Thieme

Can Opportunistic Use of Computed Tomography Help Reveal the Association Between Hepatic Steatosis and Disease Severity in Hospitalized COVID-19 Patients?

Kann der opportunistische Einsatz der Computertomografie dazu beitragen, den Zusammenhang zwischen Lebersteatose und Schweregrad der Erkrankung bei hospitalisierten COVID-19-Patienten aufzudecken?

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ABSTRACT

Purpose To measure hepatic steatosis (HS) in hospitalized COVID-19 patients using unenhanced chest computed tomography (CT) imaging and to evaluate the relationship between disease severity and prognosis in adult patients.

Materials and Methods This retrospective study included 152 consecutive hospitalized COVID-19 patients with a positive reverse transcriptase polymerase chain reaction (RT-PCR) test. The COVID-19 Reporting and Data System (CO-RADS) and the chest CT score were evaluated. HS measurements were performed based on CT images using a single region of interest placed on the right liver lobe (segments V-VII). HS was defined as a liver attenuation value <40 Hounsfield units. Data were collected and compared with the patients' prognostic parameters.

Results Of the 152 inpatients, 137 patients (90.1 %) had a CT score ≥ 3 and 109 patients (71.7 %) had a CO-RADS score ≥ 4, 43 (28.2 %) had HS. All patients with HS (100 %) and 94/109 (86.2 %) patients without HS had a CT score ≥ 3. There was a statistically significant difference between the two groups in terms of chest CT score ($p = 0.006$). There was no statistically significant difference between the two groups in terms of CO-RADS score ($p = 0.291$). The median CRP levels were significantly increased in patients with HS compared to patients without HS ($p = 0.023$). There was no significant difference in ICU hospitalization and mortality due to the presence of HS ($p > 0.05$).

Conclusion The current study revealed significantly higher chest CT scores in COVID-19 patients with HS measured on CT compared to those without HS. Opportunistic use of CT images for the detection of HS can be considered as an adjunctive tool in the risk analysis of COVID-19 patients hospitalized due to COVID-19 pneumonia.

Key Points The severity of COVID-19 disease is increased in hospitalized patients with hepatosteatosis compared to patients with a normal liver. Density measurements for the evaluation of HS using opportunistic CT applications can be considered as an adjunctive tool in the prognostic evaluation of hospitalized patients with COVID-19 pneumonia.

Citation Format

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ZUSAMMENFASSUNG

Ziel Messung der Lebersteatose (HS) bei hospitalisierten COVID-19-Patienten mittels nativer Thorax-Computertomografie (CT) und Bewertung des Zusammenhangs zwischen

Schweregrad der Erkrankung und Prognose bei erwachsenen Patienten.

Material und Methoden Diese retrospektive Studie umfasste 152 aufeinanderfolgende hospitalisierte COVID-19-Patienten mit einem positiven RT-PCR-Test (Reverse Transkriptase-Polymerase-Kettenreaktion). Das COVID-19 Reporting and Data System (CO-RADS) und der Thorax-CT-Score wurden ausgewertet. Die Messungen für HS wurden anhand von CT-Bildern mit einer einzigen Region of Interest durchgeführt, die auf dem rechten Leberlappen (Segmente V-VII) platziert wurde. HS wurde bei Leberdichtewerten von <40 Hounsfield-Einheiten definiert. Die so erhobenen Daten wurden mit den prognostischen Parametern der Patienten verglichen.

Ergebnisse Von den insgesamt 152 stationären Patienten hatten 137 Patienten (90,1 %) einen CT-Score ≥ 3 und 109 Patienten (71,7 %) einen CO-RADS-Score ≥ 4, 43 (28,2 %) eine HS. Alle Patienten mit HS (100 %) und 94/109 (86,2 %) der Patienten ohne HS hatten einen CT-Score ≥ 3. Es gab statistisch signifikante Unterschiede zwischen zwei Gruppen in Bezug auf den Thorax-CT-Score (p = 0,006). Es gab keinen statistisch signifikanten Unterschied zwischen zwei Gruppen in Bezug auf den CO-RADS-Score (p = 0,291). Die medianen CRP-Spiegel waren bei Patienten mit HS im Vergleich zu Patienten ohne HS signifikant erhöht (p = 0,023). Es gab keinen signifikanten Unterschied zwischen Krankenhausaufenthalten auf der Intensivstation und der Mortalität durch das Vorhandensein von einer HS (p > 0,05).

