

Editorial

Kidney transplant after a COVID-19[☆]

Trasplante renal después de una COVID-19

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The severity of the disease and the evolution of patients infected with the type 2 coronavirus that causes severe acute respiratory syndrome (SARS-CoV-2) has been associated with advanced age, comorbidities such as obesity, hypertension, diabetes, and chronic kidney disease.¹⁻⁸ The Spanish Society of Nephrology (SEN), the Spanish Society of Transplantation (SET) and the National Transplant Organization (ONT) have published protocols and recommendations aiming to prevent the infection of kidney patients⁸⁻¹² and professionals involved in their care.¹² Since the beginning of the first large epidemiological wave, we insisted on general and specific rules for protection (extensive information to patients, reasonable limitation of collective transport, systematic interviews to patients before each hemodialysis session, telematic visits that whenever possible, etc.). Since the initial days of pandemic there was a remarkable initiative to promote a registry of cases of renal patients that has allowed us to be informed weekly about the situation of the disease and provide clinical evidences that are highly relevant.¹³⁻¹⁸

COVID-19 in kidney transplant patients

Since the first months of the pandemic, numerous publications of clinical cases, case series, and registries have described the clinical features of COVID-19 in kidney transplantation (KT).¹³⁻³⁰ The incidence and mortality rate are higher than in the general population and it was found

that the poor prognosis was associated to similar variables as in the general population, such as advanced age or severe pneumonia. As in the general population, no specific treatment has been shown to be effective, and only general and respiratory support are truly relevant in the therapeutic strategy. The potential benefit of high-dose steroids³⁰ has not yet been confirmed in renal patients.

Safety of kidney transplants

During the months of March and April 2020, due to the collapse of the intensive care units and the almost exclusive dedication to the care of patients with COVID-19, most organ donation and transplant programs reduced their activity, or even were suspended. Thereafter, the activity progressively recovered, and expert professionals have adapted the programs to the new reality.³¹⁻³⁴ One of the most important concerns of professionals responsible of kidney transplant (KT) programs the need for a safe KT given the indisputable evidence that there are alternative renal replacement treatment techniques, such as peritoneal dialysis and hemodialysis, that allow transplantation to be deferred and done in maximum safety conditions. The fact that RT is the most favorable option of RRT with the best rehabilitation and greater survival³⁴ may not justify the risk of reducing safety of the procedure, in an epidemiological pandemic scenario (Table 1).

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Table 1 – Recommendations for safe kidney transplantation (KT) during the COVID-19 pandemic.**I) Before KT**

- Increase patient education, especially on risks of post-transplant COVID-19
- Review information sheets and informed consent form, and incorporate COVID-19 information
- In KT candidate patients, rule out active SARS-CoV-2 infection with negative nasopharyngeal exudate PCR test and absence of symptoms for at least 72 hours
- In any elective KT (e.g. live donor), repeat PCR test and confirm negative result
- Test for anti-IgG SARS-CoV-2 antibodies in serum; if present, they ensure greater safety
- Limit indication and dose of induction treatment with polyclonal antibodies

II) After KT

- Implement strict isolation measures during first admission
- Consider early removal of bladder catheter (1-4 days)
- If immediate function, limit length of first admission as much as possible (4-6 days)
- If delayed function, develop day hospital management programmes, with on-demand haemodialysis and outpatient follow-up
- Establish telemedicine consultations after discharge, and limit need for in-person visits as much as possible
- Develop monitoring strategies that do not require invasive techniques (protocol biopsies), admissions or non-essential in-person visits

As recommended by ONT to guarantee the protection of patients on the waiting list, patients will undergo an exhaustive medical history inquiring about contact with suspected or confirmed cases, or if there is any symptoms compatible with COVID-19.¹¹ SARS-CoV-2 screening should be performed by RT-PCR in a respiratory tract sample before the procedure of renal implant, antigen testing or virus serology being discouraged as an alternative to RT-PCR for screening. The transplant will not be performed until the result of the PCR is available. At this moment, there is no evidence to recommend the systematic performance of chest CT as a screening test in patients without clinical data suggestive of active infection.

