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Impact of the first wave of the SARS-CoV-2 pandemic on the outcome of neurosurgical patients: a nationwide study in Spain

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ABSTRACT

Objective To assess the effect of the first wave of the SARS-CoV-2 pandemic on the outcome of neurosurgical patients in Spain.

Settings The initial flood of COVID-19 patients overwhelmed an unprepared healthcare system. Different measures were taken to deal with this overburden. The effect of these measures on neurosurgical patients, as well as the effect of COVID-19 itself, has not been thoroughly studied.

Participants This was a multicentre, nationwide, observational retrospective study of patients who underwent any neurosurgical operation from March to July 2020.

Interventions An exploratory factorial analysis was performed to select the most relevant variables of the sample.

Primary and secondary outcome measures Univariate and multivariate analyses were performed to identify independent predictors of mortality and postoperative SARS-CoV-2 infection.

Results Sixteen hospitals registered 1677 operated patients. The overall mortality was 6.4%, and 2.9% (44 patients) suffered a perioperative SARS-CoV-2 infection. Of those infections, 24 were diagnosed postoperatively. Age (OR 1.05), perioperative SARS-CoV-2 infection (OR 4.7), community COVID-19 incidence (cases/10⁵ people/week) (OR 1.006), postoperative neurological worsening (OR 5.9), postoperative need for airway support (OR 5.38), ASA grade ≥3 (OR 2.5) and preoperative GCS 3–8 (OR 2.82) were independently associated with mortality. For SARS-CoV-2 postoperative infection, screening swab test <72 hours preoperatively (OR 0.76), community COVID-19 incidence (cases/10⁵ people/week) (OR 1.011), preoperative cognitive impairment (OR 2.784),

postoperative sepsis (OR 3.807) and an absence of postoperative complications (OR 0.188) were independently associated.
Conclusions Perioperative SARS-CoV-2 infection in neurosurgical patients was associated with an increase in mortality by almost fivefold. Community COVID-19 incidence (cases/10^5 people/week) was a statistically independent predictor of mortality.
Trial registration number CEIM 20/217.

Strengths and limitations of this study

► This was a multicentre, nationwide, observational retrospective study of patients who underwent any neurosurgical operation during the first wave of the SARS-Cov2 pandemic in Spain.
► Demographic and clinical characteristics, postoperative course, preoperative screening for SARS-CoV-2 infection as well as SARS-CoV-2 infection, community COVID-19 incidence and patient outcomes were reviewed at least up to postoperative day 30.
► An exploratory factorial analysis was performed to select the most relevant variables of the sample.
► Univariate and multivariate analyses were then performed to identify independent predictors of mortality and postoperative SARS-CoV-2 infection.
► Laboratory testing and diagnostic protocols were not standardised across the different centres, and only patients with laboratory-confirmed SARS-CoV-2 infection were considered for the analysis, probably excluding some infected patients.

INTRODUCTION

The SARS-CoV-2 pandemic has taken a terrible toll worldwide in terms of excess mortality and morbidity. The virus has a high rate of transmission and causes severe forms of COVID-19 in 15% of infected persons.[1][2] Spain, among the high-income economies of the world, has been one of the countries most severely affected by the first outbreak.[3] By 30 June 2020, 252 878 cases of COVID-19 had been diagnosed, 103 225 individuals had been hospitalised, 8372 had been admitted to intensive care units (ICUs) and 29 567 had died from the disease.[4]

This flood of patients with COVID-19 overwhelmed an unprepared healthcare system that had to rapidly adapt by taking a variety of measures, among which (but not limited to) were the relocation of patients and healthcare providers, drawing resources from different areas of the hospital and converting certain locations not originally designed for it into hospitalisation and ICU areas (ie, turning operating rooms into ICU beds).[5] This strain helped the system cope with the excess of patients attending the emergency department and requiring hospitalisation. However, these measures implied a halt of elective surgeries and outpatient clinic visits,[6] difficulties in providing ICU care to patients in critical condition and delayed diagnosis of new cases.

A collaborative effort has been established to measure this 'collateral damage' in surgical non-COVID-19 patients affected by cancer.[7] However, neurosurgeons represent a small percentage of surgeons overall, and they deal with conditions (including non-cancer cases) in which the time of treatment is paramount to patient outcome in terms of mortality and disability.

The aim of this study was to investigate what factors were related the morbidity, rate of perioperative SARS-CoV-2 infection and mortality of patients who underwent neurosurgery in Spain during the first peak of the COVID-19 pandemic to improve our preparedness for the hopefully few waves to come.

METHODS

Study design

A national call for data collection on neurosurgical patients was launched on 1 June, supported by the Sociedad Española de Neurocirugía and the Sociedad de Neurocirugía de la Comunidad de Madrid. A provider profiling questionnaire was administered in all the collaborative institutions to evaluate the characteristics of the neurosurgical service and the maximum percentage of hospital beds dedicated to COVID-19 patients during the first peak of the pandemic (online supplemental file 1).

This was a multicentre nationwide observational retrospective study of patients who underwent any neurosurgical operation from March to July 2020 that fulfilled the following inclusion criteria and none of the exclusion criteria:

Patient inclusion criteria:

► Children and adult patients undergoing any operation, irrespective of the urgency and complexity, performed between 1 March and 30 June.
► Patients for whom operations were performed to treat a confirmed diagnosis of any neurosurgical disease: intracranial and spinal tumour, haemorrhagic cerebrovascular disease, traumatic brain injury, acute spine injury, degenerative spinal disease, cerebrospinal fluid (CSF) disorders and functional neurosurgery.