Schlussfolgerung Die aktuelle Studie ergab signifikant höhere Thorax-CT-Scores bei COVID-19-Patienten mit HS, die im CT gemessen wurden, im Vergleich zu Patienten ohne HS. Die opportunistische Verwendung von CT-Bildern zur Erkennung von HS kann als zusätzliches Instrument bei der Risikoanalyse von COVID-19-Patienten angesehen werden, die aufgrund einer COVID-19-Lungenentzündung ins Krankenhaus eingeliefert wurden.

Kernaussagen Der Schweregrad der COVID-19-Erkrankung ist bei hospitalisierten Patienten mit Hepatosteatose im Vergleich zu Patienten mit normaler Leber erhöht. Dichtemessungen zur Bewertung von HS mit opportunistischen CT-Anwendungen können als ergänzendes Instrument bei der prognostischen Bewertung der hospitalisierten Patienten mit COVID-19-Lungenentzündung betrachtet werden.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or coronavirus disease 2019 (COVID-19) outbreak was first described as undetermined forms of pneumonia in Wuhan, China, in December 2019. Since then, studies have revealed that advanced age, diabetes mellitus, hypertension, obesity, and metabolic syndrome are the leading causes of poor prognosis in the disease course [1, 2].

Obesity, which is one of the main causes of poor prognosis, was also shown to be associated with COVID-19 disease progression to severe pneumonia, the need for hospitalization and mechanical ventilation due to acute respiratory failure and diffuse coagulopathy, and consequently an increased mortality risk [1, 2]. Also, a large amount of adipose tissue in obesity has been shown to increase the severity of infectious diseases and has a deleterious effect on the immune system when the tissue has chronic inflammation [3]. Hepatic steatosis (HS) is reported to have a prevalence of up to 95 % in populations with cumulative risk factors including type 2 diabetes mellitus (DM) and morbid obesity [4]. Nonalcoholic fatty liver disease (NAFLD) caused by metabolic disorders contributes to the poor prognosis in SARS-CoV-2 infection. NAFLD is known to cause significant impairment of liver function which plays an important role in the immune system [5]. The gold standard for the diagnosis of HS is liver biopsy. However, it is an invasive procedure and is not practical for all patients. Past studies revealed that alternative imaging methods can effectively identify HS [3, 4, 6]. Unenhanced chest computed tomography (CT) provides an opportunistic means of measuring liver density for the detection of fatty liver in a practical and noninvasive fashion [3].

The normal liver has slightly greater attenuation than the spleen and intrahepatic blood vessels on unenhanced CT. In HS, liver attenuation decreases, and this density reduction can be quantified by Hounsfield Units (HU) [5]. Based on past studies with biopsy verification, a liver without HS was reported as approximately 64 HU and a liver with moderate steatosis was reported as 42 HU [6]. Based on this knowledge, measuring HS on unenhanced chest CT can play a significant role in understanding whether adipose tissue has a role in disease severity. Thus far, only a small number of studies have focused on the opportunistic use of unenhanced chest CT for diagnosing HS in COVID-19 patients [3, 5, 6].

CT has been reported to have a very high sensitivity in patients infected with SARS-CoV-2 since it is a commonly used imaging method for patient management [7]. Meanwhile, CT scoring systems have been developed to stratify patients and CO-RADS classification was used to evaluate the prognosis and to understand the progression of the disease from pneumonia to pulmonary edema, acute respiratory distress syndrome, multiple organ failure, and death [8, 9].

The aim of this study was to determine the correlation between pulmonary involvement calculated by chest CT score and CO-RADS with the clinical staging of COVID-19 and to assess the role of HS in the prognosis of the disease as a new prognostic factor.

Materials and Methods

This retrospective study was pre-approved by the IRB Committee (2021/222) and was conducted in accordance with the 1964 Declaration of Helsinki; informed patient consent was waived. Pa-

tient records and information were anonymized and de-identified prior to analysis.

Study Population

Between August 2021 and March 2022, 152 consecutive hospitalized adult patients with a diagnosis of COVID-19 in a tertiary care medical center were retrospectively included in the study. The inclusion criteria were age ≥ 18 years, an initial need for hospitalization in a medical ward, a positive SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) test from nasopharyngeal swabs, routine blood tests, and a positive unenhanced chest CT examination for COVID-19 interstitial pneumonia at the time of initial admission to the emergency room.

Patients who had a negative RT-PCR test and/or negative chest CT for SARS-CoV2 interstitial pneumonia and were followed up at an outpatient clinic, those with enhanced CT studies and/or images with artifacts with the potential to alter liver density measurements, and those with a history of chronic liver disease were excluded from the study.

