Neuro-Oncology

XX(XX), 1–11, 2023 | https://doi.org/10.1093/neuonc/noad019 | Advance Access date 13 April 2023

Variation in postoperative outcomes of patients with intracranial tumors: insights from a prospective international cohort study during the COVID-19 pandemic

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Abstract

Background. This study assessed the international variation in surgical neuro-oncology practice and 30-day outcomes of patients who had surgery for an intracranial tumor during the COVID-19 pandemic.

Methods. We prospectively included adults aged ≥18 years who underwent surgery for a malignant or benign intracranial tumor across 55 international hospitals from 26 countries. Each participating hospital recorded cases for 3 consecutive months from the start of the pandemic. We categorized patients' location by World Bank income groups (high [HIC], upper-middle [UMIC], and low- and lower-middle [LLMIC]). Main outcomes were a change from routine management, SARS-CoV-2 infection, and 30-day mortality. We used a Bayesian multilevel logistic regression stratified by hospitals and adjusted for key confounders to estimate the association between income groups and mortality.

Results. Among 1016 patients, the number of patients in each income group was 765 (75.3%) in HIC, 142 (14.0%) in UMIC, and 109 (10.7%) in LLMIC. The management of 200 (19.8%) patients changed from usual care, most commonly delayed surgery. Within 30 days after surgery, 14 (1.4%) patients had a COVID-19 diagnosis and 39 (3.8%) patients died. In the multivariable model, LLMIC was associated with increased mortality (odds ratio 2.83, 95% credible interval 1.37–5.74) compared to HIC.

Conclusions. The first wave of the pandemic had a significant impact on surgical decision-making. While the incidence of SARS-CoV-2 infection within 30 days after surgery was low, there was a disparity in mortality between countries and this warrants further examination to identify any modifiable factors.

Key Points

- COVID-19 research collaborative efforts allowed international comparisons.
- Low- and low-middle-income countries were associated with higher 30-day mortality.
- This disparity required clarification and identification of modifiable factors.

Importance of the Study

Globally there is a major deficit of neurosurgeons predominantly in low- and low middle-income countries (LLMIC). There is a general paucity of studies reporting postoperative outcomes in LLMIC. COVID-19 collaborative surgical research provided an opportunity to assess neuro-oncology practice and outcomes across countries. Data from our prospective international multicenter cohort study during the COVID-19 pandemic allowed international comparisons of short-term outcomes between countries of different income groups. In the presence of a low (1.4%) perioperative COVID-19 rate, LLMIC was associated with almost 3 times higher odds of 30-day mortality compared to high income. These findings were not explained by patient characteristics and postoperative pulmonary complications. The disparity in 30-day postoperative mortality between different income countries should become a focus of global neurosurgery and warrants further examination to identify any modifiable factors that could be addressed.

The impact of the COVID-19 pandemic on the delivery of surgical care is substantial. It has been estimated that over 28.4 million elective operations were canceled or delayed during the 12-week first wave of the pandemic worldwide.[1] International studies have demonstrated that preoperative SARS-CoV-2 infection is associated with a higher risk of 30-day postoperative mortality.[2,3] Longer-term direct and indirect effects of the pandemic are yet to be realized though these are likely to result in excess mortality among people with cancer due to delays in diagnosis and treatment.[4] Few studies have evaluated neuro-oncology services during the pandemic[5–7] but they do not provide a global view. Estimating the effect of the pandemic on the initial management of brain tumors during the first wave (January–August 2020) can set a reference to compare hospital activities as the pandemic evolves and new evidence emerges.

Even before the COVID-19 pandemic, the landscape of global neurosurgery was disparate. A major deficit of neurosurgeons predominantly in low- and middle-income countries has resulted in an estimated 5 million essential neurosurgical procedures not performed each year.[8] While the direct impact of access to neurosurgery cannot be measured for neuro-oncology patients worldwide, it is reasonable to assess the variations in neuro-oncology practices of different countries since healthcare systems and patient pathways can affect patient outcomes.

