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ABDOMINAL IMAGING

ORIGINAL ARTICLE

Relationship between hepatic and pancreatic steatosis and the COVID-19 pneumonia total severity score and prognosis with an emphasis on prognostic strength

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PURPOSE

To investigate the relationship between hepatic steatosis (HS), pancreatic steatosis (PS), coexisting HS and PS and the Coronavirus disease-2019 (COVID-19) pneumonia total severity score (TSS) and prognosis, assessed through computed tomography (CT), and to evaluate the degree of effectiveness of the three steatosis conditions on TSS and prognosis.

METHODS

This retrospective study involved 461 patients (255 male and 206 female, median age of 53 years) with COVID-19 who underwent unenhanced chest CT. HS, PS, and coexisting HS and PS, assessed through CT, were compared with patient demographics, comorbidities, TSS, hospitalization and intubation requirements, and mortality rates. The parameters were compared using Mann–Whitney U and chi-square tests. The parameters of three groups of patients with only HS, only PS, and both HS and PS were compared using the Kruskal–Wallis test.

RESULTS

Results revealed that TSS ($P < 0.001$ for all) and hospitalization rates ($P < 0.001$ for all except for HS [$P = 0.004$]) were higher in patients with HS, PS, and both than in those without. Intubation ($P = 0.003$) and mortality rates ($P = 0.018$) were significantly higher solely in patients with PS. However, TSS, hospitalization, and diabetes mellitus were significantly higher than in age-standardized analyses for PS. In a comparison between only HS, only PS, and coexisting HS and PS in 210 patients, the highest TSS was in the coexistence group ($P < 0.001$).

CONCLUSION

The TSS and hospitalization rates correlate with HS, PS, and coexisting HS and PS, whereas intubation and mortality rates only correlate with PS. However, TSS correlates with coexisting HS and PS at the highest rate.

KEYWORDS

Computed tomography, COVID-19, hepatic, pancreas, steatosis

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In the last few years, Coronavirus disease-2019 (COVID-19) has become a public health concern and crisis, with a total of approximately 540 million cases and 6.3 million deaths as of June 2022.[1] Caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), the disease has similar clinical features to many other viral diseases originating in the respiratory system, such as cough, fever, and fatigue. However, it can also lead to more severe complications, resulting in hospitalization, intubation, and death.

Although it is primarily a respiratory system disease, COVID-19 can also be related to other organ systems, especially the gastrointestinal (GI) tract. Evidence suggests that SARS-CoV-2 infection can intensify pre-existing GI conditions.[2] Furthermore, GI pathologies, such as

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pre-existing liver diseases or GI cancers, have been demonstrated to be correlated with COVID-19 prognosis.[2-12] This prognosis is also related to the COVID-19 pneumonia total severity score (TSS) because it is a comprehensive and systematic structure that gathers common findings from COVID-19 chest computed tomography (CT) within one scoring system.[13,14] The hepatobiliary system also plays an essential role in determining the outcome of COVID-19, as demonstrated by studies that have analyzed the effects of hepatic steatosis (HS) on COVID-19 prognosis.[2-5,7-10,12] In addition, assessing HS during the management of COVID-19 is feasible because HS can easily be identified in unenhanced chest CT. Similarly, evaluating the pancreas can help clarify a COVID-19 prognosis because this organ can be observed in a chest CT. In a recent study by Guneyli et al.[15], correlations between pancreatic steatosis (PS) and the clinical severity of COVID-19 pneumonia in 396 patients and the prognosis in 201 hospitalized patients were reported. However, to our knowledge, no studies until now have focused on the relationship between the radiological severity of COVID-19 pneumonia and prognosis and the three following parameters in a single study: HS, PS, and the coexistence of HS and PS in a single patient.

Main points

- Hepatic steatosis (HS), pancreatic steatosis (PS), and coexisting HS and PS, which are components of metabolic syndrome, can be used for the assessment of Coronavirus disease-2019 (COVID-19) prognosis with the help of unenhanced chest computed tomography (CT).
- Of 461 patients, male sex was found to be correlated with HS, and older age showed an association with PS and coexisting HS and PS. Comorbidities such as diabetes mellitus, hypertension (HT), and coronary artery disease showed a strong association with only PS.
- HS, PS, and coexisting HS and PS were all strongly correlated with the disease severity demonstrated by the COVID-19 pneumonia total severity score (TSS) and higher rates of hospitalization, and of the three, PS was also correlated with rates of intubation and mortality.
- When only HS, only PS, and both HS and PS were compared with each other, patients with only PS were older and had higher rates of HT than those in the other two groups.
- The TSS medians in the three groups with only HS, only PS, and both HS and PS were ranked as 5 (HS), 6 (PS), and 7 (both HS and PS), of which the latter had significant correlation.

Therefore, we hypothesize that HS, PS, and their coexistence correlate with the COVID-19 pneumonia TSS, hospitalization and intubation requirements, and COVID-19 mortality rates. This study aims to understand the relationship between HS and PS, both individually and, in one case, coexisting, and COVID-19 TSS and prognosis with the assistance of chest CT and to investigate which of these parameters have a more effective role in COVID-19 pneumonia prognosis by comparing them.