Routine blood tests and arterial blood gas (ABG) tests were performed for all patients and the following parameters were evaluated: C-reactive protein (CRP), D-dimer, lymphocyte count, lactate dehydrogenase (LDH), neutrophil lymphocyte ratio (NLR), ferritin, troponin. As identified in the meta-analysis of these parameters were accepted as the prognostic markers of the severity of COVID-19 disease [10]. Poor prognostic factors were described as lymphocyte > 800, NLR > 3.13, Ferritin > 500, D-dimer > 1000, CRP > 50, LDH > 245, and Troponin > 10 [10].

Computed Tomography Imaging

All patients underwent a focused diagnostic low-dose non-enhanced chest CT examination on a multidetector [64-detector (32 × 2)] CT scanner (Siemens Somatom Go Up, Erlangen, Germany) dedicated to the COVID-19 patients in pandemic conditions. Images were acquired with the patient in a supine position during breath-hold. Both lungs were scanned in a cranio-caudal direction from the apices of the lungs at the top to the adrenal glands at the bottom. No contrast material was used during scanning. The scanning and reconstruction parameters were as follows: tube voltage 110 kV; tube current quality reference value of 73 milliamps with automatic dose modulation program; beam pitch 1.5; reconstruction kernel 170 f and 130 f; reconstruction slice thickness 3 mm and 1 mm; matrix 512 × 512; field of view 350 mm; acquisition slice thickness 0.75 mm. All images were reformatted in the axial, coronal, and sagittal planes. Following each examination, the CT device and the entire room were sanitized. After image acquisition, all images were sent to the picture archiving and communication system (PACS).

Image interpretation

Identifying information was removed from the images prior to evaluation of the chest CT images. Then, a radiologist with more than 15 years of experience reviewed the images on a PACS workstation. All images were assessed for the presence of ground glass opacities (GGOs) in bilateral multi-lobar distribution with peripheral and posterior involvement, crazy-paving pattern, GGOs with interlobular septal thickening, and consolidations described as the characteristic imaging features of COVID-19 according to the standard nomenclature of Fleischer's Society [11].

Although non-specific, findings include the presence of a prominent/enlarged sub-segmental vessel (diameter > 3 mm), reverse halo or atoll sign, consolidation with air bronchogram, bronchiectasis, and mediastinal/hilar lymphadenopathy were also noted [12].

Chest CT findings were classified into five categories according to Radiological Society of North America (RSNA) Export Consensus criteria [13] and the COVID-19 Reporting and Data System (CO-RADS) from the COVID-19 Working Group of Dutch Radiological Society [14]. Based on this system, suspicion of pulmonary involvement of COVID-19 was assessed on a scale from 1 (very low) to 5 (very high).

