COVID-19 (the disease) has become a global threat to human health

- In December 2019, an outbreak of a novel coronavirus (SARS-CoV-2)(The VIRUS), started in Wuhan, China[1]
- > 2,600,000 confirmed cases of COVID-19 have now been reported worldwide[2]
- SARS-CoV-2 shares 82% genome sequence similarity to SARS-CoV and 50% genome homology to MERS-CoV[1]
- SARS-CoV-2 binds to target cells through angiotensin-converting enzyme 2 (ACE2) (as does SARS-CoV). ACE2 occurs abundantly on liver and biliary epithelial cells, and the liver is a potential target for infection[3]

- Liver test abnormalities and in some, liver impairment, has previously been reported in up to 60% of patients with SARS and has also been reported in patients with MERS-CoV[1]
- At least seven relatively large-scale case studies in China have reported the clinical features of patients with COVID-19[1]
- 2–11% of patients with COVID-19 had liver comorbidities and 14–53% of cases reported abnormal levels of ALT and AST (dominates) during disease progression[1]
- Higher rates of liver test elevation and possible liver dysfunction appear to be associated with patients with severe COVID-19 disease[1]

1. Zhang C, et al. Lancet Gastroenterol Hepatol 2020; published online.
Available at: https://www.thelancet.com/pdfs/journals/langas/PIIS2468-1253(20)30057-1.pdf (Accessed March 2020).
2. https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases (Accessed March 25, 2020)
3. AASLD: Clinical insights for hepatology and liver transplant providers during the COVID-19 pandemic

ALT: alanine aminotransferase; AST: aspartate aminotransferase; COVID-19: coronavirus disease 2019; MERS-CoV: Middle East respiratory syndrome coronavirus; SARS-CoV: severe acute respiratory syndrome coronavirus

Recent Data on studies showing comorbidity with liver disease and liver test change in patients with COVID-19

	Patients with COVID-19	Patients with pre-existing liver conditions	Patients with abnormal liver tests during disease progression	Notes
Guan, et al[1]	1099	23 (2.3%)	AST abnormal (22.2%) ALT abnormal (21.3%)	Elevated levels of AST were observed in 112 (18.2%) of 615 patients with non-severe disease and 56 (39.4%) of 142 patients with severe disease. Elevated levels of ALT were observed in 120 (19.8%) of patients with non-severe disease and 38 (28.1%) of 135 patients with severe disease
Huang et al[2]	41	1 (2.0%)	15 (31.0%)	Patients with severe disease had increased incidence of abnormal liver tests. Elevation of AST level was observed in eight (62%) of 13 patients in the ICU compared with seven (25%) 25 patients who did not require care in the ICU
Chen, et al[3]	99	NA	43 (43.0%)	One patient with severe liver function /damage
Wang, et al[4]	138	4 (2.9%)	NA	
Shi, et al[5]	81	7 (.6%)	43 (53.1%)	Patients who had a diagnosis of COVID-19 confirmed by CT scan while in the subclinical phase had significantly lower incidence of AST abnormality than did patients diagnosed after the onset of symptoms
Xu, et al[6]	62	7 (11.0%)	10 (16.1%)	
Yang, et al[7]	52	NA	15 (28.6%)	No difference for the incidences of abnormal liver tests between survivors (30%) and non-survivors (28%)
Zhang, et al (unpublished)	56	2 (3.6%)	16 (28.6%)	One fatal case, with elevated liver tests and liver injury

Table from Zhang C, et al. Lancet Gastroenterol Hepatol 2020

1. Guan WJ, et al. N Engl Med 2020; published online Feb 28. 2. Huang C, et al. Lancet 2020;395:497–506. 3. Chen N, et al. Lancet 2020;395:507–13. 4. Wang D, et al. JAMA 2020;published online Feb 7. 5. Shi H, et al. Lancet Infect Dis 2020; published online Feb 24. 6. Xu XW, et al. BMJ 2020; published online Feb 19. 7. Yang X, et al. Lancet Respir Med 2020; published online Feb 24.

Surveillance of COVID-19 patients with pre-existing liver conditions is required

Chronic HBV or HCV[1]

Patients with chronic liver disease, especially viral hepatitis B and/or C, may be more susceptible to liver damage from SARS-CoV-2, as was the case with SARS-CoV, but supporting data are lacking.

Liver Transplant Recipient or Autoimmune Hepatitis[1]

In liver transplant recipients or patients with autoimmune hepatitis on immunosuppressive therapy, acute cellular rejection or disease flare, respectively, should not be presumed in the face of active COVID-19.

Primary Biliary Cirrhosis or Primary Sclerosing Cholangitis[1]

It is unknown whether SARS-CoV-2 infection exacerbates cholestasis in those with underlying cholestatic liver disease such as PBC or PSC or with underlying cirrhosis.

Decompensated Cirrhosis or those awaiting Liver Transplantation[1]

There are currently no clear data on the effects of SARS-CoV-2 infection in patients with decompensated cirrhosis or those awaiting liver transplantation.

