



Hot Topic Commentary

# COVID-19 and Liver Transplantation: Challenges and Opportunities



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Coronavirus disease 2019 (COVID-19) has presented humanity with a significant global challenge that has necessitated changes and adaptations at all levels. Liver transplant (LT) activity could not have been an exception, as it was impacted both by changes in the urgency of the use of medical resources, including shortage of hospital and intensive care unit beds, problems in outpatient follow-up, redefining the urgency of a LT among others. In addition to the fact that the quarantines placed and the resulting emotional isolation have led to increased alcohol use and abuse.<sup>1,2</sup> An effort by several transplant associations and the Centers for Medicare and Medicaid led to issuing guidance and recommendations regarding transplantation surgery during COVID-19.<sup>3,4</sup> In the paper “Impact of COVID-19 on Liver Transplant Activity in the USA: Variation by Etiology and Cirrhosis Complications” by Kuo *et al.*,<sup>5</sup> the authors provide us with a thorough evaluation of the impact of the COVID-19 pandemic on LT activity based on etiology in the USA, by analysing data from the United Network of Organ Sharing (UNOS) database (2018–2021). The authors looked at two different time periods, one in the pre-COVID era between April 2018 and February 2020, and one in the COVID era between March 2020 and May 2021). They evaluated the effect of COVID-19 examined LT frequency, variation in liver disease etiology, Model for End-stage Liver Disease (MELD) score, and complications of cirrhosis, with an emphasis on hepatocellular carcinoma (HCC) and acute on chronic liver failure (ACLF). The pre-COVID era was purposefully chosen to be 22 months long to include trends that developed prior to COVID-19, such as the decrease in the incidence of hepatitis C virus (HCV) in terms of etiology for LT and the increase in non-alcoholic steatohepatitis (NASH). In terms of methodology, the authors used monthly statistics and joinpoint regression models.

The results, as far as the LT frequency is concerned, showed a 3.4% monthly decrease in the number of LTs per-

formed during the COVID-19 era, with 15,312 LTs performed prior to the pandemic and 8,995 in the COVID-19 era. It should be noted that overall survival (96% at 3 months post LT) was stable in both periods, showing that quality was maintained. As far as the etiology of LT is concerned, Kuo *et al.*<sup>5</sup> showed a 4.5% monthly increase in the percentage of LTs performed for alcoholic liver disease (ALD) in the period between November 2020 and May 2021, the COVID-19 era. What was even more important was the fact that these LTs were more likely to use a poorer quality organ, to have autoimmune hepatitis and ACLF grade 2–3, and a poor performance status, which is critical in these patients. Regarding the MELD score, the main effect was seen with HCV-related LTs, where there was an increase in the average monthly MELD score by 0.7, again indicating the increased challenges for these patients. When Kuo *et al.*<sup>5</sup> evaluated the effect of the COVID-19 pandemic on the frequency of LT performed for HCC and ACLF grade 2–3, the analysis found that for HCC there was a 22% monthly decrease on a log scale of LTs performed during the COVID-19 era, with recipients having higher MELD scores, an increase of 0.36% per month, and being more likely to have ALD-related ACLF, as well as receive a poorer quality graft. As far as ACLF grade 2–3 is concerned although there was a 17% monthly increase in the LTs performed in the COVID-19 era, the recipients had a higher MELD score, and the grafts were of poorer quality. In both these cases of HCC and ACLF grade 2–3, we can see that the pandemic made it harder for LTs with, what could be considered, less of an urgent etiology harder to proceed and with lower quality grafts. Thankfully, there was no effect in the case of patients with acute liver failure needing an LT.

Overall, Kuo *et al.*<sup>5</sup> through their comparison of the pre- and COVID-19 eras and their statistical analysis of the UNOS database, found that there was an overall decrease in the number of LTs for HCC, in addition to the need for a higher MELD score for these patients, similar to HCV, to receive an LT. On the other hand, there was a proportional increase in the LTs for ALD and ACLF grade 2–3. The findings reveal the effect of the COVID-19 pandemic on LT, which was a decrease in the activity because of a diversion of resources needed, decreased outpatient visits and follow-up, as well as increased ALD prevalence because of the effect of the quarantine and the overall stressors. The study had the advantage of comparing long time periods and using joinpoints to find the best fitting log linear regression model. Also, the use of a large database, such as the UNOS one, has the advantage of a wealth of patients and data, but there is an inherent challenge in all these databases of identifying fine differences.

**Abbreviations:** ACLF, acute on chronic liver failure; ALD, alcoholic liver disease; COVID-19, coronavirus disease 2019; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LT, liver transplant; MELD, model for end-stage liver disease.

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Additionally, this was necessarily a retrospective study, and given the continuously evolving nature of organ allocation, the changes in February 2020 with capping of MELD exception points for HCC listings, may have played a role in the decrease in HCC-related LTs. Several papers have evaluated the effect of the COVID-19 pandemic on LT, and frequently there were differences regarding increased or decreased frequency of LT seen because of different time points, different populations and also the evolving nature of the pandemic and the response to it.<sup>6–8</sup> The importance of the paper by Kuo *et al.*<sup>5</sup> is that they are able, at least in this specific population, to start identifying the finer differences as to how the pandemic affected LTs of different etiology and to what extent.

