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Calcium score in COVID-19 patients: A risk predictor for severity of lung involvement?

Akin Cinkooglu[a], Mustafa Bozdag[b,*], Selen Bayraktaroglu[a], Naim Ceylan[a], Recep Savas[a]

[a]*Department of Radiology, Ege University Faculty of Medicine, 35100, Bornova, Izmir, Turkey.*
[b]*Department of Radiology, Tepecik Training and Research Hospital, 35180, Yenisehir, Konak, Izmir, Turkey.*

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Abstract

Aim: The aim of the study is to evaluate the relationship between the severity of lung involvement and the Agatston score calculated using the chest computed tomography (CT) images of patients diagnosed with COVID-19 pneumonia.

Materials and Methods: One hundred thirty-six patients (71 male, 65 female; mean age: 51.45 years ± 16,06) presented to our hospital between March 17, 2020, and April 14, 2020, and got the diagnosis of COVID-19 pneumonia, were included in the study. The patients were stratified into two disease severity groups, namely mild disease (n=118) and severe disease (n=18), based on their ICU needs. Agatston score and visual CT score, which were calculated using the CT images obtained at admission, were assessed.

Results: Calcified coronary plaques were observed in 47 patients (34.6%). Agatston score ranged from 0.8 to 5179 in these patients (n=47, median: 125.8). Overall, there was a significant, moderately positive correlation between Agatston score and visual CT score (n=136, $p < 0.001$). Visual CT score was significantly higher in patients with calcified plaques (n=47, $p < 0.001$). Among the patients with calcified plaques, the Agatston and visual CT scores were significantly higher in the severe disease group (n=9) than the mild disease group (n=38) (p=0.015 and p=0.023, respectively).

Conclusion: Agatston score calculated from CT images can be used as a risk indicator in predicting the severity of COVID-19 pneumonia.

Introduction

The novel coronavirus disease (COVID-19) pandemic continues to impact worldwide. According to official data, as of April 24, 2021, the total number of affected cases in Turkey is over 4.5 million [1]. The reverse-transcriptase polymerase chain reaction (RT-PCR) test is the reference standard in diagnosing the disease, but it may return false-negative results, especially in the early stages [2]. In these early cases, thorax computed tomography (CT) examination plays a complementary role in the diagnosis [3]. In addition, thorax CT examination is an effective method for estimating disease severity, and various scoring systems are used for this purpose [4-5].

Hypertension, diabetes, cardiovascular diseases, and chronic kidney disease, among the most common comorbidities in COVID-19 patients, have been identified as significant risk factors [6]. Severe course of COVID-19 infection and high mortality rates have been reported in patients with coronary artery disease (CAD) [7]. Coronary artery calcium scoring (CACS) is widely used in CAD risk assessment, and Agatston scoring is the most preferred method for this purpose [8-9].

Our study aims to reveal the relationship between the Agatston score and the severity of lung involvement in patients diagnosed with COVID-19 pneumonia by comparing the visual CT score (VCTS) and Agatston score (AS) calculated from the patients' thorax CT examinations obtained at the time of admission.

Materials and Methods

Patient Selection (Recruitment)

Ethical approval was obtained for this study from the local ethics committee of our institution (20.04.2021 / decision no: 21-4.1T/38).

The data of 495 patients who underwent thoracic CT examination between 17.03.2020 and 14.04.2020 with the preliminary diagnosis of COVID-19 were screened retro-

*Corresponding author:
Email address: bozdagmustafa.84@gmail.com (Mustafa Bozdag)

spectively. Inclusion criteria were as follows: 1) Presence of CT findings that support COVID-19 pneumonia, 2) Having a definitive diagnosis with a positive RT-PCR result, 3) The patient's age is 18 or older. One hundred fifty-four patients who met these criteria were evaluated. Exclusion criteria were determined as follows: 1) The patient's CT examination was not obtained by following the high-resolution CT protocol; 2) Computed tomography examination was not of sufficient quality to allow measurements to be made; 3) Presence of previous coronary artery by-pass grafting operation or coronary stenting findings on CT. CT examination of two patients was performed by following the thoracic angiography protocol. CT examination of 13 patients was not of sufficient quality. Three patients had findings consistent with previous coronary artery by-pass grafting and/or coronary stenting operation on CT. After these evaluations, 136 patients (71 male, 65 female; age range: 19-95; mean age=51.45 ± 16.06 years) who met all criteria were included in the study. The patients were examined in two separate groups such that those followed in the clinical services were included in the mild disease (MD) group (n = 118; 59 male, 59 female; age range: 19-79; mean age=49.6 ± 14.82), while the patients who needed intensive care during the follow-up were included in the severe disease (SD) group (n = 18; 12 male, 6 female; age range: 34-95; mean age=63.56 ± 18.94 years).

