



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



ELSEVIER

Contents lists available at ScienceDirect

## Journal of Liver Transplantation

journal homepage: [www.elsevier.com](http://www.elsevier.com)

Original article

## Impact of COVID-19 on 2020 transplant activity and waiting lists in France ☆,☆☆

C. Legeai<sup>a,\*</sup>, E. Savoye<sup>a</sup>, C. Cantrelle<sup>a</sup>, C. Jasseron<sup>a</sup>, G. Santin<sup>a</sup>, G. Brousse<sup>b</sup>, M. Duman<sup>b</sup>, F. Foubert<sup>b</sup>, R. Mahmoudi<sup>b</sup>, A. Deshayes<sup>b</sup>, C. Antoine<sup>a</sup>, F. Kerbaul<sup>a</sup><sup>a</sup> Organ and Tissue Procurement and Transplantation Department, Agence de la biomédecine, Saint Denis La Plaine, France<sup>b</sup> Data Quality Department, Agence de la biomédecine, Saint Denis La Plaine, France

## ARTICLE INFO

## Article History:

Received 18 October 2021

Accepted 21 October 2021

Available online 23 October 2021

## Keywords:

COVID-19

Solid organ procurement

Solid organ transplant

## ABSTRACT

The COVID-19 pandemic strongly affected organ procurement and transplantation in France, despite the intense efforts of all participants in this domain. In 2020, the identification and procurement of deceased donors fell by 12% and 21% respectively, compared with the mean of the preceding 2 years. Similarly, the number of new registrations on the national waiting list declined by 12% and the number of transplants by 24%. The 3-month cumulative incidence of death or drop out for worsening condition of patients awaiting a liver transplant was significantly greater in 2020 compared to the previous 2 years. Continuous monitoring at the national level of early post-transplant outcomes showed no deterioration for any organ in 2020. At the end of 2020, less than 1% of transplant candidates and less than 1% of graft recipients — of any organ — had died of COVID-19.

© 2021 The Author(s). Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## Abbreviations

CI	confidence interval
cDCD	controlled donation after circulatory death
CUSUM	cumulative sum
ICU	intensive care unit

## 1. Introduction

On March 11, 2020, the World Health Organization qualified the COVID-19 epidemic as a pandemic. From the onset of the first cases in France, the French high council for public health (Haut Conseil de la Santé Publique) issued guidelines intended for transplantation professionals to specify the conditions in which organ procurement and transplantation could be continued, in view of the risks linked to the circulation of SARS-CoV-2. The Agence de la biomédecine (the French public health authority of reference for tissue and organ transplantation) provided its expertise for these guidelines and has widely forwarded them to the professionals concerned to maintain both procurement and transplant activity, while ensuring the

<sup>\*</sup>Declaration of interestsThe authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

<sup>\*\*</sup>All co-authors report no associations of interest in relation to this article.

\* Corresponding author: Dr Camille Legeai.

E-mail address: [camille.legeai@biomedecine.fr](mailto:camille.legeai@biomedecine.fr) (C. Legeai).

<https://doi.org/10.1016/j.liver.2021.100051>

2666-9676/© 2021 The Author(s). Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

maintenance of the safety and quality of organ transplants. The epidemic continues to mobilize healthcare facilities, care providers, and in particular, intensive care departments (ICUs). It involves hospital organization requirements and human and logistic constraints that affect procurement and transplant activity considerably throughout France and Europe. The purposes of this article are to describe the guidelines that were established and to assess the consequences of this current health crisis on organ procurement and transplant activity in 2020.

## 2. Guidelines concerning organ procurement and transplantation in 2020

From the start of the epidemic in France, it was recommended that organs be recovered from donors only when all of the following conditions could be met:

- ✓ Negative RT-PCR test of a nasopharyngeal or endotracheal sample, possibly combined with a blood sample, in the 24 h preceding the procurement;
- ✓ Thoracic imaging that is not suggestive of COVID-19;
- ✓ Absence of clinical symptoms suggestive of COVID-19, contact with a person infected or screened positive in the 28 days before the organ recovery [1].