The aim of this study was to assess the changes to routine neuro-oncology management that resulted from the COVID-19 pandemic, and to compare 30-day postoperative mortality between countries of different income groups.

Methods

Study Design

The COVIDSurg-Cancer is an international, observational cohort study that assessed treatment pathways and perioperative events in patients undergoing surgery for a tumor during the pandemic.[9] This study also presents a unique opportunity to assess patient presenting features, neuro-oncology practice, and short-term surgical outcomes in different countries. Investigators from participating centers obtained the appropriate study approval according to the local and national requirements.

This study was a preplanned subgroup analysis of patients from the COVIDSurg-Cancer study who underwent surgery for an intracranial tumor during the first wave (January–August 2020) of the pandemic. Any hospital providing brain tumor surgery in an area affected by COVID-19 was eligible and participation was voluntary. Each investigator identified a start date for the respective center. This start date corresponded to the date of admission of the first patient with confirmed SARS-CoV-2 infection in the hospital. In hospitals operating a Covid-free surgical pathway, the start date was the date of admission of the first SARS-CoV-2 positive patients in another hospital in the city. Patient recruitment ended 3 months after the start date. The follow-up period was 30 days after tumor surgery. Collaborators entered anonymized data into a secure server using the Research Electronic Data Capture online system.[1]

Participants

Collaborators recruited all consecutive adults aged ≥18 years who underwent any surgery for an intracranial tumor during the 3-month recruitment period. Patients with primary or secondary malignant or nonmalignant tumors were eligible. Collaborators reviewed hospital records to collect information about postoperative outcomes.

Definitions of Co-variables

The explanatory variable of interest was The World Bank income group 2020 (https://data.worldbank.org/country) of the country where each participating hospital was located. The main outcome of interest was all-cause mortality within 30 days of tumor surgery. Collaborators ascertained mortality data based on their hospital records. We collected baseline, operative, and tumor characteristics of included patients. Healthcare system characteristics included the local 14-day SARS-CoV-2 cumulative notification rate, COVID-19 free surgical pathway, preoperative Covid screening, and preoperative swab test results. Community SARS-CoV-2 incidence is a proxy measure of the risk of SARS-CoV-2 infection and was calculated for

2-week windows from March to April 2020. We extracted this for each participating hospital from the World Health Organization, European Centre for Disease Prevention and Control, or United States Centers for Disease Control and Prevention statistics. We trichotomized patients into high (≥58 cases per 100 000 population) medium (10.3–58 cases per 100 000 population) and low (<10.3 cases per 100 000 population) SARS-CoV-2 risk groups according to the population data at the time of surgery. COVID-19 free surgical pathway referred to hospitals that utilized a system where patients without SARS-CoV-2 infection underwent surgery and perioperative care in hospital areas completely separated from patients treated for COVID-19. When there were changes to the intended management plan due to the COVID-19 pandemic, the local study team recorded this as a change from usual care. For example, these changes may have occurred because of hospital bed shortages, staff redeployment, or perceived high risk of SARS-CoV-2 infection risks. Other postoperative data included pulmonary complications, which included pneumonia, acute respiratory distress syndrome, or unplanned postoperative ventilation, and postoperative SARS-CoV-2 infection confirmed by a positive swab, positive thoracic CT imaging, or a clinical diagnosis of symptomatic COVID-19 in patients for whom these tests were unavailable. We also recorded postoperative complications identified by the participating hospitals.

Sample Size and Mitigation Against Bias

There was no sample size calculation for this exploratory analysis of data generated from a rapid response research collaborative. To account for potential bias that hospitals more severely affected by Covid would participate, we collected data on both community and postoperative COVID-19 status. To minimize ascertainment bias, we requested for additional validation of patient identification in hospitals recruiting ≤5 patients. Testing and screening capacity for COVID-19 was variable internationally during the study period, which would introduce measurement bias of perioperative COVID-19 status. We used postoperative pulmonary complication as a proxy variable to account for this since pulmonary complication was less likely to be affected by measurement bias in this 30-day study period.

