Use of liver ultrasound and transient elastography in risk stratification in COVID-19 patients

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ABSTRACT

Background: Elevated liver enzymes is common in patient infected with COVID-19 and recent cohorts found that it present in 17% - 57% of COVID-19 patients. Transient elastography (TE) is a widely used non-invasive tool to measure liver stiffness (LS). LS measurements are a sensitive method to detect liver damage, and increased LS values are seen in compromised liver tissue like in chronic and in acute hepatitis(1).
Aim and objectives: To identify the validity of liver transient elastography in assessing the severity of disease in COVID-19 patients.
Subjects and methods: This was a prospective observational cohort study that included patients hospitalized due to covid-19 infection documented by reverse transcription polymerase chain reaction (PCR) to kasr el-Ainy isolation unit during the period from June 2021 To March 2023.
Results: there was a statistically significant difference between the studied groups regarding , liver biomarkers(ALT, AST, LDH, ALK and LDH), inflammatory biomarkers, oxygenation, Length of hospital stay, SOFA score and Mortality.
Conclusion: Transient elastography is a useful and non-invasive tool to assess onset and severity of acute liver injury in patients with COVID-19 patients. Increased LS seems to be predictive for a more severe and complicated course of disease.
Keywords: transient elastography, risk stratification, COVID-19.

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INTRODUCTION

Severe acute respiratory syndrome corona virus 2 (SARS-COVID) was first detected in Wuhan, Hubei province in China at December 2019. Since then, the coronavirus disease 2019 (COVID-19) has spread globally with over 599,227,808 millions cases and to date more than 76300 000 disease related fatalities.

Coronaviruses are a diverse group of large, enveloped, positive-stranded RNA viruses that cause a broad spectrum of diseases, including pneumonitis, hepatitis, nephritis, enteritis and encephalitis in animals, and several of these viruses are significant veterinary pathogens(2) Six coronavirus species have been identified to be pathogenic in humans as well.(3) Among them, two coronaviruses have emerged as major global health threats: the severe acute respiratory syndrome coronavirus (SARS-CoV; in 2002) that spread to 37 countries, and the Middle East respiratory syndrome coronavirus (MERS-CoV; in 2012) that reached 27 countries(4)

Both, the SARS-CoV and the MERS-CoV, had a low basic reproductive number, whereas SARS-CoV-2 virus has a very high potential for community transmission and causes the current pandemic threat.

The typical symptoms of a SARS-CoV-2 infection, such as fever, cough, sore throat or dyspnea, are well recognized and have been widely described.(5–9) Additionally, the Centers of Disease Control and Prevention (CDC) announced gastrointestinal (GI) symptoms as pathognomonic in COVID-19.(10) Little is known about SARS-CoV-2 induced-liver diseases, although abnormalities of liver function indexes are common in patients with COVID-19(11,12)

Transient elastography (TE) is a widely used non-invasive tool to measure liver stiffness (LS). LS measurements are a sensitive method to detect liver damage, and increased LS values are seen in compromised liver tissue like in chronic and in acute hepatitis(1)

The aim of this work was to identify the validity of liver transient elastography and ultrasound in assessing the severity of disease in COVID-19 patients.

PATIENTS AND METHODS

This was a prospective observational cohort study that included patients hospitalized due to covid-19 infection documented by reverse transcription polymerase chain reaction (PCR) to kasr el-Ainy isolation unit during the period from June 2021 To March 2023. The study was approved by Cairo university ethics committee.

Exclusion Criteria: Patients younger than 18 years old, Pre-existing chronic liver disease (determined by the history and review of past laboratory results and/or abdominal ultrasound), Presence of ascites, Pregnancy, History of liver transplantation, Significant alcohol consumption (≥20 g per week for women and ≥30 g per week for men),Unable to give written informed consent, Prior antiviral treatment for hepatotropic viruses 3months before the study and Patient with cardiogenic pulmonary oedema.

All patients were subjected to the following: History taking, Full clinical assessment and Investigations.

laboratory investigation: Routine laboratory investigations (PCR for COVID-19, CBC, SGPT, SGOT, Bilirubin, Urea, Creatinine, uric acid, coagulation profile including PT, PC, ferritin, d-dimer, CRP, LDH, GGT, ALKALINE PHOSPHATASE and INR(and Arterial blood gases (ABG.(

Radiological investigations: chest X-ray to all patients, Performance of transient elastography and Abdominal ultrasound.