Imaging Technique

Computed tomography images were obtained with a 160-slice scanner (Aquilion Prime, Toshiba Medical Systems, Tokyo, Japan) using the high-resolution protocol. No contrast agent was given during imaging. Volumetric scanning was performed from the thorax inlet to the end of the diaphragm during inspiration, within a single breath-holding time of the patient. The images were obtained in the axial plane. The imaging parameters were as follows: tube voltage: 120 kV; tube current: 100-200 mA; collimation: 80x0.5 mm. Reconstruction images with a section thickness of 0.5 mm were created using a sharp reconstruction kernel.

Calculation of the Visual CT Score

Computed tomography images were evaluated separately by two radiologists with 15 years and 16 years of experience in thoracic imaging. Visual CT scoring was performed using the method described by Chung et al. [10]. Areas of infiltration with a ground-glass density (pure ground glass or crazy-paving pattern), consolidation, or both were considered pathological. Evaluations were done visually and for five lung lobes separately. The total score was calculated by summing the individual lobar scores obtained. Scoring criteria were as follows: '0 points' if there is no pathological area; '1 point' if the pathological area covers 1% to 25% of the lobe; '2 points' if it covers 26% to 50%; '3 points' if it covers 51% to 75%; '4 points' if it covers 76% to 100%. With this scoring system, the lobar score ranged from 0 to 4, with the highest total score being 20 (Table 1). In cases where two radiologists could not agree on scoring, the images were re-evaluated by a third radiologist with 25 years of experience in thoracic imaging, and the measurements were completed by reaching a consensus.

Table 1. Visual CT Scoring

Areas of infiltration	Point
None	0
1-25%	1
26-50%	2
51-75%	3
76-100%	4

Calculation of the Agatston Score

Agatston scores of the patients were calculated from the CT images on the workstation. Dedicated software designed for this measurement (Myrian, Intrasense, Paris, France) was used for analysis. Plaques identified by automatic subtraction by the software were manually marked by a radiologist with seven years of experience in cardiac imaging (Figure 1). Final scores calculated by the software were recorded.

Statistical Analysis

Statistical evaluation was performed using SPSS statistical package software (IBM, version 25.0, SPSS Inc., Chicago, Illinois, USA). Continuous data with a normal distribution were expressed as mean ± standard deviation (SD). Continuous data that did not fit the normal distribution were expressed as median values. Independent groups were compared using the Mann-Whitney U test or the two-sample t-test. Spearman correlation test was used for correlation analysis. The confidence interval was taken as 95%, and P values less than 0.05 were accepted as statistical significance.

Results

In our study, CT images of 136 patients were evaluated. Lung involvement was bilateral in 120 (88.2%) patients, and involvement of all five lung lobes was observed in 88 (64.7%) patients. Involvement was limited to one lobe in only 16 patients (11.8%). As for the lesion-based evaluation, the most common type was pure ground-glass lesions (80.9%). This was followed by ground-glass and consolidation (30.1%), crazy-paving pattern (22.8%), and pure consolidation (18.4%). Visual CT scores ranged from 1 to 20 (n=136; median=5). The highest total score of '20' was present in two patients. In these patients, crazy-paving pattern and consolidation formed the dominant infiltration pattern (Figure 2).

Coronary calcific plaques were observed in 47 patients (34.6%) in the study. All these patients were over the age of 40. The AS in these patients ranged from 0.8 to 5179 (n=47; median=125.8). Overall, a moderate positive correlation was found between AS and VCTS (n=136, $p < 0.001$) (Figure 3). Visual CT score was significantly higher in patients with coronary calcific plaque (n=47, $p < 0.001$).

