

# Coronaviruses and Immunosuppressed Patients: The Facts During the Third Epidemic

## TO THE EDITOR:

We read with interest the letter by D'Antiga evaluating the early experience with coronavirus disease 2019 (COVID-19) in liver transplantation (LT) recipients in Bergamo, Italy, suggesting that immunosuppression would not increase the risk of severe infections.<sup>(1)</sup> Another recent report also showed that mortality in LT patients affected by COVID-19 appeared to be limited to longterm (>1 years after LT) recipients with mild immunosuppression and affected by metabolic and vascular comorbidities.<sup>(2)</sup> Even though the pathophysiology of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is still under investigation, the immune system appears to play a major role especially in patients with severe disease,<sup>(3)</sup> thus supporting previous observations.

Between February 21, 2020—the day the first Italian case of COVID-19 was confirmed in Codogno, near Milan—and April 21, 2020, 16 LTs were performed in our center. Regular screening for SARS-CoV-2 was carried out in LT candidates at admission and

repeated weekly in hospitalized recipients as well as in all the potential deceased donors. No candidate tested positive at admission, although 2 recipients were diagnosed with COVID-19 (9 and 45 days after LT) and showed an almost asymptomatic course of the infection. The immunosuppressive regimen was left unchanged. Concomitantly, in our preliminary experience, SARS-CoV-2 infection was diagnosed in 5 longterm LT recipients (>1 year after LT) transplanted at our center (>100 transplants/year performed in the last 5 years) who required hospital admission. Among these patients, 2 needed noninvasive ventilation, 2 died due to respiratory failure, and 1 died of septic shock in neutropenia following chemotherapy for lymphoma. Among the 5 patients, 3 patients were affected by diabetes mellitus, 4 were affected by arterial hypertension, and 2 were affected by advanced cancer, supporting a previous report<sup>(2)</sup> on the role of comorbidities in LT recipients with COVID-19. As recently observed,<sup>(1)</sup> severe immunosuppression, as used in the early posttransplant period, did not appear to negatively affect the outcomes, and calcineurin inhibitors may also partly suppress the innate immune response,<sup>(4)</sup> which appears to play a relevant role in the pathophysiology of severe disease in SARS-CoV-2 infection. Nonetheless, because other immunomodulating therapies are emerging in the treatment of COVID-19 (ie, tocilizumab or high-dose steroid), caution is warranted to limit the risk of superimposing bacterial and fungal infections, especially in critically ill patients. Moreover, prompt identification of cases and their management in COVID-19–dedicated areas by a multidisciplinary team can limit the nosocomial spreading of the infection without negatively affecting regular care to hospitalized patients.

*Abbreviations: COVID-19, coronavirus disease 2019; LT, liver transplantation; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.*

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## REFERENCES

- 1) D'Antiga L. Coronaviruses and immunosuppressed patients: the facts during the third epidemic. *Liver Transpl* 2020;26:832-834.
- 2) Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *Lancet Gastroenterol Hepatol* 2020;5:532-533.
- 3) Giamarellos-Bourboulis EJ, Netea MG, Rovina N, Akinosoglou K, Antoniadou A, Antonakos N, et al. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. *Cell Host Microbe* 2020;27:992-1000.
- 4) Zaza G, Leventhal J, Signorini L, Gambaro G, Cravedi P. Effects of antirejection drugs on innate immune cells after kidney transplantation. *Front Immunol* 2019;10:2978.