Liver stiffness measurement LSM was measured using a FibroScan® 530 compact device equipped with both M and XL probes at the beginning of hospitalization.(13) All patients were asked to fast for at least 3 hours before the examination. Probe selection was performed using the automatic probe selection tool embedded in the device software. For the examination, the patients were placed in the dorsal decubitus position and the transducer probe was positioned in the intercostal space of the right lobe of the liver 6cm in depth.

LSM is an average estimate of stiffness (Young's modulus) at a shear wave frequency of 50 Hz and is expressed as kPa.(14)Severe liver fibrosis (fibrosis ≥ 3) was defined as LSM higher than 9.6 kPa, as published several times.' (15) a value above 5kpa was considered to be elevated and reflect acute liver damage(16–18) The procedure was repeated at day 0,3,6.

Table 1: Sequential organ failure assessment (SOFA SCORE): was applied to all included patients within 24 hours. (19)

Sequential [Sepsis-Related] Organ Failure Assessment (SOFA) Score

System	0	1	2	3	4
Respiration PaO2/FiO2, mmHg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation Platelets, x10³/uL	≥150	<150	<100	<50	<20
Liver Bilirubin, mg/dL (umol/L)	<1.2 (20)	1.2 - 1.9 (20 - 32)	2.0 - 5.9 (33 - 101)	6.0 - 11.9 (102 - 204)	>12.0 (204)
Cardiovascular	MAP ≥70mmHg	MAP <70mmHg	Dopamine <5 or Dobutamine (any dose)	Dopamine 5.1 - 15 or Epinephrine ≤0.1 or Norepinephrine ≤0.1	Dopamine >15 or Epinephrine >0.1 or Norepinephrine >0.1
CNS GCS Score	15	13 - 14	10 -12	6 - 9	<6
Renal Creatinine, mg/dL (umol/L) Urine Output, mL/d	<1.2 (110)	1.2 - 1.9 (110 - 170)	2.0 - 3.4 (171 - 299)	3.5 - 4.9 (300 - 440) <500	>5.0 (440) <200
*Catecholamine Doses = ug/kg/min for at least 1hr					

Statistical analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test in normally distributed quantitative variables while non-parametric Mann-Whitney test was used for non-normally distributed quantitative variables **(14)**. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5 **(14)**. Correlations between quantitative variables were done using Spearman correlation coefficient **(14)**. ROC curve was constructed with area under curve analysis performed to detect best cutoff value of LS for detection of mortality, ICU admission and ventilation. P-values less than 0.05 were considered as statistically significant**.**

RESULTS

Table (2) Age in group A and group B .

	LS score above 5 kpa(A)					LS score less than 5 kpa(B)					P value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Age	62.74	11.43	64.00	36.00	83.00	62.91	11.97	63.00	35.00	82.00	0.939

There was no statistically significant difference between both groups regarding gender and age.

Table (3) Risk factors and comorbidities in group A and group B .

	Group				
	LS score above 5 kpa(A)		LS score less than 5 kpa(B)		P value
	Count	%	Count	%	
Smoker	19	35.8%	22	46.8%	0.266
Copd	11	20.8%	11	23.4%	0.750
Diabetic	25	47.2%	26	55.3%	0.416
Hypertensive	37	69.8%	23	48.9%	0.033
Malignancy	1	1.8%	1	2.1%	

Apart from hypertension there was no statistically significant difference between both groups regarding(COPD, Diabetes mellitus, malignancy and smoking).

Table (4) liver biomarkers in group A and group B on admission, on day three and on day six .

	LSM above 5 kpa(A)					LSM less than 5 kpa(B)					P value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
ALT on admission	108.68	83.92	93.00	11.00	616.00	40.74	31.41	27.00	13.00	126.00	< 0.001
ALT on day three	124.13	93.85	115.00	8.00	538.00	43.13	37.00	28.00	13.00	206.00	< 0.001
ALT on day six	112.09	80.34	90.00	13.00	488.00	40.39	36.60	29.50	13.00	213.00	< 0.001
AST on admission	107.70	64.68	93.00	7.00	389.00	44.49	31.17	35.00	10.00	146.00	< 0.001
AST on day three	113.06	60.72	96.00	17.00	306.00	50.51	57.86	35.00	12.00	377.00	< 0.001
AST on day six	94.66	56.92	81.00	16.00	324.00	44.08	38.10	34.00	14.00	224.00	< 0.001
LDH on admission	961.00	508.93	896.00	112.00	2540.00	495.81	209.93	430.00	266.00	1055.00	< 0.001
Alkaline on phosphatase on admission	103.89	81.56	77.00	30.00	376.00	57.02	20.84	49.00	32.00	133.00	< 0.001