An anonymised online database was used to collect data and stored on a secure data server running the Research Electronic Data Capture web application (REDCap platform).[8] Research Electronic Data Capture (REDCap) is a secure, web-based software platform designed to support data capture for research studies.[8][9]

Data variables

Demographic and clinical characteristics, operative technique, surgical resources, operating time, postoperative course, postoperative neurological worsening (defined as new focal deficit or as a decrease of two or more points on the GCS), the length of hospital stay the and outcome at the end of the follow-up period were recorded (online supplemental file 2). Patient outcomes were reviewed at least up to postoperative day 30, although we encouraged participants to extend their follow-up to the deadline of the study period. Patients follow-up was done through revision of the patient's record both during admission and outpatient visits. Periodic communication with local principal investigators was maintained during the study

period, and final case ascertainment and data completeness were checked with them, mitigating missing data as much as possible.

Surgeons were asked, for each patient, whether they thought the patient was operated on with fewer resources than the standard practice and the main reasons that determined the decision to maintain the indication for a surgical procedure during the COVID-19 pandemic.

Patients who had clinical symptoms, recent contact with a patient confirmed to have COVID-19 and laboratory or radiological findings suggestive of SARS-CoV-2 infection were considered COVID-19 suspected patients. Preoperative screening for SARS-CoV-2 infection was defined as a nasopharyngeal/oropharyngeal swab test (real time PCR or RT-PCR) and/or chest CT imaging performed in the 72 hours before surgery to confirm SARS-CoV-2 infection status. Irrespectively of the screening method, all SARS-CoV-2 infections were confirmed with a positive swab test (RT-PCR).

Community COVID-19 incidence
The community COVID-19 incidence within each participating hospital's local community was extracted from the Ministry of Health official data.[4 10] COVID-19 incidence was calculated for each epidemiological 1 week (from Monday to Sunday) window on the basis of the number of confirmed COVID-19 cases at the smallest available administrative level (province), and each patient was assigned with the 7-day incidence of the week he or she was operated on.

Outcome measures
The primary outcome was the mortality rate within the first 30 postoperative days. The secondary outcomes were postoperative SARS-CoV-2 infection and complications. SARS-CoV-2 infection was considered perioperative if it was diagnosed between 30 days preoperatively and 30 days postoperatively. Only postoperatively diagnosed SARS-CoV-2 infections were considered for risk assessment of acquiring the infection in the postoperative period, while all perioperative infections were considered as risk factors for mortality.

Statistical analysis
The study was conducted according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[11] Descriptive statistics are presented as the median and IQR for quantitative measures and absolute frequency and its relative percentage for qualitative measures.

An exploratory factorial analysis was performed to the entire sample to search for those variables that explain most of the variance of the sample. An optimal coordinates method was used, with the next setting: extraction method of maximum likelihood, number of factors 6 and rotation method varimax with Kaiser normalisation. Variables with loadings greater than 0.3 after extraction were used for the subsequent analysis (variables entered

and subsequently extracted in the factorial analysis are provided in online supplemental file 3).

Differences between groups in quantitative and categorical data were calculated by the Mann-Whitney U test and χ^2 test, respectively (univariate analysis). Factors selected in the exploratory factorial analysis and that were significantly related to the outcome of interest in the univariate analysis were included for adjusted analyses to identify independent predictors of mortality and postoperative SARS-CoV-2 infection. Thus, a multivariable logistic regression analysis was used to calculate ORs and 95% CIs for each independent covariate significantly related to the outcome of interest.

All statistical analyses were performed using SPSS V.20 (IBM) and R V.3.3.3 packages ("psych", "lavaan", "see" "nFactors", "corrr", "parameters", "GPArotation", and "mvtnorm", among others).

Patient and public involvement
No patient involved.

RESULTS
Centres and setting
Sixteen hospitals from 11 provinces, attending an approximate population of 17 250 170 people,[12] provided a positive response to our call and registered patients undergoing neurosurgery in the period of study. All the participating centres are based on public health systems and are tertiary-level hospitals, out of 40 potentially responder hospitals. Patient distribution by region is shown in figure 1.

Systematic preoperative screening for COVID-19 was established in epidemiological week 21 (range 12–33). Patients whose preoperative screening test was positive were postponed until it turned negative, unless their condition threaten to worsen during the waiting time. They were only included if they were operated during the study period. We could not identify the date when the screening was established as a routine preoperative study in four centres (742 patients), and this variable was not considered reliable. In the case of emergency surgery, in 13 out of 16 centres, surgery was started under conditions recommended for confirmed COVID-19 patients. Only one centre performed chest CT imaging for preoperative screening in emergency cases. Twenty-three neurosurgeons were diagnosed with SARS-CoV-2 infection during the study period.

