

Liver Transplantation During COVID-19 Pandemic: Experience of a Single High-Volume Italian Center in the Eye of the Storm

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ABSTRACT

The first wave of coronavirus disease 2019 (COVID-19) pandemic accounted for roughly 35,000 deaths in Italy and was mainly concentrated in the industrial north of the country. Despite Italy returned to a partial lockdown during December, the number of people dying in the second wave has now surpassed the toll recorded in the first. This report aims to provide a snapshot of the impact of COVID-19 on liver transplantation activity in our Institution, with special regard to the measures put in place to guarantee through the two waves of the pandemic. LT activity continued in our Institution despite the heavy pandemic burden without being stopped a priori, but evaluating each organ offer based on the resources available. During the first wave of COVID-19 (February 2020–June 2020), 48 LTs were performed in our Institution with minor monthly variations. As of December 31, 2020, during the ongoing second wave of COVID-19, 118 LTs have been performed. Yet, the number of LTs performed remained stable in 2020 compared to the 127 LTs performed in 2019. Preserving LT activity was possible and safe with specific precautions, strong team motivation, and cooperation.

Key words: severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), organ donation and transplantation, donor and recipient screening, immunosuppression

Abbreviations:

BAL: Bronchoalveolar lavage;
COVID-19: coronavirus disease 2019;
HCC: hepatocellular carcinoma;
ICU: intensive care unit;
LDLT: living donor liver transplantation;
LT: liver transplantation;
NFS: nasopharyngeal swabs;
RT-PCR: reverse transcription-polymerase
chain reaction.

INTRODUCTION

The impact on the Italian national healthcare service of the coronavirus disease 2019 (COVID-19) pandemic has already been reported (1,2). Starting at the end of July, a potential second wave of COVID-19 infection seemed to arise differently in Europe. Indeed, after a decrease during summer, Italy suffers a disproportionate toll in the second COVID-19 wave (3,4). The first wave of pandemic accounted for roughly 35,000 deaths and was mainly concentrated in the industrial north of the country. Despite Italy returns to a partial lockdown during December, the number of people dying in the second wave has now surpassed the toll recorded in the first.

As of January 31, 2021, the ongoing pandemic COVID-19 outbreak has continued to spread with over 2.494.758 confirmed cases and 85.664 deaths (3,4).

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The number of patients infected in Italy since 21 February 2020 through the two waves challenged our universal-coverage public healthcare system especially in terms of the availability of intensive care unit (ICU) beds, and healthcare provider, and potentially affected liver transplantation (LT) programs.

The mission of the COVID-19 Lombardy Intensive Care Unit (ICU) Network was to coordinate the critical care response to the outbreak, identifying top priorities such as increasing ICU capacity and implementing containment measures (2).

Through the two COVID-19 waves, respectively from March 2020 to June 2020 and from September 2020 to January 2021, the ICU bed capacity of our public tertiary hospital (ASST Grande Ospedale Metropolitano Niguarda, Milano) was increased up to 250% (from 35 to >150), and almost all of the anesthesiologists and operative room nurses have been progressively moved to the COVID-19 ICUs, complicating logistics for organ procurement and transplant surgery at the same time (5,6).

In these circumstances, COVID-19 could have inevitably impacted transplant activity. Before the COVID-19 pandemic, the dedicated ICU serving abdominal organ transplant recipients admitted approximately 150 patients/year to our Hospital. As a result of the emergency measures put in place, especially during the first wave, almost all elective surgery has been canceled, except for major urgent oncological procedures.

Our Hospital's trauma center and its neuro-ICU for patients with all types of neurosurgical and neurological injuries continue to be operational, and we have a dedicated ICU bed for donor management. Critical admissions use dedicated COVID-19-free pathways.

Mitigation strategies were put in place to ensure the availability of transplant activity in our Hospital, and a special COVID-19 donor/recipient protection protocol introduced, as already reported by others (7-9).

In Italy, the National Center for sharing and management of the Transplant network (CNT) has recommended some guidelines for solid organ transplantation as mentioned below in the text (5).

