL, SA). Continuous variables were expressed as mean (standard deviation) and categorical variables were defined as percentages (%).

Results

Between March 22 and April 13, 2020, we obtained 855 nasopharyngeal swabs from suspicious cases and evaluated 49 patients with RT-PCR confirmed COVID-19 infection in the hospital. Twenty (40.9%) of the cases were females and 29 (59.1%) were males. The mean age of the patients was 56.20 (17.65) years, ranging between 17-88 years. Two patients had international contact (Saudi Arabia and France). Six of the patients had family contact and two cases were healthcare professionals. Fifteen (30.6%) cases were current smokers, 31 (61.3%) were non-smokers and 3 (6.1%) were ex-smokers. There were no patients who resided in nursing homes or were homeless. The fever of the cases ranged from 36 to 39 ^{o}C, with a mean of 36.75^{o}C (0.66). The respiratory rate of the patients ranged between 18 and 32 breaths per minute with a mean of 21.19 (3.47) breaths. The mean systolic blood pressure of cases

was 110.20 (9.01) mmHg, ranging between 100 and 130 mmHg. The heart rate of the cases varied between 58 and 105 beats per minute, with a mean of 76.89 (8.95) beats. The mean oxygen saturation was 92.71 (5.63) (range: 82-99%) on room air. Clinical symptoms and signs of patients and their comorbidities are presented in Table 1. The most common symptom was cough (75.5%). Hypertension (HT) (26.5%) was the most prevalent coexisting disease. Demographics of the patients admitted to ICU are shown in Table 2.

Table 1: Clinical symptoms and signs of patients and their comorbidities

| | | COVID-19 patients (n=49) | |
		No.	%
Gender	Male	29	59.1
	Female	20	40.9
Smoking status	Current smoker	15	30.6
	Non-smoker	31	63.3
	Ex-smoker	3	6.1
Hypertension		13	26.5
Diabetes mellitus		3	6.1
Coronary artery disease		4	8.2
COPD		5	10.2
Asthma		-	-
Nursing home resident		-	-
Neoplastic disease		2	4.1
Chronic liver diseases		-	-
Congestive heart failure		2	4.1
Cerebrovascular diseases		-	-
Chronic renal diseases		-	-
Confusion		1	2.05
Pleural effusion		3	6.1
ICU admission		10	20.4
Mortality		2	4.1
	Min-Max	Mean	SD
Respiratory rate (min)	18-32	21.19	3.47
Systolic blood pressure (mmHg)	100-130	110.20	9.01
Temperature (°C)	36-39	36.75	0.66
Heart rate (min)	58-105	76.89	8.95
Age (years)	17-88	56.20	17.65

Table 2: Demographics of patients admitted to ICU

| | | COVID-19 patients (n=10) | |
		No.	%
Gender	Male	8	80
	Female	2	20
Smoking status	Current smoker	5	50
	Non-smoker	3	30
	Ex-smoker	2	20
Hypertension		2	20
Diabetes mellitus		2	20
Coronary artery disease		3	30
COPD		3	30
Neoplastic disease		1	10
Congestive heart failure		1	10
Confusion		1	10
Pleural effusion		2	20
Mortality		2	20
	Min-Max	Mean	SD
Systolic blood pressure (mmHg)	100-120	107	6.74
Temperature (°C)	36-39	37.2	1.06
Heart rate (min)	72-90	79.4	7.12
Age (years)	38-80	62.7	12.9
Albumin, g/L	20-38.1	28.2	5.91
Creatinine, mg/dL	0.52-1.26	0.82	0.24
Troponin I, ng/L	0.04-4.01	0.49	1.23
CRP, mg/L	3.97-246.9	108.8	70.6
Hemoglobin, g/dL	5.7-14.9	11.8	2.45
Lymphocyte, 10*9 L	0.4-1.73	1.07	0.46
Platelet, 10*3/uL	153-503	298	123
Neutrophil, 10*3/uL	0.93-26.92	9.93	7.74
D-dimer	0.88-2.53	1.46	0.74