Statistical Analyses

We used descriptive statistics to present characteristics of patients in different income groups without univariable analyses to avoid multiple testing. To account for the different operational characteristics of hospitals and the expected few number of deaths, we used Bayesian multilevel logistic regression models with population stratification by hospitals incorporated as random intercepts for our multivariable analyses. Informative priors were based on existing literature on the association between covariates and 30-day postoperative mortality[10–12] and experts in the study group. Covariates in the multivariable model on 30-day mortality included the World Bank income groups, age groups, sex, WHO performance status, ASA status, urgency of surgery, and postoperative respiratory complications. Sensitivity analysis using weakly informative priors assessed the influence of informative priors on the posterior distributions. Credible interval (CrI) represented the 95% highest density interval of the posterior distributions, which can be interpreted as 95% confidence interval but is philosophically distinct. WHO performance status may have different prognostic value depending on the context; a model including an interaction between income groups and WHO performance status evaluated this potential effect modification. Interaction terms had weakly informative priors. We took a complete case analysis approach. We accepted model as convergent if R-hat diagnostic was <1.05. Other diagnostics checked for correct specification, independence, and linearity. We performed all data handling and analyses in R (v4.1.0) using "tidyverse" (v1.3.1), "gtsummary" (1.4.1), "brms" (v2.15.5), and "ROCR" (v1.0-11) packages. We used "shinystan" (v.2.5.0) and "loo" (v.4.2.1) for model parameters and convergence diagnostics.

Results

Participating Hospitals

There were 1016 patients who underwent surgery for an intracranial tumor in 55 participating hospitals from 26 countries. The 3-month patient recruitment periods across the hospitals spanned between January 13, 2020 and August 9, 2020. Countries that contributed >50 patients were United Kingdom (40.4%; *N* = 410), United States (9.7%; *N* = 99), Saudi Arabia (9.5%; *N* = 97), Serbia (7.7%; *N* = 78), Morocco (6.2%; *N* = 63) and Italy (5.7%; *N* = 58). There were 11 high-income countries (HICs) contributing 765 (75.3%) patients, 7 upper-middle income countries (UMICs) contributing 142 (14.0%) patients, and 8 low and lower-middle income countries (LLMICs) contributing 109 (10.7%) patients. The median number of patients from each hospital during the respective 3-month consecutive recruitment period was 7 (interquartile range [IQR] 2–34) patients.

Patient Characteristics

The proportions of patients in communities with low, medium, and high SARS-CoV-2 risk were 26.8%, 35.9%, and 36.6%, respectively (Table 1). Eleven (1.1%) patients had confirmed or probable COVID-19 that had resolved before the time of surgery, of which 9 occurred within 4 weeks preoperatively. Most (85.5%) underwent surgery in hospitals without a COVID-19-free surgical pathway. 753 (74.1%) patients had preoperative Covid screening, of which 551 (73.2%) had a swab test. There were 10 patients who tested positive using preoperative swab test within 7 days. Most (83.3%) patients were <70 years of age and 8.0% had a preexisting respiratory condition (Table 1). Gliomas were the most common tumor type (42.9 %) followed by meningiomas (18.3%). Nine hundred eleven (89.7%) patients had a tumor resection, and a gross total resection was achieved in 521 (51.6%) patients.

Table 1. Characteristics of 1016 Patients Who Underwent Surgery for an Intracranial Tumor