Patients and procedures
A total of 1677 operated patients were reported. The sex distribution was 888 (53%) and 789 (47%) for males and females, respectively. The median age was 57 years (IQR=26). American Society of Anesthesiologists (ASA) grade 1 or 2 was assigned to 984 patients (58.7%). According to the patient's medical history, 356 patients (21.2%) had no remarkable medical history. We frequently found patients who had hypertension (623,
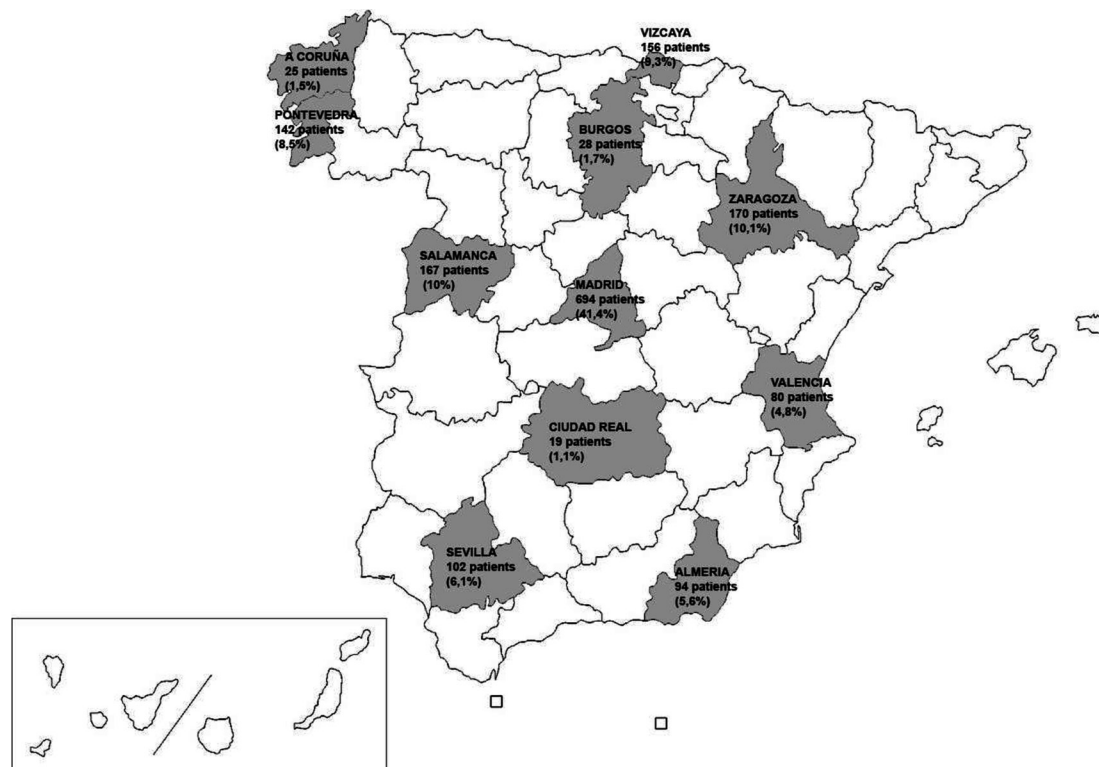
Figure 1 Registered distribution of operated patients in provinces of Spain.

37.1%), diabetes mellitus (278, 16.6%), smoking (257, 15.3%), cancer (185, 11%) and dyslipidaemia (170, 10.1%).

Regarding neurosurgical disease, among adult patients, 522 patients (32.3%) underwent surgery because of cranial (457, 87.5%) or spinal tumours (65 patients, 12.5%), and 59 procedures were related to tumours in the sellar region. Only 90 (17.2%) of the oncological surgeries were performed in relapsing central nervous system (CNS) tumours. Degenerative spinal disease (324, 20.1%), haemorrhagic cerebrovascular disease (187, 11.6%) and traumatic brain injury (191, 11.8%) followed oncology in frequency. Among 63 children, 23 patients (36.5%) underwent surgery because of CNS tumours, and 22 patients (34.9%) underwent surgery due to CSF disorders.

In relation to the urgency of the procedures, 652 (38.9%) of surgeries were considered elective surgeries, 515 (30.7%) expedited surgeries (<4 weeks after diagnosis), 204 (12.2%) urgent surgeries (<48 hour after diagnosis) and 306 (18.2%) emergency surgeries. Surgeries were dichotomised into urgent (<48 hours after diagnosis) and non-urgent for further analysis. The most frequent reason to not postpone the procedures to the end of the pandemic was evidence of a mass effect on neuroimaging or progressive neurological decline (703 patients, 41.9%), followed by an imminent effect on survival or suspicion of malignancy (512 patients, 30.5%). However, in 562 cases (33.5%), the neurosurgeon in charge considered that there was no reduction in surgical resources or excess risk at their institution. Although all

patients underwent surgery, 391 (23.3%) experienced a delay, as considered by the neurosurgeon, while waiting for their procedure. Additionally, seven patients underwent surgery with a different surgical technique (eg, three pituitary adenomas were operated on by craniotomy instead of by the transsphenoidal route), five patients required neoadjuvancy due to the mentioned delay and six patients were transferred to a COVID-19 free hospital.

When the opinion about the operating resources was asked, 65 procedures were considered to be performed under inadequate conditions, but in just 7 out of the 65 procedures, the limited resources were thought to affect postoperative outcome.

Complete patient and procedure characteristics and comparisons of groups of patients according to the kind of neurosurgical disease are described in tables 1 and 2.

Preoperative screening
Overall, 909 patients (54.3%) were tested for SARS-CoV-2 infection within 72 hours before the procedure (swab test and RT-PCR). Only 14 out of 909 patients had a positive result. Among 768 patients without a recent swab test, 30 patients were evaluated by chest CT imaging, and 95 patients were assessed only by a structural interview.

Outcomes
The overall mortality was 6.4% (107 patients within the first 30 days postoperatively). A total of 22.2% (372 patients) suffered at least one complication (median: one complication, range: 1–7 complications), and 2.9% (47 patients) suffered a SARS-CoV-2 infection. Of those

Table 1 Baseline patients characteristics and comparison between main neurosurgical pathologies

