Brazilian Journal of TRANSPLANTATION

https://doi.org/10.53855/bjt.v27i1.530_ENG
Preprint deposited on: Nov 27, 2023 [https://doi.org/10.1590/SciELOPreprints.7285]
ORIGINAL PAPER

Perioperative Analysis of Patients Undergoing Liver Transplantation at the Hospital de Clínicas of Unicamp in the Context of SARS-Cov-2 Pandemic

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Section Editor: Edna Montero

Received: 01 Sep 2023 | Accepted: 11 Jan, 2024

ABSTRACT

Introduction: SARS-CoV-2 began in 2020 and caused important changes in the number of transplants performed in hospitals and in the protocols for admitting candidates to perform the procedure. The Brazilian Association of Organ Transplantation (ABTO) recommends not performing transplants from donors with active COVID-19 infection, positive test results or with Severe Acute Respiratory Syndrome. The hepatic repercussions related to COVID-19 are presented in some reports in the medical literature. Liver changes resulting from other corona viruses such as SARS-CoV and MERS-CoV are well documented. The Hospital de Clínicas of the State University of Campinas is a tertiary center that performs solid organ transplants. **Objectives:** To carry out a perioperative, retrospective, descriptive analysis of liver transplants in the context of the SARS-CoV-2 pandemic carried out at the Hospital das Clínicas of the State University of Campinas from March 2020 to July 2021. **Materials and Methods:** Retrospective, descriptive, longitudinal cohort study based on the review of medical records of patients undergoing liver transplantation in the context of the SARS-CoV-2 pandemic from March 2020 to July 2021 at the clinical hospital of the State University of Campinas. **Results:** Retrospective analysis was performed on 57 patients in the period. Only 1 patient needed to be excluded because he was under 18 years old. Of the 56 patients, 52 underwent RT-PCR laboratory testing and chest tomography (CT). Of these 52 patients, only 2 tested positive, one pre-transplant (TX) and one post-operatively (post-op). Regarding chest CT scans, none of them showed typical changes for COVID pre-TX, in the post-op 4 patients presented typical chest CT scans. The average age was 55.86 years. The mortality rate was 38% and no deaths were attributed to COVID 19. The average MELD-Na scale was 20.94. **Conclusion:** The present study carried out at the Hospital de Clínicas da Unicamp analyzed the clinical, laboratory and radiological association to better elucidate the variables determined by COVID-19 in its diagnosis and in-hospital management. It is concluded that the SARS-CoV-2 pandemic had an impact on the routine of liver transplantation worldwide and on the service in which the study was carried out.

Descriptors: COVID 19; Chest CT; Liver Transplant; RT-PCR.

Análise Perioperatória dos Pacientes Submetidos a Transplante Hepático no Hospital de Clínicas da Unicamp no Contexto da Pandemia de SARS-Cov-2

RESUMO

Introdução: A pandemia causada pelo SARS-CoV-2 teve início no ano de 2020 e ocasionou mudanças importantes no número de transplantes realizados nos hospitais e nos protocolos de admissão de candidatos para realização do procedimento. A Associação Brasileira de Transplante de Órgãos (ABTO) recomendava não realizar transplante de doadores com infecção COVID-19 ativa, teste positivo ou com Síndrome Respiratória Aguda Grave. As repercussões hepáticas relacionadas a COVID-19 são apresentadas em alguns relatos presentes na literatura médica. Estão bem documentadas as alterações hepáticas decorrentes de outros coronavírus tais como SARS-CoV e MERS-CoV. O Hospital de Clínicas da Universidade Estadual de Campinas é um centro terciário que realiza transplantes de órgãos sólidos. **Objetivos:** Realizar a análise retrospectiva descritiva perioperatória dos transplantes hepáticos no contexto da pandemia