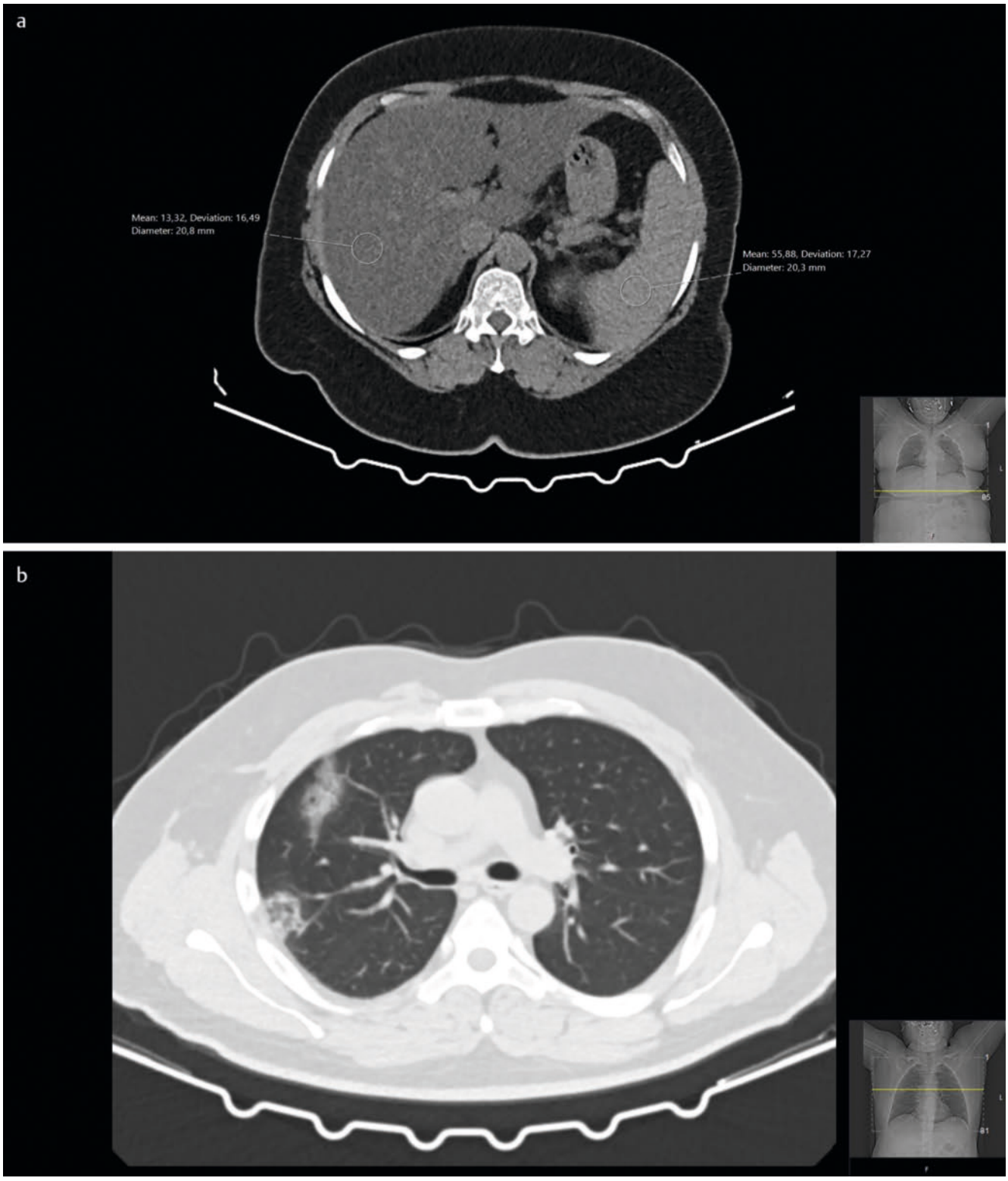
Chest CT scores were calculated based on the degree of involvement of each lung lobe as described by Francone et al. [7]. Regarding the extent of anatomic involvement, a chest CT score was calculated for each of the 5 lung lobes as follows: (0) no involvement; (1) <%5 involvement, (2) 5–25 % involvement, (3) 26–50 % involvement, (4) 51–75 % involvement, and (5) > 75 % involvement. After calculating all scores from the five lobes, summation of each score yielded a total CT score, ranging from 0–25 [7]. Based on the cut-off values used in previous studies, a chest CT score ≥ 3 in each lobe was determined to represent severe cases [8].

HS measurements were performed from the upper abdominal sections involved in the unenhanced chest CT images. A single circular region of interest (ROI) of 4–10 cm^2 was drawn for particular places on the right liver lobe (segments V–VII). Care was taken to avoid blood vessels and parenchymal calcifications while performing measurements [15]. Normal liver was determined based on a slightly higher attenuation than the spleen provided that relatively hypoattenuated intrahepatic blood vessels are visible. HS was determined if the attenuation of the liver was less than 40 HU (▶ **Fig. 1**) [3].

Statistical Analyses

IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY) was used for data analysis. The Shapiro–Wilk test was used to test the normality of the data. Continuous data were presented using mean ± SD for normally distributed data and median (interquartile range: 25–75 percentile) for non-normally distributed data. Categorical variables were given with n (%) and compared with Pearson chi-square test and Fisher's Exact test. Mann-Whitney U test and Independent t-test were performed for non-parametric and parametric comparisons of continuous data between groups, respectively. The stepwise backward logistic regression analyses were performed for multivariate analysis for ICU hospitalization and mortality. Receiver operating characteristics (ROC) curves were created for the chest CT score for ICU hospitalization and mortality. The sensitivity, specificity, area under the curve (AUC), and optimal cut-off values were determined for various cut-off points.

A two-sided p-value less than 0.05 was considered statistically significant.



▶ **Fig. 1** **a** Upper abdominal axial section of a non-enhanced chest computed tomography (CT) image of a 45-year-old female with COVID-19 diagnosis demonstrates the ROI measurement with an area of 4 cm^2 from the right lobe of the fatty liver. **b** Parenchymal window of chest CT scan of the same patient reveals the ground glass opacities in the upper lobe of the right lung.

Results

In this study 152 consecutive patients [79 females (% 52), age range: 21–92; 73 males (48%), age range: 24 to 94; mean (±SD) age 59.82 (±15.94)] were included. Among all these patients 43/152 (28.2%) had HS and 109/152 (71.8%) did not have HS. There were no statistically significant differences in terms of age and gender between the two groups ($p>0.05$).