GGT on admission	85.74	49.35	75.00	29.00	230.00	44.43	15.01	39.00	24.00	90.00	< 0.001

Regarding liver biomarkers , (ALT, AST, LDH, ALP, GGT) there was statistically significant difference between both groups on admission, on day three and on day six as shown in the table.

Table (5) inflammatory biomarkers in group A and group B on admission, on day three and on day six .

	LSM above 5 kpa					LSM less than 5 kpa					P value
	Mean	**SD**	**Median**	**Minimum**	**Maximum**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	
Procalcitonin	1.17	1.78	0.50	0.03	9.60	0.50	0.74	0.16	0.01	3.00	0.007
CRP on admission	154.00	98.09	143.00	2.00	345.00	139.47	92.29	109.00	9.00	343.00	0.454
CRP on day three	112.75	87.01	79.00	3.00	328.00	98.02	91.03	56.00	4.00	298.00	0.153
CRP on day six	78.34	102.38	28.00	1.00	398.00	56.41	66.36	22.00	1.00	233.00	0.627
FERRITIN on admission	951.45	640.08	869.00	2.87	2650.00	608.43	523.35	428.00	12.00	2100.00	0.002
FERRITIN on day three	1029.89	804.49	760.00	83.00	3428.00	418.83	291.85	335.00	14.00	1032.00	< 0.001
D-DIMER	1.14	0.98	0.89	0.25	5.66	0.66	0.50	0.55	0.20	2.50	0.002
TLC on admission	10.07	4.98	10.00	2.30	27.00	7.31	3.52	6.80	2.50	16.20	0.004
TLC on day three	11.15	6.30	11.40	1.90	29.80	8.44	4.71	6.90	2.00	18.00	0.034
TLC on day six	11.91	5.59	11.60	3.50	25.20	9.50	4.89	9.50	2.50	22.00	0.035

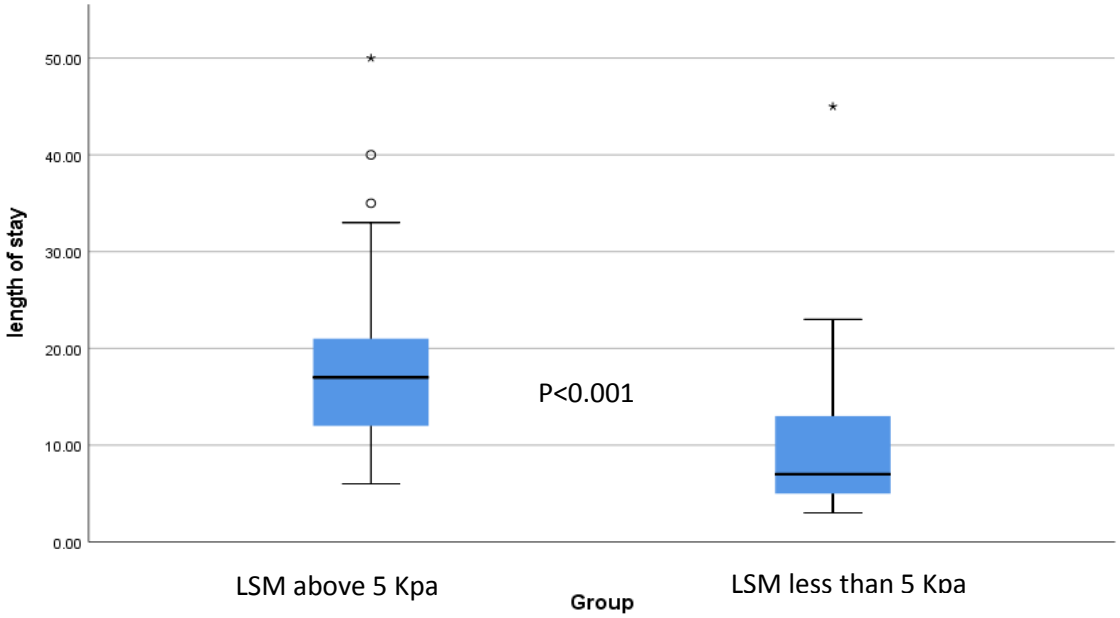
Despite the statistically significant difference between both groups regarding inflammatory markers including (procalcitonin, ferritin, D-dimer and TLC) , yet CRP showed no statistically significant difference between both groups (A) and (B).