por SARS-CoV-2 realizados no hospital das clínicas da Universidade Estadual de Campinas no período de março de 2020 a julho de 2021. **Materiais e Métodos:** Estudo retrospectivo, descritivo de coorte longitudinal baseado na revisão dos prontuários dos pacientes submetidos ao transplante hepático no contexto da pandemia por SARS-CoV-2 no período de março de 2020 a julho de 2021 no hospital de clínicas da Universidade Estadual de Campinas. **Resultados:** A análise retrospectiva foi realizada em 57 pacientes no período. Apenas 1 paciente precisou ser excluído por ter menos de 18 anos. Dos 56 pacientes, 52 realizaram coleta do exame laboratorial RT-PCR e tomografia (TC) de tórax. Desses 52 pacientes apenas 2 positivaram o exame, um pré transplante (TX) e um no pós-operatório (pós-op). Em relação às TC de tórax nenhuma apresentava alterações típicas para COVID pré-TX, no pós-op 4 pacientes apresentaram TC típicas. A média de idade foi de 55,86 anos. A taxa de mortalidade foi de 38% e nenhum óbito foi atribuído ao COVID 19. A escala de MELDNa média foi de 20,94. **Conclusão:** O presente estudo realizado no Hospital de Clínicas da Unicamp analisou a associação clínica, laboratorial e radiológica para melhor elucidar as variáveis determinadas pela COVID-19 no seu diagnóstico e manejo intra-hospitalar. Conclui-se que a pandemia por SARS-CoV-2 teve impacto na rotina de realização do transplante hepático mundialmente e no serviço no qual o estudo foi realizado.

Descritores: COVID 19; Tomografia de Tórax; Transplante de Fígado; RT-PCR.

INTRODUCTION

The pandemic that began in 2020, caused by SARS-CoV-2, has led to major changes in the number of liver transplants (Tx) performed in hospitals and in the protocols for admitting candidates for this procedure[1,2].

At the time, it was suggested that patients infected with COVID-19 (C-19) undergoing solid organ transplantation could have worse outcomes compared to those transplanted without this disease3. In a systematic review, Nacif and collaborators demonstrated a higher mortality rate in patients over the age of 60 affected by this pathology[4].

Since the beginning of the pandemic, several countries have seen a significant reduction in the number of transplants performed, with a decline of up to 90% [2,5,6].

The Brazilian Organ Transplant Association (ABTO, in Portuguese) advised against transplanting donors with active COVID-19 infection, a positive test, or with Severe Acute Respiratory Syndrome[7].

The recommendation for asymptomatic recipients, according to ABTO, was to collect a swab and perform a chest computed tomography (CT) scan, and even with negative tests, patients should be warned about the risk-benefit of surgery[8].

Hepatic repercussions related to COVID-19 were described in a systematic review by Kumar-M and collaborators, highlighting hypoalbuminemia as the main repercussion, followed by elevated gamma-glutamyl transferases and aminotransferases[9].

Other extrapulmonary systemic disorders, such as alterations in the immune system, cardiovascular system, gastrointestinal system, genitourinary system, endocrine and neurological systems, have also been reported[10].

An important relationship has been observed between the C-19 virus and angiotensin-converting enzyme 2 receptors, as well as inflammatory cytokines in organ damage in general[11].

Complications such as bile stasis resulting in liver damage and dilated bile ducts, direct pancreatic cell damage, direct effects of renal endothelial cell damage, and inflammatory response with coagulopathy, interstitial or hemorrhagic cystitis or solid organ infarcts can occur in COVID-19 patients[11-13].

The "Hospital de Clínicas" of the State University of Campinas, a tertiary center that performs solid organ transplants[14], was also impacted by the global event related to SARS-CoV-2, presenting changes in the internal management of the transplant service.

The perioperative analysis during this period remained unknown, becoming an important factor in the prognosis and management of these patients.

OBJECTIVES

To carry out a retrospective descriptive perioperative analysis of liver transplants in the context of the SARS-CoV-2 pandemic, carried out at the Hospital de Clínicas of the State University of Campinas between March 2020 and July 2021. In addition, to relate factors associated with the evolution and outcome of this population.

MATERIALS AND METHODS

This study adopts a retrospective, descriptive, longitudinal cohort approach, based on a review of anesthetic records and the medical records of patients who underwent liver transplantation between March 2020 and July 2021 at the Hospital de Clínicas of the State University of Campinas. The project was approved by the Research Ethics Committee (CAAE 52496821.0.0000.5404).

Inclusion criteria:

Patients undergoing liver transplantation over the age of 18.

Exclusion criteria:

Patients undergoing liver transplantation under the age of 18 in the period studied.