	All patients	Oncology	Degenerative spine disease	TBI	Haemorrhagic cerebrovascular disease	CSF disorder	Functional	Traumatic spine injury	Paediatrics	Infection
Number of patients	1677	522	324	191	187	157	104	78	63	51
Age (median. (IQR))	57 (IQR=26)	59 (IQR=22)	57 (IQR=22)	74 (IQR=31)	57 (IQR=17)	57 (IQR=31)	52 (IQR=29)	55 (IQR=72)	3.5 (IQR=7)	56 (IQR=34)
Sex	Males: 888 (53) Females :789 (47)	Males: 252 (48.3) Females: 270 (51.7)	Males: 174 (48.3) Females: 150 (46.3)	Males: 126 (66) Females: 65 (14)	Males: 93 (49.7) Females: 94 (50.3)	Males: 74 (47.1) Females: 83 (52.9)	Males: 54 (51.9) Females: 50 (48.1)	Males: 51 (65.4) Females: 27 (34.6)	Males: 34 (54) Females: 29 (46)	Males: 30 (58.8) Females: 21 (41.2)
Epidemiological week*	19th week (7–13 May)	18th week (30 April–6 May)	21st week (21–27 May)	17th week (23–29 April)	18th week (30 April–6 May)	16th week (16–22th Apr)	22th week (28 May–3 June)	19th week (7–13 May)	22th week (28 May–3 June)	17th week (23–29 April)
Community SARS-CoV-2 incidence*	8 cases/10^5 population (IQR=19)	9 cases/10^5 population (IQR=20)	5 cases/10^5 population (IQR=11)	10 cases/10^5 population (IQR=32)	8 cases/10^5 population (IQR=20)	9 cases/10^5 population (IQR=53)	6 cases/10^5 population (IQR=8)	9 cases/10^5 population (IQR=26)	6 cases/10^5 population (IQR=9)	13 cases/10^5 population (IQR=53)
Weight/ BMI	72 kg (IQR=20) 27.1 kg/m^2 (IQR=6)	73.3 kg (IQR=17) 28.1 kg/m^2 (IQR=7)	75 kg (IQR=22) 27.4 kg/m^2 (IQR=7)	70 kg (IQR=17) 27 kg/m^2 (IQR=3)	75 kg (IQR=20) 25 kg/m^2 (IQR=7)	75 kg (IQR=30) 29 kg/m^2 (IQR=6)	55 kg (IQR=39) 26.4 kg/m^2 (IQR=11)	75.5 kg (IQR=12) 28 kg/m^2 (IQR=6)	16kg (IQR=13) 16 kg/m^2 (IQR=6)	75 kg (IQR=27) 27.7 kg/m^2 (IQR=5)
ASA grade, n (%)										
Unknown	40 (2.4)	6 (1.1)	2 (0.6)	13 (6.8)	8 (4.3)	3 (1.9)	1 (1)	3 (3.8)	0	4 (7.8)
Grades I and II	984 (58.7)	288 (55.2)	252 (77.8)	92 (48.1)	114 (60.9)	77 (49)	55 (52.8)	44 (56.4)	42 (66.6)	20 (39.2)
Grades III and IV	640 (38.2)	228 (43.7)	70 (21.6)	81 (42.4)	59 (31.6)	76 (48.4)	48 (46.2)	31 (39.7)	20 (31.7)	27 (53)
Grade V	13 (0.8)	0	0	5 (2.6)	6 (3.2)	1 (7.7)	0	0	1 (1.6)	0
Medical history, n (%)										
None	356 (21.2)	113 (21.6)	88 (27.2)	35 (18.3)	33 (17.6)	22 (14)	20 (19.2)	19 (24.4)	18 (28.6)	8 (15.7)
Hypertension	623 (37.1)	193 (37)	98 (30.2)	98 (51.3)	92 (49.2)	70 (44.6)	21 (20.2)	32 (41)	0	19 (37.3)
Diabetes	278 (16.6)	80 (15.3)	46 (14.2)	53 (27.7)	31 (16.6)	33 (21)	8 (7.7)	18 (23.1)	0	9 (17.6)
DL	170 (10.1)	56 (10.7)	34 (10.5)	26 (13.6)	17 (9.1)	20 (12.7)	7 (6.7)	5 (6.4)	0	5 (9.8)
Current smoker	257 (15.3)	84 (16.1)	57 (17.6)	22 (11.5)	51 (27.3)	16 (10.2)	10 (9.6)	9 (11.5)	0	8 (15.7)
COPD	78 (4.7)	21 (4)	21 (6.5)	12 (6.3)	8 (4.3)	5 (3.2)	1 (1)	8 (10.3)	0	2 (3.9)
IHD	74 (4.4)	23 (4.4)	9 (2.8)	18 (9.4)	10 (5.3)	2 (1.3)	3 (2.9)	6 (7.7)	0	3 (5.9)
Obesity	55 (3.3)	21 (4)	11 (3.4)	0	7 (3.7)	10 (6.4)	1 (1)	2 (2.6)	0	3 (5.9)
CHF	34 (2)	10 (1.9)	4 (1.2)	8 (4.2)	6 (3.2)	1 (0.6)	0	2 (2.6)	0	3 (5.9)
Priority of the surgery, n (%)										
Emergent	306 (18.2)	15 (2.9)	6 (1.9)	105 (55)	102 (54.5)	47 (29.9)	0	8 (10.3)	11 (17.5)	12 (23.5)
Urgent (<48 hours)	204 (12.2)	28 (5.4)	12 (3.7)	60 (31.4)	23 (12.3)	34 (21.7)	1 (1)	20 (25.6)	11 (17.5)	15 (29.4)
Expedite (<4 weeks)	515 (30.7)	315 (60.3)	46 (14.2)	18 (9.4)	16 (8.6)	33 (21)	14 (13.5)	39 (50)	12 (19)	22 (43.1)
Elective (>4 weeks)	652 (38.9)	164 (31.4)	260 (80.2)	8 (4.2)	46 (24.6)	43 (27.4)	89 (85.6)	11 (14.1)	29 (46)	2 (3.9)
Days on surgical list	10 days (IQR=98)	12 days (IQR=50)	118 days (IQR=161)	0 days (IQR=1)	0 days (IQR=38)	2 days (IQR=25)	88 days (IQR=156)	3 days (IQR=10)	21 days (IQR=151)	2 days (IQR=9)