Table (7) oxygenation in group A and group B on admission, on day three and on day six.

		Group				
		LS score above 5 kpa		LS score less than 5 kpa		P value
		Count	%	Count	%	
Oxygenation	**Off**	3	5.7%	17	36.2%	< 0.001
	Nasal	10	18.9%	21	44.7%	
	simple mask	11	P<0.001	4	8.5%	
	mask reservoir	23		2	4.3%	
	HFNC	1	1.9%	1	2.1%	
	CPAP	2	3.8%	1	2.1%	
	Mechanical ventilation	3	5.7%	1	2.1%	
oxygenation	**Off**	10	18.9%	28	60.9%	< 0.001
	Nasal	4	7.5%	10	21.7%	
	simple mask	9	17.0%	0	0.0%	
	mask reservoir	10	18.9%	2	4.3%	
	HFNC	5	9.4%	1	2.2%	
	CPAP	10	18.9%	4	8.7%	
	Mechanical ventilation	5	9.4%	1	2.2%	
oxygenation 3	**Off**	10	18.9%	29	74.4%	< 0.001
	Nasal	6	11.3%	2	5.1%	
	simple mask	10	18.9%	0	0.0%	
	mask reservoir	5	9.4%	4	10.3%	
	HFNC	1	1.9%	0	0.0%	
	CPAP	12	22.6%	3	7.7%	

	Mechanical Ventilation	9	17.0%	1	2.6%	

Regarding oxygen requirement including NIPV and invasive mechanical ventilation among studied patients it was statistically significant higher in group A than group B with p <0.001 all through the study.

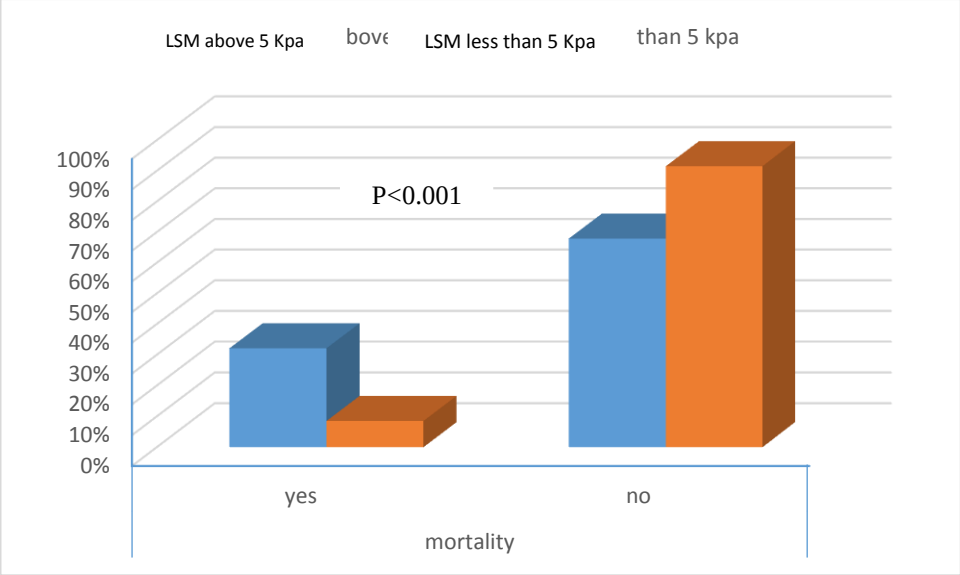


{Figure (3)} Length of hospital stay in group A and group B.

Table (8) SOFA score in group A and group B on admission, on day three and day six.