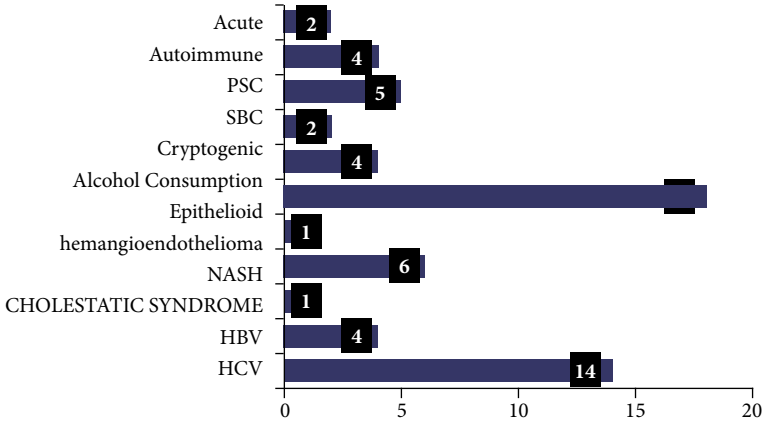
RESULTS

We carried out a retrospective analysis involving 57 patients from March 2020 to July 2021 at the Hospital de Clínicas of the State University of Campinas. During this evaluation, we consulted laboratory and radiological data and medical records. The median age of the patients was 55.9 years (range 24–75 years), with only one patient excluded for being under 18 years.

The median pure MELD-Na score (without the addition of exception points) was 20.9 (range 6 to 42), excluding the two cases of acute hepatitis. In terms of gender distribution, 17 patients (30.4%) were female gender, and 39 patients (69.6%) were male gender.

The most common underlying diseases that led to liver transplantation were alcoholism in 18 cases (32.1%), hepatitis C virus infection in 14 cases (25%), non-alcoholic fatty liver disease in 6 cases (10.7%), primary sclerosing cholangitis in 5 cases (8.9%), and autoimmune hepatitis in 4 cases (7.1%). It should be noted that some patients had more than one underlying disease.

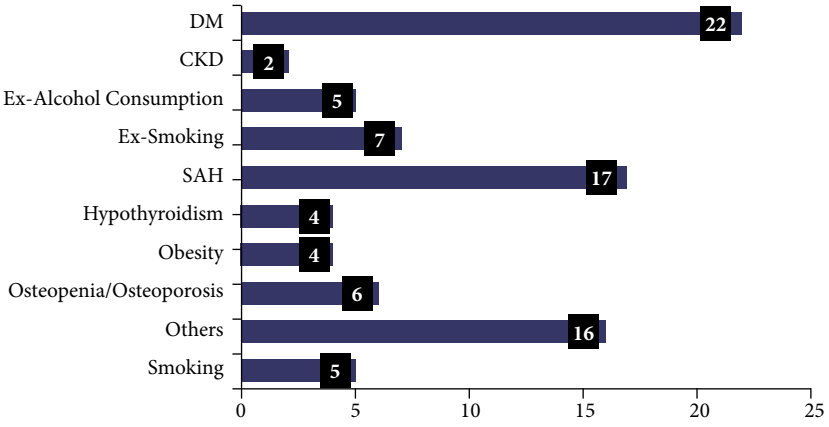
Regarding the presence of hepatocellular carcinoma (HCC), 15 patients (26.8%) were diagnosed with this condition, while 41 patients (73.2%) were not affected by this pathology (Fig. 1).



Source: Elaborated by the author, data from the Hospital de Clínicas Unicamp electronic medical record.

Figure 1. Underlying diseases of transplant patients.

The most frequent comorbidities were diabetes mellitus in 22 (39.2%), hypertension in 17 (30.3%), and some patients had more than one pathology (Fig. 2).



Source: Elaborated by the author, data from the Hospital de Clínicas Unicamp electronic medical record.

Figure 2. Comorbidities of transplant patients.

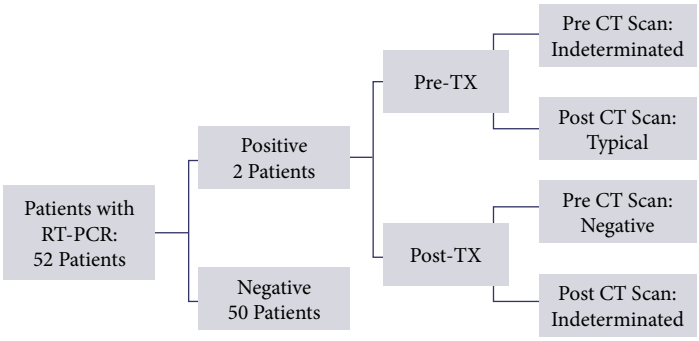
The mortality rate during the study period was 21 (38%). According to the records in the medical charts and progress reports, no deaths were attributed to the infection caused by COVID-19. It is worth noting that three patients (5.3%) were on dialysis with grade 3 ACLF (acute to chronic liver failure), and one patient (1.8%) had grade 4 ACLF. Postoperatively, 27 patients (48.2%) required dialysis and seven (12.5%) required re-intubation.