Among patients with HS, 23/43 (53.5%) were female and 20/43 (46.5%) were male. Patients were similar in terms of age ($p=0.319$) and gender ($p=0.814$) in both the steatotic and non-steatotic groups. Among all patients, 53/152 (34.9%) had hypertension (HT), 41/152 (27%) had DM, 22/152 (14.5%) had asthma, 18/152 (11.8%) had coronary heart disease (CHD), and 21/152 (13.8%) had miscellaneous diseases including congestive heart failure (CHF), chronic renal failure (CRF), cerebrovascular accident (CVA) and neurological diseases, hematologic diseases (HD), chronic obstructive lung disease (COLD), and neoplastic diseases (▶ **Table 1**).

Of the 41 patients with DM, 17/41 (41.4%) had HS while 24/41 (58.6%) did not have HS.

The number of patients with DM (17/43, 39.5%) in the HS group was significantly higher than those without HS (24/109, 22%) ($p=0.028$). There were no statistically significant differences in terms of HS in other systemic disease groups including HT, asthma, CHD, and miscellaneous diseases ($p>0.05$). There was a trend towards an increased number of patients with lung cancers in the HS group ($p=0.079$) (▶ **Table 1**). The median CRP levels were significantly increased in patients with HS compared to patients without HS ($p=0.023$). The median ferritin levels were marginally increased in patients with HS compared to patients without HS ($p=0.060$). Although not statistically significant, LDH and lymphocyte ferritin levels were slightly increased in patients with HS compared to patients without HS ($p=0.467$ and $p=0.186$, respectively). The distribution of other parameters by the presence of HS is presented in detail in ▶ **Table 2**.

There were 137 patients (90.1%) with a CT score ≥3 and 109 patients (71.7%) with a CO-RADS score ≥4. There was no statistically significant difference between the two groups in terms of CO-RADS score ($p=0.291$). All 43 patients with HS (100%) had a CT score ≥3, while 94/109 (86.2%) patients without HS had a CT score ≥3. There was a statistically significant difference between the two groups in terms of chest CT score ($p=0.006$).

31 patients (20.4%) were hospitalized in the intensive care unit (ICU). 24 (22%) of these patients did not have HS whereas 7 (16.3%) had HS. 25 (16.4%) patients passed away. Among the patients who died, 19 (17.4%) had HS and 6 (14%) did not have HS. There was no statistically significant difference in terms of ICU hospitalization or mortality between the two groups

▶ **Table 1** Distribution of patient demographics and clinical parameters of the patient groups by the presence of hepatic steatosis.

Variables	All patients (n=152)	Nonsteatotic (n=109)	Steatotic (n=43)	p
Age (year)	59.82±15.94	60.52±17.11	58±12.41	0.319
Gender				
Female	79 (52)	56 (51.4)	23 (53.5)	0.814
Male	73 (48)	53 (48.6)	20 (46.5)	
Systemic Disease	88 (57.9)	60 (55)	28 (65.1)	0.257
DM	41 (27)	24 (22)	17 (39.5)	**0.028**
HT	53 (34.9)	40 (36.7)	13 (30.2)	0.451
CHD	18 (11.8)	14 (12.8)	4 (9.3)	0.781
CHF	1 (0.7)	1 (0.9)	0 (0)	0.999
CRF	2 (1.3)	2 (1.8)	0 (0)	0.999
CVA	3 (2)	3 (2.8)	0 (0)	0.559
Hematologic disease	3 (2)	2 (1.8)	1 (2.3)	0.999
Neurological	1 (0.7)	1 (0.9)	0 (0)	0.999
COLD	3 (2)	2 (1.8)	1 (2.3)	0.999
Asthma	22 (14.5)	18 (16.5)	4 (9.3)	0.255
Lung tumor	2 (1.3)	0 (0)	2 (4.7)	0.079
Non-lung tumor	6 (3.9)	3 (2.8)	3 (7)	0.352

Findings were presented as median ± standard deviation, median (interquartile range), or number and percentages (%). Independent t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's Exact test were used to analyze data. $P<0.05$ was considered statistically significant.
N = number of patients; DM = Diabetes Mellitus; HT = Hypertension; CHD = Coronary heart disease; CHF = Congestive heart failure; CRF = Chronic renal failure; CVA = Cerebrovascular accident; COLD = Chronic obstructive lung disease

▶ **Table 2** Comparison of laboratory parameters of the patients with respect to steatosis between the groups.

