

RESEARCH ARTICLE

Evaluation of thorax computed tomography findings of patients with COVID-19 associated myocarditis

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Abstract

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COVID-19, myocarditis, pleural effusion, pneumonia, computed tomography Introduction: It is known that human coronaviruses cause myocarditis, and during the pandemic, a series of coronavirus disease (COVID-19) related myocarditis cases have been reported. It is stated that cardiac magnetic resonance (CMR) has a specificity of up to 91% and a sensitivity of 67% for the diagnosis of myocarditis. The present study aims to determine whether patients at risk for myocarditis might be recognized on thoracic CT, comparing thoracic computed tomography (CT) and laboratory findings of patients with COVID-19-associated myocarditis that can be a significant consequence for COVID-19 patients and controls. Methods: The study included 51 patients with elevated troponin levels, CMR, and suspected myocarditis to meet this aim. As a result of the evaluation, while myocarditis findings such as a signal change in myocardial contrast involvement on T1 and T2 weighted images and contrast involvement in myocarditis in post-contrast series were detected in 31 patients, no abnormality was detected in the CMRs of 20 patients Results: When the thoracic CT findings of the groups were compared, no significant difference was detected in the volumetric evaluations of infiltration frequency, distribution, lateralization, lobar involvement, and lung involvement. No infiltration related to COVID-19 was observed in most of the patients in both groups. Pleural and pericardial effusion were more frequently observed in the group with myocarditis. Conclusion: The present study revealed that myocardial involvement can occur without COVID-19-related distinct lung involvement and that pleural-pericardial effusion can be an alert for myocarditis diagnosis.

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Introduction

The virus, named SARS-CoV-2 by the World Health Organization, emerged in China's Wuhan city, spread to the whole world and infected millions of people in a brief time after its emergence in December 2019.¹ The infection named Coronavirus Disease 2019 (COVID-19) can progress asymptomatic or with mild symptoms. However, approximately 20% of the cases can have severe symptoms requiring hospitalization.²

Thoracic Computed Tomography (CT) is the most susceptible radiological method used for the evaluation of lung involvement in COVID-19 patients. In CT, there is a ground-glass appearance compatible with viral pneumonia, whether accompanied by consolidation. CT findings are usually bilaterally or peripherally distributed and include the lower lobes.³

Myocarditis is an inflammatory heart disease characterized by inflammatory infiltrations and myocardial damage without ischemic reasons. It is known for a long time that human coronaviruses cause myocarditis. During the pandemic, a series of COVID-19-related myocarditis cases were reported.³

The clinical manifestation of SARS-CoV-2 myocarditis varies between cases. While some patients can admit to the hospital with relatively mild symptoms such as fatigue and shortness of breath, some patients describe chest pain on exertion and chest tightness.^{4,5} The American Heart Association (AHA) recommends performing tests with further cardiac imaging such as echocardiography or cardiovascular magnetic resonance (CMR) on patients with symptoms consistent with myocarditis.⁶

In this study, we aim to obtain data that can establish the possible connection between the CT and laboratory findings of patients with COVID-19-associated myocarditis, which can have fatal effects and cause serious problems for COVID-19 patients and the control group, and myocarditis. We wanted to examine which CT findings are common in patients with myocarditis, and whether there is a relationship between involved lung volume and myocarditis or not. In addition, we intended to use laboratory data to support CT findings. In conclusion, we aimed to determine whether thoracic CT findings could be used to detect patients at risk for COVID-19-related myocarditis.

Material and Methods

The study was conducted as an observational and retrospective study. Ethical committee approval

(Ankara City Hospital Clinical Research Committee No. 2 Decision dated June 2, 2021, numbered E2-21-526) and the Republic of Türkiye Ministry of Health's permission were obtained. The study included 51 patients over 18 years of age who had or were having COVID-19 infection and applied to our hospital with complaints such as chest pain, shortness of breath, and palpitation between April 1, 2020, and June 30, 2021 and had high troponin values that raised myocarditis suspicions and whose CMR examination were conducted. Lake Lous criteria, updated in 2018, were used to diagnose myocarditis.⁷ As a result of CMR, 31 patients with myocarditis findings such as myocardial signal changes on T1A and T2A images and myocardial contrast involvement in post-contrast series and 20 patients without any pathological CMR findings were divided into two groups: the myocarditis group and the normal group.

Thoracic CT scanning is standard for all patients and obtained with a multi sectional GE 128 Revolution Evo model (GE Healthcare, US, 2018) in the supine position and inspiration phase. Scanning parameters are 100 kV tube voltage, 50-399 mAs, and a section thickness of 1.3mm

Patients' CMR were performed with a GE 1.5 Tesla Signa Explorer model (GE Healthcare, USA, 2018) MRI device, and they consist of cine sequences, morphological sequences, flow sequences, perfusion, and late contrast sequences.