At the beginning of the epidemic, sufficient data to ensure that the benefits of transplants would outweigh their risks were not available [2–5]. Accordingly, with the agreement of several professional societies, the transplantation of kidneys (except for pediatric transplantation), intestines, whole pancreases, islets of Langerhans, and tissue was suspended from March 19 through May 11, 2020 (the period of the first lockdown in France). These resumed progressively, as means of, like other transplants, RT-PCR screening of recipients in the 24 h before their arrival in the operating room, the absence of both symptoms suggestive of COVID-19 and contact with an infected person in the 28 days before the intervention, and the existence in both the procurement and transplantation facilities of a strict "COVID-free" environment. Initially, new transplants were possible only for patients on dialysis awaiting a kidney graft that was not combined with a pancreas, who were at low risk of severe COVID-19 because of the absence of comorbidities (advanced age, overweight, diabetes, respiratory history, cardiovascular or respiratory disease) or who were considered urgent due to poor vascular access for dialysis, hyperimmunization or a long waiting time. Then, as knowledge about SARS-CoV-2 infections in transplant recipients progressed, the criteria were slowly expanded to a larger number of individuals as benefit-risk assessments favored transplantation rather than dialysis.

Given the possibility of an epidemic rebound and to maintain organ procurement and transplant activities as much as possible, including for organs for which a transplant is not an emergency treatment because alternative replacement therapies are available (kidneys and pancreas), the Agence de la biomédecine, in partnership with the relevant professional societies and associations representing patients awaiting an organ transplant, issued new guidelines in the autumn of 2020. Unlike in the previous spring, hospitals were asked to:

- ✓ ensure the availability of the medical and paramedical staff, who comprise the medicosurgical teams that contribute to organ procurement and transplantation, as well as the hospitals' organ/tissue procurement teams;

- ✓ plan COVID-19-free treatment pathways to enable procurement and transplants to take place in the optimal conditions for health security;
- ✓ maintain the maximum identification of potential donors and organ/tissue procurement.

Finally, in March 2021, these guidelines were completed by encouraging these establishments to promote priority access to vaccination against COVID-19 for transplant recipients and for candidates on the national waiting list. It was also specified that the subjects who died after having been immunized by an mRNA vaccine against COVID-19 remained eligible for organ and tissue donation, as stated in the HCSP opinion dated January 15, 2021 [6].

### 3. Trends in the donor identification and organ procurement in France in 2020

In 2020, the deceased donor identification and organ procurement fell by 12% and 21% respectively, compared with the mean of the preceding 2 years (Fig. 1). The proportion of donors from whom organs were recovered among those identified fell from 49% for the 2018–2019 period to 45% in 2020. This reduction in procurement from deceased donors in 2020 concerned essentially brain-dead donors; the number of controlled donation after circulatory death (cDCD) donors from whom organs were procured did not decline compared with the means of the previous 2 years. The proportion of cDCD donors among all actual deceased donors rose from 8% on average in 2018–2019 to 10% in 2020. The number of living donors in 2020 fell by 25% compared with the previous 2 years and accounted for 21% of actual donors in 2020 versus a mean of 22% in 2018–2019.