Variables	All patients (n = 152)	Nonsteatotic (n = 109)	Steatotic (n = 43)	p
LDH	301 (226–442)	297.5(225.5–426.5)	329 (232–445)	0.467
CRP	78.4 (25.7–154.1)	64.75 (21.7–133.2)	107.8 (40.5–192.8)	**0.023**
Lymphocyte	1160 (785–1570)	1060 (750–1510)	1300 (890–1740)	0.186
NLR	3.99 (2.7–7.21)	4.08 (2.84–8.22)	3.93 (2.11–6.33)	0.386
Ferritin	239 (123–438)	221 (121–388)	366 (156–637)	0.060
Troponin	6 (0–13)	7 (0–15)	4 (0–10)	0.096
D-DIMER	292 (170–478)	313 (162.5–593.5)	229 (190–359)	0.278
Chest CT score	9 (6–12)	8 (5–12)	10 (6–12)	0.142
≥3	137 (90,1)	94 (86.2)	43 (100)	**0.006**
CORADS	4 (3–5)	4 (3–5)	4 (4–5)	0.291
≥4	109 (71.7)	75 (68.8)	34 (79.1)	0.206
ICU hospitalization	31 (20.4)	24 (22)	7 (16.3)	0.429
Mortality	25 (16.4)	19 (17.4)	6 (14)	0.602

Findings were presented as median ± standard deviation, median (interquartile range), or number and percentages (%). Independent t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's Exact test were used to analyze data. P < 0.05 was considered statistically significant.
N = number of patients

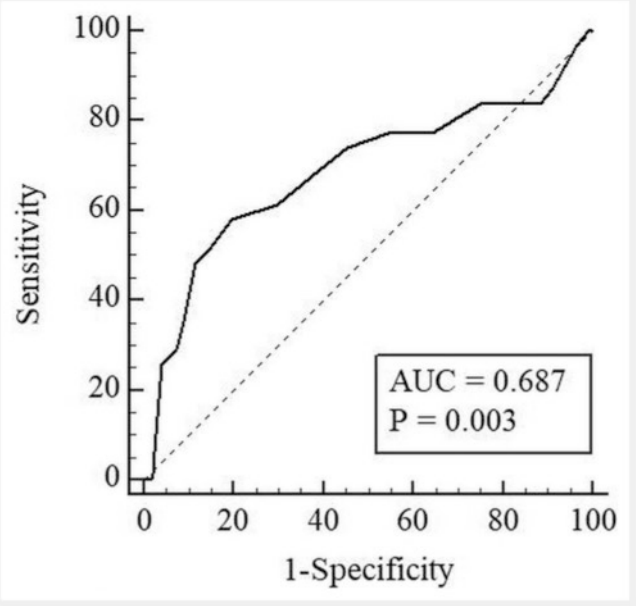
(p = 0.429 and p = 0.602, respectively). There was no significant difference in ICU hospitalization or mortality based on the presence of HS (p > 0.05) (Tables 1, 2).

The stepwise backward logistic regression analysis of the parameters that affect ICU hospitalization revealed that older age and higher chest CT score increased the likelihood of ICU hospitalization with odds ratios of 1.095 (95 % CI: 1.039–1.155; p = 0.001) and 1.205 (95 % CI: 1.06–1.375; p = 0.004), respectively, among hospitalized COVID-19 patients.

Based on the ROC analysis, the optimal cut-off value for the chest CT score for predicting ICU hospitalization was > 11 for an AUC value of 0.687 (CI%95: 0.607–0.760; p = 0.003) with a specificity of 80.17 % and sensitivity of 58.06 % (▶ **Fig. 2**).

The stepwise backward logistic regression analysis of the parameters showed that older age and a higher chest CT score increased the likelihood of mortality with odds ratios of 1.102 (95 % CI: 1.047–1.161; p = < 0.001) and 1.173 (95 % CI: 1.031–1.334; p = 0.015), respectively. ROC analysis showed that the optimal cut-off value for the chest CT score for the prediction of mortality was > 12 with an AUC value of 0.654 (CI%95: 0.572–0.729; p = 0.031) with a specificity of 82.68 % and a sensitivity of 48 % (▶ **Fig. 3**).

As for the clinical factors predicting a poor prognosis, 25.7 % of patients had a lymphocyte count < 800, 67.8 % had NLR > 3.13, 24.6 % had ferritin > 500, 14.8 % had D-dimer > 1000, 60.3 % had CRP > 50, 68.9 % had LDH > 245, and 31.8 % had troponin > 10. The presence of ferritin > 500 was marginally increased in patients with HS (37.9 %) compared to patients without HS (20.2 %) (p = 0.054) (▶ **Table 3**).



