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## ORIGINAL ARTICLE

# Impact of the first Covid-19 outbreak on liver transplantation activity in France: A snapshot



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## Abstract

**Background:** The global pandemic of Coronavirus Disease 2019 (COVID-19) has potentially affected liver transplantation (LT) programs worldwide. The aim of this study was to determine whether the COVID-19 outbreak affected organ donation and LT activity in France.

**Methods:** Data on the number of brain-dead donor procurements and adult liver transplantations were compared between two periods (1<sup>st</sup> January- 31<sup>st</sup> May 2019 vs. 1<sup>st</sup> January-31<sup>st</sup> May 2020).

**Abbreviations:** ABM, Agence de la Biomédecine; COVID-19, coronavirus disease 2019; ICU, intensive care unit; LT, liver transplantation.

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**Main findings:** There was a 28% decrease in the number of organ donations in 2020 (543 in 2020 vs. 752 organ donations in 2019). A 22% decrease in the number of liver transplantations was also observed: 435 in 2020 vs. 556 LTs in 2019. Overall, the North East area which was the main COVID-19 cluster area, had > 25% decrease of the multiorgan procurement (-33% compared to 2019), and liver transplantation (-26% compared to 2019) activities in 2020

**Conclusion:** This analysis confirmed that during the COVID-19 outbreak there was a significant decrease in the number of organ donations and liver transplantations performed in France.

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## Introduction

As of June 17<sup>th</sup> 2020, the ongoing pandemic of Coronavirus disease 2019 (COVID-19) outbreak, a new infectious viral disease, has continued to spread, with over 8,061,550 confirmed cases in more than 215 countries and 440,290 deaths [1]. Initial confirmed cases of COVID-19 were declared in Wuhan (China) on December 31<sup>st</sup> 2019 [2]. On January 30<sup>th</sup> 2020, the COVID-19 outbreak was formally declared as a Public Health Emergency of International Concern [3].

In Europe, the first documented case of COVID-19 was observed in France in a French citizen from China on January 24<sup>th</sup> 2020. In France, the first COVID-19 death was declared on February 14<sup>th</sup> 2020. National lockdown was declared by the French government and implemented on March 17<sup>th</sup> 2020. The lockdown ended on May 11<sup>th</sup> 2020. On June 6<sup>th</sup> 2020, French authorities reported over 153,634 confirmed cases of COVID-19 with more than 29,142 deaths [4].

Due to the rapid spread of COVID-19, the French Society of Transplantation and the French society of nephrology, dialysis and transplantation have recommended some guidelines for solid organ transplantation, adult recipients and donors [5,6]. These latter have been validated by the French Biomedicine Agency (Agence de la Biomédecine, ABM) that manages organ procurement and transplantation in France [7]: 1) to stop live donor organ transplantations, 2) to stop deceased kidney and pancreas transplantations, 3) to maintain heart, lung and liver transplantations but to limit transplantations only to urgent cases, and 4) all organ transplantation recipients and donors, regardless of the presence or absence of symptoms, should be systematically tested for the presence of COVID-19 before validating organ procurement and transplantation surgery [8]. The aim of this study was to provide a snapshot of the impact of COVID-19 on a national liver transplantation (LT) program.

## Material and methods

### Study design

This study is a retrospective analysis of data regarding the number of organ donations (brain-dead donors) and adult LTs performed from 1<sup>st</sup> January to 31<sup>st</sup> May 2020. This period was compared to the same period in 2019. All data were retrieved from the prospective French national database "CRISTAL" (from the ABM). Pediatric transplant centers were excluded from the analysis.

There are 16 adult LT centers, namely Pitié-Salpêtrière Hospital (Paris); Paul Brousse Hospital (Villejuif); Beaujon

Hospital (Clichy); Croix-Rousse Hospital (Lyon); Grenoble Alpes Hospital (Grenoble); Estaing Hospital (Clermont-Ferrand); Archet Hospital (Nice); Saint-Eloi Hospital (Montpellier); Claude Huriez Hospital (Lille); Hautepierre Hospital (Strasbourg); Jean Minjot Hospital (Besançon); Rangueil Hospital (Toulouse); Haut-Lévêque Hospital (Bordeaux Pessac); Pontchaillou Hospital (Rennes); Trousseau Chambray Hospital (Chambray les Tours); Timone Hospital (Marseille) (Fig. 1).