Continued

Table 1 Continued

	All patients	Oncology	Degenerative spine disease	TBI	Haemorrhagic cerebrovascular disease	CSF disorder	Functional	Traumatic spine injury	Paediatrics	Infection
Reason to maintain the indication, n (%)										
Life threatening	512 (30.5)	217 (40)	0	92 (48.2)	117 (62.6)	60 (38.2)	2 (1.9)	3 (3.8)	12 (19)	14 (27.5)
Mass effect/neurol decline	703 (41.9)	295 (54.4)	87 (26.9)	123 (64.4)	40 (21.4)	52 (33.1)	9 (8.7)	51 (65.4)	34 (54)	20 (39.2)
No limited resources	562 (33.5)	138 (25.5)	183 (56.5)	23 (12)	35 (18.7)	47 (29.9)	80 (76.9)	21 (26.9)	29 (46)	17 (33.3)
Patients assume risks	350 (20.9)	85 (15.7)	109 (33.6)	12 (6.3)	20 (10.7)	31 (19.7)	51 (49)	21 (26.9)	19 (30.2)	8 (15.7)

*Median week and SARS-CoV-2 rate of new cases at province level at which the procedure for the specific neurosurgical pathology was performed.
ASA, American Society of Anesthesiologist; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CSF, cerebrospinal fluid; DL, dyslipidaemia; IHD, ischaemic heart disease; TBI, traumatic brain injury;

infections, 6 occurred while waiting for the surgery, 14 occurred during the preoperative screening, 13 occurred in the postoperative period while still in the hospital, 11 occurred after discharge within the first 30 days and 3 occurred after the 30th day (and therefore were not considered for further analysis).

According to the univariate analysis, mortality was higher among those suffering SARS-CoV-2 infection (OR 7.72; 95% CI 3.96 to 15.07). The weekly incidence of COVID-19 in the community was higher for the patients who died (60 vs 29.8 cases/10^5 population, p<0.0001). Other related variables are shown in table 3.

A binary logistic regression with the variables selected in the factorial analysis and significantly related to mortality in the univariate analysis was performed: age (OR per year increase 1.05; 95% CI 1.034 to 1.068), perioperative SARS-CoV-2 infection (OR 4.7; 95% CI 1.81 to 12.1), 7-day COVID-19 incidence in the local population (OR per point increase 1.006; 95% CI 1.002 to 1.009), postoperative neurological worsening (OR 5.9; 95% CI 3.27 to 10.66), postoperative need for airway support (OR 5.3; 95% CI 2.81 to 10.3), ASA grade ≥3 (OR 2.5; 95% CI 1.31 to 4.79) and preoperative GCS 3–8 (OR 2.82; 95% CI 1.34 to 5.94) were independently associated with mortality (table 4).

Then, we constructed an ROC curve to assess which cut-off value of the community 7-week incidence of COVID-19 better discriminated 30-day mortality. The AUC was 0.661 (95% CI 0.605 to 0.718; p<0.001); according to the values of sensitivity (69.8%) and specificity (59.8%), the best cut-off was 10 cases/10^5. Mortality with an incidence greater than 10 cases/10^5 was 10.9% versus 3.6% (OR 3.285; 95% CI 2.169 to 4.975).

Of the 47 patients suffering from COVID-10, 44 suffered it in the perioperative period. Among them, the mortality rate was 31.8% (14 out of 44). Of those 44 infections, 6 occurred while waiting for the surgery and 14 were diagnosed in the preoperative screening test. The other 24 infections were diagnosed after the surgery and within the first 30 days. Risk factors for postoperative infection in the univariate analysis were weekly COVID-19 incidence (30.2 vs 143.2 cases/10^5 population; p<0.0001), swab test within 72 hours prior to surgery, suffering one or more complications and postoperative need for intubation, among others (table 3). After a binary logistic regression with the variables selected in the factorial analysis (and significantly related in the univariate analysis) was performed, 7-day COVID-19 incidence (OR per point increase 1.013 95% CI 1.008 to 1.018), swab test within 72 hours prior to surgery (OR 0.098; 95% CI 0.012 to 0.778), preoperative cognitive impairment (OR 2.784 95% CI 1.037 to 7.471), postoperative sepsis (OR 3.807; 95% CI 0.968 to 14.976) and an absence of postoperative complications (OR 0.188; 95% CI 0.068 to 0.521) remained in the model as independently associated with a SARS-CoV-2 postoperative infection (table 4).

Postoperative infections occurred between epidemiological weeks 9 and 16. Only two postoperative infections