The distribution of the main causes of brain death of identified donors were similar to those identified in the preceding years; in 2020, 58% were from vascular causes, 20% traumatic, and 20% anoxic. Two-thirds of the decrease in the number of actual brain-dead donors in 2020 compared to 2019 was due to the decrease

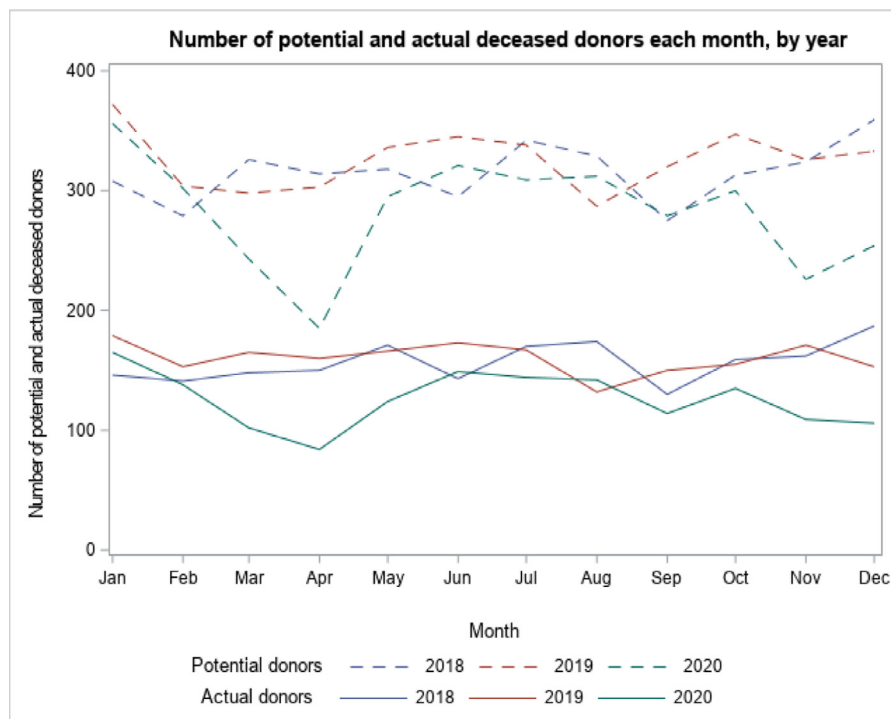


Fig. 1. Number of potential and actual deceased donors each month, by year.

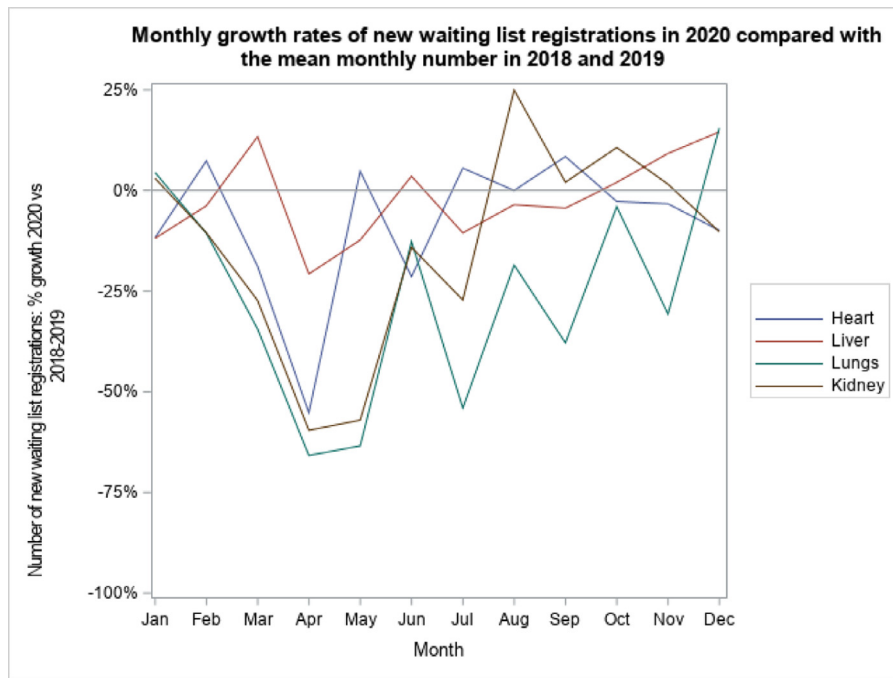


Fig. 2. Monthly growth rates of new waiting list registrations in 2020 compared with the mean monthly number in 2018 and 2019.

in those whose death was of vascular origin. The rate of opposition to donation increased in 2020, touching 33% of the identified brain-dead donors, climbing from a mean of 30% in 2018–2019.