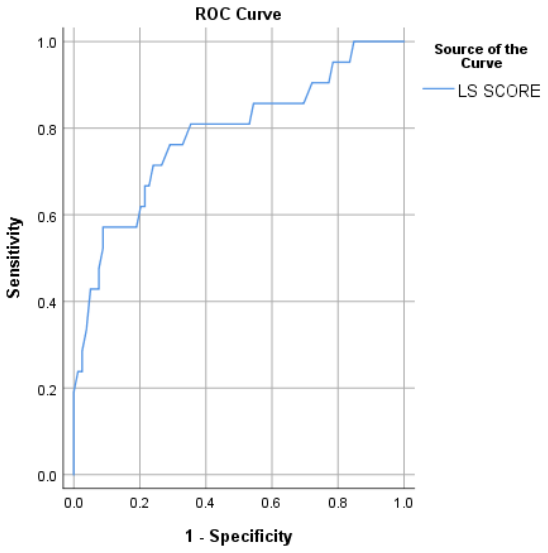
	LSM above 5 kpa					**LSM less than 5 kpa**					**P value**
	Mean	**SD**	**Median**	**Minimum**	**Maximum**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**	
SOFA score	3.04	2.38	3.00	0.00	12.00	1.81	1.90	1.00	0.00	11.00	0.002
SOFA SCORE 2	3.42	3.17	3.00	0.00	14.00	1.47	2.25	0.00	0.00	11.00	< 0.001
SOFA SCORE 3	3.81	3.80	2.00	0.00	14.00	1.46	2.72	0.00	0.00	14.00	< 0.001

The mean of SOFA score was (3.04±2.38 vs 1.81±1.90) with p= 0.002 on admission, (3.42±3.17 vs 1.47±2.25) with (p <0.001).on day three and (3.81±3.80 vs 1.46±2.72) on day six with (p <0.001). among group A and group B respectively.

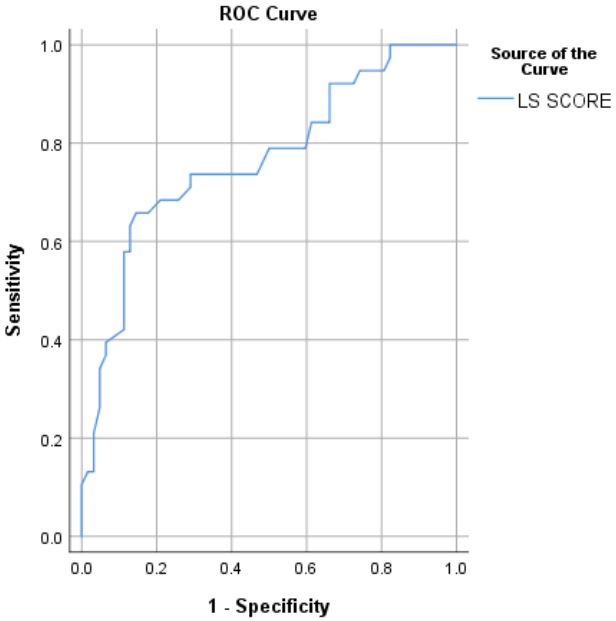


{Figure (4)} Mortality in group A and group B

The cut off value for LSM to predict mortality was 6.25 KPA with a sensitivity of 71.4% and a specificity of 75.9 % and with a P value of 0.001. The area under curve [AUC] was 0.784 [95% confidence Interval (0.663-0.906).



The cut off value for LSM to predict ICU admission was 6.25 KPA with a sensitivity of 65.8% and a specificity of 85.5 % and with a P value of 0.001. The area under curve [AUC] was 0.766[95% confidence Interval (0.666-0.865]



DISCUSSION

Elevated liver enzymes is common in patient infected with COVID-19 and recent cohorts found that it present in 17% - 57% of COVID-19 patients(20). Fraquelli and coworkers(21)showed a stepwise increase of LS going along with the inflammatory activity in a cohort of patients with acute on chronic liver disease. (22) The relationship of LS and aminotransferase levels and even with the degree of histologically proven liver inflammation was demonstrated convincingly several times.(23,24)This encourage us to deem LS measurements proper to uncover liver damage, and therefore, we proposed that acute liver damage caused by COVID-19 can be detected with non-invasive LS measurements.

Our study showed that SOFA score was significantly higher in patients with higher LSM with statistically significant positive correlation between SOFA score and LSM.