Data collection included the overall number of donors procured, and the number of LTs performed. The analyses were also stratified according to four different regions in France: North East (Nord-Est), South West (Grand-Ouest), South East/French Islands in Indian Ocean (Sud Est/Océan Indien) and Paris region/French Guiana/French Antilles (Ile-de-France/Guyane/Antilles). As for the LT centers, North East area includes Besançon, Lille and Strasbourg centers; South East/French Islands in Indian Ocean area includes Clermont-Ferrand, Grenoble, and Lyon centers; South West area includes Bordeaux, Marseille, Montpellier, Nice, Rennes, Toulouse and Tours centers; and Paris region area includes Paris, Villejuif, and Clichy centers.

### Statistical analysis

All the statistics were performed using Excel software for Windows (Microsoft Office Excel 2007). Results are given as number and percentage.

## Results

The Mulhouse cluster; which was the initial hotspot involved in the spread of COVID-19 is located in the North East area in France (Fig. 1).

### Multiorgan procurement activity

From January 1<sup>st</sup> to May 31<sup>st</sup>, the number of brain-dead donors in France has decreased from 752 in 2019 to 543 in 2020 (-28%; Fig. 2A). There were regional variations in the decrease of the organ procurement activity in 2020: 33%, 29%, 30%, and 9% in the North East, South East/French Islands in Indian Ocean, South West and Paris region/French Guiana/French Antilles areas, respectively (Fig. 3A and B). The North East area, i.e. the initial regional cluster (Fig. 1), had the highest decrease (from 209 in 2019 to 141 in 2020) in organ procurement activity in 2020 (-33%).

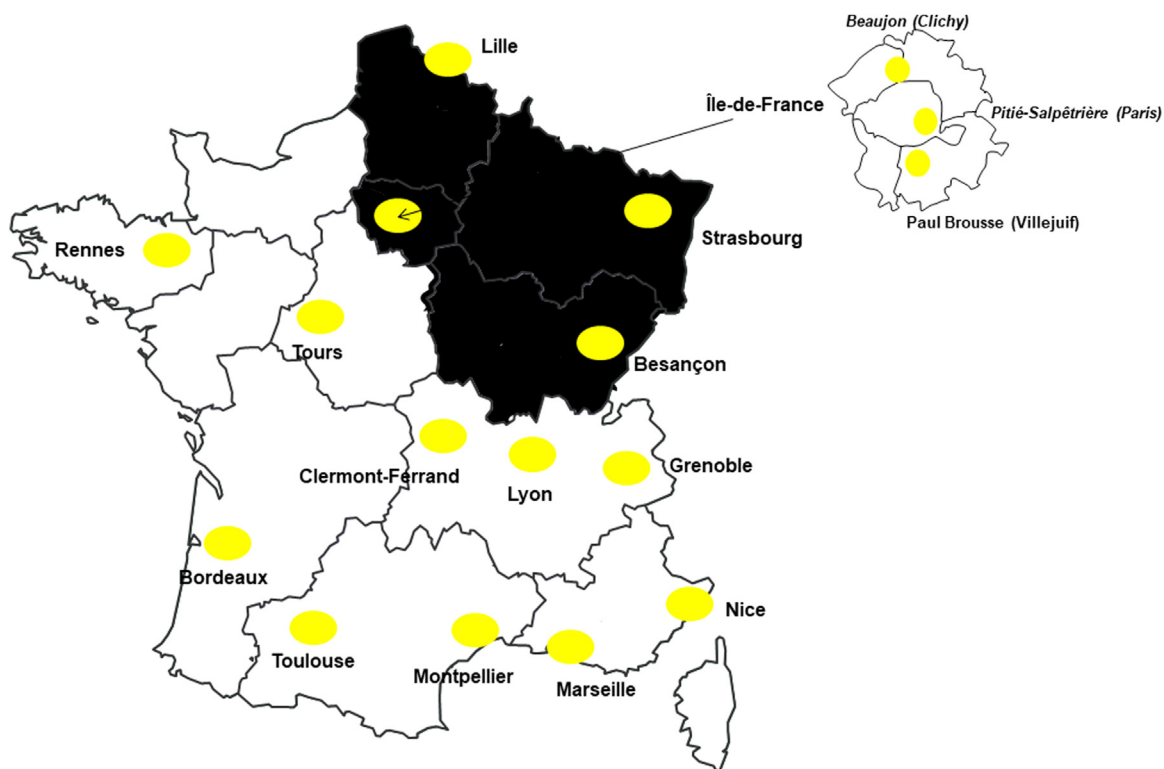


Figure 1 2020 COVID-19 pandemic in France (black) and the 16 adult liver transplantation centers (yellow).