Table 2 Perioperative patient condition and support, surgical data and outcome

	All patients	Oncology	Degenerative spine disease	TBI	Haemorrhagic cerebrovascular disease	CSF disorder	Functional	Traumatic spine injury	Paediatrics	Infection
Number of patients	1677	522	324	191	187	157	104	78	63	51
Preoperative airway support (at least venturi mask) (n (%))	165 (9.8)	9 (1.7)	1 (0.3)	52 (27.2)	72 (38.5)	15 (9.6)	2 (1.9)	11 (14.1)	1 (1.6)	2 (3.9)
Preoperative suspect of COVID-19? (n (%))	45 (2.7)	5 (1)	0	11 (5.8)	10 (5.3)	14 (8.9)	0	2 (2.6)	2 (3.2)	1 (2)
Screening swab test<72 hour preoperatively (n (%))										
Non tested	768 (45.7)	249 (47.7)	145 (46.6)	84 (45.4)	101 (50.2)	66 (42)	35 (33.7)	32 (41)	10 (15.9)	17 (33.3)
Negative	895 (53.5)	272 (52.1)	164 (52.9)	97 (52.4)	96 (47.9)	87 (55.4)	69 (66.3)	46 (59)	53 (84.1)	34 (66.7)
Positive	14 (0.8)	1 (0.2)	1 (0.3)	4 (2.2)	4 (2)	4 (2.5)	0	0	0	0
Postoperative airway support (n (%))	250 (14.9)	49 (9)	3 (0.9)	54 (28.3)	93 (49.7)	23 (14.6)	3 (2.9)	16 (20.5)	5 (7.9)	6 (11.8)
Length of hospital stay	5 days (IQR=9)	5 days (IQR=5)	2 days (IQR=3)	4 days (IQR=11)	15 days (IQR=29)	6 days (IQR=19)	2 days (IQR=3)	7 days (IQR=11)	5 days (IQR=4)	8 days (IQR=25)
Complications (n (%))										
None	1243 (74.1)	370 (70.9)	370 (90.4)	139 (72.8)	105 (56.1)	108 (68.8)	92 (88.5)	53 (67.9)	52 (82.5)	31 (60.8)
Perioperative SARS-CoV-2 infection (n (%))										
Awaiting surgery	6 (0.4)	3 (0.6)	0	0	0	2 (1.3)	0	1 (1.3)	0	0
Preoperatively screening	14 (0.8)	1 (0.2)	1 (0.3)	4 (2.1)	4 (2.1)	4 (2.5)	0	0	0	0
In-hospital admission	13 (0.8)	7 (1.3)	0	1 (0.5)	2 (1.1)	2 (1.3)	0	0	0	1 (2)
After hospital discharge<30days	11 (0.7)	5 (0)	0	1 (0.5)	2 (1.1)	1 (0.6)	0	2 (2.6)	0	0
After hospital discharge>30days	3 (0.2)	1 (0.2)	0	1 (0.5)	0	0	0	0	0	0
Outcome after 3 months of study entry (n (%))										
Alive, at home	1376 (82.1)	440 (84.3)	315 (97.2)	143 (74.9)	107 (57.2)	115 (73.2)	102 (98.1)	50 (64.1)	62 (98.4)	42 (82.4)
Alive, in-hospital	61 (3.6)	20 (3.8)	3 (0.9)	5 (2.6)	13 (7)	14 (8.9)	1 (1)	2 (2.6)	1 (1.6)	2 (3.9)
Alive, transfer to other hosp.	33 (2)	5 (1)	3 (0.9)	9 (4.7)	5 (2.7)	4 (2.5)	0	5 (6.4)	0	2 (3.9)
Alive, at nursing facility	91 (5.4)	13 (2.5)	3 (0.9)	12 (6.3)	32 (17.1)	14 (8.9)	1 (1)	13 (16.7)	0	3 (5.9)
Dead	114 (6.8)	43 (7.9)	0	22 (11.5)	29 (15.5)	10	0	8	0	2 (.9)
Unknown	2 (0.1)	1 (0.2)	0	0	1 (0.5)	0	0	0	0	0
Cause of death, n (%)										
Neurosurgical disease	77 (4.6)	29 (5.6)	0	14 (7.3)	26 (13.9)	5 (3.2)	0	3 (3.8)	0	0
New medical condition	26 (1.6)	9 (1.7)	0	6 (3.1)	2 (1.1)	0	0	4 (5.1)	0	2 (3.9)
COVID-19 or its complications	8 (0.5)	1 (0.2)	0	1 (0.5)	1 (0.5)	2 (1.3)	0	1 (1.3)	0	0
Other	2 (0.1)	1 (0.2)	0	1 (0.5)	0	3 (1.9)	0	0	0	0

Continued

Table 2 Continued

	All patients	Oncology	Degenerative spine disease	TBI	Haemorrhagic cerebrovascular disease	CSF disorder	Functional	Traumatic spine injury	Paediatrics	Infection
Time of death, n (%)										
Postoperative day 0–7	28 (1.7)	7 (1.3)	0	8 (4.2)	10 (5.3)	2 (1.3)	0	0	0	1 (2)
Postoperative day 8–30	79 (4.7)	33 (6.3)	0	12 (6.3)	17 (9.1)	8 (5.1)	0	8 (10.3)	0	1 (2)
Postoperative>30	7 (0.4)	3 (0.6)	0	2 (1)	2 (1.1)	0	0	0	0	0

CSF, cerebrospinal fluid; TBI, traumatic brain injury.

occurred after strict preoperative SARS-CoV-2 screening had been established.

Of the 44 patients who suffered an infection in the perioperative period, 25 needed admission to the ICU, 11 required intubation and 8 out of 14 deaths were considered secondary to the infection itself. The mortality was similar (p=0.546) among those infected preoperatively (5 of 20; 25%), postoperatively during admission (4 of 13; 30.8%) or after discharge (5 of 11; 45.5%).

The majority of patients did not experience any complications (1243; 74.1%). Among those experiencing at least one, neurological worsening was the most frequent (121, 7.2%), followed by pneumonia (75, 4.5%) and CSF fistula (43, 2.3%).

DISCUSSION

SARS-CoV-2 has stricken our society in an unprecedented way and, in some countries, has hit fast and hard. This first blow of the first wave caught many healthcare systems unprepared, and they were completely overwhelmed.[3] Many countries, such as Spain, fought to relocate resources and increase their stock in a world full of countries also struggling to obtain the same resources.[13] This global crisis negatively affected the way patients with COVID-19 were taken care of,[14] the way healthcare providers protected themselves[15] and (less thoroughly studied) the way other non-COVID-19 pathologies were treated.[6 16 17]