Regarding ICU admission and mortality our study showed that among patients with higher LSM there were 28 patients admitted to ICU (52%) while in group B there were 10 patients admitted to ICU(21.3%) . The mortality rate in group A was 32% (17 patients) while in group B 8.9% (4 patients).

likely Da et al 2021. a single-center retrospective cohort study of consecutive patients hospitalized with severe and critical COVID-19 with or without liver injury and who underwent immunologic testing (interleukin [IL]-6, IL-8, tumor necrosis factor alpha [TNF-α], and IL-1β). Peak inflammatory markers and IL-6 were higher in the liver injury group. The liver injury group had a longer length of stay in the hospital and more severe COVID-19 despite having less diabetes and chronic kidney disease(25)

It worth that all patients in this study is severely disease which different from our type of patients.

Suffredini, et al. showed that Each unit increase in liver stiffness, treated as a continuous variable, was associated with an increase of 0.32 ± 0.10 days in the hospital (p = 0.002).(26)

Mortality rate, ICU admission and SOFA score were higher in group A as patients in group A were more diseased with elevated, sepsis parameters due to over whelming infections.

Krishnasamy et al. found that the presence of elevated liver enzymes is associated 5 times higher odds of mortality in retrospective analysis of hospitalized COVID-19 patients.(27)

Likely Medetailbeyoglu A et al. included 614 patients who were hospitalized with COVID-19. Mortality rate and need for intensive care unit were statistically higher in subjects that had high ALT–AST levels at hospital admission. They also identified the AST/ALT ratio as a predictor for ICU admission and mortality (AUC = 0.636 and 0.713) respectively.(28)

Liver stiffness assessment by TE measurement was evaluated by ***Lindvig , et al,*** a cohort of word admission. They found a significantly higher 30-day mortality in patients with LSM >8 KPa. Those patients with LSM >8KPa had about 7 times higher odds of 30- day mortality.(29)

Several authors evaluated the use of TE in heart failure patients (30), (31) ***(Soloveva, et al*** and ***Taniguchi, et al)*** and in ICU patients (32)(***Kosh, et al)***. Patients with highest LSM group had a hazard of 3 times higher mortality and heart failure rehospitalization compared with other tertiles. (30), (31) In medical ICU, liver stiffness value >18 KPa

was associated with high ICU admission and even long-term mortality even in noncirrhotic patients. (32)

Despite that Campos-Varela, et al. Identified that elevated baseline AST is a predictor of worse outcome in the term of either 28 day death or composite of death for ICU admission in COVID-19 patients, these finding were not seen with elevated ALT or increased liver stiffness using TE. The difference seen in this study may be attributed to sample size ,type of patients and geographical distribution.(33)

CONCLUSION

Transient elastography is a useful and non-invasive tool to assess onset and severity of acute liver injury in patients with COVID-19 patients. Increased LS seems to be predictive for a more severe and complicated course of disease.

REFERANCES

1. Cobbold JF, Taylor-Robinson SD. Transient elastography in acute hepatitis: All that's stiff is not fibrosis. Hepatology. 2008;47(2):370–2.
2. Sutton TC, Subbarao K. Development of animal models against emerging coronaviruses: From SARS to MERS coronavirus. Virology. 2015;479:247–58.
3. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England journal of medicine. 2020;
4. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. The Lancet. 2020;395(10225):689–97.
5. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. New England journal of medicine. 2020;
6. Guan W jie, Ni Z yi, Hu Y, Liang W hua, Ou C quan, He J xing, et al. Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine. 2020;382(18):1708–20.
7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020;395(10223):497–506.
8. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet. 2020;395(10223):507–13.
9. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–9.
10. Jin X, Lian JS, Hu JH, Gao J, Zheng L, Zhang YM, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut. 2020;69(6):1002–9.
11. Lescure FX, Bouadma L, Nguyen D, Parisey M, Wicky PH, Behillil S, et al. Clinical and virological data of the first cases of COVID-19 in Europe: a case series. Lancet Infect Dis. 2020;20(6):697–706.
12. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020;5(5):428–30.
13. Sandrin L, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, et al. Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. Ultrasound Med Biol. 2003;29(12):1705–13.
14. Newsome PN, Sasso M, Deeks JJ, Paredes A, Boursier J, Chan WK, et al. FibroScan-AST (FAST) score for the non-invasive identification of patients with non-alcoholic steatohepatitis with significant activity and fibrosis: a prospective derivation and global validation study. Lancet Gastroenterol Hepatol. 2020;5(4):362–73.
15. Ziol M, Handra- Luca A, Kettaneh A, Christidis C, Mal F, Kazemi F, et al. Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with chronic hepatitis C. Hepatology. 2005;41(1):48–54.
16. Viganò M, Massironi S, Lampertico P, Iavarone M, Paggi S, Pozzi R, et al. Transient elastography assessment of the liver stiffness dynamics during acute hepatitis B. Eur J Gastroenterol Hepatol. 2010;22(2):180–4.
17. Kim SU, Choi GH, Han WK, Kim BK, Park JY, Kim DY, et al. What are 'true normal'liver stiffness values using FibroScan®?: a prospective study in healthy living liver and kidney donors in South Korea. Liver International. 2010;30(2):268–74.
18. Liver EA for S of. EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for