Table 3 presents the blood results of patients including renal functions (urea, creatinine), liver tests (alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin), lactate dehydrogenase (LDH), sodium, glucose, c-reactive protein (CRP), albumin and complete blood count (white blood cell (WBC), neutrophil, hemoglobin, platelets, eosinophil, basophil. Troponin I result of 42 (85.7%) patients were negative (reference value <0.1 ng/mL). In Table 4, chest CT findings of the cases are presented. Three patients (6.1%) had pleural effusion and 14 patients (28.5%) had bilateral lung infiltration. Ground glass densities were detected in 28 (57.1%)

and consolidation in 7 (14.2%) patients. Ten patients (18.4%) were admitted to the ICU and the overall mortality rate was 4.1% (n=2). The important characteristics of two non-survivors were as follows: i) A 67-year-old-man, high fever (38.5°C), current smoker, diabetes mellitus (+) and chronic obstructive pulmonary disease (+), congestive heart failure (+), first admission to ICU, bilateral infiltration on the chest CT, lower serum albumin level (20 g/L), CRP:3.97 mg/L and higher AST (6755 U/L), and ALT (256 U/L), troponin I: 4.01 ng/L, LDH: 1058 U/L, ii) A 38-year-old-man, current smoker, chronic obstructive pulmonary disease (+), first admission to ICU and higher CRP (120.86 m/L). The samples of CT findings of six patients are shown in Figures 1a-1f.

Table 3: Blood parameters of the cases

	n	Minimum	Maximum	Mean (SD)
Albumin, g/L	39	20	47.6	37.24 (6.86)
Creatinine, mg/dL	49	0.52	1.29	0.84 (0.19)
AST, U/L	47	14	6755	173.93 (98.94)
ALT, U/L	47	6	256	29.85 (37.35)
Total bilirubin, mg/dL	46	0.16	1.54	0.48 (0.26)
LDH, U/L	46	142	1058	320.28 (164.67)
Sodium, mmol/L	47	134	146	139.68 (3.03)
Glucose, mg/dL	47	76	427	118.34 (54.4)
CRP, mg/L	49	0.46	246.9	54.06 (58.58)
Eosinophil, 10*9 L	47	0	0.7	0.08 (0.12)
Hemoglobin, g/dL	49	5.7	15.5	12.83 (1.65)
Neutrophil, 10*3/uL	47	0.93	26.9	5 (4.55)
Platelet, 10*3/uL	49	108	503	227.5 (87.02)
Lymphocyte, 10*9 L	47	0.40	2.93	1.47 (0.57)
Troponin I, ng/L	49	0.04	4.01	0.119 (0.55)
D-dimer, ng/mL	31	0.40	310	11.14 (55.47)

Table 4: Chest CT findings of the patients

	n	%
Pleural effusion	3	6.1
Bilateral infiltration	14	28.5
Infiltration		
Right lung upper lobe	19	38.7
Right lung middle lobe	12	24.4
Right lung lower lobe	24	48.9
Left lung upper lobe	17	34.6
Left lung lower lobe	20	40.8
Left lung lingula	12	24.4
Consolidation	7	14.2
Ground glass densities	28	57.1
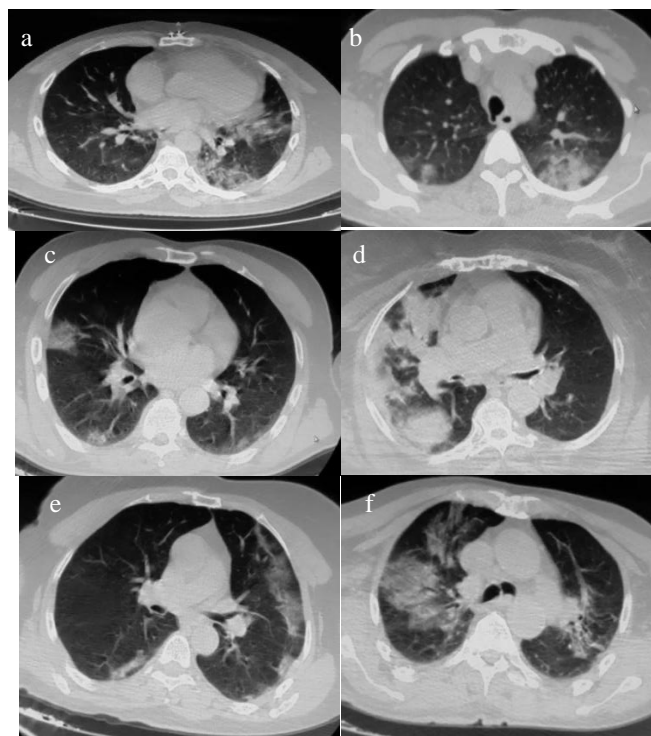
Figure 1: Chest CT samples of the patients (a: consolidation and peribronchial thickening in the left lower lobe, b: ground glass densities and alveolar consolidation in the posterior segment of the right lung upper lobe and the apicoposterior segment of the left lung lobe, c: patchy infiltration and ground glass densities in the right lung, d: consolidation and ground glass densities in right lung parenchyma, e: multifocal patchy infiltration and ground glass densities in the right and left lung, f: diffuse ground glass densities and multifocal pneumonic infiltration)