**4. Trends in the number of new registrations on the organ transplant waiting list in France in 2020**

After a fall of 50 to 70% in the number of new registrations on the waiting lists for heart, pulmonary and kidney transplants in

April 2020 compared with mean for the months of April 2018 and 2019, the monthly number of new listings reached a level similar to that of the preceding 2 years from the beginning of the second half of 2020. There was one exception: the monthly number of new registrations for lung transplants did not catch up with those of the preceding 2 years until the end of 2020 (Fig. 2). Overall, at the end of 2020, the number of new waiting list registrations fell by 27% for lung transplants, by 15% for kidneys, by 10% for hearts, and by 2% for livers, compared with the mean of the new listings in 2018 and 2019.

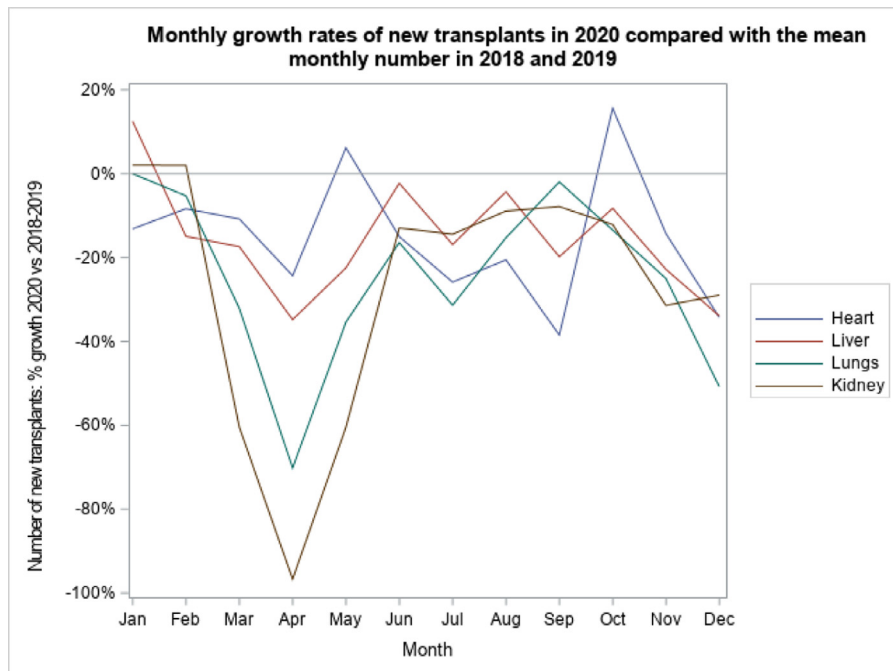


Fig. 3. Monthly growth rates of new transplants in 2020 compared with the mean monthly number in 2018 and 2019.

**Table**

Cumulative incidence rate of transplants and of death or drop out for worsening condition at 3 months post-inscription according to the year of inclusion on the national waiting list and the type of organ.

	Kidney	Liver	Heart	Lungs
Registered between January 1, 2018, and September 30, 2019, censored as of December 31, 2019	1 [1–1]	7 [6–8]	9 [7–11]	2 [2–4]
Registered between January 1, 2020, and December 31, 2020, censored as of March 31, 2021	1 [1–1]	10 [9–12]	11 [8–13]	4 [2–6]
<b>p value</b>	0,16	$p < 0.01$	0,23	0,35
<b>Cumulative incidence rate of transplant access at 3 months (95% CI), temporary contraindication time not excluded</b>				
Registered between January 1, 2018, and September 30, 2019, censored as of December 31, 2019	5 [5–5]	32 [30–33]	50 [47–53]	55 [52–59]
Registered between January 1, 2020, and December 31, 2020, censored as of March 31, 2021	3 [2–3]	27 [25–29]	45 [40–49]	45 [39–51]
<b>p value</b>	$p < 0.001$	$p < 0.001$	0,1	$p < 0.01$