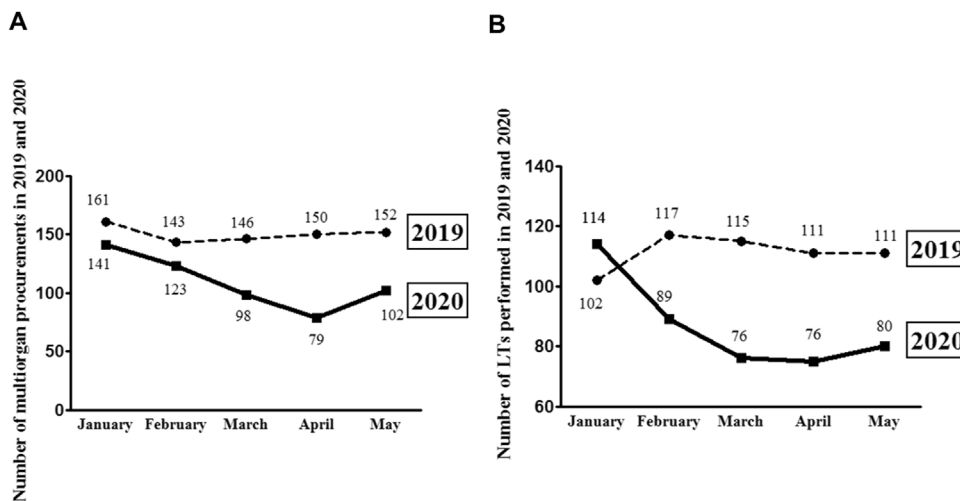


Figure 2 Time variations of the organ procurement (A) and liver transplantation (B) activities.

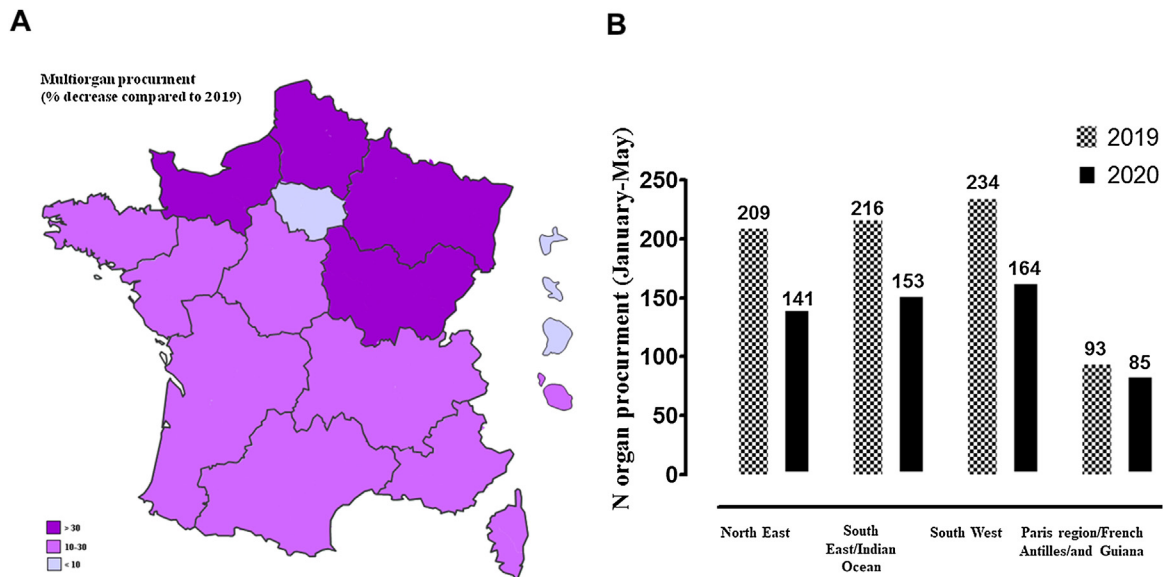
### Liver transplantation activity

The number of LTs performed in France also decreased from 556 in 2019 to 435 in 2020 (-22 %, Fig. 2B). There were variations between different areas: 26%, 22%, 27%, and 16% in the North East, South East/French Islands in Indian Ocean, South West and Paris region/French Guiana/French Antilles areas, respectively (Fig. 4A). The North East and South West areas had the highest decrease (from 90 in 2019 to 67 LTs in 2020 for North East and from 143 in 2019 to 105 in 2020 for South West) (Fig. 4A and B). At a LT center level (except

for 4 centers including Clermont-Ferrand, Lyon, Clichy and Nice in which the numbers of LTs performed were stable or increased), the number of LTs performed has decreased between 1 and 18 in 2020 compared to 2019 (Fig. 4C and D).