Most importantly, regardless of the presence or the absence of COVID-19 symptoms, all organ transplant recipients and donors have been systematically tested for the presence of covid-19 before approving organ procurement and transplantation procedure.

This report aims to provide a snapshot of the impact of COVID-19 on LT activity in our Institution, and measures put in place to guarantee LT through the two waves of the pandemic.

Living donor liver transplantation activity

Living donor LT (LDLT) poses significant issues during the pandemic due to the risk of nosocomial transmission to donors and recipients. During the first pandemic wave, LDLT activity nearly stopped in most European countries and was performed seldomly in the US (7–9). Given the elective nature of the procedure, we considered postponing LDLT, as well as living donor kidney transplantation, as the ethically appropriate action, and no cases of LDLT were performed in our Institution through 2020. In urgent cases we put the patients in the deceased donor waiting list.

Donors and recipients' screening

In all cases, we performed molecular testing with reverse transcription-polymerase chain reaction (RT-PCR) on donors and recipients, as strongly recommended by most scientific societies worldwide (10–12). Significant variability in the false-negative rate has been reported in the literature in testing for SARS-CoV-2 by nasopharyngeal swabs (NFSs) (8,13). For this reason, we interpreted the results alongside clinical history and chest X-ray. Bronchoalveolar lavage (BAL) was used for deceased donor screening, as it has a very low false-negative rate (14).

Positive donors and recipients were excluded from the program in this setting.

Hospitalization

The Niguarda Hospital was heavily involved in the management of COVID-19 since the very beginning of the outbreak in Italy on 21 February 2020. We were therefore obliged to design COVID-safe clinical pathways for LT recipients during their entire hospital stay.

In compliance with our transplant protection strategy, every transplant patient was admitted to a dedicated ICU strictly not serving COVID-19 patients.

Like other centers during the first pandemic wave, we preferred suspending family visits during the post-transplant course and giving information to the relatives by phone (15).

There is limited guidance related to immunosuppression management during the pandemic. Some authors have initially suggested a reduction in using lymphocyte depletion therapy for induction immunosuppression during the pandemic to reduce the risk of nosocomial infection (11,16).

We maintained our standard immunosuppression protocol, including basiliximab induction with steroid, tacrolimus, and the addition of mycophenolate in the case of encephalopathy or kidney injury.

Patients follow-up

A recent survey from Germany has shown that LT patients more often canceled or postponed scheduled clinical visits for fear of becoming infected with SARS-CoV-2 (17). A thorough follow-up is crucial for LT patients, who are prone to surgical and medical complications. At our Institution, the follow-up was performed preferably by telemedicine. We established a telephone and email hotline that enabled the transplanted patients to get consultation directly from the liver transplant team. This practice drastically reduced the ambulatory and hospital access of this high-risk group of patients.

Liver transplantation activity at Niguarda Hospital

In Italy, the first lockdown started on March 9th and ended on May 18th, and Lombardy, which includes Milan, was the worst-hit area in Italy's March crisis - and it was one of Europe's first coronavirus hotspot (3,4).

September 2020 signed the beginning of the second wave of the COVID-19 outbreak in Italy. From November 4, 2020, a partial lockdown started, and Italy was split into three zones: red for high risk, then

orange and yellow, and Lombardy has always been red or, less frequently, orange.

During the period of the first outbreak, we performed 16 liver transplantations (LT), accounting for 66% (16/24) of all the LTs performed in Lombardy (5) which includes other 3 liver transplant centers, and 8 local donors were used, while 2 others were rejected because of a Covid-19 positivity. Compared to the same study period in 2019 (17 LT performed; 8 local donors evaluated), transplant activity in our Hospital has been fairly similar, although data for the whole of Italy show a 25% reduction in organ procurement during the first month of the COVID-19 outbreak (3). Besides, considering the entire period (the year 2020), 118 LTs were performed at our Institution, accounting for 45.4% (118/260) of all the LT activity in Lombardy in the 4 operative LT Centers. Overall, the number of LTs performed in Italy also decreased from 1277 in 2019 to 1202 in 2020 (-5.9%) (3).