Methods

Study population

The Institutional Review Board authorized the waiver of informed consent for this retrospective investigation (decision number of the ethics committee approval: 2021.468. IRB1.135). We searched the data of 724 individuals who had received a positive SARS-CoV-2 reverse transcription-polymerase chain reaction test result and had undergone a chest CT using a 64-slice CT scanner between March 2020 and March 2021 at a single institution. Patients under the age of 18 (n = 9), those with a pancreatic or liver mass (n = 6) or diffuse liver disease (n = 2) or splenectomy (n = 1), those who had a contrast-enhanced chest CT (n = 26), those whose CT scans did not cover the pancreas (n = 206), and those with significant artifacts (n =13) were all excluded, leaving 461 patients (255 male and 206 female) with a median age of 53 (minimum 18, maximum 91) years. No patient with hemochromatosis or amiodarone use, both of which may change the density measurements, was included.

Throughout the research procedure, patient demographics and associated chronic conditions, including diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), and cerebrovascular disease (CVD), were recorded. In addition, hospitalization and intubation requirements and mortality rates were documented.

CT image acquisition

All CT scans were performed without contrast material using a 64-slice scanner (Siemens, Somatom Definition Flash, Erlangen, Germany). The patients were placed in a supine position, and the images were taken while they held their breaths. The upper abdomen and the whole thoracic cavity were scanned. The CT technique was as follows: helical scanning mode; tube voltage, 120 kV; tube current-time product, 50–350 mAs; pitch, 1.2 and 1.375; matrix, 512x512; reconstructed in lung and soft tissue windows; reconstructed slice thickness, 1.00 mm.

Assessment of PS and HS

The Hounsfield unit (HU) of fat tissue ranges from −150 to −30 HU on unenhanced CT.[16] Two radiologists with expertise in thoracic and abdominal radiology (E.U. with 9 years and H.D. with 3 years of clinical expertise), blinded to patient information, reviewed the CT scans using a dedicated workstation; their decisions were based on consensus. Four regions of interest (ROIs), each separated by the hepatic veins, were drawn using a circular ROI of 1 cm^2 from four distinct places on both lobes (Figure 1a), and the top, middle, and lower sections of the spleen were marked with three ROIs.[16,17] To assess the HU values more accurately, ROIs were generated while avoiding vessels and parenchymal calcifications. The average attenuation values of both organs pointing to the final hepatic and splenic attenuation values were obtained. The liver-to-spleen (L/S) attenuation ratio was then calculated by dividing the liver's attenuation value by that of the spleen. If the L/S attenuation ratio was less than 0.9, HS was assumed to be present in the patient.[9]

The uncinate process, head, neck, body, and tail of the pancreas were marked with five ROIs (Figure 1b, c). After calculating the average attenuation value of the pancreas, the pancreas-to-spleen (P/S) attenuation ratio was calculated by dividing the pancreatic attenuation value by the spleen attenuation value. If the P/S attenuation ratio was less than 0.70, a patient was classified as having PS.[18]

Assessment of TSS

Two radiologists (E.U. with 9 years and H.D. with 3 years of clinical expertise) assessed all images while blinded to patient information, and agreement was reached on the patients with varied scores. The amount of lobar involvement in each of the five lung lobes was measured and categorized as none (0%), minimal (1–25%), mild (26–50%), moderate (51–75%), or severe (76–100%), with reference scores ranging from 0 to 4 (Figure 2). After adding all the scores from the five lobes, a total TSS ranging from 0 to 20 was calculated.[13]

Statistical analysis

For the data analysis, SPSS version 17.0 software (IBM, Chicago, IL, USA) was used. The Kolmogorov–Smirnov test was used to determine if there was a normal distribution.

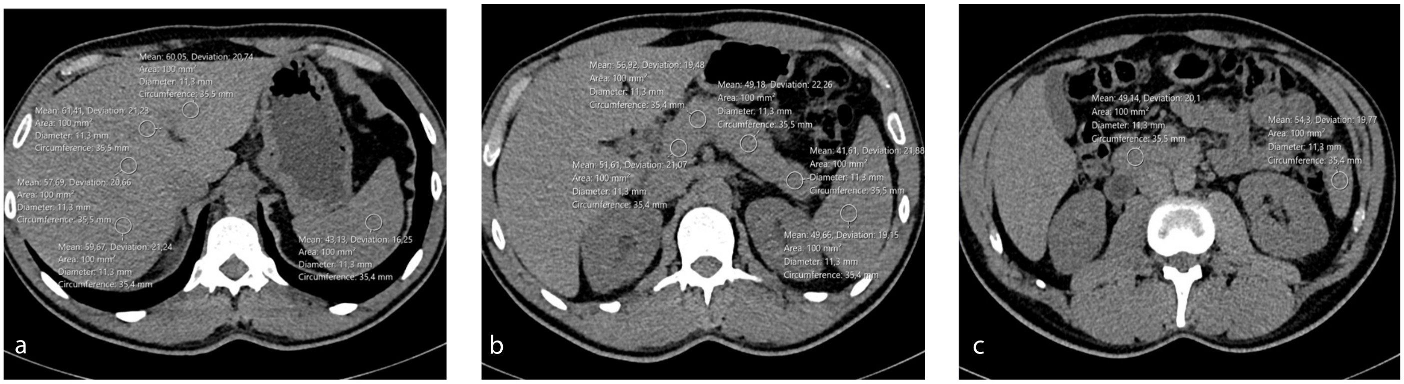

Figure 1. Axial computed tomography images at three levels: **(a)** upper part of the liver and spleen; **(b)** head, neck, body, and tail of the pancreas and the middle part of the spleen; **(c)** uncinate process of the pancreas and lower part of the spleen. The average attenuation value of the four regions of interest (ROIs) in the liver, five ROIs in the pancreas, and three ROIs in the spleen were 59.56, 49.69, and 49.03 Hounsfield units, respectively. The liver-to-spleen attenuation ratio of 1.21 confirmed "liver without steatosis," and the pancreas-to-spleen attenuation ratio of 1.01 confirmed "pancreas without steatosis."