### Analysis stratified according to the lockdown period

In France, the lockdown started on March 17<sup>th</sup> and ended on May 11<sup>th</sup>. While the number of organ procurement was > 140 per month between January and May 2019, it was < 100



**Figure 3** Regional variations of the organ procurement activity. Variations shown in regard to: (A) the percentage of decrease in organ procurement, (B) the number of organ procurement.

per month during the lockdown period (March-April 2020). Yet, the number of LTs remained > 110 per month between January and May 2019 and it was < 80 per month during the lockdown period (March-April 2020).

## Discussion

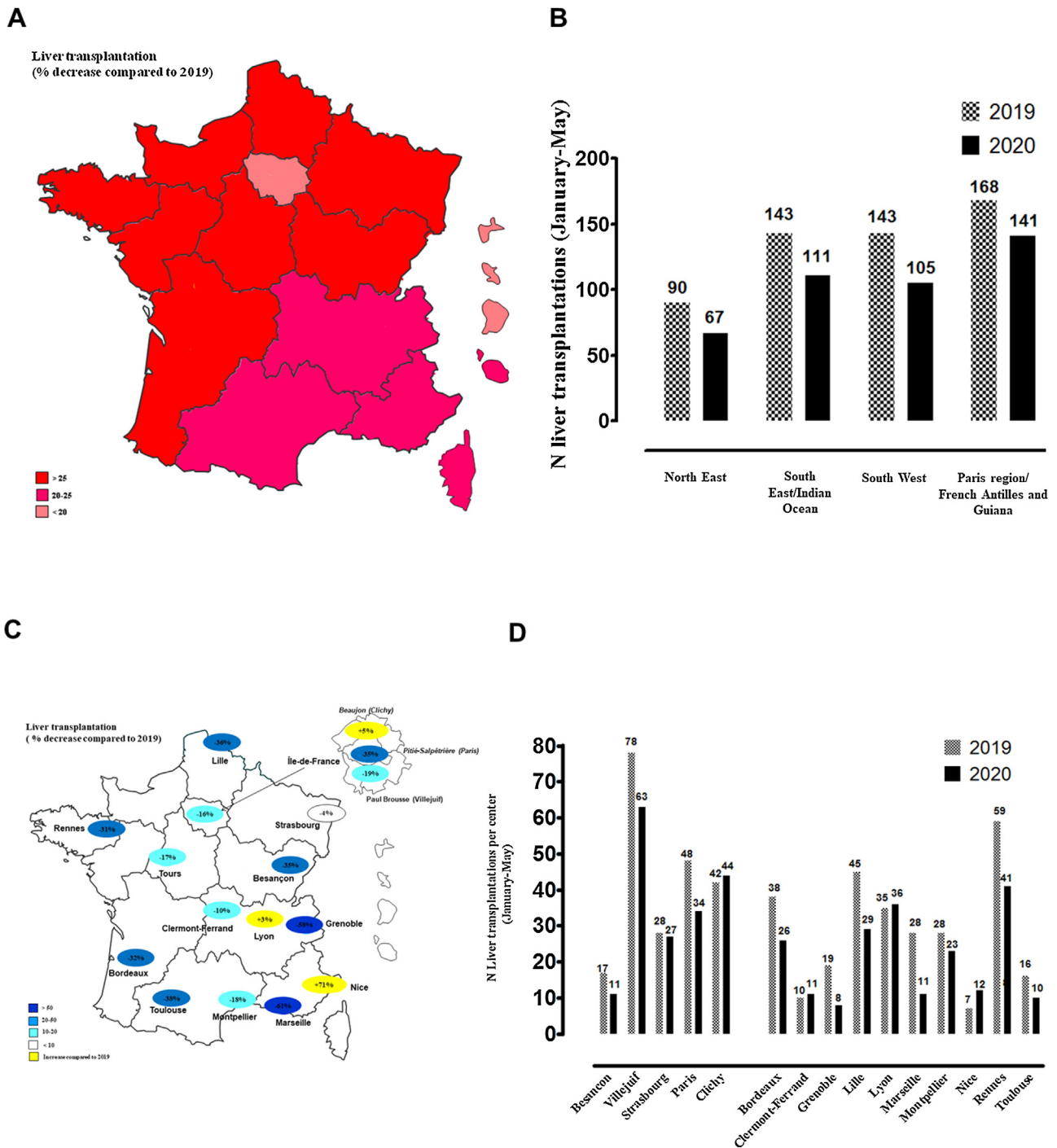
This interim analysis showed the following results: 1) a 28% decrease in the number of deceased donors procured at a national level in 2020; this reduction in the number of organ donations was also observed in the number of liver donations, 2) a 22% decrease in the number of LTs performed at national and center levels in 2020, 3) more importantly, this reduction in the LT program activity was mainly observed in the North East area, which is the initial COVID-19 cluster in France, and 4) finally, this reduction in the organ procurement and LT program activities was more pronounced during the lockdown period.