The groups' thoracic CT were compared in terms of COVID-19 findings. The distribution of lesions (especially ground glass opacities (GGO), crazy-paving pattern (CPP), and consolidation areas which are often encountered in COVID-19 pneumonia (irregular peripheral nodular, confluent peripheral, peribronchovascular, perilobular, and peripheric linear irregular opacities), lobar involvement (upper lobe, middle lobe, lower lobe, middle and lower lobe, upper and lower lobes, and all lobes), and lateralization) were evaluated. In addition, peripheral irregular reticulation-atelectasia, pericardial-pleural effusion, and lymphadenopathy findings were recorded. In addition, lung volumes and involvement percentages were calculated. D-dimer (mg/L), CK-MB (µg/L), and troponin (ng/L) values were recorded from the groups' laboratory data.

In computed tomography, attenuation was measured with Hounsfield Unit (HU) and the density of water was accepted as 0 HU, while the den-





sity of air was accepted as -1000 HU. In several studies, the normally aerated lung parenchyma was measured at -900 and -500/-700 HU. In line with case studies and software suggestions, lung parenchyma aerated with -1024 and -705 HU was accepted as -705 and +5 consolidation and ground glass opacities. In the study, the affected lung volume was obtained with the measurements of unaerated and poorly aerated lung areas. Patients' thoracic CT images were uploaded to the AW Volume Share 7 workstation with Thoracic VCAR software for volume measurement. The software provides the affected percentage and volume according to the whole lung volume by calculating the unaerated and poorly aerated parenchyma areas through attenuation values.

First, the groups with and without myocarditis were demographically evaluated and compared. Then, thoracic CT findings in terms of COVID were evaluated separately for both groups and compared within themselves and between the groups. In addition, with the special Thoracic VCAR program, lung volumetric measurements (right lung volume, left lung volume, total lung volume, right lung involvement percentage, left lung involvement percentage, total lung involvement percentage, total lung involvement percentage, total lung involvement percentage, and total lung involvement volume) were conducted, and data were obtained for statistical analysis. Finally, the laboratory values of the patients were combined with other data and forwarded for statistical analysis.

In the evaluation of data, SPSS 25.0 (IBM Corp. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp) statistics package program was used. In the study, descriptive statistics for categorical and continuous variables (mean, standard deviation, median, number, and quantile) were given. And the homogeneity of the variances, which is among the preconditions of parametric tests, was checked with the "Levene" test. The "Shapiro-Wilk" test was used to check the normality assumption. When it was desired to evaluate the differences between the two groups, the "Student's t-Test" was used in the conditions where parametric test preconditions were met, and if not, the "Mann Whitney-U test" was used. The relationships between the categorical variables were analyzed using Fisher's Exact Test and Pearson's Chi-Square Test. p<0,05 and p<0.01 levels were considered statistically significant.

Results

Of the study participants, 19 were female and 32 were male. The mean age of the myocarditis group and the normal group were respectively $37.74\pm13,757$ and $46,4\pm16,188$. It was found that there was no statistically significant difference in terms of sex and age between the groups (p>0,05) (Table 1).

Table 1: Evaluation of Demographic Information

		Patier		р	
		Myocarditis (n=31)	Normal (n=20)		
Gender	Female	10 (%32.3)	9 (%45)	0.844	0.358 2
	Male	21 (%67.7)	11 (%55)		0.550
Age		37.74±13.757	46.4±16.188	-1.976	0.056 ¹
		41 (25;46)	45 (35;53)		

1: Independent sample t test (t); 2: Chi-Square Test ($\chi 2$)

When the thoracic CT findings of the study groups were examined (Table 2), while GGO was present in 25,8% of the myocarditis group, it was present in 55% of the normal group. There is a statistically significant difference between the groups in terms of GGO prevalence ($\chi 2=4,432$ p=0,035).

While pleural effusion was observed in 12,9% of the myocarditis group, effusion was not observed in any patient in the normal group. There is a statistically significant relationship between the groups in terms of pleural effusion prevalence ($\chi 2=4,200 \text{ p}=0,040$).

Between the groups, no statistically significant relationship was found in terms of lobar involvement ($\chi 2=4,563$ p=0,207). While 63% bilateral and 38% unilateral parenchymal involvement were observed in the myocarditis group; the normal group demonstrated 91% bilateral and 9% unilateral involvement. No significant difference was found between the groups in terms of lateralizing involvement ($\chi 2=2,249$ p=0,134). No significant difference was observed between the groups in terms of lung volumes, involvement percentages, and mean values obtained from laboratory parameters (p>0,05) (Table III and IV).