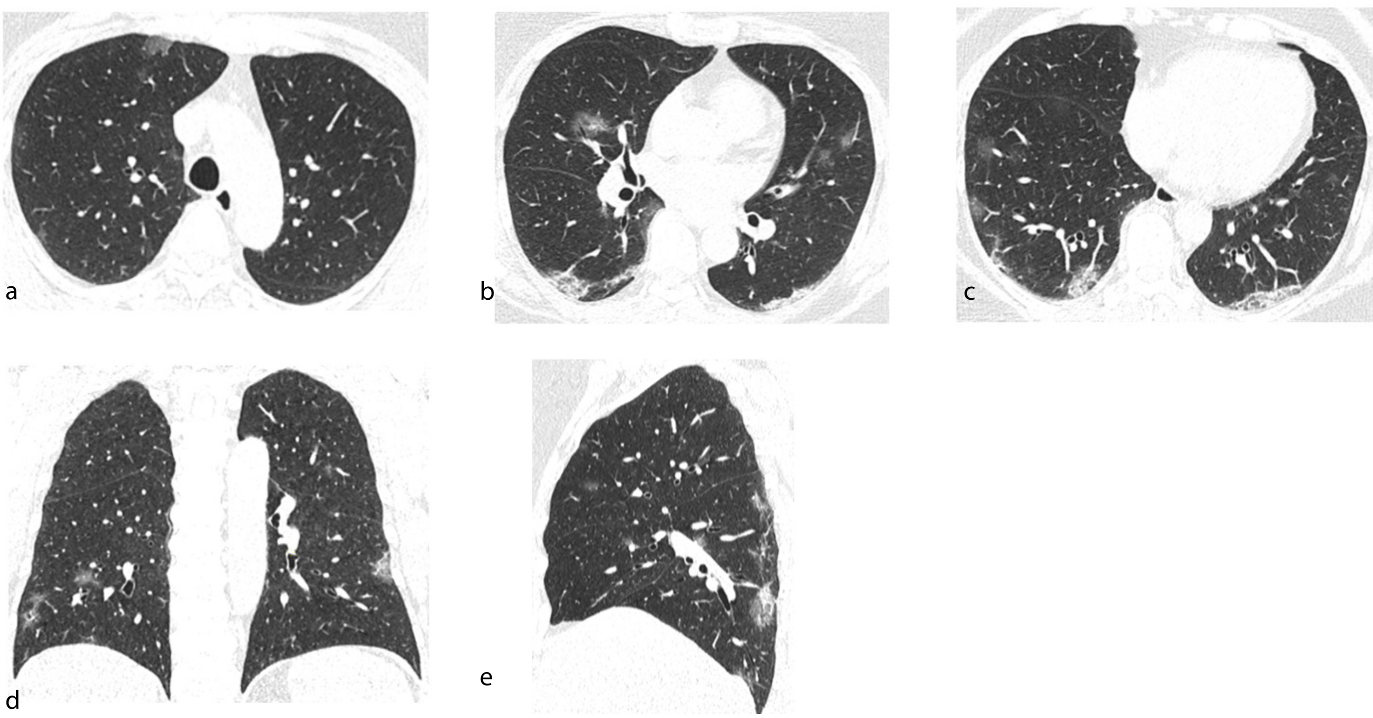

Figure 2. Axial computed tomography images at three levels and the other two planes: **(a)** axial image at the level of the upper lung lobes; **(b)** axial image at the level of the right middle lung lobe; **(c)** axial image at the level of the lower lung lobes; **(d)** coronal image; **(e)** sagittal image. Multifocal, mild involvement of bilateral lungs was revealed, and the COVID-19 pneumonia total severity score was 6. COVID-19, coronavirus disease-2019.

The chi-square test was used to compare HS, PS, and coexisting HS and PS with sex, comorbidities, hospitalization and intubation requirements, and mortality rates, and the Mann–Whitney U test was used to compare HS, PS, and coexisting HS and PS with age and TSS. Age-standardized analyses for PS based on comorbidities, hospitalization, intubation, and mortality rates were investigated using logistic regression, and the unstandardized B value for PS based on TSS was evaluated using linear regression. The parameters were then compared using the Kruskal–Wallis test across the three groups of patients with only HS, only PS, or both. The Mann–Whitney U test was performed for double comparisons. The medians of age and TSS were calculated. Fisher's exact test and Fisher–Freeman–Halton test were also used when required. Statistical significance was defined as a *P* value less than 0.05.

Results

From a total of 461 patients, HS (n = 104, 22.55%), PS (n = 151, 32.75%), and coexisting HS and PS (n = 45, 9.76%) rates were determined. The comparisons of the patients with and without HS, PS, or both according to age, sex, and comorbidities are presented in Table 1.