### 5. Trends in transplant activity in France in 2020 by organ

The pandemic affected transplant activity differently according to the organ concerned. Non-urgent adult kidney transplants, suspended for 7 weeks in 2020, and lung transplants, which underwent a net slowdown in April, were the most strongly affected, with decreases of 28% and 25% respectively, compared with their mean activity levels in the preceding 2 years (Fig. 3). Liver and heart transplants maintained levels around 85% of the mean in 2018 and 2019.

### 6. Access to organ transplants in France in 2020 according to the organ

The decrease in transplantation activity observed in 2020 had an immediate influence on the cumulative incidence of access to a graft within 3 months of waiting-list registration in 2020, which was significantly lower than that for new registrants between 2018 and 2019 for all types of transplants, except hearts (Table). The

cumulative incidence of death or drop out for worsening condition on the waiting list during the first 3 months in 2020 was statistically higher than in preceding years for patients awaiting a liver transplant. On the other hand, no significant difference in this 3-month incidence rate was observed for candidates awaiting another organ.

### 7. Transplant activity in Europe

As in France, transplant activity in Europe was affected by the health crisis, with reductions in the number of transplants in 2020 relative to the mean activity of the preceding 2 years of:

- 28% in Great Britain (3801 transplants in 2020 versus 5256.5 in 2018–2019) [7],
- 18% in Spain (4425 in 2020 versus 5383 in 2018–2019) [8],
- 9% in Italy (3441 in 2020 versus 3769 in 2018–2019) [9] and
- 7% in Germany (3016 in 2020 versus 3228 in 2018–2019) [10].