However, there are more lessons to be learned here. First we have to acknowledge the facts that (1) COVID-19 is a reality of our times, albeit more manageable with the advent of the vaccines, and (2) LT is and should continue to be a social priority, not only because it has to do with a life-saving procedure, but also because we need to honor the noble decision that families make during a difficult time to donate the organs of their loved ones. The points raised above mean that as a society and as a health care system, we need to prioritize LTs, even in the case of living donors, especially as with the use of the vaccines, the overall need for intensive care unit (ICU) beds is not such a problem. The mention of the vaccines brings us to the need to continue to improve the types of vaccines, but also clarify their effectiveness in the transplant population. We have to remember that patients on the transplant waiting list and those that have undergone a LT are immunosuppressed, and thus more vulnerable to COVID-19, but it is this same immunosuppression that makes the response to the vaccines unpredictable. Transplant recipients are reported to have increased mortality from COVID-19 (15–30%), altered viral kinetics and often atypical presentations.<sup>9</sup> Thus, issues such as evaluating the antibody response after vaccination, the risk of thrombosis and immunosuppression adjustments are issues that are not universally agreed upon, and thus fertile ground for discussion and research. However, there is one fact that we can all agree upon: that although vaccines may not be able to completely prevent a COVID-19 infection, they are effective in protecting against the more severe form of the disease, necessitating ICU care.<sup>10</sup>

Another key lesson from the pandemic is that we can continue to take care of our cirrhotic and LT patients and address their needs through the use of technology. The increased use of web-based platforms and social media has been a critical factor in addressing communication issues with our patients, in addition to our newly found admiration for webinars.<sup>11</sup> In addition, the use of telemedicine has simplified the follow-up of these patients by avoiding over-crowding in the outpatient transplant clinics and yet still being able to maintain communication.

There are several other issues that the management of the COVID-19 pandemic has forced us to address, such as the physical and mental welfare of the transplant providers,

the role of the transplant infectious disease teams, the need for an organized approach by transplant societies and associations and of course the existence of regional and national variations. For all the reasons and challenges mentioned above we have to acknowledge the importance of papers such as the one by Kuo *et al.*,<sup>5</sup> which provide us with the necessary data to start making the necessary adjustments. We need to understand that we do not have the full picture yet; the only thing that we have is the opportunity to gain from the lessons we learn from addressing the pandemic.

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### Conflict of interest

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### References

- [1] Maggi U, De Carlis L, You D, Colledan M, Regalia E, Rossi G, *et al.* The impact of the COVID-19 outbreak on liver transplantation programs in Northern Italy. *Am J Transplant* 2020;20:1840–1848. doi:10.1111/ajt.15948, PMID: 32330351.
- [2] Cholankeril G, Goli K, Rana A, Hernaes R, Podboy A, Jalal P, *et al.* Impact of COVID-19 pandemic on liver transplantation and alcohol-associated liver disease in the USA. *Hepatology* 2021;74:3316–3329. doi:10.1002/hep.32067, PMID:34310738.
- [3] Non-Emergent, Elective Medical Services, and Treatment Recommendations. Centers for Medicare and Medicaid Services. Available from: <https://www.cms.gov/files/document/31820-cms-adult-elective-surgery-and-procedures-recommendations.pdf>.
- [4] Strauss AT, Boyarsky BJ, Garonzik-Wang JM, Werbel W, Durand CM, *et al.* Liver transplantation in the United States during the COVID-19 pandemic: National and center-level responses. *Am J Transplant* 2021;21:1838–1847. doi:10.1111/ajt.16373, PMID:33107180.
- [5] Kuo YF, Kwo P, Wong RJ, Singal AK. Impact of COVID-19 on Liver Transplant Activity in the USA: Variation by Etiology and Cirrhosis Complications. *J Clin Transl Hepatol* 2023;11(1):130–135. doi:10.14218/JCTH.2022.00129, PMID:36406316.
- [6] Reddy MS, Hakeem AR, Klair T, Marcon F, Mathur A, Samstein B, *et al.* Trinal study exploring the early impact of the COVID-19 pandemic on organ donation and liver transplantation at national and unit levels. *Transplantation* 2020;104:2234–2243. doi:10.1097/TP.0000000000003416, PMID: 32804803.
- [7] Goff RR, Wilk AR, Toll AE, McBride MA, Klassen DK. Navigating the COVID-19 pandemic: initial impacts and responses of the Organ Procurement and Transplantation Network in the United States. *Am J Transplant* 2021;21:2100–2112. doi:10.1111/ajt.16411, PMID:33244847.
- [8] Dominguez-Gil B, Coll E, Fernandez-Ruiz M, Corral E, Del Rio F, Zaragoza R, *et al.* COVID-19 in Spain: Transplantation in the midst of the pandemic. *Am J Transplant* 2020;20:2593–2598. doi:10.1111/ajt.15983, PMID: 32359194.
- [9] Lembach H, Hann A, McKay SC, Hartog H, Vasanth S, El-Dalil P, *et al.* Resuming liver transplantation amid the COVID-19 pandemic. *Lancet Gastroenterol Hepatol* 2020;5(8):725–726. doi:10.1016/S2468-1253(20)30187-4, PMID:32534603.
- [10] Wadei HM, Leoni JC, Shah SZ, Aslam N, Speicher LL. COVID-19 Infection in Solid Organ Transplant Recipients after SARS-CoV-2 vaccination. *Am J Transplant* 2021;21(10):3496–3499. doi:10.1111/ajt.16618, PMID: 33890410.
- [11] Bellini MI, Parisotto C, Dor FJMF, Kessar N. Social Media Use Among Transplant Professionals in Europe: a Cross-Sectional Study from the European Society of Organ Transplantation. *Exp Clin Transplant* 2020;18(2):169–176. doi:10.6002/ect.2019.0078, PMID:31724925.