Age was positively correlated with PS ($P < 0.001$) and coexisting PS and HS ($P = 0.014$), and HS ($P = 0.001$) was higher in male than in female patients (Figure 3). Regarding comorbidities, DM ($P < 0.001$), HT ($P < 0.001$), and CAD ($P < 0.001$) showed a significant correlation with PS, whereas CVD ($P = 0.105$) did not show any significant correlation with this group. Of the four comorbidities, HS and co-

Table 1. Comparisons of patients with and without HS, PS, and both HS and PS according to age, sex, and comorbidities from a total of 461 patients

	Age (years)	Sex (male)	Sex (female)	DM +	DM –	HT +	HT –	CAD +	CAD –	CVD +	CVD –
HS + (n = 104)	54 (26–85)	72 (69.2%)	32 (30.8%)	35 (33.7%)	69 (66.3%)	40 (38.5%)	64 (61.5%)	12 (11.5%)	92 (88.5%)	0 (0%)	104 (100%)
HS – (n = 357)	52 (18–91)	183 (51.3%)	174 (48.7%)	58 (16.2%)	299 (83.8%)	113 (31.7%)	244 (68.3%)	34 (9.5%)	323 (90.5%)	4 (1.1%)	353 (98.9%)
P	0.300	**0.001***		**<0.001***		0.194		0.546		0.579‡	
PS + (n = 151)	63 (31–91)	84 (55.6%)	67 (44.4%)	53 (35.1%)	98 (64.9%)	85 (56.3%)	66 (43.7%)	31 (20.5%)	120 (79.5%)	3 (2%)	148 (98.0%)
PS – (n = 310)	46 (18–87)	171 (55.2%)	139 (44.8%)	40 (12.9%)	270 (87.1%)	68 (21.9%)	242 (78.1%)	15 (4.8%)	295 (95.2%)	1 (0.3%)	309 (99.7%)
P	**<0.001***	0.924		**<0.001***		**<0.001***		**<0.001***		0.105‡	
Coexistence of HS and PS + (n = 45)	57 (35–85)	28 (62.2%)	17 (37.8%)	18 (40.0%)	27 (60.0%)	19 (42.2%)	26 (57.8%)	6 (13.3%)	39 (86.7%)	0 (0%)	45 (100%)
Coexistence of HS and PS – (n = 416)	52 (18–91)	227 (54.6%)	189 (45.4%)	75 (18.0%)	341 (82.0%)	134 (32.2%)	282 (67.8%)	40 (9.6%)	376 (90.4%)	4 (1%)	412 (99.0%)
P	**0.014***	0.327		**<0.001***		0.176		0.431‡		1.000‡	

*Statistically significant values (*P* < 0.05 was used as the significance level). Numeric parameters are expressed as medians. ‡Fisher's exact test was used. CAD, coronary artery disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HS, hepatic steatosis; HT, hypertension; PS, pancreatic steatosis.

existing HS and PS correlated only with DM ($P < 0.001$).

The comparisons of the patients with and without HS, PS, or both according to the TSS, hospitalization and intubation requirements, and mortality rates are presented in Table 2.

Higher TSSs were determined in patients with HS ($P < 0.001$), PS ($P < 0.001$), and both ($P < 0.001$), and higher hospitalization rates were identified in patients with HS ($P = 0.004$), PS ($P < 0.001$), and both ($P < 0.001$) than in patients without (Figure 4). Intubation ($P = 0.003$) and mortality rates ($P = 0.018$) were significant only in patients with PS. The requirement for intubation in patients with and without PS were 9.3% and 2.9%, respectively, whereas mortality rates were 6% and 1.6%, respectively.

The age-standardized odds ratios for PS according to the comorbidities, hospitalization, intubation, mortality rates, and unstandardized B value for PS according to the TSS are presented in Table 3. When the effect of age on the results was eliminated, the presence of DM was 1.8 times greater, hospitalization was 1.7 times greater, and TSS was higher in the patients with PS than in those without PS.

Following these comparisons, three novel groups of interest were formed: Patients with only HS, patients with only PS, and finally, patients with both HS and PS that do not co-