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Table II: Evaluation of Clinical Findings According to Study Groups Patients

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Table III: Evaluation of Lung Volume and Percentage of Involvement in Thorax CT Examination by Study Groups

Patients

		Myocarditis (n=31)	Normal (n=20)		
Consumed allows	no	23 (%74.2)	9 (%45)		
Ground glass		20 (777 112)	5 (1010)	4.432	0.035 1
opacity	yes	8 (%25.8)	11 (%55)		
Ground glass	no	26 (%83.9)	13 (%65)		
opacity and		5 (%16.1)	7 (%35)	2.406	0.121 1
consolidation	yes	5 (7010.1)	7 (7655)		
Peripheral nodular	no	26 (%83.9)	14 (%70)		
patern	yes	5 (%16.1)	6 (%30)	1.383	0.240 1
		20 (0/05 8)	17 (0/05)		
Peripheral confluen	no	30 (%96.8)	17 (%85)	2.332	0.127 ¹
involvement	yes	1 (%3.2)	3 (%15)		
	no	30 (%96.8)	20 (%100)		
Diffuse involvement	yes	1 (%3.2)	0 (%0)	0.658	0.417 1
Peribronchovascular	no	30 (%96.8)	18 (%90)	1.008	0.315 1
nodular involvement	yes	1 (%3.2)	2 (%10)		
	no	30 (%96.8)	19 (%95)	0.102	0.750 -
Crazy paving	yes	1 (%3.2)	1 (%5)		
pattern		. ,	. ,		
Irregular	no	31 (%100)	19 (%95)		
reticulations	yes	0 (%0)	1 (%5)	1.581	0.209 1
	,				
Pleural effusion	no	27 (%87.1)	20 (%100)	4.200	0.040 1*
	yes	4 (%12.9)	0 (%0)		
	no	29 (%93.5)	20 (%100)		
Pericardial effusion	2005	2 (%6.5)	0 (%0)	2.044	0.153 ¹
	yes	2 (/00.3)	0 (200)		
	Upper lobe	3 (%38)	1 (%9)		
	Lower lobe	1 (%13)	0 (%0)		
	All lobes	4 (%50)	9 (%82)		
Lober involvement				4.563	0.207 ¹
	Upper and	0 /	4 (****)		
	lower	0 (%0)	1 (%9)		
	lobes				
Lataraliz-ti	Bilateral	5 (%63)	10 (%91)	2.242	0.1011
Lateralisation	Unilateral	3 (%38)	1 (%9)	2.249	0.134 1

	Myocarditis (n=31)	Normal (n=20)		
	(Mean+Sd)	(Mean+Sd)		
Left lung	5.06±11.73	9.51±17.648		
involvement(%)	0 (0;5.7)	0 (0;13)	-1.342	0.180 ²
Left lung	2.18±0.757	1.96±0.713		
volume	2.1 (1.7;2.75)	2 (1.4;2.7)	0.907	0.370 ¹
Right lung	3.82±8.243	11.08±16.796		
involvement(%)	0 (0;5.85)	7.7 (0;16)	-1.883	0.060 ²
Right lung	2.46±0.803	2.24±0.858		
volume	2.45 (1.93;2.98)	2.3 (1.5;3.1)	0.815	0.420 ¹
Total lung	4.27±9.352	10.2±16.954		
involvement(%)	0 (0;4.18)	6.8 (0;14)	-1.582	0.114 ²
Total lung	4.68±1.553	4.22±1.55		
volume	4.55 (3.65;5.65)	4.3 (2.8;5.7)	0.907	0.370 ¹
Total lung	0.22±0.475	0.35±0.505		
involment volume	0 (0;0.25)	0.26 (0;0.47)	-1.335	0.182 ²

¹:Independentsamplettest(t);²:ManWhitneyUtest(z)

Table IV: Evaluation of Laboratory Data by Study Groups

	Myocarditis (n=31)	Normal (n=20)			
	(Mean+Sd)	(Mean+Sd)		p.	
D-dimer	2.47±6.042	102.53±442.545			
(mg/L)	0.68 (0,27;1.73)	0.57 (0.24;2)	-0.288	0.773 ²	
CK-MB	6.71±20.753	12.7±35.201			
(µg/L)			-0.098	0.922 ²	
	1.23 (0.83;2.45)	1.44 (0.49;5.77)			
Troponin I	2017.26±5759.237	2302.52±6638.941			
(ng/L)	9 (2.5;510)	7 (3;17)	-0.111	0.911 ²	