Evidently, to avoid aggravation of the infection, if a patient on the KT waiting list is a suspected or confirmed case of COVID-19, he will be excluded from the list and will remain a temporary contraindication for KT until complete cure occurs. This will be established after a minimum period of 14 days since the onset of symptoms, with at least three days free of symptoms and a negative CRP; at this point the patient can be included in kidney transplant list.

In this sense, the ONT also recommends the review of informed consents for transplantation, including relevant information about the COVID-19 infection as part of the general process of information to the potential recipient or their legal representative.¹¹

Based on data from the SEN COVID-19 registry, we have reported a special risk of severe COVID-19 and high mortality in recent KT recipients.^{16,17} Therefore, strategies should be developed whereby the hospital admission time is as short as possible, including intensive telematic monitoring, management strategies as outpatient in hospital facilities with SARS-CoV-2 free circuits, and very early diagnosis of any symptoms potentially related with COVID-19.³²⁻³⁵ The

development of non-invasive monitoring tools, that were already relevant, now become essential; and of course, quality research and development in this area should be a priority.³⁵

Kidney transplant after a COVID-19 episode

There is little published evidence about the safety of KT in patients who have survived a mild³⁶ or asymptomatic³⁷ episode of COVID-19. In this issue of the journal, two very interesting experiences are being reported, in which the authors describe the cases of three patients who received a KT after having overcome the disease.^{38,39}

The two cases reported from India are unique and constitute original contributions.³⁸ It is the first patient reported to undergo a transplant after overcoming COVID-19 pneumonia (four weeks after the initial diagnosis), and the first recipient of a kidney from living donor in which both donor and recipient simultaneously presented previous mild symptomatic COVID-19. In both cases, the recipients were negative at the time of renal implantation and presented anti-SARS-CoV-2 IgG antibodies.

The case from Spain³⁹ is the first case reported of advanced age (70 years). On this occasion, COVID-19 was found when the patient did not present symptoms, as a screening immediately prior to a KT from a deceased donor. After several positive PCR tests, alternating with some negative ones, it was decided to put him back on the list and he was transplanted with a negative PCR that was repeated frequently after transplantation. Although the authors acknowledge that there is no supporting evidence, they decided to confirm negativity to the virus with three consecutive PCR tests. It is possible that the specific characteristics of kidney patients, especially those who

undergo periodic dialysis treatment, make it advisable to wait at least four weeks after a negative PCR, before proceeding with intense immunosuppression of a KT. In addition, it must not be forgotten that the sensitivity of PCR does not exceed 75–80%, and therefore it is advisable its repetition on at least two to three consecutive occasions. Besides certainty in the negativity of the PCR, it seems pertinent to verify the existence of sufficient titers of anti-SARS-CoV-2 IgG antibodies while the patient is awaiting for a KT. In this patient the disappearance of IgG antibodies was verified after having demonstrated their presence. It seems reasonable to think that the disappearance of IgG antibodies does not contraindicate KT, but with the current state of our knowledge, the documentation of each case should be as exhaustive as possible. This experience reinforces the concept that a past COVID-19 episode does not guarantee adequate long term protection, and in no way should preventive measures against possible infection should be relaxed.