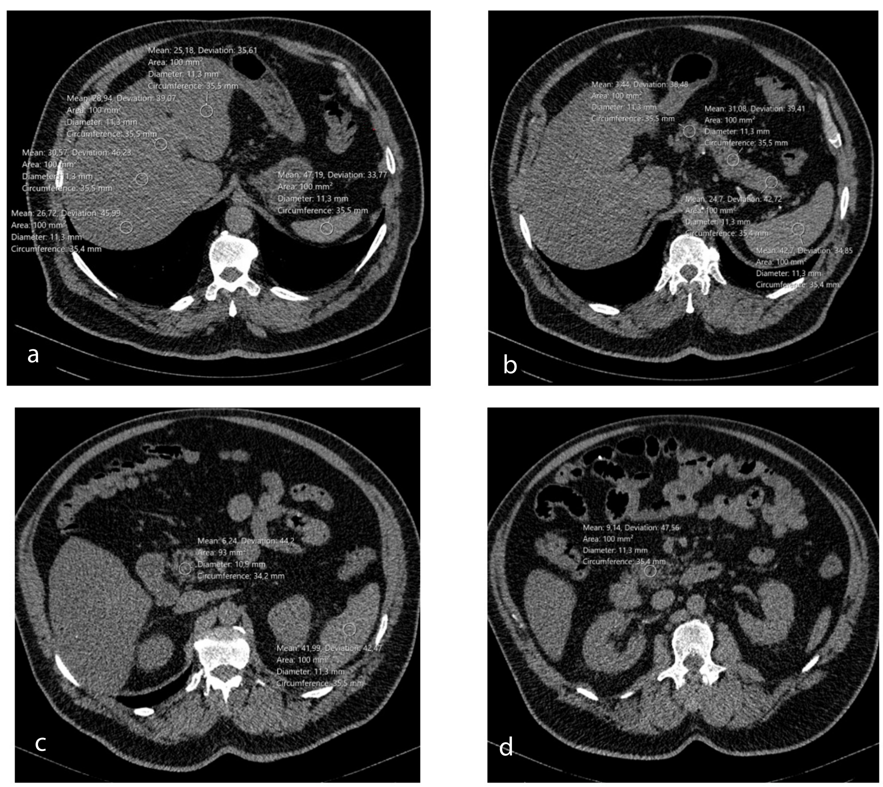

Figure 3. Axial computed tomography images at three levels: **(a)** upper part of the liver and the spleen; **(b)** neck, body, and tail of the pancreas and the middle part of the spleen; **(c)** head of the pancreas and lower part of the spleen; **(d)** uncinate process of the pancreas. The average attenuation value of four regions of interest (ROIs) in the liver, five ROIs in the pancreas, and three ROIs in the spleen were 27.85, 14.92, and 43.96 Hounsfield unit, respectively. The liver-to-spleen attenuation ratio of 0.63 (<0.9) confirmed hepatic steatosis, and the pancreas-to-spleen attenuation ratio of 0.33 (<0.7) confirmed pancreatic steatosis.

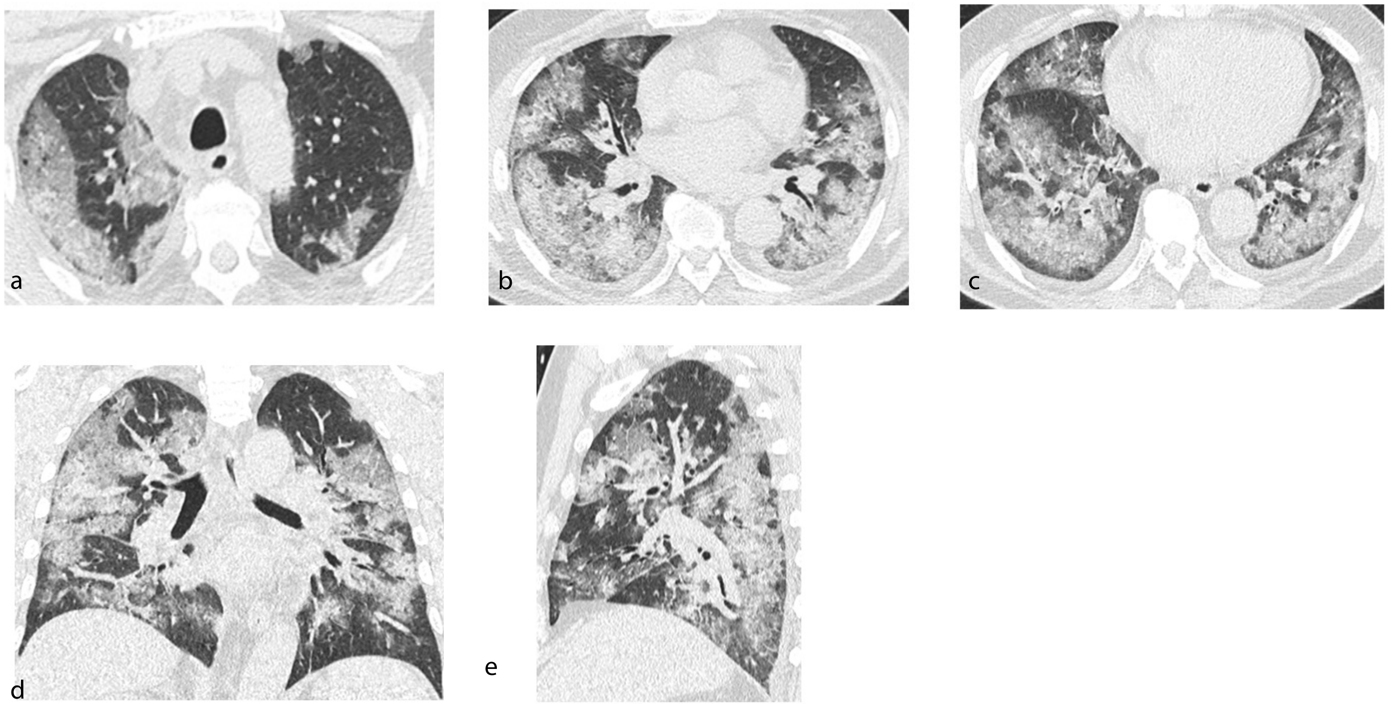

Figure 4. Axial computed tomography images at three levels and the other two planes: **(a)** axial image at the level of the upper lung lobes; **(b)** axial image at the level of the right middle lung lobe; **(c)** Axial image at the level of the lower lung lobes; **(d)** coronal image; **(e)** sagittal image. Severe involvement of bilateral lungs was revealed, and the COVID-19 pneumonia total severity score was 17. COVID-19, coronavirus disease-2019.