The occurrence of SARS-CoV-2 infection during the perioperative period was associated with almost fivefold increase in mortality in our cohort, following adjustment for other predictors. The fatality rate of SARS-CoV-2 infection is highly dependent on the patient's age, but it has been globally estimated to be between 1% and 2%.[18] We found a fatality rate among neurosurgical patients of 31.8%, which was strikingly higher. Neurosurgically infected patients fated badly, since 25 required ICU admission, and 8 of the 14 deaths were considered directly related to COVID-19. The mortality distribution did not vary greatly if the infection occurred before the surgery (25%), after the surgery during admission (30.8%) or after discharge (45.5%); therefore, the combination of a neurosurgical procedure and SARS-CoV2 infection greatly worsened the prognosis irrespective of the time of infection. Our mortality rate among infected patients was in line with, although greater than, the 23.8% found by the CovidSurg collaborative[16] in surgical patients. Age, postoperative neurological worsening, postoperative need for intubation, ASA grade ≥3 and worse preoperative GCS were also independent predictors of mortality, irrespective of the infection status. Interestingly, the weekly incidence of COVID-19 correlated with mortality once adjusted by the previous factors, irrespective of the infection status of the patient itself. This fact is probably secondary to the degree of healthcare system overload. It is also possible that some degree of therapeutic nihilism

Table 3 Univariate analysis for mortality and postoperative SARS-CoV-2 infection, with the variables selected in the exploratory factorial analysis

	Mortality			Postoperative SARS-CoV-2 infection		
	Alive (30 days)	Dead (30 days)	P value	Not infected (30 days)	Infected (30 days)	P value
Age	54	63.5	**<0.001**	54.5	58.1	**0.393**
ASA grade			**<0.001**			**0.261**
1, n (%)	376 (96.4)	14 (3.6)		389 (99.5)	2 (0.5)	
2, n (%)	571 (96.1)	23 (3.9)		584 (98.3)	10 (1.7)	
3, n (%)	482 (91.8)	43 (8.2)		515 (98.1)	10 (1.9)	
4, n (%)	98 (85.2)	17 (14.8)		113 (98.3)	2 (1.7)	
5, n (%)	7 (53.8)	6 (46.2)		13 (100.0)	0 (0.0)	
Previous medical conditions			**0.033**			**0.039**
At least one, n (%)	1228 (93.0)	93 (7)		1282 (98.2)	23 (1.8)	
None, n (%)	342 (96.1)	14 (3.9)		352 (99.7)	1 (0.3)	
High blood pressure			**0.002**			**0.082**
No, n (%)	1002 (95.1)	52 (4.9)		1043 (99.0)	11 (1.0)	
Yes, n (%)	568 (91.2)	55 (8.8)		610 (97.9)	13 (2.1)	
Diabetes mellitus			**0.013**			**0.572**
No, n (%)	1319 (94.3)	80 (5.7)		1380 (98.6)	19 (1.4)	
Yes, n (%)	251 (90.3)	27 (9.7)		273 (98.2)	5 (1.8)	
GCS 3–8			**<0.001**			**0.183**
No, n (%)	1492 (95.5)	71 (4.5)		1539 (98.5)	24 (1.5)	
Yes, n (%)	78 (68.4)	36 (33.6)		114 (100)	0 (0)	
Preoperative neurological deficit, n (%)						
None	573 (97.0)	18 (3.0)	**<0.001**	577 (98.5)	9 (1.5)	**0.826**
Language	137 (88.4)	18 (11.6)	**0.005**	145 (96)	6 (4)	**0.006**
Motor	391 (92.2)	33 (7.8)	**0.172**	408 (97.6)	10 (2.4)	**0.062**
Cognitive impairment	264 (91.0)	26 (9.0)	**0.048**	277 (97.2)	8 (2.8)	**0.035**
No reliable (altered mental status)	66 (67.6)	32 (32.7)	**<0.001**	93 (100)	0 (0)	**0.229**
Community COVID-19 incidence (cases/10^5 people/week) (median; IQR)	8 (19)	22 (67)	**<0.001**	8 (19)	132 (216)	**<0.001**
Screening swab test <72 hours preoperatively			**0.064**			**<0.001**
No, n (%)	704 (92.5)	57 (7.5)		743 (97.1)	23 (2.9)	
Yes, n (%)	861 (94.7)	48 (5.3)		908 (99.9)	1 (0.1)	
SARS-CoV-2 perioperative infection			**<0.001**			
No, n (%)	1540 (94.3)	93 (5.7)				
Yes, n (%)	30 (68.2)	14 (31.8)				
Urgent surgery			**<0.001**			**0.166**
No, n (%)	644 (98.8)	8 (1.2)		1163 (98.3)	20 (1.7)	
Yes, n (%)	446 (87.5)	64 (12.5)		490 (99.2)	4 (0.8)	

Continued

Table 3 Continued

	Mortality			Postoperative SARS-CoV-2 infection		
	Alive (30 days)	Dead (30 days)	P value	Not infected (30 days)	Infected (30 days)	P value
General anaesthesia, n (%)	1373 (93.4)	97 (6.6)	0.338	1447 (98.4)	23 (1.6)	0.222
Preoperative airway support, n (%)	90 (70.9)	37 (29.1)	<0.001	124 (97.6)	3 (2.4)	0.359
Postperative airway support, n (%)	144 (74.6)	49 (25.4)	<0.001	187 (96.9)	6 (3.1)	0.017
Length of surgery (min)	163.41	152.58	0.370	162.3	186.8	0.324
Postoperative sepsis, n (%)	38 (84.4)	7 (15.6)	0.011	39 (90.7)	4 (9.3)	<0.001
Postoperative neurological worsening, n (%)	88 (72.7)	33 (27.3)	<0.001	113 (96.6)	4 (3.4)	0.064
Postoperative pneumonia, n (%)	56 (74.7)	19 (25.3)	<0.001	70 (93.3)	5 (6.7)	<0.001
Postoperative blood transfusion, n (%)	28 (77.8)	8 (22.2)	<0.001	30 (96.8)	1 (3.2)	0.403
Suffering one or more complications, n (%)	309 (83.1)	63 (16.9)	<0.001	348 (96.1)	14 (3.9)	<0.001
Reoperation			0.007			0.078
No, n (%)	1371 (94.2)	84 (5.8)		1420 (98.7)	18 (1.3)	
Yes, n (%)	195 (89.4)	23 (10.6)		209 (97.2)	6 (2.8)	
Resources shortage (surgeon opinion)			0.664			0.256
No, n (%)	1505 (93.7)	102 (6.3)		1585 (98.6)	22 (1.4)	
Yes, n (%)	60 (92.3)	5 (7.7)		63 (96.9)	2 (3.1)	

ASA, American Society of Anesthesiologists; GCS, Glasgow Coma Scale.

governed medical decisions at the worst moments of the pandemic.