Discussion

In our hospital, the fever of all patients admitted to emergency department is measured first in the triage and patients demonstrating any of the fever, cough or sputum complaints are considered as patients with suspected COVID-19. Typical symptoms in patients with COVID-19 are commonly known as fever, cough, dyspnea, muscle weakness, malaise, sore throat and respiratory symptoms (cough, dyspnea), but some patients are also known to present with chest pain and palpitations [1,11]. The diagnostic test usage, demographics and mortality rates of COVID-19 can differ between countries [1]. We particularly focused on clinical and basic-simple cardiac features of our patients.

Cardiac arrhythmias and elevation of troponin I can be seen with COVID-19, and the specific effect of this disease on the cardiovascular system remains uncertain [8]. Based on our current knowledge, the pathophysiology of the high pathogenicity of COVID-19 is not fully understood in elderly patients or those with severe comorbidities, but it is stated that there is a relationship between increased age, cardiovascular disease and COVID-19 [8]. In a study, it is stated that the overall case-mortality rate associated with the disease in China is 2.3%, however, this rate increased to 8.0% in patients between the ages of 70-79 years and to 14.8% in patients over the age of 80 [8,11]. In this study, the mean age of patients was 56.20 (17.65) years and the mortality rate was 4.1%. One of our patients who died due to COVID-19 was a 67-year-old male, current smoker, with DM, CHF and COPD, and a high serum troponin value (4.01 ng/L). The other non-survivor was 38-year-old male, current smoker, with COPD and he had a high serum CRP level (120.86 m/L). Although only mild signs of infection are seen in the majority of patients, increased troponin level, which indicates the cardiac complication of COVID-19, is seen in 20-30% of patients, especially in the elderly with hypertension, heart failure, CAD and DM [1,12,13]. It is reported that in patients with COVID-19, mortality rate increases up to 70% in case of high troponin level and CAD [1,13]. Ventricular dysfunction and increased inflammatory markers including CRP and NT-proBNP are also associated with poor prognosis [1,13]. In another meta-analysis including patients with COVID-19, the presence of HT was reported as 17.1%, the presence of cardiovascular and cerebrovascular disease was 16.4%, and the rates of comorbid HT and CAD in our study were 26.5% and 8.2%, respectively [8,14].

Several studies in hospitalized patients in China report that heart damage is more common and may be associated with a poor prognosis in patients who are followed up and die in the ICUs [8,15-17]. In our study, the number of patients admitted to ICU was 10 (20.4%) and two (20%) of those died. Seven (80%) patients recovered from the ICU and were discharged, including one patient who was intubated and resuscitated due to cardiopulmonary arrest, and the other, a current smoker who had previously received a coronary artery bypass-graft. The troponin levels of five (10.2%) patients in our study were relatively high, and this may be due to the low average age of our group and their relatively low comorbidities such as CAD and DM (8.2% and 6.1%, respectively). One of the two patients (50%) who died had a high troponin value and three of five patients (60%) with increased troponin needed ICU. The frequency of cardiac arrhythmia is twice as high in patients with COVID-19 admitted to ICU [8,15].

Previous studies showed that patients with COVID-19 had prominent levels of proinflammatory cytokines [8,17]. In one of our two patients who died, CRP value was very high (120.86 mg/L) and ICU was needed in 24.3% (n=9) of 37 patients whose CRP value was above the reference value (0-5 mg/L). Cytokine discharge associated with systemic inflammation may lead to atherosclerotic plaque instability, rupture, and myocarditis [1,18]. The mean CRP value in our patients was 54.06 (58.58) mg/dL, and this relatively low value may be due to less coexisting diseases such as CAD and DM.

Limitations

This single-centered study had some limitations. To begin with, the size of the patient population was relatively small, and we could not compare the data of survivors and non-survivors. Only patients diagnosed with COVID-19 and treated in the hospital were included in the study, and patients with home isolation were excluded. In the future, multicenter and large-scale studies are needed in Turkey.

Conclusions

According to our current knowledge, clinical parameters that determine the prognosis of COVID-19 are acute respiratory exacerbation, accompanied by cardiovascular diseases such as hypertension and coronary artery disease. We think that cardiac enzyme monitoring including troponin is important especially in patients with cardiovascular risk factors.

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