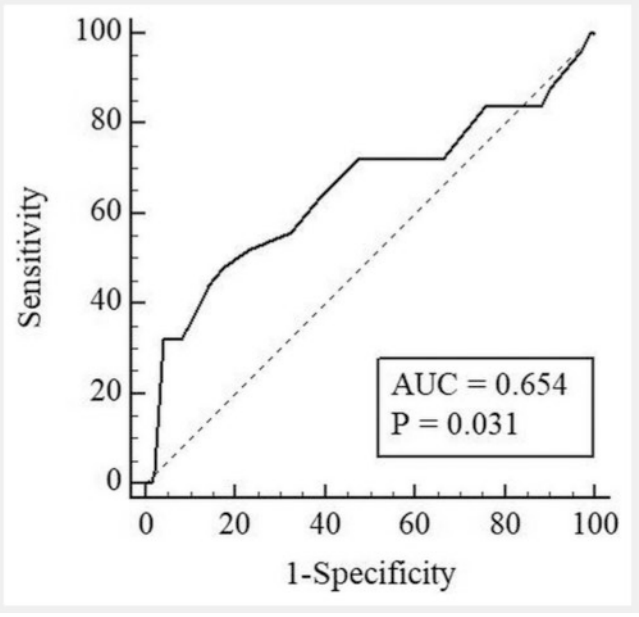
▶ **Fig. 2** ROC curve for chest CT score for ICU hospitalization.

Discussion

The current study demonstrated that chest CT scores and serum CRP levels were significantly increased in hospitalized COVID-19 patients with HS compared to non-steatotic patients as well as that factors indicating a marginally increased poor prognosis including ferritin > 500 and a trend towards an increase in lympho-

cyte, ferritin, and LDH levels were detected in those with HS compared to those without. Also, older patients and those with a higher chest score are more likely to require ICU hospitalization with odds ratios of 1.095 (95% CI: 1.039–1.155; p = 0.001) and 1.205 (95% CI: 1.06–1.375; p = 0.004) among hospitalized COVID-19 patients, respectively. Similarly, older age and a higher chest CT score increased the likelihood of mortality with odds ratios of 1.102 (95% CI: 1.047–1.161; p = < 0.001) and 1.173 (95% CI: 1.031–1.334; p = 0.015), respectively. ROC analyses for both mortality and ICU hospitalization revealed optimal cut-off values for chest CT score of > 12 and > 11, respectively, with AUC values of 0.654 and 0.687, respectively.

A small number of recent studies have explored the relationship between obesity and COVID-19 after SARS-COV-2 outbreak [2]. This study focused on a more specific issue related to metabolic disorders. A meta-analysis of COVID-19 patients showed that cardio metabolic risk factors potentiate mortality [16]. HS is commonly related to metabolic conditions including insulin resistance, DM, obesity, and dyslipidemia. We conducted this study to see whether HS was associated with severity and related to the prognosis of COVID-19 disease. There are many theories about the effects of fatty liver disease on COVID-19 disease. Moreover, it has been reported that the production of proinflammatory cytokines is increased in patients with HS. Therefore, HS affects the liver's effect on the immune system and influences the prognosis of infectious diseases [3, 16]. In this study, we solely evaluated patients who had been hospitalized and had higher chest CT scores as well as serious laboratory findings.



▶ **Fig. 3** ROC curve for chest CT score for mortality.

A multicenter study conducted by Palomar-Lever et al. [5] reported that HS was independently associated with severe COVID-19 pneumonia in outpatients. In a recent study, Dogan et al. also assessed HS in both inpatient and outpatient groups and reported a correlation with the total severity scores and HS in COVID-19 patients with an emphasis on prognostic strength [15]. Our study results were compatible with the results of past studies, namely that there is a correlation between chest CT scores and HS. The difference is that we only evaluated patients in our study who had been hospitalized, i. e., we included a more homogeneous group from a single medical center. Therefore, clinical tests, imaging studies, and measurement values were optimally standardized within the groups.

Palomar-Lever et al. also reported an association between HS and risk factors including HT, DM, and obesity in COVID-19 patients [5]. Similarly, DM was significantly higher in HS patients compared to non-steatotic patients. Although there was no statistically significant increase in lymphocyte count, NLR, ferritin, D-dimer, or LDH, we found a significant correlation between increased CRP levels and HS in COVID-19 patients. Past studies also revealed that there was a correlation between increased CRP and disease severity. Villard et al. [17], Yang et al. [18], and Ahnach et al. [19] also reported that CRP levels were associated with disease severity. Another difference regarding our study is that to our knowledge this is the first study to evaluate the relationship between clinical prognostic parameters and HS along with disease severity.

▶ **Table 3** Distribution of poor prognostic factors in patients by the presence of hepatic steatosis.