Table 2. Comparisons of patients with and without HS, PS, and both HS and PS according to TSS, hospitalization, intubation, and mortality rates from a total of 461 patients

	TSS	Hospitalization +	Hospitalization –	Intubation +	Intubation –	Mortality +	Mortality –
HS + (n = 104)	5 (0–17)	59 (56.7%)	45 (43.3%)	6 (5.8%)	98 (94.2%)	4 (3.8%)	100 (96.2%)
HS – (n = 357)	5 (0–17)	146 (40.9%)	211 (59.1%)	17 (4.8%)	340 (95.2%)	10 (2.8%)	347 (97.2%)
P	**<0.001***	**0.004***		0.678		0.529‡	
PS + (n = 151)	6 (0–17)	98 (64.9%)	53 (35.1%)	14 (9.3%)	137 (90.7%)	9 (6.0%)	142 (94.0%)
PS – (n = 310)	4 (0–17)	107 (34.5%)	203 (65.5%)	9 (2.9%)	301 (97.1%)	5 (1.6%)	305 (98.4%)
P	**<0.001***	**<0.001***		**0.003***		**0.018*‡**	
Coexisting HS and PS + (n = 45)	7 (0–15)	33 (73.3%)	12 (26.7%)	3 (6.7%)	42 (93.3%)	2 (4.4%)	43 (95.6%)
Coexisting of HS and PS – (n = 416)	5 (0–17)	172 (41.3%)	244 (58.7%)	20 (4.8%)	396 (95.2%)	12 (2.9%)	404 (97.1%)
P	**<0.001***	**<0.001***		0.482‡		0.637‡	

Numeric parameters are expressed as medians. *Statistically significant values ($P < 0.05$ was used as the significance level). ‡Fisher's exact test was used. HS, hepatic steatosis; PS, pancreatic steatosis; TSS, total severity score.

incide with the first two groups. Of the 210 patients with HS, PS, or both, 59 (28.09%) had only HS, 106 (50.47%) had only PS, and 45 (21.42%) had both. The comparisons of the three groups of patients with only HS, only PS, and both according to the parameters in patients with HS and/or PS are presented in Tables 4, 5. In this study, the median age was found to be 65.5 years in patients with only PS, which was higher than the median ages (53 and 57 years) determined in the other groups ($P < 0.001$). The rate of HT was also demonstrated as 62.3% in patients with PS, which was higher than the rates (42.4% and 42.2%) determined in the other groups ($P = 0.015$). The TSS medians were 5, 6, and 7 in the patients with only HS, only PS, and both, revealing the TSS of the group with coexisting HS and PS to be significantly higher than those of the other two groups ($P < 0.001$). The other parameters were not significant between the groups.

Discussion

This research determines that HS, PS, and coexisting HS and PS are related to TSS and

Table 3. Age-standardized odds ratios for PS according to comorbidities, hospitalization, intubation, mortality rates, and unstandardized B value for PS according to TSS

	Odds ratio (95% CI) and *P* value
DM	**1.81 (1.06–3.10), *P* = 0.029***
HT	1.53 (0.92–2.55), *P* = 0.097
CAD	1.81 (0.86–3.79), *P* = 0.115
CVD	3.95 (0.31–50.17), *P* = 289
TSS‡	**1.04 (0.43–1.66), *P* = 0.001***
Hospitalization	**1.70 (1.07–2.72), *P* = 0.024***
Intubation	1.01 (0.37–2.73), *P* = 979
Mortality	0.62 (0.16–2.34), *P* = 0.486

*Statistically significant values (*P* < 0.05 was used as the significance level). ‡Unstandardized B value is expressed for TSS. CAD, coronary artery disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HT, hypertension; PS, pancreatic steatosis; CI, confidence interval; TSS, total severity score.

Table 4. Comparisons of the three groups of patients with only HS, only PS, and both according to age, sex, and comorbidities from a total of 210 patients with HS and/or PS

	Age (years)	Sex (male)	Sex (female)	DM +	DM –	HT +	HT –	CAH +	CAH –	CVD +	CVD –
HS + (n = 59)	53 (23–87)	33 (55.9%)	26 (44.1%)	16 (27.1%)	43 (72.9%)	25 (42.4%)	34 (57.6%)	9 (15.3%)	50 (84.7%)	1 (1.7%)	58 (98.3%)
PS + (n = 106)	**65.5 (31–91)**	56 (52.8%)	50 (47.2%)	35 (33.0%)	71 (67.0%)	**66 (62.3%)**	40 (37.7%)	25 (23.6%)	81 (76.4%)	3 (2.8%)	103 (97.2%)
Coexisting HS and PS + (n = 45)	57 (35–85)	28 (62.2%)	17 (37.8%)	18 (40.0%)	27 (60.0%)	19 (42.2%)	26 (57.8%)	6 (13.3%)	39 (86.7%)	0 (0%)	45 (100%)
P	**<0.001***	0.568		0.382		**0.015***		0.232		0.812‡	

Numeric parameters are expressed as medians. *Statistically significant values (*P* < 0.05 was used as the significance level). ‡Fisher–Freeman–Halton test was used. CAD, coronary artery disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HS, hepatic steatosis; HT, hypertension; PS, pancreatic steatosis.