¹: Independent sample t test (t); ²: Man Whitney U test (z)

Discussion

Thoracic CT findings of COVID-19 infection and involvement frequencies have been defined in detail as the pandemic has progressed. In 10.6% of the symptomatic patients, thoracic CT findings are normal within 4-5 days after the beginning of the symptoms. In the following days, this ratio decreases gradually (1.2-4%). CT findings are normal in approximately 46% of asymptomatic patients.^{1, 8, 9, 10}

Ground glass opacities, vascular enlargement, bilateral involvement, lower lobe, and posterior lung are among the common thoracic CT findings and are observed in 70% of the cases. Consolidation, linear opacities, septal thickenings and reticulations, crazy-paving pattern, air bronchogram, pleural thickening, halo sign and reversed halo sign are less common findings and reported in the literature with a 10% to 70% prevalence. In addition, among less common findings, one-sided involvement (15%), single or focal lesion (10,5%), middle or upper lobe involvement (49%), and extensive involvement (26%) were reported. Pleural effusion, tree-in-bud appearance, lymphadenopathy, central lesion distribution and pericardial effusion are rare findings and detected in less than 10% of the cases.^{8,11}

In the study conducted by Ashar Pirzada et al. using Louise criteria, it is stated that CMR has a specificity of up to 91% and a sensitivity of 67% for the diagnosis of myocarditis.¹² Another study reported that if no contraindications exist, CMR can be used as the primary diagnostic in COVID-19-related myocarditis examination.¹³ With this information, CMR was accepted as the standard diagnostic tool.

Males predominated in both the CMR-detected myocarditis group and the normal group, accounting for 67.7% of the myocarditis group and 55% of the non-myocarditis group. The mean ages of the CMR-detected myocarditis group and non-myocarditis group were respectively $37,7\pm13$ and $46,4\pm16$. In the study of Sawalha et al., conducted on the cases published in the literature, the mean age of 14 myocarditis/myopericarditis cases was 50.4, and male dominancy was present (58%). Troponin levels were elevated in 91% of cases.^{14,15} In a compilation by Kariyanna et al., the mean age of the COVID-19 patients with myocarditis was 51.8, the male/female ratio was equal and troponin levels were elevated in all patients.¹⁶ In a compilation by Ho et al.,



the mean age was 55, and 69% of the cases were males. In addition, troponin levels were higher in most of the cases.^{16,17} Male dominancy in the current study showed a similarity between the studies in the literature, and mean age was shown to be lower.

While late myocardial enhancement was detected in most of the patients (90.3%), accompanying pericardial enhancement was only detected in eight patients (25,8%) (Figure 1,2). In the series conducted by Esposito et al. on ten patients who underwent a CMR test for COVID-19-related myocarditis suspicion, generalized myocardial edema was demonstrated in all cases, but eight patients' late contrast images were found to be normal.¹⁸ In the current study, late myocardial enhancement was detected in all patients.

Figure 1



Figure 1. Cardiac magnetic resonance and thorax computed tomography examinations (CT) of the same patient. Myocardium showing contrast enhancement in the late contrast series on the left(asterix). Normal thorax CT on right

Figure 2



Figure 2. Cardiac magnetic resonance and thorax computed tomography examinations (CT) of the same patient. Subendocardial patchy contrast enhancement(asterix) is observed in the late contrast series on the left(A). Widespread involvement due to CO-VID-19 pneumonia on the right (B).



When the thoracic CT results of the patient group with myocarditis compatible CMR findings were examined, infiltration was not monitored in the majority of them (74.2%). Infiltration was present only in eight patients' lungs. All of these patients had infiltration ground-glass opacity-shaped regions, and five of them had accompanying consolidations. In addition, these patients' involvements are mostly bilateral (62.5%), involve all lobes, and show the distribution in a peripheral nodular pattern (62.5%), compatible with the literature. Pleural effusion was detected in four of the patients, and pericardial effusion in two patients. In the normal group, where pathology was not detected on CMR, infiltration was identified in 11 patients (55%) and not in nine patients (45%) on thoracic CT. Ground glass appearance was present in all patients with involvement. And in seven patients, accompanying consolidations were present. Most of the infiltrations consisted of opacities displaying bilateral distribution (90.9%), involving all lobes (81.8%), irregular peripheral weighted nodular (54.5%), and peripheral weighted confluent (27.7%). While the group without myocarditis displayed a pattern more consistent with the literature, findings which can be considered atypical were more common in the group with myocarditis. When both groups were compared, no statistical difference was found in thoracic CT findings. Interestingly, it was seen that in the group without myocarditis, thoracic infiltration was observed more, in a statistically detected ratio.