Given the high incidence of COVID-19 in dialysis patients, it is very likely that throughout the world, patients with a past COVID-19 infection are being transplanted, especially in countries with very high transplantation activity as in Spain. It is necessary to collect experiences in this regard and to know the evolution with detail, learn whether respiratory or other sequelae are detected, if IgG antibodies are preserved over time and if reinfections occur.⁴⁰ Transplant teams must be most careful in the analysis and orderly follow-up of these cases.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323:1239–42, <http://dx.doi.org/10.1001/jama.2020.2648>.
2. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020;323:1775–6, <http://dx.doi.org/10.1001/jama.2020.4683>. Published online March.
3. Gansevoort RT, Hilbrands LB. CKD is a key risk factor for COVID-19 mortality. *Nat Rev Nephrol*. 2020;26:1–2, <http://dx.doi.org/10.1038/s41581-020-00349-4>. PMID: 32848205.
4. Posso M, Comas M, Román M, Domingo L, Louro J, González C, et al. Comorbidities and mortality in patients with COVID-19 aged 60 years and older in a university hospital in Spain. *Arch Bronconeumol*. 2020;56:756–8, <http://dx.doi.org/10.1016/j.arbres.2020.06.012>. Epub 16 July 2020. PMID: 32782092.
5. Collado S, Arenas MD, Barbosa F, Cao H, Montero MM, Villar-García J, et al. COVID-19 in grade 4-5 chronic kidney disease patients. *Kidney Blood Press Res*. 2020;45:768–74, <http://dx.doi.org/10.1159/000511082>. Epub 8 September 2020. PMID: 32898845 Free PMC article.
6. Arenas MD, Crespo M, Pérez-Sáez MJ, Collado S, Redondo-Pachón D, Llinàs-Mallol L, et al. Clinical profiles in renal patients with COVID-19. *J Clin Med*. 2020;9:2665, <http://dx.doi.org/10.3390/jcm9082665>. PMID: 32824683 Free PMC article.
7. Coca A, Burballa C, Centellas-Pérez FJ, Pérez-Sáez MJ, Bustamante-Munguira E, Ortega A, et al. Outcomes of COVID-19 among hospitalized patients with non-dialysis CKD. *Front Med Front Med*. 2020;7, <http://dx.doi.org/10.3389/fmed.2020.615312>.
8. Arenas MD, Villar J, González C, Cao H, Collado S, Crespo M, et al. Management of the SARS-CoV-2 coronavirus epidemic (COVID-19) in hemodialysis units. *Nefrología*. 2020;40:258–64, <http://dx.doi.org/10.1016/j.nefro.2020.04.001>. Epub 8 April 2020.
9. López V, Vázquez T, Alonso-Titos J, Cabello M, Alonso Á, Beneyto I, et al. Recommendations on management of the SARS-CoV-2 coronavirus pandemic (COVID-19) in kidney transplant patients. *Nefrología*. 2020;40:265–71, <http://dx.doi.org/10.1016/j.nefro.2020.03.002>. Epub 3 April 2020.
10. Domínguez-Gil B, Coll E, Fernández-Ruiz M, Corral E, Del Río F, Zaragoza R, et al. COVID-19 in Spain: transplantation in the midst of the pandemic. *Am J Transplant*. 2020;20:2593–8.
11. Organización Nacional de Trasplantes. <http://www.ont.es/infesp/RecomendacionesParaProfesionales/Recomendaciones%20Donaci%C3%B3n%20y%20Trasplante%20frente%20a%20la%20COVID-19%20ONT.pdf>, 2020.
12. Arenas MD, Villar J, González C, Cao H, Collado S, Barbosa F, et al. Protection of nephrology health professionals during the COVID-19 pandemic. *Nefrología*. 2020;40:395–402, <http://dx.doi.org/10.1016/j.nefro.2020.06.001>. Epub 1 July 2020. PMID: 32703645 Free PMC article.
13. Sánchez-Álvarez E, Pérez-Fontán M, Jiménez-Martín C, Blasco-Pelicano M, Cabezas Reina CJ, Sevillano-Prieto AM, et al. SARS-CoV-2 infection in patients on renal replacement therapy. Report of the COVID-19 Registry of the Spanish Society of Nephrology (SEN). *Nefrología*. 2020;40:272–8, <http://dx.doi.org/10.1016/j.nefro.2020.04.002>. Epub 16 April 2020.
14. Crespo M, Mazuecos A, Rodrigo E, Gavela E, Villanega F, Sánchez-Álvarez E, et al. Respiratory and gastrointestinal COVID-19 phenotypes in kidney transplant recipients. *Transplantation*. 2020;104:2225–33, <http://dx.doi.org/10.1097/TP.0000000000003413>.
15. Pérez-Sáez MJ, Blasco M, Redondo-Pachón D, Ventura-Aguir P, Bada-Bosch T, Pérez-Flores I, et al. Use of tocilizumab in kidney transplant recipients with COVID-19. *Am J Transplant*. 2020;20:3182–90, <http://dx.doi.org/10.1111/ajt.16192>. Epub 4 August 2020. PMID: 32654422.
16. Pascual J, Melilli E, Jiménez-Martín C, González-Monte E, Zárraga S, Gutiérrez-Dalmau A, et al. COVID-19-related mortality during the first 60 days after kidney transplantation. *Eur Urol*. 2020;78:641–3, <http://dx.doi.org/10.1016/j.eururo.2020.06.036>. Epub 19 June 2020. PMID: 32624283.
17. Crespo M, Pérez-Sáez MJ, Redondo-Pachón D, Llinàs-Mallol L, Montero MM, Villar-García J, et al. COVID-19 in elderly kidney transplant recipients. *Am J Transplant*. 2020;20:2883–9, <http://dx.doi.org/10.1111/ajt.16096>. Epub 6 July 2020. PMID: 32471001.
18. Zhong Z, Zhang Q, Xia H, Wang A, Liang W, Zhou W, et al. Clinical characteristics and immunosuppressants management of coronavirus disease 2019 in solid organ transplant recipients. *Am J Transplant*. 2020;20:1916–21, <http://dx.doi.org/10.1111/ajt.15928>. Epub 2020 May 4.
19. Zhang H, Chen Y, Yuan Q, Xia QX, Zeng XP, Peng JT, et al. Identification of kidney transplant recipients with coronavirus disease 2019. *Eur Urol*. 2020;77:742–7,

