

## **COVID-19: an overview of worldwide recommendations for management of patients with liver diseases or liver transplantation**

Hugo Perazzo<sup>1</sup>, Juliana Piedade<sup>1</sup>, Rodolfo Castro<sup>2,3</sup>, Laura Pinto<sup>1</sup>, Valdiléa G Veloso<sup>1</sup>, Beatriz Grinsztejn<sup>1</sup>, Gustavo Pereira<sup>4</sup>, Flavia F Fernandes<sup>4</sup>,

### **Institutions**

<sup>1</sup> Fundação Oswaldo Cruz, FIOCRUZ, Instituto Nacional de Infectologia Evandro Chagas (INI), Rio de Janeiro, Brazil

<sup>2</sup> Fundação Oswaldo Cruz, FIOCRUZ, Escola Nacional de Saúde Pública Sergio Arouca (ENSP), Rio de Janeiro, Brazil

<sup>3</sup> Universidade Federal do Estado do Rio de Janeiro, UNIRIO, Instituto de Saúde Coletiva (ISC), Rio de Janeiro, Brazil

<sup>4</sup> Hospital Federal de Bonsucesso, Serviço de Gastroenterologia & Hepatologia, Ministério da Saúde-RJ, Rio de Janeiro, Brazil.

### **Corresponding Author**

Hugo Perazzo; MD, PhD

Fundação Oswaldo Cruz

Instituto Nacional de Infectologia Evandro Chagas

Av. Brasil, 4365 - CEP 21040-360 - Rio de Janeiro - Brazil

E-mail: hugo.perazzo@ini.fiocruz.br / perazzohugo@gmail.com

Tel: +55 21 3865-9128 / Fax +55 21 2564-4933

**Word count:** 750 words

### **Conflict of Interest Statement**

The following authors have nothing to disclose : **Hugo Perazzo, Juliana Piedade, Rodolfo Castro, Laura Pinto, Valdiléa G Veloso, Beatriz Grinsztejn, Gustavo Pereira, Flavia F Fernandes**

### **Authors' contributions**

**Hugo Perazzo:** study concept and design, study supervision, data collection, interpretation of data, statistical analysis, drafting and critical revision of the manuscript. **Juliana Piedade:** data collection, interpretation of data and drafting and critical revision of the manuscript; **Rodolfo Castro:** study concept and design, data collection, analysis and interpretation of data and critical revision of the manuscript; **Laura Pinto:** data collection, interpretation of data and critical revision of the manuscript; **Valdilea G Veloso:** interpretation of data and critical revision of the manuscript; **Beatriz Grinsztejn:** interpretation of data and critical revision of the manuscript, **Gustavo Pereira:** study supervision, data collection, interpretation of data, statistical analysis, drafting and critical revision of the manuscript; **Flavia F Fernandes:** study supervision, data collection, interpretation of data, statistical analysis, drafting and critical revision of the manuscript.

### **Financial Support**

This work was supported by funding from INI-FIOCRUZ [Programa de Incentivo à Jovens Pesquisadores for HP grant number INI-003-FIO-19-2-5] and from University Estacio de Sa (UNESA) [Programa Pesquisa e Produtividade for GP]. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

## 1 **To the Editor**

2 We read with great interest the recent manuscript published in Clinical  
3 Gastroenterology and Hepatology by Donato et al. reporting the results of a survey  
4 administered to a large sample of transplanted patients during the Coronavirus 2019  
5 disease (COVID-19) outbreak.<sup>1</sup> The authors used telemedicine for providing measures  
6 to prevent SARS-CoV-2 infection and to follow the development of COVID-19  
7 symptoms in transplant recipients in Italy. We aimed to overview the recommendations  
8 provided by national and international gastroenterology/hepatology societies for the  
9 management of patients with chronic liver diseases or liver transplantation during the  
10 COVID-19 pandemic.