Table 5. Comparisons of the three groups of patients with only HS, only PS, and both according to TSS, hospitalization, intubation, and mortality rates from a total of 210 patients with HS and/or PS

	TSS	Hospitalization +	Hospitalization –	Intubation +	Intubation –	Mortality +	Mortality –
HS + (n = 59)	5 (0–16)	32 (54.2%)	27 (45.8%)	6 (10.2%)	53 (89.8%)	3 (5.1%)	56 (4.9%)
PS + (n = 106)	6 (0–17)	65 (61.3%)	41 (38.7%)	11 (10.4%)	95 (89.6%)	7 (6.6%)	99 (93.4%)
Coexisting HS and PS + (n = 45)	**7 (0–15)**	33 (73.3%)	12 (26.7%)	3 (6.7%)	42 (93.3%)	2 (4.4%)	43 (95.6%)
P	**<0.001***	0.137		0.762		0.929‡	

Numeric parameters are expressed as medians. *Statistically significant values (*P* < 0.05 was used as the significance level). ‡Fisher–Freeman–Halton test was used. HS, hepatic steatosis; PS, pancreatic steatosis; TSS, total severity score.

the requirement for hospitalization. However, PS alone was correlated with the requirement for intubation and mortality rates in patients with COVID-19. In addition, TSS, hospitalization, and DM were significant in patients with PS when age-standardized analyses were conducted for PS. Furthermore, the contrast between patients with only HS, only PS, and both using an analysis of variance revealed that patients that only had PS had a higher age and level of HT, whereas patients with both PS and HS had a higher TSS.

Visceral steatosis can affect the overall outcome of diseases. For instance, in hemochromatosis and hepatitis C virus infections, having HS influences the progression of the fibrotic changes in the liver.[19,20] Moreover, infections in organs other than those where the steatosis originated can be affected. For example, research indicates that non-alcoholic fatty liver disease is associated with increased mortality in patients with community-acquired pneumonia.[21] In the present study, we hypothesized that steatosis of the GI organs could aggravate COVID-19 outcomes, considering its effects on human metabolism and its concomitant nature with obesity. There is a gap in the literature in this respect in relation to some of the GI organs. Although previous research has revealed that HS is a factor that worsens the outcomes of patients with COVID-19,[3,4,7,9] the gap is more evident in the research on PS and COVID-19. Furthermore, PS does not need to be a single steatotic entity but can co-occur with HS. Hence, we chose the three main groups of focus to be patients with COVID-19 with HS, PS, and both in our study.

The prevalence of HS and PS in patients with COVID-19 was 22.5% and 32.7%, respectively. In line with our study, previous studies have reported the rates of HS in patients with COVID-19 as 25.6–30%, and the global prevalence of HS has been stated as 25.4%.[7,8] In a case–control study,[16] PS assessed through CT was found in 71.9% and 45.3% of the prediagnostic pancreatic ductal adenocarcinoma cases and controls, respectively, identifying a relatively high rate of PS even in the healthy control participants. Although a limited number of studies have been conducted, we believe that the prevalence of PS may be higher than the prevalence of HS.

In a study by Guneyli et al.[15], PS accounted for approximately one third of patients with COVID-19 pneumonia. They also reported that PS correlated with clinical severity and hospitalization in all patients with COVID-19 pneumonia.[15] In the present study, we found that patients with PS presented with higher TSS and hospitalization rates, and intubation and mortality rates were significant in patients with PS in all 461 patients. In comparison, PS did not correlate with intubation and mortality in the 201 hospitalized patients with COVID-19 included in the study by Guneyli et al.[15], possibly because of the small number of intubations and low death rates.

Initially, we investigated the three groups according to their relationships with epidemiologic data. Older age exhibited a substantial correlation in patients with PS and with coexisting HS and PS. Although those with HS lacked this connection with age, this group correlated with the male sex. It was also crucial to compare the essential manifestations of the metabolic syndrome among the patients in this study, as these comorbidities have previously proven to worsen the COVID-19 diagnosis.[12] In this study, PS became more prominent because its existence in a patient with COVID-19 was correlated with DM, HT, and CAD. A correlation between DM and having HS and both PS and HS was also noted. However, CVD was not associated with any of the three groups. Previously, Singh and Khan[11] conducted an extensive multicentered study of 250 patients with COVID-19, and liver disease predominantly comprised of HS. They demonstrated that pre-existing liver disease was associated with older age and comorbidities such as HT and DM. Among the other studies focusing on HS, Çoraplı et al.[7] noted that HS did not correlate with older age or sex. In contrast with our study, Chen et al.[3] demonstrated that although younger age was correlated with HS, sex, HT, and DM had no association with this condition. Additionally, Forlano et al.[8] found that the median age was higher in patients with COVID-19 without HS than in those with HS. However, sex and comorbidities were not correlated with HS in the same study.

To clarify the relationship between these three groups of steatosis and COVID-19 prognosis, we used four parameters for comparison: TSS and the presence of hospitalization, intubation, and mortality. TSS was notably detected in direct proportion to all three groups of steatoses, thus supporting the hypothesis that PS, HS, and coexisting PS and HS are factors that exacerbate COVID-19 severity. This correlation also existed for the presence of hospitalization in all three groups. Subsequently, intubation was correlated with only the presence of PS. However, no correlation was uncovered between intubation and HS or the coexistence of the two steatoses. Finally, mortality rates followed a similar pattern; mortality exhibited a significant change of 4.4% only with PS. The significant correlation between intubation and mortality with only PS may be because PS is a more specific prognostic factor in patients with COVID-19 than HS or coexisting HS and PS. Furthermore, the concept of PS being a more specific prognostic factor can also be affiliated with the presence of metabolic syndrome. Singh and Khan[11] demonstrated higher hospitalization and mortality rates among patients with pre-existing liver disease (predominantly HS) and COVID-19. Among the studies focusing more specifically on HS and COVID-19, Parlak et al.[10] had similar results to ours in terms of severity after investigating CT findings indicating that severity, such as upper lobar involvement and paving pattern lung lesions, was more common in patients with a fatty liver. Compared with this and other similar studies, our research uses an even more tangible severity indicator, TSS.[13,14] Çoraplı et al.[7], who also focused only on HS, found that HS was notably correlated with TSS and hospitalization rates. Furthermore, Chen et al.[3] demonstrated that HS was correlated with intubation rates, whereas mortality rates were inversely correlated with HS. Furthermore, Forlano et al.[8] revealed that higher mortality was not associated with patients with COVID-19 having fatty liver disease.