Several factors associated with a worse condition of the patient (such as preoperative cognitive impairment or postoperative sepsis) or a longer hospital stay (postoperative absence of complications was protective) were also associated with a higher postoperative infection rate. This suggests that there was a non-negligible number of intrahospital infections. The implementation of systematic preoperative screening for COVID-19 with the swab test occurred at different moments of the first wave in the different centres included; thus, it was difficult to assess its specific role in the postoperative infection rate. However, it seems to be an independent factor in diminishing the infection rate; therefore, some of the postoperative infections may have actually been preoperatively acquired but not diagnosed until the postoperative period. It is difficult to weigh the burden of each individual factor on the infection rate, which is a rapidly evolving situation, and improvements are constantly being implemented. For example, the segregation of patients into COVID-19 free surgical pathways has proven to decrease the infection rate[17] and pulmonary complications and that measure was implemented at different moments and with different success rates in each hospital. No credible COVID-19-free surgical pathways could have been implemented until systematic screening (with the swab test in the majority of cases) was performed; therefore, those two factors might be tightly intertwined. Every postoperative infection occurred between epidemiological weeks 9 and 16, and only two of them after a strict screening protocol had been established; therefore, although a considerable amount of data are missing for that variable, the implementation of those protocols seemed to greatly benefit the patients. Even considering all of the above, the 7-day COVID-19 community incidence was still one of the main predictors of postoperative infection.

In Spain, by 4 May, 2.6 million people were estimated to have been infected,[19 20] while only 226 557 cases had been officially diagnosed.[10 12] These figures are subject to many interpretations, but we can roughly assume that the official COVID-19 incidence was 8%–10% of the real incidence. In our cohort of patients, when the incidence was above 10 cases/10^5 a week, the chances

Table 4 Binary logistic regression for mortality and SARS-CoV-2 postoperative infection.

Binary logistic regression for mortality			
Variables	OR	95% CI	P value
Age*	1.05*	1.034 to 1.068	<0.001
Community COVID-19 incidence (cases/10^5 people/week)*	1.006*	1.002 to 1.009	<0.001
SARS-CoV-2 perioperative infection	4.7	1.81 to 12.1	<0.001
Postoperative neurological worsening	5.9	3.27 to 10.66	<0.001
GCS 3–8	2.82	1.34 to 5.94	0.006
Postoperative airway support	5.38	2.81 to 10.3	<0.001
ASA grade ≥3	2.5	1.31 to 4.79	0.005
Nagelkerke R square=0.338			
Binary logistic regression for postoperative SARS-CoV-2 infection			
Community COVID-19 incidence (cases/10^5 people/week)*	1.013*	1.008 to 1.018	<0.001
Screening swab test <72 hours preoperatively	0.098	0.012 to 0.778	0.028
Preoperative cognitive impairment	2.784	1.037 to 7.471	0.042
Postoperative sepsis	3.807	0.968 to 14.976	0.056
No postoperative complications	0.188	0.068 to 0.521	0.001
Nagelkerke R square=0.351			

The OR, 95% CI and level of significance (P) are provided for each variable, as well as the constant of the model and the Nagelkerke R square.

*OR provided per unit increase.

ASA, American Society of Anesthesiologists; GCS, Glasgow Coma Scale.

of death increased by 3.2-fold and that incidence best discriminated the mortality chances. Diagnosis capabilities have greatly increased since then, and it is difficult to estimate the current incidence that could be comparable with that one. However, if the above estimation is correct, an incidence of 100–120 cases/10^5 could be the current threshold. Even if that estimation is correct, patients are better managed now, and it is possible that incidences far above that number are needed to see a comparable increase in mortality. Regardless of the threshold number that we chose, a rise in the COVID-19 incidence in the community seems to be associated with a mortality rise. On that basis, it seems reasonable to recommend that every effort should be made by authorities and the general population to avoid increases in worrisome numbers. Nevertheless, if the incidence rises, consideration should be given to delay neurosurgical interventions until the incidence lowers or to transfer neurosurgical patients to areas with lower incidence if feasible.

This study has several limitations. Laboratory testing and diagnostic protocols were not standardised across the different centres. Only patients with laboratory-confirmed SARS-CoV-2 infection were considered for the analysis, thus reducing variability but probably excluding some infected patients. Every neurosurgical patient was meant to be included; therefore, it is possible that high-volume centres, or those under a high strain due to the pandemic, might not have identified all patients.

CONCLUSIONS

Perioperative SARS-CoV-2 infection in neurosurgical patients was associated with an increase in mortality by almost fivefold. The local 7-day COVID-19 incidence in the community was a statistically independent predictor of mortality. An incidence greater than 10 cases/10^5 was associated with a 3.2-fold increase in the chance of mortality. Routine preoperative screening with swab tests within 72 hours prior to surgery has proven to be effective in reducing postoperative infections.

If the local incidence of COVID-19 is high, consideration should be given to delaying elective surgeries or transferring neurosurgical patients to low-incidence areas.

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