- <http://dx.doi.org/10.1016/j.eururo.2020.03.030>. S0302-2838(20)30205-0. [Epub ahead of print].
20. Alberici F, Delbarba E, Manenti C, Econimo L, Valeria F, Pola A, et al. A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia. *Kidney Int.* 2020;97:1083-8, <http://dx.doi.org/10.1016/j.kint.2020.04.002>. Epub 9 April 2020.
 21. Banerjee D, Popoola J, Shah S, Ster IC, Quan V, Phanish M. COVID-19 infection in kidney transplant recipients. *Kidney Int.* 2020;97:1076-82, <http://dx.doi.org/10.1016/j.kint.2020.03.018>. Epub 9 April 2020.
 22. Gandolfini I, Delsante M, Fiaccadori E, Zaza G, Manenti L, Degli Antoni A, et al. COVID-19 in kidney transplant recipients. *Am J Transplant.* 2020;20:1941-3, <http://dx.doi.org/10.1111/ajt.15891>. Epub 12 April 2020.
 23. Columbia University Kidney Transplant Program. Early description of coronavirus 2019 disease in kidney transplant recipients in New York. *J Am Soc Nephrol.* 2020;31:1150-6, <http://dx.doi.org/10.1681/ASN.2020030375>. Epub 21 April 2020.
 24. Kates OS, Fisher CE, Stankiewicz-Karita HC, Shepherd AK, Church EC, Kapnadak SG, et al. Earliest cases of coronavirus disease 2019 (COVID-19) identified in solid organ transplant recipients in the United States. *Am J Transplant.* 2020;20:1885-90, <http://dx.doi.org/10.1111/ajt.15944>. Epub 8 May 2020.
 25. Fernández-Ruiz M, Andrés A, Loinaz C, Delgado JF, López-Medrano F, San Juan R, et al. COVID-19 in solid organ transplant recipients: a single-center case series from Spain. *Am J Transplant.* 2020;20:1849-58, <http://dx.doi.org/10.1111/ajt.15929>. Epub 10 May 2020.
 26. Akalin E, Azzi Y, Bartash R, Seethamraju H, Parides M, Hemmige V, et al. Covid-19 and Kidney Transplantation [published online ahead of print, 2020 Apr 24]. *N Engl J Med.* 2020;382:2475-7, <http://dx.doi.org/10.1056/NEJMc2011117>. Epub 24 April 2020.
 27. Pereira MR, Mohan S, Cohen DJ, Husain SA, Dube GK, Ratner LE, et al. COVID-19 in solid organ transplant recipients: initial report from the US epicenter. *Am J Transplant.* 2020;20:1800-8, <http://dx.doi.org/10.1111/ajt.15941>. Epub 10 May 2020.
 28. Nair V, Jandovitz N, Hirsch JS, Nair G, Abate M, Bhaskaran M, et al. COVID-19 in kidney transplant recipients. *Am J Transplant.* 2020;20:1819-25, <http://dx.doi.org/10.1111/ajt.15967>. Epub 27 May 2020.
 29. Coll E, Fernández-Ruiz M, Sánchez-Álvarez JE, Martínez-Fernández JR, Crespo M, Gayoso J, et al. COVID-19 in transplant recipients: the Spanish experience. *Am J Transplant.* 2021;21(May (5)):1825-37, <http://dx.doi.org/10.1111/ajt.16369>. Online ahead of print. PMID: 33098200.
 30. van Paassen J, Vos JS, Hoekstra EM, Neumann KMI, Boot PC, Arbous SM. Corticosteroid use in COVID-19 patients: a systematic review and meta-analysis on clinical outcomes. *Crit Care.* 2020;24:696, <http://dx.doi.org/10.1186/s13054-020-03400-9>. PMID: 33317589.