When the disease severity groups were compared, VCTS and AS were significantly higher in the SD group (n=18)

Table 2. Comparison of patient groups

Patients with calcified coronary plaques (n=47)	Mild disease group(n=38)	Severity disease group (n=9)	
Age (Mean ± SD)	61.21 ± 8.58	79.22 ± 10.58	p = 0.431
VCTS (Median)	5	9	p = 0.023*
AS (Median)	86,15	1142	p = 0.015*

* Independent groups were compared using the Mann-Whitney U test or the two-sample t-test., P-value of < 0.05 was considered to be statistically significant. VCTS, Visual computed tomography score; AS, Agatston score; SD, Standart deviation.

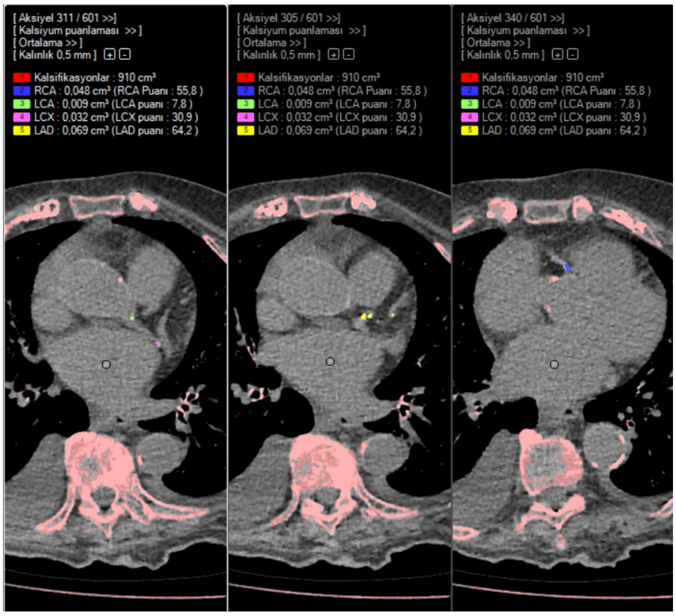

Figure 1. Agatston scoring on the workstation. Plaques determined by automatic subtraction by the software are marked using different colors for each vessel.

than in the MD group (p=0.002 and p=0.035, respectively). When only patients with a calcific coronary plaque were evaluated, AS was found to be significantly higher in patients in the SD group (n=9) compared to those in the MD group (n=38) (p=0.015) (Figure 4). Similarly, the VCTS of the patients in the CS group was also found to be significantly higher (p=0.023) (Table 2). When the cases in the mild disease group were evaluated within themselves (n=118), VCTS was significantly higher in patients with calcific plaque (n=38, p=0.001).

Discussion

In this study, thorax CT scans of the patients were evaluated to reveal the relationship between Agatston score and severity of COVID-19 pneumonia. We believe that the significant correlation found in this study between VCTS, which quantitatively shows the prevalence of pneumonia, and AS, which is used in CAD risk assessment, is an important finding. In addition, the fact that AS was found to be significantly higher in severe cases who needed intensive care during follow-up, as well as the significant increase in AS and VCTS in severe patients with calcific plaque, stand out as the other remarkable findings of our study.

The main CT findings of pulmonary involvement developing during the course of the disease are bilateral lesions located predominantly in the periphery and basal parts of the lungs. In the early stages of the disease, the lesions are primarily of pure ground-glass density. During the progression stage of pneumonia, the ground-glass areas become more diffuse, and lesions begin to appear in crazy-paving and consolidation patterns [11]. Considering that we analyzed the CT images of patients taken at the time of admission to the hospital, we believe that the most common lesion pattern being pure ground glass is a finding consistent with expectations. In addition, ground-glass with consolidation, and crazy-paving pattern with consolidation were other findings that we found at different rates in CTs. We used a scoring system to convert these pneumonia findings into quantitative data and compare them with the coronary calcium score. Such scoring systems may use either visual or computer-aided calculations. In this study, we used the visual scoring system designed by Chung et al., for which the significant relationship between high scores and the need for intensive care was previously demonstrated [10]. Similarly, in our study, we showed that the visual CT score of the cases who developed a need for intensive care during follow-up was significantly higher. In another study using the same scoring system, Ufuk et al. showed a significant correlation between the clinical severity score they described and the CT score. In that study, in which computer-assisted scoring was also used, it was emphasized that computer-assisted scoring gave better results in distinguishing between disseminated- and limited disease [12]. In another study using computer-assisted scoring, Wang et al. reported that the deep learning model they developed successfully estimated the risk of acute respiratory distress syndrome that may develop during follow-up, based on the density characteristics of the lesions [13]. The most significant advantage of such scoring approaches is that they are not user-dependent and provide objective data. However, measurement variability arising from the different software used is also a matter to be considered [14].