The causes of death recorded were infections not related to COVID-19 in nine cases (16.1%), primary graft failure in five cases (8.9%), complications resulting from severe graft dysfunction in four cases (7.1%), two hepatic artery thromboses (3.6%), and one recurrence of HCC (1.8%).

Of the 56 patients, 52 underwent laboratory tests and a pre-X-ray chest CT scan. Four patients did not have a chest CT scan or RT-PCR due to a lack of tests at the start of the pandemic, following ABTO's determination to only collect RT-PCR for some patients.

Of the 52 patients, only 2 showed positive results in the RT-PCR test. The first had a positive result preoperative (pre-op.), but the test was released after the anesthetic-surgical procedure. This patient was asymptomatic, and his chest CT scan was negative for COVID-19. Postoperatively, the CT scan became typical for COVID-19. The second patient tested positive in the postoperative period (post-op) of his liver transplant while he was on the ward, after having contact with another patient who tested positive. It should be noted that this patient's CT was undetermined during the positive PCR.

RT-PCR tests were collected in the post-operative period regardless of the presence of respiratory symptoms, following the protocols of the Hospital Infection Commission. These protocols changed over the year, but on average, the tests were carried out within 3 to 5 days (Fig. 3).



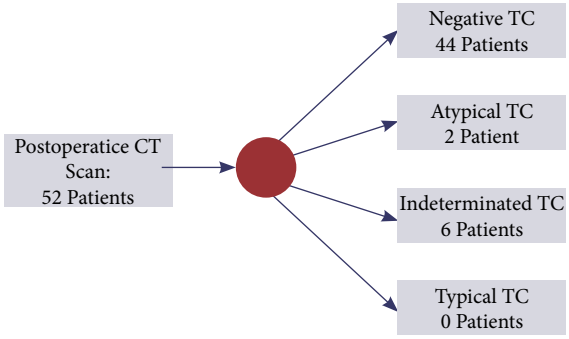
Source: Elaborated by the author, data from the Hospital de Clínicas Unicamp electronic medical record.

Figura 3. Pacientes com RT-PCR coletados.

Radiological findings were analyzed according to the Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19[15].

Of the 56 patients, 52 underwent pre-X-ray CT and 32 underwent post-operative CT. Post-op CT scans were performed when the transplant patient had any respiratory symptoms.

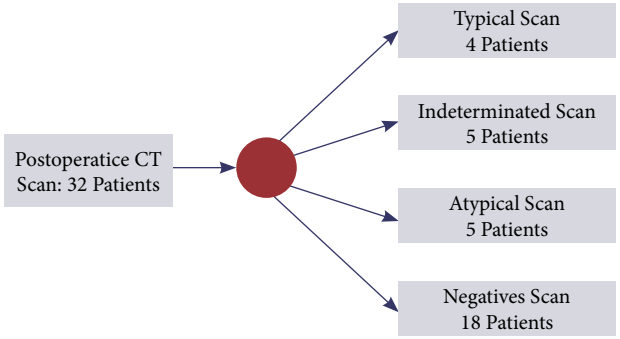
The results of the pre-transplant CT scans were as follows: 44 negative, 2 atypical, 6 indeterminate, and no typical (Fig. 4).



Source: Elaborated by the author, data from the Hospital de Clínicas Unicamp electronic medical record.

Figure 4. Pre-TX chest CT scan

The results of the 32 postoperative (post-op) CT scans were as follows: 4 patients had typical CT scans for COVID-19, including the patient with a positive RT-PCR pre-transplant (TX - whose result was released after surgery) and who initially had an indeterminate CT scan on entry; 5 patients had indeterminate CT scans; 18 showed negative characteristics; and 5 were considered atypical (Fig. 5).



Source: Elaborated by the author, data from the Hospital de Clínicas Unicamp electronic medical record.

Figure 5. Post-TX chest scan.

DISCUSSION

Regarding the patients studied, a higher pure MELDNa score was observed compared to that found in the scientific literature, as well as a higher mortality rate. A study using the United Network for Organ Sharing database, carried out between February 2002 and June 2016 (n=64977), showed a mortality rate of 5% in 90 days and 10% in 1 year after liver transplantation[16]. Naturally, the difference in mortality between the sample in that study and the one in our study may be influenced by the size of the sample itself, the high MELDNa score and the seriousness of the patients in our analysis.

We can infer that the measures adopted, such as performing RT-PCR pre-surgery and every three to five days on all patients, preoperative chest CT scans, postoperative CT scans on symptomatic patients as well as early isolation of suspicious patients, were highly effective regarding the mortality rate since no deaths can be attributed to COVID-19.