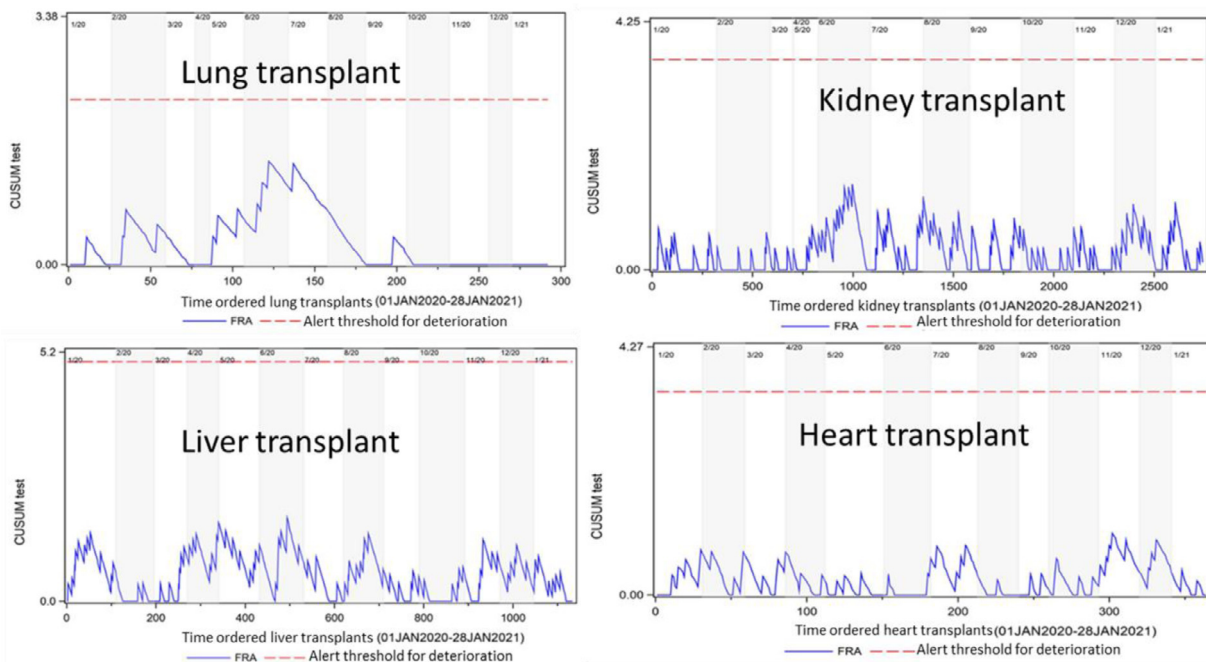


Fig. 4. Continuous surveillance of failures 1 month posttransplant (CUSUM method).

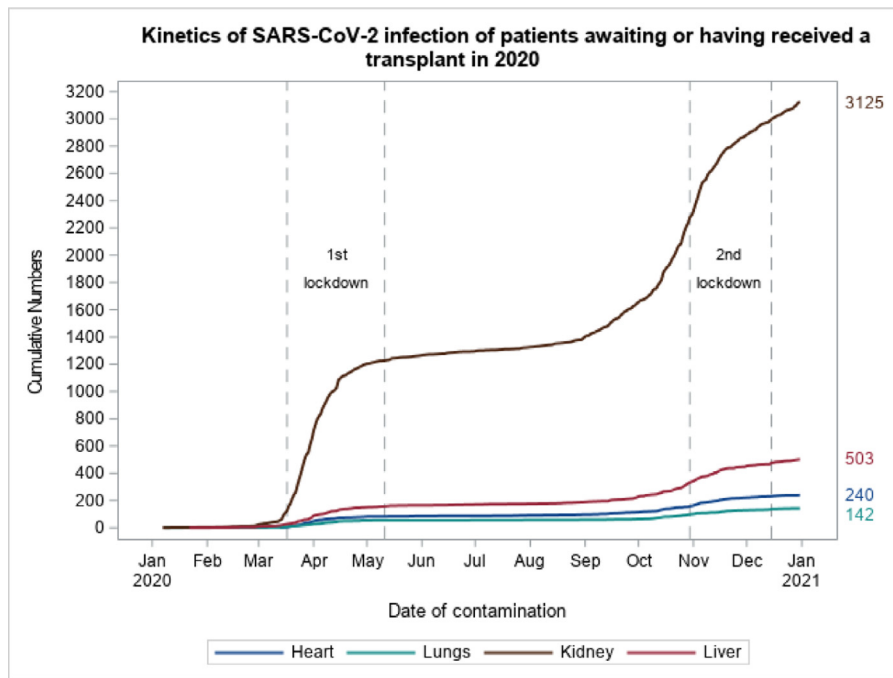


Fig. 5. Kinetics of SARS-CoV-2 infection of patients awaiting or having received a transplant in 2020.

### 8. Monitoring of posttransplant results

To ensure the safety of newly transplanted patients, from the start of the epidemic in France, the Agence de la biomédecine set up continuous monitoring of early national posttransplant results by organ type. The 1-month death or graft failure rate was compared monthly with the rate observed between September 2018 and June 2019, by using the cumulative sum (CUSUM) chart method (Fig. 4) [11], which makes it possible to determine graphically if the results observed

differ statistically from the reference results. The result of each transplant is reported on the graph in chronological order of performance. If a failure is observed, the curve rises. Inversely, if no failure occurs, it descends. A threshold with specific sensitivity and specificity is established in advance to detect a predefined level of deterioration. When the curve reaches this threshold, the failure rate observed is significantly higher than the reference rate. In 2020, no significant deterioration in the early posttransplant failure rate was shown for any organ.