Three reasons may explain the observed reduction in organ donation in France in 2020. First, like other European countries, in particular Italy (the first European country with the highest incidence of confirmed COVID-19 cases outside China), the French government has made tremendous efforts to dramatically increase the overall number of intensive care unit (ICU) beds all over the country growing from 5,000 in early March to approximately more than 10,000 in April 2020. The vast majority of these ICU beds was specifically dedicated to the management of critical patients infected by COVID-19 and this certainly contributes to the decrease in organ donation activity. Second, all surgical teams including intensivists, anesthesiologists, surgeons and operative room nurses have been progressively redirected to manage COVID-19 patients, complicating logistics for organ procurement and transplantation surgery at the same time. Third, kidney and pancreas transplantation programs in France have been suspended since March 20<sup>th</sup> 2020,

greatly contributing to the decrease in organ procurement activity.

Meanwhile, there has been a reduction in LT program activity. This result was particularly observed in the departments and transplant centers located in the North East region (the main cluster area in France). This finding was also reported by other European centers [9,10]. Again, this may be due to several reasons: 1) as all ICU beds and the majority of healthcare transplant professionals were specifically dedicated to the management of severe COVID-19 infected patients, this led to the restriction of ICU beds for the management of LT recipients in the postoperative course, 2) as data regarding the impact of organ donation from donors infected with COVID-19 do not exist, these patients were excluded from organ donation, 3) all French centers have limited LT to the most urgent cases on a case-by-case selection process (i.e, acute liver failure or high MELD score > 30). Hence, all remaining patients including those with hepatocellular carcinoma (who usually had low MELD score) are put in temporary contraindication for LT [11]. Further studies will be necessary to evaluate the impact of the COVID-19 outbreak on waitlist mortality and dropout rate due to HCC progression, and 4) like many other countries [12], the French government ordered the containment on March 17<sup>th</sup> 2020, to limit the extent and speed of diffusion of the COVID-19 epidemic. The debate about the shortage of masks only reserved for health professionals and patients at risk of infection from the COVID-19, as well as the higher incidence of severe forms, eventually lethal, of COVID-19 in elderly and patients with comorbidities, often led liver transplant candidates to be reluctant to receive LT during this endemic period [2,13].

Finally, the proportion of patients who underwent "urgent" LT due to severe acute liver failure was relatively stable during the study period, demonstrating our strong voluntarist policy to maintain LT only to most "urgent" cases



**Figure 4** Regional and center variations of the liver transplantation program activity. Variations shown in regard to: (A) the percentage of decrease in liver transplantations at a regional level, (B) the number of liver transplantations at a regional level, (C) the percentage of decrease in number of liver transplantations at a center level, (D) the number of liver transplantations at a center level.

for which the risk of death within the 3 months is higher than the risk of being infected with COVID-19.

Finally, similar to data from the United States and Italy and to what has already been published on the impact of COVID-19 on transplants in France, our findings are somewhat different because we specifically investigated

regional and monthly variations in procurement and number of transplants. Another limitation of this study was the relatively short study period of six months. However, as this is a highly dynamic topic and the available information is changing continuously, we feel that this study is contemporary and provides novel information based

on the current, rapidly changing landscape of COVID-19.

In conclusion, this observational study showed that the COVID-19 outbreak dramatically impacts on organ and liver transplantation programs. Further studies are needed to evaluate the impact of the COVID-19 outbreak on survival of liver transplant candidates who will be temporarily contraindicated for LT due to the COVID-19 storm:

### Funding sources

None.

### Declaration of interests

None.

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