Time variations of the organ procurement and LT activities stratified according to the different pandemic periods were reported in *fig. 1*. During the first wave of COVID-19 (February 2020 – June 2020) 48 LTs were performed in our Institution with minor monthly variations. As of December 31, 2020, during the ongoing second wave of COVID-19, 118 LTs have been performed. Yet, the number of LTs performed remained stable in 2020 compared to the 127 LTs performed in 2019.

Recipients receiving LT in the two lockdown periods had similar indications with respect to other time

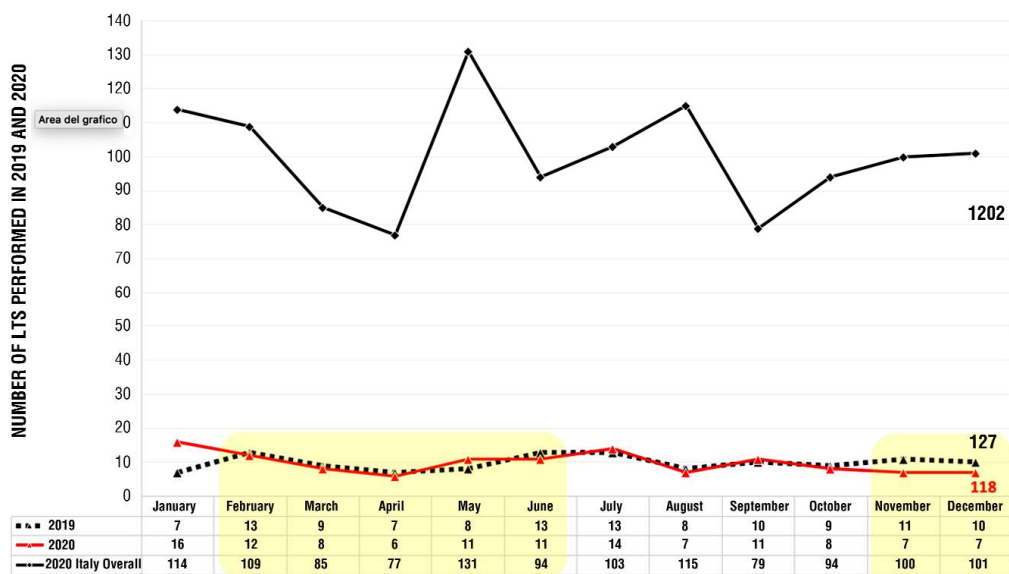


Figure 1 - Time variations of liver transplant activities at our Institution during the COVID-19 pandemic

periods. The majority were more likely to have hepatocellular carcinoma (HCC) (28/46; 60.9%) with a relatively low MELD score (mean MELD, 24; range 16-36) except for 5 urgent retransplantations. The predominance of HCC recipients is a specific feature of our waitlist. No restrictions to our allocation policy, which is not based exclusively on the MELD score, were introduced during this period (5).

Fortunately, there has been no significant increase in waitlist mortality and dropout due to HCC progression during the pandemic waves.

CONCLUSIONS

The numbers reported confirm the need to protect the donation and transplant process while of course ensuring that all procurement and transplant procedures follow a coronavirus-free pathway for donors, recipients, and the clinicians involved.

Further studies will be necessary to evaluate the impact of organ procurement from COVID-19 donors on transplant activity. LT activity continued in our Institution despite the heavy pandemic burden without being stopped a priori but evaluating each organ offer based on the resources available at the moment. Our hospital, despite its severe involvement in the treatment of COVID-19 patients, resulting the second hospital in Lombardy, after Bergamo, for the number of patients admitted to hospital, maintained a routine transplant activity.

Preserving LT activity was possible and safe with specific precautions, strong team motivation, and cooperation.

Conflict of interest

The authors of this manuscript have no conflicts of interest to disclose.

Ethics of approval

No formal ethical approval was required, given the retrospective, observational, and anonymous nature of this report.

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