Cardiovascular diseases are among the common comorbidities in COVID-19 infection, and their overall prevalence has been reported as 12% [15]. In addition, if myocardial damage occurs due to COVID-19 in patients with underlying cardiovascular disease, the mortality rate was found to be significantly higher than in other patients [16]. Considering their need for more aggressive treatment, we believe that triage of these patients at admission may be an appropriate approach for disease management, and that, CACS, which is a widely used marker to predict the risk of cardiovascular events, can be used for such a stratification. The significant correlation between VCTS and AS found in our study, as well as the significantly higher AS in pa-

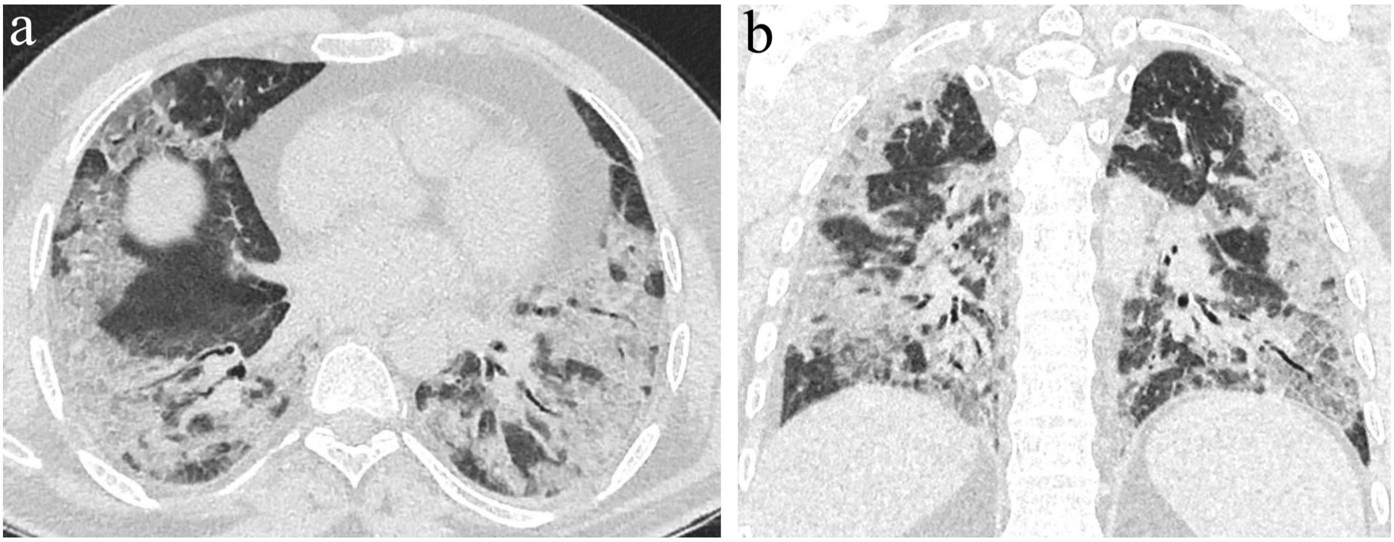

Figure 2. A sample case with diffuse parenchymal involvement. In the axial (a) and coronal (b) CT images of a 51-year-old male patient, diffuse consolidation and crazy-paving pattern infiltrations are observed in both lungs. The visual CT score of this patient was 20, and the patient who needed intensive care during the follow-up was included in the SD group.

tients who need intensive care during follow-up, may serve as the basis for potential approaches to be designed for this triage purposes. Recently, several studies have been published addressing the same issue. In their study conducted with 1093 subjects, which aimed to evaluate the relationship between coronary artery calcium and disease mortality in COVID-19 patients, Giannini et al. concluded that AS is an important predictor of in-hospital mortality [17]. In another study, Gupta et al. used the visual CACS method and showed that high scores were associated with increased intubation requirements and mortality rates [18]. It is important to make such evaluations without additional imaging through calculations performed on thorax CT examinations that were obtained for lung parenchyma evaluation. Since calcium score measurements are affected by cardiac motion, calculations made on CT images obtained using electrocardiography triggering constitute the traditional method. However, there are studies showing that calculations can also be made on non-contrast thorax CTs obtained without electrocardiography triggering. A meta-analysis of five validation studies conducted for this purpose showed an excellent correlation between scores from both methods. It was also emphasized that evaluating the coronary artery score in categories would provide more reliable data in cardiovascular risk assessment [19].

