Title of study: Impact of the SARS-CoV-2 (COVID19) pandemic on the morbidity and mortality of patients undergoing surgery at Bellvitge University Hospital

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Idibell Group: Perioperative physiology and pain

Introduction:

The coronavirus have been the cause of mild and moderate respiratory infections. Types 229E, HKU1, NL63 and OC43 are responsible for the common cold. But others like SARS CoV (2002) and MERS-CoV (2012) will generate severe respiratory infections and nosocomial infections[1].

In December 2019, a disease produced by a new coronavirus, SARS-CoV-2, was detected in Wuhan (Hubein Province, China) and was named COVID-19 (Coronavirus Disease 2019). Since then, it has spread rapidly throughout the world and was declared a pandemic by the WHO on 11 March 2020. At least 15% of the total number of cases develop significant respiratory complications (adult respiratory distress syndrome) and significant morbidity and mortality.

Actually, Spain is one of the countries with the highest rate of infection. The latest statistics (dated on 24th May 2020)[2,3] refer to a total of 235,290 confirmed cases, and 28,706 of them have died. This situation has required the transformation of conventional hospitalisation beds into specific areas for COVID patients.

Bellvitge University Hospital (HUB) need to increase the number of COVID-19 critical care beds to a total of 108 during the period of maximum health emergency, which has been determined since 11th March 2020 (when the first case of COVID-19 was admitted to the ICU at our hospital) until 15th May 2020. The number of COVID-19 patients who required an ICU at the HUB during this period of time was 224.

In order to cover the needs of critical COVID-19 pathology, a specific care circuit was generated for these patients and surgical spaces had to be reconverted into critical care areas. During this period, Bellvitge University Hospital treated 186 patients with non COVID-19 critical pathology.

Despite this reorganisation and during this same period, the number of surgeries performed at the HUB, amounts to 789.

Different authors have assessed that during the pandemic, there has been an increase in morbimortality in patients who have undergone surgery[4,5,6,7]. In a similar analysis, a rate of infection of 16% and a mortality rate, due to respiratory failure, of 1.7% in cancer patients who were operated in the month before and during the peak of the pandemic[8].

The aim of this study is to evaluate the complications generated in patients during this period of COVID crisis in our centre. The analysis of these data will help us to assess which measures are essential to take into account in the event of a future outbreak.

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Hypothesis:

At Bellvitge University Hospital (HUB), a specific circuit was created in order to keep the emergent and the scheduled surgical activity that cannot be delayed, following measures of security established during the pandemic. We consider that this measures have contributed to contain the rate of infection of these patients and the post-operative complications that have occurred during the maximum crisis period, generating a control of quality of care and security.

For this reason, the sample of operated patients will be compared with a sample of patients adjusted to the month of January, before the crisis of the pandemic.

As a working hypothesis, we consider that there are no differences, and therefore, we propose the study as a non inferiority in terms of the assistance results.

Objective:

Our objectives are:

1. Assess all patients who have underwent surgery in our hospital during the period of maximum crisis of the pandemic, from March 11, 2020 to May 15, 2020.

2. Determine the post-surgical complications that have occurred during this period.

3. Determine the rate of COVID-19 infections in these patients and the secondary complications generated by them.

4. Be able to compare with series adjusted for types of surgery, characteristics of the surgery, age and sex in the pre-pandemic period (January 2020).

5. Propose some potential improvements in the context of the health crisis

Methodology:

Design and sample size:

Observational study, that includes all patients who have undergone emergent or scheduled surgery from March 11th 2020 until May 15th 2020, with a total of 789 surgical interventions recorded during this period.

Data collection:

Our source of information will be basically the access to the virtual clinical history (SAP) of the patients and the closing of the episode according to the Minimum Data Set (MDS). Only data of

interest for this research will be obtained, and in any cases, data that can be directly linked to patients (name, address, telephone number, etc.) will be used, preserving the confidentiality of the data. The variables of interest to be extracted from the clinical history to configure our data base will be:

- Age.
- Sex.
- Functional State according to ECOG (available in the annex).
- Personal antecedents of interest.
- Diagnosis of the pathology to be operated.
- Day of surgery.
- Type of surgery:
    - Specialty: general surgery, thoracic surgery, traumatology, neurosurgery, vascular surgery, neck and face surgery, urology...
    - I fit consists on an emergent surgery or a scheduled surgery.
    - Delayable (benign) or non-delayable (malignant) surgery.
- Postoperative complications according to Clavien Dindo classification (available in the annex).
- Infection by COVID-19?
- Date of confirmation of the SARS-CoV-2.
- Treatment required by SARS; determined by groups.
- Hospital stay in days.
- Mortality.
- To asses the severity of the COVID-19 infection, we will use the Brescia Respiratory COVID19 Severity Scale (available in the annex).
- In addition, we will evaluate the therapeutic measures applied in each patient in case of COVID-19 infection (available in the annex).

Exclusion criteria:

1. Surgeries related to complications in the treatment of COVID patients.
2. Patients with incomplete data.

Selection criteria of the control sample (January 2020):

The selection will be made according to the type of surgery, sex and age range. In order to ensure that the sample is not inferior, the procedures chosen will be analysed with a ratio of 2:1 and 1:1 for patients undergoing emergent surgery, using as a reference the patients included during the COVID19 period, according to the list elaborated by Surgical Planification Department, where no operating results have been recorded (blind).

Statistical treatment:

It is considered a non-inferiority study, with a maximum difference in the percentage of patients with complications according to the Clavien Dindo classification of 10% and 2% in the percentage of patients with death result.