Additional considerations[2]

- Liver inflammation in mild cases of COVID-19 is often transient and may return to normal without any special treatment. Liver protective drugs have usually been administered in Chinese patients when severe liver damage occurs
- Immune-mediated inflammation, such as cytokine storm and pneumonia-associated hypoxia, may also contribute to liver injury or develop into liver failure in critically ill COVID-19 patients
- Concomitant drug therapies may also result in hepatotoxicities, which may explain some of the variation across cohorts

1. AASLD: Clinical insights for hepatology and liver transplant providers during the COVID-19 pandemic
2. Zhang C, et al. Lancet Gastroenterol Hepatol 2020; published online.
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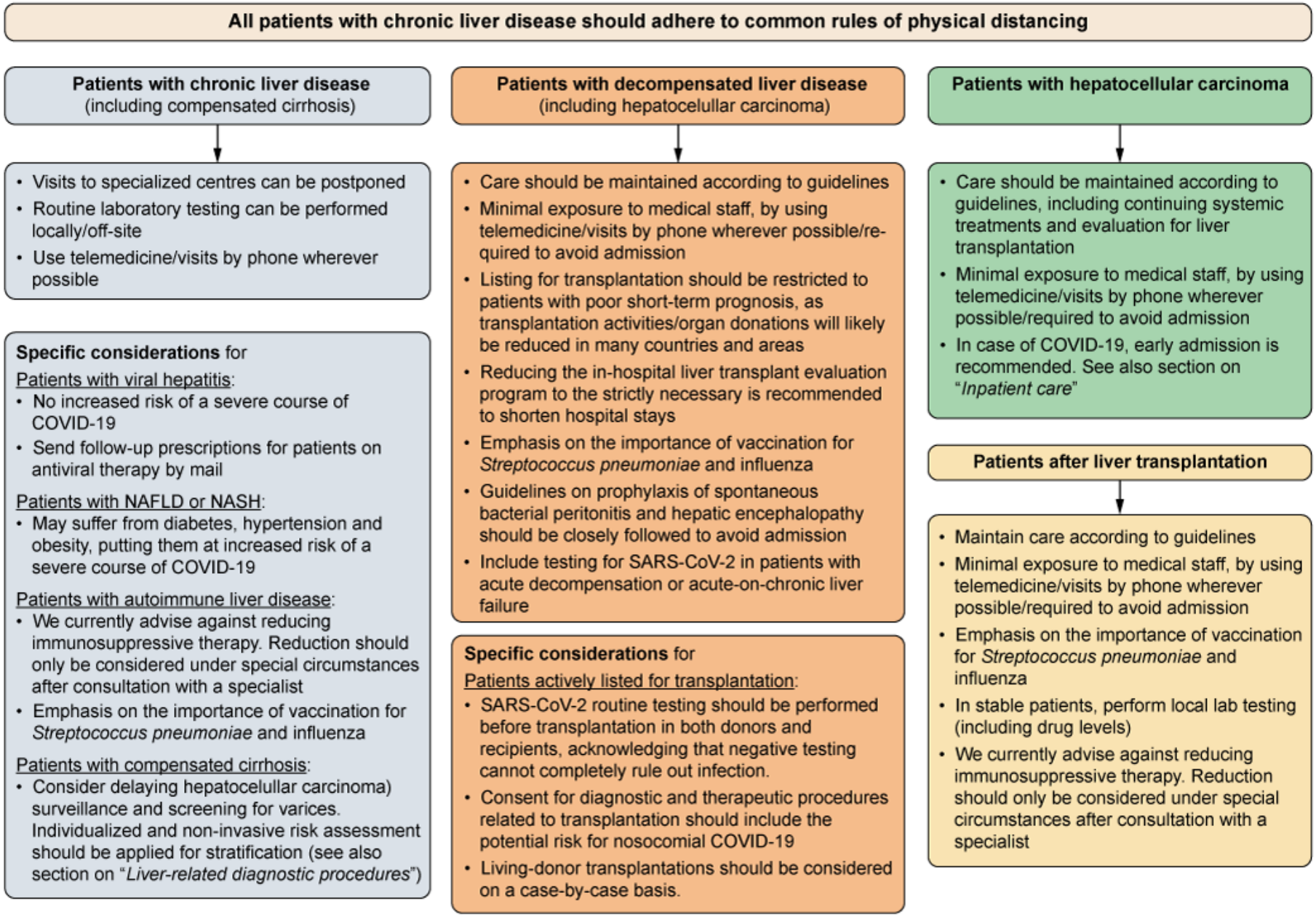
GGT: gamma-glutamyl transferase; HCC: hepatocellular carcinoma; NAs: nucleos(t)ide analogues

Flow chart for the prioritization of patient care in patients with chronic liver disease.

The individual management of these patients strongly depends on the local COVID-19 burden and officially implemented rules and regulations. In some countries and areas, maintenance of standard care might not be able and transplantation activities might be reduced. COVID-19, coronavirus disease 2019; HCC, hepatocellular carcinoma; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.



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AASLD: COVID and the Liver

Major Updates to COVID-19 Clinical Insights Document

4/16/2020

- Emerging data suggest that patients with NAFLD may be at higher risk for COVID-19
- Patients with chronic liver disease and transplant recipients are potentially at increased risk for severe COVID-19 until further data become available
- Consider etiologies unrelated to COVID-19, including other viruses such as hepatitis A, B, and C when assessing patients with COVID-19 and elevated liver biochemistries
    - Updated Figure 1
- Proceed with treatment of hepatitis B and C in patients *without* COVID-19 as clinically warranted
- Initiating treatment of hepatitis B in a patient *with* COVID-19 is not routinely warranted but should be considered if there is clinical suspicion of a hepatitis B flare or when initiating immunosuppressive therapy
- Initiating treatment of hepatitis C in a patient *with* COVID-19 is not routinely warranted
- Consider the following issues in hospitals with a high prevalence of COVID-19:
    - The risk of nosocomial transmission during the transplant admission
    - Difficulty obtaining procedures or other resources when complications arise
    - Limitations on family/caregiver visitation for a postoperative period that often relies on the engagement of caregivers
- Due to cancelations of elective/non-urgent endoscopy:
    - Consider, in the interim, primary prophylaxis with beta blocker therapy for patients with clinically significant portal hypertension or high risk of decompensation
- Data suggest that a surgical mask worn by infected individuals may reduce the risk of transmission (source control)
    - All healthcare workers should wear a surgical mask in patient care settings