 31. O'Neill S, Brown TJ, McCaughan JA, Magowan H, Courtney AE. Resetting healthcare services during the coronavirus disease 2019 pandemic: a multi-disciplinary team approach to delivering kidney transplantation. *Br J Surg.* 2020;107:e496-7, <http://dx.doi.org/10.1002/bjs.11951>. Epub 21 August 2020. PMID: 32822064.
 32. Domínguez-Gil B, Fernández-Ruiz M, Hernández D, Crespo M, Colmenero J, Coll E, et al. Organ donation and transplantation during the COVID-19 pandemic: a summary of the Spanish experience. *Transplantation.* 2021;105:29-36, <http://dx.doi.org/10.1097/TP.0000000000003528>. Online ahead of print. PMID: 33165237.
 33. Stock PG, Wall A, Gardner J, Domínguez-Gil B, Chadban S, Muller E, et al. Ethical issues in the COVID era: doing the right thing depends on location, resources, and disease burden. *Transplantation.* 2020;104:1316-20, <http://dx.doi.org/10.1097/TP.0000000000003291>. PMID: 32569002.
 34. Arcos E, Pérez-Sáez JM, Comas J, Lloveras J, Tort J, Pascual J. Catalan Renal Registry. Assessing the limits in kidney transplantation: use of extremely elderly donors and outcomes in elderly recipients. *Transplantation.* 2020;104:176-83, <http://dx.doi.org/10.1097/TP.0000000000002748>. PMID: 30985579.
 35. Potter SR, Hinojosa R, Miles CD, O'Brien D, Ross DJ. Remote monitoring using donor-derived, cell-free DNA after kidney transplantation during the coronavirus disease 2019 pandemic. *Kidney Res Clin Pract.* 2020;104:176-83, <http://dx.doi.org/10.23876/j.krcp.20.107>.
 36. Varotti G, Dodi F, Garibotto G, Fontana I. Successful kidney transplantation after COVID-19. *Transpl Int.* 2020;33:1333-4, <http://dx.doi.org/10.1111/tri.1370>.
 37. Singh N, Tandukar S, Zibari G, Naserr MS, Amiri HS, Samaniego-Picota MD. Successful simultaneous pancreas and kidney transplant in a patient post-COVID-19 infection. *Kidney Int.* 2020;98:1615-6, <http://dx.doi.org/10.1016/j.kint.2020.09.004>.
 38. Kanchi P, Sambandam S, Siddhan R, Soundappan S, Vaseekaran VP, Gupta A. Successful kidney transplantation after COVID-19 infection in two cases. *Nefrología.* 2021, <http://dx.doi.org/10.1016/j.nefro.2020.12.004>.
 39. Villanego F, Vigara LA, Torrado J, Naranjo J, García AM, García T, et al. Infección por SARS-COV-2 en lista de espera de trasplante renal: ¿se puede trasplantar un paciente con antecedente de COVID-19? *Nefrología.* 2021, <http://dx.doi.org/10.1016/j.nefro.2020.12.003>.
 40. Kang H, Wang Y, Tong Z, Liu X. Retest positive for SARS-CoV-2 RNA of "recovered" patients with COVID-19: persistence, sampling issues, or re-infection? *J Med Virol.* 2020;92:2263-5, <http://dx.doi.org/10.1002/jmv.26114>.