11 We searched websites of 125 national and international societies of  
12 gastroenterology/hepatology from 7 international associations and 83 countries to  
13 extract data on the recommendations for management of patients with chronic liver  
14 disease, autoimmune hepatitis (AIH), hepatocellular carcinoma (HCC) or liver  
15 transplantation during the COVID-19 pandemic. The final sample included  
16 recommendations for patients with chronic liver disease from 20 national or  
17 international societies, seven specifically concerning patients with AIH, seven for those  
18 with HCC and nine on liver transplantation (Supplementary Material). Six societies  
19 stated to follow recommendations from other societies. Therefore, we analyzed the  
20 recommendations from 14 societies (Table 1). Briefly, all societies recommended the  
21 use of telemedicine (100%) and 12 societies (86%) temporarily postponing non-urgent  
22 appointments. Questionnaire of symptoms (29%) and/or patient's body temperature  
23 measurement (29%), limiting the number of consultations/day and restricting number of  
24 family/companions (57%) were recommended in case of face-to-face consultation. Few  
25 societies recommended checking influenza/*Streptococcus pneumoniae* vaccination

26 (29%), delaying HCC surveillance (29%) and/or postponing all elective/non-urgent  
27 liver biopsy or elastography (29%). A majority of the societies recommended  
28 temporarily postponing all elective/non-urgent endoscopy exams (86%) and to continue  
29 immunosuppressive therapy (93%). On the other hand, few societies recommended  
30 testing for SARS-CoV-2 in patients with hepatic decompensation.

31       Concerning patients with AIH, HCC or liver transplantation, telemedicine was  
32 extensively recommended for patients with AIH or liver transplanted (86%), but in  
33 lower rates for patients with HCC (57%) (Supplementary Material). The maintenance of  
34 the same dosage of immunosuppressive agents was highly recommended for patients  
35 with AIH (86%) or liver transplantation (100%). The majority of societies (67%)  
36 recommended performing SARS-CoV-2 testing for liver transplantation recipients and  
37 donors. All seven societies with recommendations for patients with HCC recommended  
38 continuation of HCC therapy and four (57%) of them continuing to perform regular  
39 exams during the pandemic. Most societies recommended to perform liver  
40 transplantation only for life-threatening situations, such as HCC or acute liver failure.

41       The impact of COVID-19 in patients with liver diseases or liver transplantation  
42 remains unclear. Preliminary results of combined data from registries that have been  
43 collecting outcomes of suspected/confirmed COVID-19 in patients with liver diseases  
44 showed high mortality rates in patients with cirrhosis.<sup>2</sup> However, there are no published  
45 results of prospective studies which followed patients with chronic liver disease/liver  
46 transplantation and COVID-19. Telemedicine is low-cost, widely available and well  
47 accepted by patients and clinicians.<sup>3</sup> However, this technology might be challenged by  
48 differences in local regulations for telehealth services and/or reimbursement in each  
49 country/region.<sup>4</sup> The risk of a flare of AIH or acute cellular rejection after liver  
50 transplantation secondary to unnecessary immunosuppressive reduction/withdrawal,

51 would overcome the risk of SARS-CoV-2 infection.<sup>5</sup> High rates of hospital admission  
52 in critical care units have been leading to a shortage of healthcare workers, beds,  
53 ventilators and blood products for HCC therapies and liver transplantation during  
54 COVID-19 pandemic. Thus, health authorities should consider deviations from the  
55 current standard of care until definitive therapy can be delivered.<sup>6</sup> It is worth noting that  
56 we relied this overview on current available recommendations from international and  
57 national societies of gastroenterology/hepatology. However, the results of our  
58 worldwide overview are aligned with the clinical recommendations and policies to  
59 mitigate the impact of the COVID-19 pandemic on patients with chronic liver diseases  
60 recently published by expert consensus.<sup>7,8</sup> Large scale testing might benefit patients at  
61 high risk of complications. Furthermore, while we wait for effective vaccines, the  
62 knowledge of the extent of immunity in each country will later guide health authorities  
63 to elaborate strategies when facing a potential second wave of COVID-19. Patients with  
64 cirrhosis and those under immunosuppressive medicines should be prioritized for  
65 testing until further evidenced-based data become available. In summary, worldwide  
66 gastroenterology and hepatology societies support the use of telehealth for managing  
67 patients with liver disease or liver transplantation. Hepatology and liver transplantation  
68 providers should follow the current recommendations to protect their patients during the  
69 COVID-19 pandemic. However, future studies addressing the impact of COVID-19 in  
70 patients with chronic liver diseases or liver transplantation are urgently needed.