A descriptive analysis will be carried out using the usual statistical tests: Chi-square test to compare the category variables, and the subtraction of variables using parametric or non-parametric tests for the continuous variables (depending on the normality of the variables). For all the variables, bilateral tests with a significance level of 5% will be used.
It should be noted that the results will be analysed after the selection of patients included.

Possible limitations of the study:

The retrospective aspect of the study will limit the value of the study. There may be a lack of information about some interesting facts in the clinical history in the postoperative follow-up after the surgical episode at the HUB. In case that some important information is required and not reflected in the Shared Clinical History of Catalonia, it could be completed by telephone contact with patient and/or relatives to avoid information bias. In case of not having it, it will be treated as "missing data" in the subsequent analysis of the data.

Expected Benefits of the Project:

The comparison with the previous cohort will help us to know if there has been a higher rate of morbidity and mortality.

We will also analyse the rate of infection by COVID-19 in post-operative patients during this period of time.

This will allow us to know the complications and infections that occurred during this period of pandemic and we will be able to search and discover avoidable situations and establish our own circuits and protocols to avoid them in the future.

It will help us to establish a quality control in our centre, because, since now, it will be necessary to coexist with COVID-19 for an undetermined period of time (infections still happen daily and, by the moment, there is not a treatment or an effective vaccine to eradicate it)

If we are able to identify the weak points of our system, if they are detected, we will avoid repercussions on the health of our patients and we will adapt our health resources better.

Ethical Aspects:

As we have already mentioned, only data of interest will be obtained for the research and, in any cases, we will use data that can be directly related to the patients (names, surname, address, telephone numbers...) in order to keep the confidentiality of the data.

Both the centre and the researchers are responsible for data processing and are committed to complying with Regulation (EU) 2016/679 of the European Parliament and the Council of 27th April 2016 on Data Protection (RGPD), as well as other applicable laws and regulations (Organic Law 3/2018 on the Protection of Personal Data and the Guarantee of Digital Rights).

Data collected for the study will be identified by a code, so that it does not include information that could identify it, and only the principal investigators/collaborators will be able to relate these data to the patient and his/her clinical history.

Working Plan:

The timeline is as follows:

1. Presentation and approval by the Ethical Committee.

2. Selection of the study sample according to inclusion and exclusion criteria.

3. Selection of the historical cohort (January 2020) according to adjusted criteria based on surgical planning.

4. Creation of the database of study groups and historical cohort.

5. Analysis and introduction into the database of the patients in the groups based on the closure of the surgical episode.

6. Statistical analysis of the data.

7. Editing and publication.

A working team performed by faculty and residents of the Anaesthesiology and Reanimation Service Department, will collect all the previously mentioned data. It is estimated that in a period of 2 months it is possible to have all the necessary information collected for the analysis and presentation of the results.

Annex:

Degree	ECOG
0	Normal activity without restriction or help.
1	Restricted activity. Walk
2	Incapacity for any working activity. <50% of the time in bed.
3	Restricted capacity for the personal care and personal hygiene. >50% of the time in bed.
4	Total incapacity. Cannot take care of himself. 100% of the time in bed.
5	Dead.

Figure 1: Eastern Cooperative Oncology Group Classification

Degree		Definition
I		Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grades also includes wound infections opened at the bedside.
II		Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions, antibiotics and total parenteral nutrition are also included.
III		Requiring surgical, endoscopic or radiological intervention
	a	Intervention under regional/local anaesthesia.
	b	Intervention under general anaesthesia.
IV		Life-threatening complications requiring intensive care/intensive care unit management.
	a	Single organ dysfunction.
	b	Multi-organ dysfunction.
V		Patient demise.

Figure 2: Clavien Dindo classification. It allows the use of a common language for classifying complications, expressing the degree of them according to the complexity of the treatment used for their resolution, which is easy to apply.

Group	Therapeutical measures applied
O	Symptomatic treatment.
1	Hospitalization with oxygen, antiretrovirals and/or immunomodulators.
2	Hospitalization and ned of corticosteroids at high doses.
3	UCI admittance or Mechanical Ventilation needed.

Figure 3: Stratification of the COVID-19 patients in groups, according to the therapeutical measures applied

the patient is sibling or unable to complete a sentence while at rest or under minimal effort	+1
Respiratory frequency > 22 rpm?	+1
PaO2 <65mmHg o SpO2 <90%?	+1
The Rx chest is getting worse significatively?	+1

Taula 4: BRCSS (Brescia Respiratory COVID-19 Severity Scale)

O ➔ keep patient monitored with pulse oximetry and clinical evaluation. Medications: Lopinavir/ritonavir.

1➔ provide supplemental O2. Keep patient monitored with pulse oximetry and clinical evaluation Medications: lopinavir/ritonavir.

2➔ perform CXR and ABG. Provide supplemental O2. Keep patient monitored with pulse oximetry and clinical evaluation. Medications: lopinavir/ritonavir. Consider dexamethasone Consider age/comorbidities, cognitive decline

3 ➔ trial of non-invasive ventilation (CPAP/BiPAP) or high-flow nasal canula (HFNC) recommended. If above clinical criteria worsening or patient clinically worsening despite this trial, intubation recommended. Otherwise, perform CXR every 2 days and ABG twice a day. Medications: lopinavir/ritonavir Consider dexamethasone and considering starting tocilizumab. Consider age/comorbidities, cognitive decline.