The small number of patients in the severe disease group, the lack of additional clinical data of the patients, and the retrospective design constitute the limitations of our study. We think that studies with larger patient groups, including clinical data, can statistically better reveal the relationship between AS and disease severity.

Conclusion

Agatston score, which can be calculated from CT images obtained from patients admitted to the hospital with a preliminary diagnosis of COVID-19 to reveal the lung parenchymal involvement of the disease, can be used as a risk indicator in predicting the severity of the disease. The ability to triage patients at the time of admission through this scoring system will strengthen the clinician's hand in the management of the disease.

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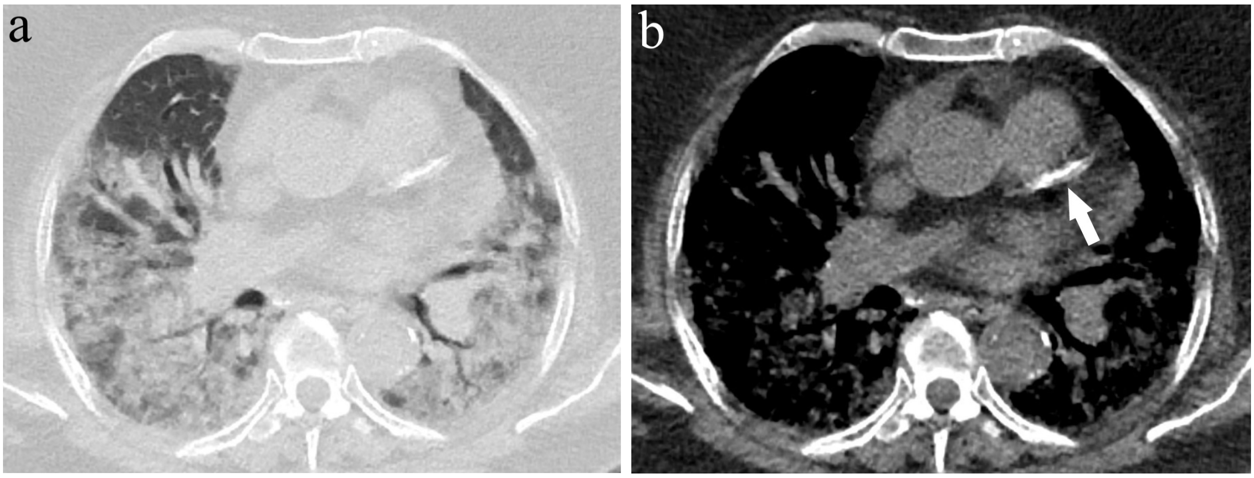

Figure 3. Widespread parenchymal involvement and its association with calcific plaque. CT slice obtained in the parenchyma window of a 78-year-old female patient (a) shows diffuse parenchymal consolidations in both lungs. CT slice obtained in the mediastinal window (b) shows calcific plaque in the left anterior descending coronary artery (arrow). This patient had a visual CT score of 19 and an Agatston score of 1659, and the patient followed up in the intensive care unit was included in the SD group.

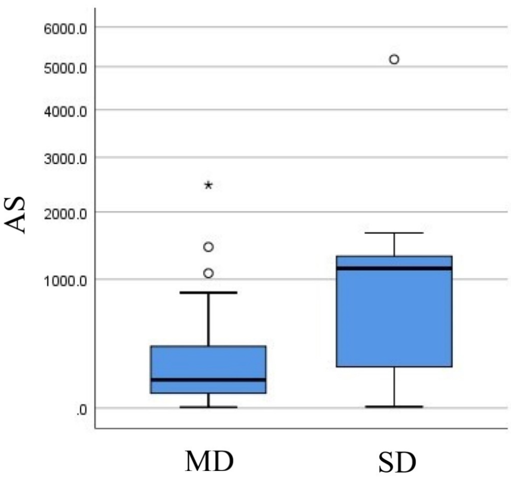

Figure 4. Box plot showing the distribution of Agatston scores obtained from patients with calcific plaque according to patient groups. AS: Agatston score; MD: mild disease; SD: severe disease.

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