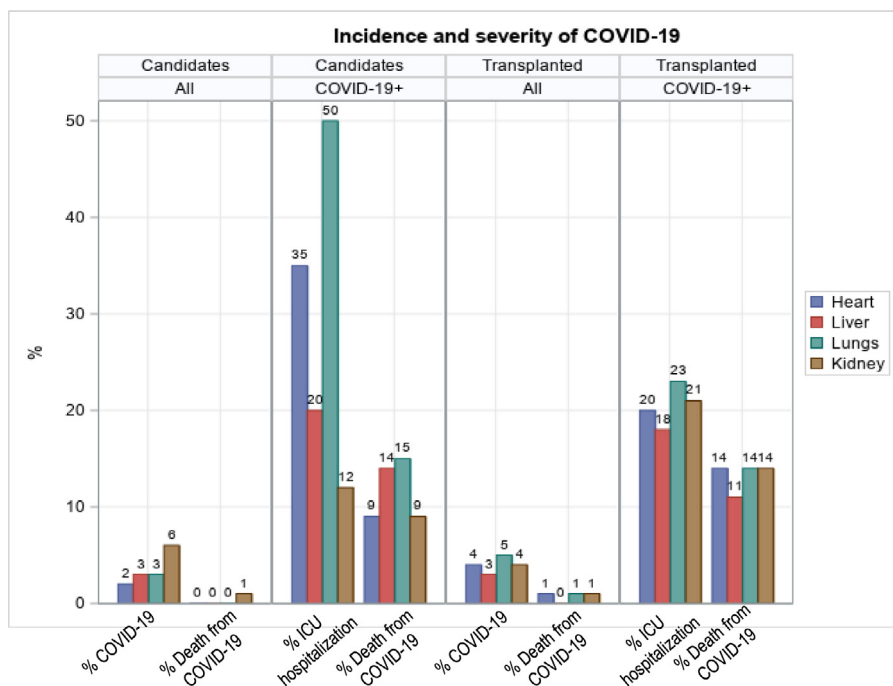


Fig. 6. Incidence and severity of COVID-19.

## 9. COVID-19 in patients awaiting a transplant or already transplanted

By December 31, 2020, among the patients awaiting or having already received a transplant who had been diagnosed with COVID-19 and reported to the CRISTAL database (the French national registry, administered by the Agence de la biomédecine, that prospectively collects data about all organ transplant candidates) [12], 3125 were awaiting or had received a kidney graft, 503 a liver graft, 240 a heart transplant, and 142 a lung graft (Fig. 5). Those infected by SARS-CoV-2 represented 6% of the transplant candidates and 4% of those with a functional graft in 2020. Nonetheless, a reporting bias probably exists for infections, induced by the closer monitoring of candidates compared with recipients. Caution is thus required in comparing the incidence of infection in these 2 populations. Similarly, this potential reporting bias could partially explain the greater severity of infections in graft recipients (21% required ICU admission and 13% died) than in candidates (13% needed ICU admission and 10% died). That is, the underreporting in the CRISTAL database of infections in transplant recipients relative to candidates may primarily concern the least severe infections. The COVID-19-associated death rates in candidates and recipients in 2020 were similar, around 0.5%, again subject to the absence of underreporting of COVID-associated deaths in transplanted individuals compared with candidates in 2020. The severity of infection in graft recipients has not varied much by organ, since the percentage of ICU admissions ranged from 18% for liver transplant recipients to 23% for lungs, and the percentage of deaths from 11% for liver transplant recipients to 14% for other organ recipients (Fig. 6). Nor did the percentage of deaths in infected candidates differ by organ (from 9% awaiting heart and kidney to 15% for lungs). On the other hand, although the figures for infection in candidates for lung or heart transplants have been low, the percentage of ICU admissions of infected candidates seems notably higher for those awaiting lung (50%) and heart (35%) transplants than for those awaiting livers (20%) and kidneys (12%).