Factors, n (%)	All patients (n = 152)	Non-steatotic (n = 109)	Steatotic (n = 43)	p
Lymphocyte count < 800	39 (25.7)	31 (28.4)	8 (18.6)	0.211
NLR > 3.13	103 (67.8)	76 (69.7)	27 (62.8)	0.410
Ferritin > 500	29 (24.6)	18 (20.2)	11 (37.9)	0.054
D-dimer > 1000	22 (14.8)	18 (16.7)	4 (9.8)	0.288
CRP > 50	91 (60.3)	62 (57.4)	29 (67.4)	0.255
LDH > 245	104 (68.9)	74 (68.5)	30 (69.8)	0.881
Troponin > 10	47 (31.8)	37 (34.9)	10 (23.8)	0.191

Pearson chi-square test, Fisher's Exact test
N = number of patients

The current study provides new insight about the fact that increased CRP levels and HS association may provide additional information about disease severity. Therefore, we suggest that clinicians examine COVID-19 patients for the presence of HS. We propose that HS may be an additional marker for disease prognosis.

Past studies conducted on patients with nonalcoholic HS exploring parameters including AST, ALT, body mass index, and presence of DM revealed an association with disease prognosis [20, 21]. Our study results revealed that there was a correlation between HS and COVID-19 disease severity which was detected on already acquired non-enhanced CT images which is a readily available tool to predict disease prognosis. We propose that adding this parameter would help physicians to manage COVID-19 patients with HS with caution.

CO-RADS classification is an effective method in the early diagnosis of COVID-19 patients with a negative RT-PCR test. Similar to the Breast Imaging Reporting and Data System (BI-RADS) or Lung Imaging Reporting and Data System (Lung-RADS), it has been reported in past literature [9, 22]. In a study conducted by Özel et al., CO-RADS was found to be useful in identifying COVID-19 disease in those with a negative RT-PCR test result. CT score was also found to be beneficial for the determination of disease severity in cases with COVID-19 pneumonia. Although the primary aim of the current study was not to compare CO-RADS and CT score, we found that chest CT score associated with HS was significantly higher compared to CO-RADS which is an important tool in the early diagnosis of the disease. This study showed that CO-RADS was superior with respect to the early and precise detection of the disease, while chest CT score was superior and compatible with the studies in the literature with respect to the evaluation of disease severity and prognosis. An explanation for the statistical insignificance of CO-RADS in those patients might be the inclusion of hospitalized patients with an advanced CO-RADS stage which narrowed the statistical range. This might have caused decreased sensitivity of CO-RADS with respect to disease severity. Similarly, we did not find a statistically significant association between mortality and hospitalization and HS. One explanation for this situation might be that the study population comprised of hospitalized patients with a poor prognosis might have caused a decrease in the sensitivity of the parameters.

Recently, Doğan et al. [15] conducted a study on COVID-19 patients to investigate the relationship between HS and disease severity and found a correlation with hospitalization and the presence of HS although they could not find a correlation between mortality and HS [15]. Our results were consistent with their study results in terms of an association between HS and disease severity. Our study was different from their study in that they included all patients admitted to the hospital who underwent chest CT, whereas we omitted outpatients and only focused on inpatients in order to achieve a more homogeneous group [15]. Among all hospitalized patients, those with HS had the worst prognosis in the disease process.

Our study was not without limitations. The retrospective study design restricted the size of the study population since we could only perform measurements from chest CT exams including upper abdominal sections. We could have used other imaging methods to detect HS. However, the nature of the disease would still only allow limited contact with patients. Similarly, we could not use spleen HU to compare with liver HU since not all included CT exams were appropriate for optimal splenic sections for the measurements.

Conclusion

In conclusion, the current study revealed a significantly higher prevalence of HS in those with a higher chest CT score. Moreover, it showed a significant correlation between disease severity and HS measured on CT. We conclude that the measurement of liver density is an easy, quick, and readily available method. The measurement can be performed using chest CT images already acquired for the detection of pneumonia. Therefore, opportunistic use of CT images for the detection of HS can be considered an adjunctive tool in the risk analysis of patients hospitalized due to COVID-19 pneumonia and may provide preliminary beneficial information for providing guidance for clinicians in future potential pandemics with respect to the prognostic evaluation of diseased individuals.

Clinical Relevance of the Study

1. There was a correlation between hepatic steatosis and disease severity in hospitalized COVID-19 patients.
2. Chest CT scores and serum C-reactive protein levels were significantly increased in hospitalized COVID-19 patients with hepatic steatosis compared to those without hepatic steatosis.
3. Opportunistic use of CT density measurements for the detection of HS can be considered an adjunctive tool in the prognostic evaluation of hospitalized patients with COVID-19 pneumonia.

Conflict of Interest

The authors declare that they have no conflict of interest.

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