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**Table 1.** Recommendations for the management of patients with chronic liver disease during the COVID-19 pandemic from International/National Societies of Gastroenterology or Hepatology updated on April 10<sup>th</sup>, 2020

Society name	Date	Screening of symptoms	Check patients' body temperature	Postpone elective consultation	Limit number of patients/family in consultation	Use of telemedicine	Prescription for next months	Vaccination for influenza/ <i>S.pneumoniae</i>	Continue immunosuppressive therapy	Delay HCC / varices screening	Postpone elective GIE	Postpone elective liver biopsy/TE
<b>International</b>												
European Association for the Study of the Liver (EASL)	April 2, 2020	NR	NR	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<b>USA/Canada</b>												
American College of Gastroenterology (ACG)	March 15, 2020	Yes	Yes	Yes	Yes	Yes	NR	NR	Yes	NR	Yes	NR
American Gastroenterological Association (AGA)	March 15, 2020	Yes	Yes	Yes	Yes	Yes	NR	NR	Yes	NR	Yes	NR
American Association for the Study of Liver Diseases (AASLD)	April 7, 2020	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes
<b>Europe</b>												
Association Française Pour l'Etude du Foie (AFEF)	April 6, 2020	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Swiss Association for the Study of the Liver (SASL)	April 3, 2020	NR	NR	Yes	NR	Yes	NR	NR	Yes	NR	Yes	Yes
British Society of Gastroenterology (BSG)	March 14, 2020	NR	NR	Yes	NR	Yes	NR	NR	Yes	NR	Yes	NR
The British Association for the Study of the Liver (BASL)	March 18, 2020	NR	NR	Yes	Yes	Yes	NR	NR	Yes	NR	NR	NR
<b>Latin America</b>												
Asociación Argentina para el Estudio de las Enfermedades de Hígado (AAEEH)	NA	NR	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR
Sociedade Brasileira de Hepatologia (SBH)	March 22, 2020	NR	NR	Yes	NR	Yes	Yes	NR	Yes	NR	Yes	NR
Asociación Chilena de Hepatología	NA	NR	NR	NR	NR	Yes	NR	NR	NR	NR	Yes	NR
<b>Asia-Pacific</b>												
Gastroenterological Society of Australia (GESA)	March 19, 2020	NR	NR	NR	Yes	Yes	NR	Yes	Yes	NR	NR	NR
Pakistan Society for the Study of Liver Diseases (PSSLD)	NA	NR	NR	Yes	Yes	Yes	NR	NR	Yes	NR	Yes	NR
<b>Africa</b>												
Société Algérienne d'Hépatogastro-entérologie et d'Endoscopie Digestive (SAHGEED)	March 15, 2020	NR	NR	Yes	Yes	Yes	Yes	NR	Yes	NR	Yes	NR

GIE, gastrointestinal endoscopy; NA, not available; NR, not reported; TE, transient elastography. SAHGEED is affiliated to EASL. ACG and AGA recommendations were based in a joint document from AGA, ACG, AASLD and American Society of Gastrointestinal Endoscopy (ASGE). Other recommendations : continuation of current HBV/HCV treatment [AASLD, EASL and GESA], consider to delay new HCV treatments [AASLD and AFEF] and test SARS-CoV-2 in patients with hepatic decompensation [EASL]. Urgent procedures which could not be stopped during COVID-19 pandemic : liver biopsy to rule out rejection or to diagnose autoimmune hepatitis [AASLD, AFEF, SBH], therapeutic paracentesis [AASLD, AFEF], TIPS [AASLD, SBH], upper GIE for variceal bleeding and endoscopic band-ligation [AASLD, AFEF, SBH]. A total of six societies stated to follow current recommendations for COVID-19 from other societies: United European Gastroenterology (UEG) [AASLD/EASL]; World Gastroenterology Organisation (WGO) [AASLD/EASL]; Belgian Association for the Study of the Liver (BASL) [EASL]; Société Royale Belge de Gastro-Entérologie [EASL]; Indian National Association for Study of the Liver (INASL) [AASLD] and New Zealand Society of Gastroenterology (NZSG) [not reported]