Regarding the screening of patients who are candidates for liver transplantation, we can infer that the standards recommended by the Brazilian Association for Organ Transplantation (ABTO) have proved to be effective in dealing with this disease.

Of the 52 patients who underwent chest CT and RT-PCR, only 1 had a positive PCR for COVID-19 (a result released after surgery).

The norms were for asymptomatic patients to have a negative chest CT and RT-PCR, and these guidelines are still in force today.

In the post-operative period, we can consider that the measures adopted to contain the spread of COVID-19 were satisfactory, since, among these 52 patients, 4 were diagnosed as positive for SARS-CoV-2, 1 with a positive RTC-PCR and 4 with typical alterations on chest CT.

The definitive diagnosis of COVID-19 is obtained through RT-PCR; however, this can be false negative even in symptomatic patients[17,18].

According to Rosa et al., changes characteristic of the disease can be identified in the chest CT[19] even before the RT-PCR results become positive.

Imaging findings do not replace RT-PCR for diagnosis, but using these tests together is an extremely valuable tool[19].

In our study, the importance of this association is evident, since only 2 patients had positive RTCs. The patient who had a positive RTC before transplantation (TX) only had a typical CT scan in the postoperative period, and the patient who had a positive scan in the postoperative period had an indeterminate CT scan. The other 3 patients who had typical CT changes had a negative CTC.

Other important issues to be addressed in this period include the stress of healthcare teams, the exhaustion caused by overwork (known as burnout), and the costs involved.

The emergence of a new disease led to changes in hospital routines during the period studied[20].

The new measures adopted were aimed at containing the disease, including the early isolation of patients with any respiratory symptoms, the collection of multiple tests, the intensive assessment of hospitalized patients, and the frequent change of protective equipment, among other actions[20].

These new routines have brought an overload of work for professionals, aggravated by the absence of several of them. Some of the remaining professionals developed burnout[21,22], stress[23] as well as depression[24].

It was not uncommon for professionals to report insomnia, tiredness, crying, and a change in behavior at home and the workplace, among other symptoms. This issue will possibly be addressed in a future paper.

As for hospital costs, it is assumed that there may have been an increase during this period. In addition to the tests usually carried out for this type of surgery, such as blood count, coagulation, chest X-ray, urea, creatinine, and albumin[25], among others,

there were also numerous pre-transplant and post-transplant RT-PCRs, pre-transplant chest CT scans, CT scans on all patients who presented any respiratory symptoms, and excessive use of protective equipment, among other factors.

Measuring this increase correctly or conducting a cost-effectiveness study in this period would be an extremely arduous task in the Brazilian Unified Health System (SUS, in Portuguese).

As examples of these difficulties, we have the price of computed tomography (CT) scans by the SUS[26], while the RT-PCR test is listed as zero cost. We would only have the price of private laboratories[27] at the time. We can cite other difficulties, such as calculating the cost of a health professional's leave of absence and the cost of Personal Protective Equipment (PPE), as this was also donated.

CONCLUSION

This study carried out at Hospital de Clínicas Unicamp analyzed the clinical, laboratory, and radiological association to better elucidate the variables determined by COVID-19 in its diagnosis and in-hospital management. Although in a small sample, the selection of candidates for transplantation (TX) with the triad: asymptomatic patient, negative RT-PCR, chest CT without typical alterations for SARS-CoV-2 proved to be effective in avoiding the anesthetic-surgical procedure in the presence of COVID-19. In the postoperative period, early isolation of patients with respiratory symptoms, chest CT, and laboratory testing are the best means of preventing the spread of the disease.

We conclude that the SARS-CoV-2 pandemic has had an impact on the routine of liver transplantation at the service where the study was conducted. In addition, the repercussions and data from this pandemic context collected in this study can serve as a basis for other future analyses, as well as contribute to better elucidating the impact of COVID-19 on liver transplantation.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

CONTRIBUTION OF THE AUTHORS

Substantive scientific and intellectual contributions to the study: Caruy CAA, Melo MS, Boin IFSFB; **Conception:** Melo MS, Munhoz DC; **Data analysis and interpretation:** Dertkigil SSJ, Miyoshi AH, Mecchi TL, Miyoshi IC, Perales SR; **Writing of the article**: Melo MS; **Critical revision:** Cardoso AR, Ataíde EC; **Final approval:** Boin IFSFB.

AVAILABILITY OF RESEARCH DATA

The entire set of data supporting the results of this study has been published in the article itself.

FUNDING

Not applicable.

ACKNOWLEDGEMENTS

Not applicable.

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