## 10. Conclusion

Due to the mobilization of all those involved in organ procurement and transplantation in France, and despite the human and logistic constraints imposed by the pandemic, the reduction in transplant activity in France in 2020 was limited to 24% of the mean activity of the preceding 2 years. Overall, 4421 transplants were performed in 2020, 59% of them kidneys, 26% livers, and 15% thoracic. At the end of 2020, less than 1% of transplant candidates and less than 1% of graft recipients — of any organ — had died of COVID-19. The 1-

month posttransplant death or graft failure rate did not deteriorate significantly in 2020. However, the pandemic notably accentuated the already existing organ shortages. The repercussions of this crisis on short-, medium-, and long-term access of candidates to grafts are under evaluation. The beginning of 2021 unfortunately turned out to be as difficult as 2020 for the hospital teams. Nonetheless, the third confinement and the perspectives of vaccination suggest a possible return of procurement and transplant activity to normal in the near future.

## Acknowledgments

The authors warmly thank all of the registry participants, in particular those who collected the data and controlled its quality. Many thanks also to Jo-Ann Cahn for her translation work.

## References

- [1] HCSP. Sécurisation des dons de sang, cellules, tissus et organes en période de circulation active du SARS-CoV-2. Haut Conseil de la Santé Publique 2020 Accessed August 20, 2020 <https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefi=778>.
- [2] Thauinat O, Legeai C, Anglicheau D, et al. IMPact of the COVID-19 epidemic on the moRTAlity of kidney transplant recipients and candidates in a French Nationwide registry sTudy (IMPoRTANT). *Kidney Int* 2020;98(6):1568–77. doi: 10.1016/j.kint.2020.10.008.
- [3] Dumortier J, Duvoux C, Roux O, et al. Covid-19 in liver transplant recipients: the French SOT COVID registry. *Clin Res Hepatol Gastroenterol* 2021;45(4):101639. doi: 10.1016/j.clinre.2021.101639.
- [4] Caillard S, Anglicheau D, Matignon M, et al. An initial report from the French SOT COVID Registry suggests high mortality due to COVID-19 in recipients of kidney transplants. *Kidney Int* 2020;98(6):1549–58. doi: 10.1016/j.kint.2020.08.005.
- [5] Thauinat O, Legeai C, Bastien O, Caillard S. The authors reply. *Kidney Int* 2021;99(3):771–2. doi: 10.1016/j.kint.2020.12.008.
- [6] HCSP. Critères d'exclusion des donneurs ayant fait l'objet d'une vaccination anti-Covid-19. Haut Conseil de la Santé Publique 2021 Accessed April 16, 2021 <https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefi=977>.
- [7] weekly-report-on-covid-19-nhsbt-9-april-2021.pdf. Accessed April 16, 2021. <https://nhsbtdeb.blob.core.windows.net/umbraco-assets-corp/22866/weekly-report-on-covid-19-nhsbt-9-april-2021.pdf>
- [8] Documentos - Todos los documentos. Accessed April 16, 2021. <http://www.ont.es/Documents/Forms/AllItems.aspx?View={4650b2e2-fae1-43d6-bd61-cbe7dd2315fa}&SortField=Modified&SortDir=Desc>
- [9] Salute M della. Dati italiani ed europei. <http://www.trapianti.salute.gov.it/trapianti/archivioDatiCnt.jsp>
- [10] Deutsche Stiftung Organtransplantation Statistiken zur Organspende. Accessed April 16, 2021. <https://www.dso.de/organspende/statistiken-berichte/organspende>
- [11] Alexandrine B, Savoye E, Pessione F, et al. Continuous Monitoring of Transplant Center Performance: different Options for Different Goals. *Transplantation* September 2019 Published online. doi: 10.1097/TP.0000000000002591.
- [12] Agence de la biomédecine. Accessed October 15, 2021. <https://rams.agence-bio-medecine.fr/organes>