Pericardial and pleural effusions are only observed in the group with myocarditis and arise as a distinctive feature. When the lung volumes and involvement percentages were compared, no statistical difference was found between the groups. However, the lung involvement percentage in the group without myocarditis was higher. This indicates that there is no correlation between the percentage of lung parenchyma involvement and myocardial involvement.

No significant difference was found between the groups in terms of troponin I, CK-MB, and D-dimer levels, and all patients' troponin I levels were high. In 16 patients in the myocarditis group (51.6%) and 11 patients in the non-myocarditis group (55%), D-dimer levels were above 500 ng/mL.

COVID-19-related myocarditis and acute heart failure cases in patients who did not have CO-VID-19 pneumonia despite a positive PCR test or overcame COVID-19 reported in the literature indicate the possibility of late-onset cardiac complications and myocarditis, even in those with mild symptoms.¹⁹⁻²¹ In the current study, infiltration was not monitored in thoracic CT tests in most of the cases in both the myocarditis and non-myocarditis groups. This case proves that even when COVID-19 pneumonia is not present, myocarditis may occur in PCR-positive patients, which is consistent with the literature.

In a study conducted on 26 patients, the majority of whom recovered from moderate COVID-19 pneumonia (85%), had no cardiovascular disease other than hypertension (8%) before and who applied for CMR, myocardial damage symptoms were present in 58% of the patients (n=15). Late gadolinium enhancement was detected in eight patients (31%) and myocardial edema in 14 patients (54%).²² Several studies have shown that patients who recovered from COVID-19 and had no active cardiac symptoms had widespread myocardial damage in the early stages of their recovery period.^{19, 23, 24}

In the early studies on COVID-19-related myocarditis, it was reported that acute heart damage is more commonly observed in patients with more severe COVID-19 infection, and patients who suffered heart damage were old individuals with comorbidities such as hypertension, CAH, and diabetes.²⁵ The findings cannot be confirmed in the current study. The patient group consists of younger patients and severe lung involvement due to COVID-19 is not observed. Based on this case, as mentioned in the studies above, even patients who did not have COVID-19 pneumonia or had a mild disease can develop COVID-19-related pneumonia.

Some of the study's limitations is that clinical findings such as shortness of breath and chest pain, as well as results such as echocardiography findings, elevated sPAP, and systolic dysfunction, were not compared between the patient and normal groups.

Conclucion

Myocarditis is an important complication of COVID-19 infection and has recently become a frequently discussed topic. Many studies have demonstrated that CMR is the best non-invasive diagnostic tool in the diagnosis of COVID-19-related myocarditis. The findings of our study reveal that myocardial involvement in CMR can occur without



prominent lung involvement. Therefore, we recommend that patients who have had COVID-19 infection but do not show obvious pneumonia signs and with cardiovascular findings or elevated troponin levels be evaluated with CMR in terms of myocarditis, and myocarditis retraction be performed. In addition, we observed that there was no linear relationship between the severity of lung involvement and myocardial involvement. While patients with severe lung involvement may not have myocarditis, a CO-VID-19 infection that has not caused parenchymal involvement can cause myocarditis. This situation indicates the possibility of other mechanisms or liability situations other than the common mechanisms regarding disease-related lung damage or myocardial damage. We believe that studies on this situation should continue. Pleural effusion and pericardial effusion have been demonstrated to frequently accompany myocarditis, and there may be warning symptoms in suspected patients when contemplating CMR imaging. As a result of our study, we also found that our myocarditis patient group was represented by a younger population compared to the literature. We discovered that complications such as myocarditis can occur post-COVID-19 infection, especially in young and healthy people. Therefore, we believe that, especially in the younger age group, in the case of clinical suspicion, the patients should be evaluated with CMR for myocarditis retraction. There are many studies in the literature on COVID-19 infection-related myocarditis. These studies focused on the relationship between myocarditis presence and CO-VID-19, myocardial damage occurrence mechanisms, and diagnosis with CMR. We attempted to present a new perspective by approaching the 51-patient case series in terms of CT findings. Thoracic CT is known to be performed on many COVID-19 patients for diagnosis or follow-up. CMR is a test that is not widely available and is requested rarely. Therefore, we focused on obtaining information regarding myocarditis by focusing on thoracic CT findings. fered heart damage were old individuals with comorbidities such as hypertension, CAH, and diabetes25. The findings cannot be confirmed in the current study. The patient group consists of younger patients and severe lung involvement due to COVID-19 is not observed. Based on this case, as mentioned in the studies above, even patients who

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