evaluation of liver disease severity and prognosis. J Hepatol. 2015;63(1):237–64.
19. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA. 2001;286(14):1754–8.
20. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England journal of medicine. 2020;
21. Fraquelli M, Rigamonti C, Casazza G, Conte D, Donato MF, Ronchi G, et al. Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease. Gut. 2007;56(7):968–73.
22. Coco B, Oliveri F, Maina AM, Ciccorossi P, Sacco R, Colombatto P, et al. Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. J Viral Hepat. 2007;14(5):360–9.
23. Sagir A, Erhardt A, Schmitt M, Häussinger D. Transient elastography is unreliable for detection of cirrhosis in patients with acute liver damage. Hepatology. 2008;47(2):592–5.
24. Arena U, Vizzutti F, Corti G, Ambu S, Stasi C, Bresci S, et al. Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology. 2008;47(2):380–4.
25. Da BL, Kushner T, el Halabi M, Paka P, Khalid M, Uberoi A, et al. Liver injury in patients hospitalized with coronavirus disease 2019 Correlates with hyperinflammatory response and elevated interleukin- 6. Hepatol Commun. 2021;5(2):177–88.
26. Suffredini G, Slowey C, Sun J, Gao WD, Choi CDW, Aziz H, et al. Preoperative Liver Stiffness is Associated With Hospital Length of Stay After Cardiac Surgery. J Cardiothorac Vasc Anesth. 2022;36(11):4093–9.
27. Krishnasamy N, Rajendran K, Barua P, Ramachandran A, Panneerselvam P, Rajaram M. Elevated Liver Enzymes along with Comorbidity Is a High Risk Factor for COVID-19 Mortality: A South Indian Study on 1,512 Patients. J Clin Transl Hepatol. 2022;10(1):120.
28. Medetalibeyoglu A, Catma Y, Senkal N, Ormeci A, Cavus B, Kose M, et al. The effect of liver test abnormalities on the prognosis of COVID-19. Ann Hepatol. 2020;19(6):614–21.
29. Lindvig K, Mössner BK, Pedersen C, Lillevang ST, Christensen PB. Liver stiffness and 30- day mortality in a cohort of patients admitted to hospital. Eur J Clin Invest. 2012;42(2):146–52.
30. Soloveva A, Kobalava Z, Fudim M, Ambrosy AP, Villevalde S, Bayarsaikhan M, et al. Relationship of liver stiffness with congestion in patients presenting with acute decompensated heart failure. J Card Fail. 2019;25(3):176–87.
31. Taniguchi T, Ohtani T, Kioka H, Tsukamoto Y, Onishi T, Nakamoto K, et al. Liver stiffness reflecting right-sided filling pressure can predict adverse outcomes in patients with heart failure. Cardiovascular Imaging. 2019;12(6):955–64.
32. Koch A, Horn A, Dückers H, Yagmur E, Sanson E, Bruensing J, et al. Increased liver stiffness denotes hepatic dysfunction and mortality risk in critically ill non-cirrhotic patients at a medical ICU. Crit Care. 2011;15(6):1–15.
33. Campos-Varela I, Villagrasa A, Simon-Talero M, Riveiro-Barciela M, Ventura-Cots M, Aguilera-Castro L, et al. The role of liver steatosis as measured with transient elastography and transaminases on hard clinical outcomes in patients with COVID-19. Therap Adv Gastroenterol. 2021;14:17562848211016568.