When the effect of age was eliminated following the initial comparisons, hospitalization was 1.7 times greater, and TSS was higher in the patients with PS than in those without PS. This validates the view that severe disease is more commonly demonstrated in patients with PS. Although intubation and mortality rates did not correlate with PS in these analyses, a significant correlation of PS with hospitalization and TSS would potentially contribute to the management of patients with COVID-19 pneumonia. Among the comorbidities, only the presence of DM was more commonly seen in patients with PS, which can be expected during DM.

Several studies have reported that increased age, cardiometabolic risk factors, and comorbidities lead to a poor prognosis in patients with COVID-19, and HS is considered part of metabolic syndrome.[3,4,7-12] Although the underlying mechanisms of HS indicate that patients with HS are more susceptible to severe COVID-19 than those without HS, some factors are considered contributing factors to the severity of the disease. First, HS can accompany DM, increasing the risk and severity of infection. Second, the prevalence of cardiovascular and pulmonary diseases, in which an impaired patient response tends to occur, is higher among patients with HS than among those without HS. Finally, the cytokine storm appears to be the main culprit behind severe disease and high mortality rates in these patients.[8] Forlano et al.[8] reported that patients with HS presented with higher levels of C-reactive protein than those without HS. They also demonstrated that in patients with HS, the survival rates were lower in those who presented with higher inflammatory markers (ferritin, prothrombin time, and lactate dehydrogenase) than in those with lower inflammatory markers. Interleukin-6 levels and the production of proinflammatory cytokines, such as tumor necrosis factor-alpha from Kupffer cells that have negative impacts on infectious diseases, were also found to be increased in patients with COVID-19 with HS.[7] PS, also known to be a risk factor for metabolic syndrome, is thought to allow mechanisms similar to HS to occur, resulting in a poor prognosis.[17]

The groups with HS and/or PS were also compared to fully understand their role in the disease. To this end, the number of patients corresponding to the earlier parameters was analyzed again in each group. However, this time, the groups did not overlap, meaning that each patient with one of the types of steatoses was not included in the coexisting group. Age was the only substantial parameter for the epidemiological parameters, as patients with only PS were significantly older than those in the other two groups. Similarly, for the comorbidities, patients with only PS exhibited higher percentages of HT than those with only HS or both.

Moreover, TSS was the only parameter that demonstrated a significant difference in terms of severity factors, as patients with coexisting HS and PS had a higher TSS than the other two groups. This finding must be emphasized because a higher TSS has been observed previously in patients with and without HS, PS, or both. The fact that a higher TSS is the only severity factor that exceeds the number of patients with coexisting HS and PS demonstrates that this coexistence is a potentially helpful prognostic parameter for COVID-19. In this study, the lack of substantial correlations between the three groups and the prognostic parameters except TSS can be attributed to the low numbers of patients, especially for those who were deceased or intubated. As the literature lacks extensive research on this matter, we could not compare these final findings with existing data.

This study has several limitations. First, the study was retrospective and conducted in a single center. Second, the baseline chest CT findings for the patients were not considered in our study; some might have overlapped with the chest CT findings attributed to COVID-19 pneumonia. Third, the disease course at the time of CT varied among patients, and CT images with the highest TSS were considered for patients who underwent multiple CT examinations. However, this affected only six patients, making the possible effect of this issue minimal in the study. Some of the routine chest CTs we reviewed did not cover the entire pancreas in several patients, making the sample size smaller, and coverage may lead to increased radiation doses. In addition, HS can be visually evaluated in most patients on CT, whereas density measurements are required in nearly all patients during the evaluation of PS through CT, which may not be routinely feasible in all patients in busy radiology departments. Additionally, the degree of HS was not considered in our study. As another limitation, the HU values of the pancreas were obtained with the consensus of two radiologists. Finally, HS can have a geographical appearance that can affect density measurements, and the assessment of HS and PS based on histopathologic specimens can be more accurate than that assessed on CT. However, using ≥4 ROIs in the liver and pancreas rendered more accurate assessments.

In conclusion, the unenhanced chest CT imaging of COVID-19 patients allows the assessment of HS and PS without difficulty. These two conditions, both separately and together, are vital tools for understanding the severity of COVID-19. The presence of HS, PS, and their coexistence have been demonstrated to play a role in TSS and hospitalization rates. Furthermore, PS is correlated with intubation and mortality rates among patients with COVID-19. Age-standardized analyses for PS revealed that TSS, hospitalization, and DM were statistically meaningful in individuals with PS. Patients with only HS, only PS, or HS and PS together were compared, with the TSS being the greater among patients with coexisting HS and PS, making this coexistence a possible prognostic factor. Future investigations with larger sample sizes may reveal any probable links by comparing other prognostic features of COVID-19 with HS, PS, or both.

Conflict of interest disclosure

The authors declare no conflicts of interest.

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