		Income groups		
Variables	**Overall** ***N*** **= 1016**	**HIC** ***N*** **= 765**	**UMIC** ***N*** **= 142**	**LLMIC** ***N*** **= 109**
Community SARS-CoV-2 risk				
Low	272 (26.8%)	129 (16.9%)	49 (34.5%)	94 (86.2%)
Medium	365 (35.9%)	291 (38.0%)	63 (44.4%)	11 (10.1%)
High	372 (36.6%)	343 (44.8%)	26 (18.3%)	3 (2.8%)
Unknown	7 (0.7%)	2 (0.3%)	4 (2.8%)	1 (0.9%)
Hospital type				
COVID-19-free surgical pathway	147 (14.5%)	21 (2.7%)	100 (70.4%)	26 (23.9%)
Hospital with no defined pathway	869 (85.5%)	744 (97.3%)	42 (29.6%)	83 (76.1%)
Preoperative Covid screening	753 (74.1%)	551 (72.0%)	119 (83.8%)	83 (76.1%)
Age				
<50 years	357 (35.1%)	255 (33.3%)	52 (36.6%)	50 (45.9%)
50–59 years	256 (25.2%)	180 (23.5%)	38 (26.8%)	38 (34.9%)
60–69 years	233 (22.9%)	184 (24.1%)	36 (25.4%)	13 (11.9%)
70–79 years	150 (14.8%)	129 (16.9%)	14 (9.9%)	7 (6.4%)
>80 years	20 (2.0%)	17 (2.2%)	2 (1.4%)	1 (0.9%)
Sex				
Female	509 (50.1%)	387 (50.6%)	79 (55.6%)	43 (39.4%)
Male	507 (49.9%)	378 (49.4%)	63 (44.4%)	66 (60.6%)
BMI				
Underweight	26 (2.6%)	20 (2.6%)	2 (1.4%)	4 (3.7%)
Normal	466 (45.9%)	297 (38.8%)	92 (64.8%)	77 (70.6%)
Overweight	317 (31.2%)	264 (34.5%)	31 (21.8%)	22 (20.2%)
Obese	204 (20.1%)	181 (23.7%)	17 (12.0%)	6 (5.5%)
Unknown	3 (0.3%)	3 (0.4%)	0 (0.0%)	0 (0.0%)
Preexisting respiratory condition	81 (8.0%)	72 (9.4%)	7 (4.9%)	2 (1.8%)
Current smoker	83 (8.2%)	67 (8.8%)	5 (3.5%)	11 (10.1%)
WHO performance status				
0	418 (41.1%)	351 (45.9%)	38 (26.8%)	29 (26.6%)
1–2	514 (50.6%)	372 (48.6%)	80 (56.3%)	62 (56.9%)
3–4	78 (7.7%)	36 (4.7%)	24 (16.9%)	18 (16.5%)
Unknown	6 (0.6%)	6 (0.8%)	0	0
ASA grade				
ASA grade 1–2	709 (69.8%)	492 (64.3%)	125 (88.0%)	92 (84.4%)
ASA grade 3–5	307 (30.2%)	273 (35.7%)	17 (12.0%)	17 (15.6%)
Urgency of surgery				
Planned	406 (40.0%)	297 (38.8%)	65 (45.8%)	44 (40.4%)
Unplanned	610 (60.0%)	468 (61.2%)	77 (54.2%)	65 (59.6%)
Tumor location				
Supratentorial	854 (84.1%)	632 (82.6%)	123 (86.6%)	99 (90.8%)
Infratentorial	162 (15.9%)	133 (17.4%)	19 (13.4%)	10 (9.2%)
Tumor type				
Glioma	436 (42.9%)	319 (41.7%)	63 (44.4%)	54 (49.5%)
Meningioma	186 (18.3%)	143 (18.7%)	26 (18.3%)	17 (15.6%)
Primary CNS lymphoma	22 (2.2%)	13 (1.7%)	6 (4.2%)	3 (2.8%)
Vestibular schwannoma	29 (2.9%)	22 (2.9%)	5 (3.5%)	2 (1.8%)

Table 1. Continued

	Income groups			
Variables	**Overall** *N* = 1016	**HIC** *N* = 765	**UMIC** *N* = 142	**LLMIC** *N* = 109
Pituitary adenoma	74 (7.3%)	58 (7.6%)	8 (5.6%)	8 (7.3%)
Metastasis	147 (14.5%)	120 (15.7%)	17 (12.0%)	10 (9.2%)
Other	122 (12.0%)	90 (11.8%)	17 (12.0%)	15 (13.8%)
Extent of resection				
Biopsy	105 (10.3%)	81 (10.6%)	8 (5.6%)	16 (14.7%)
Subtotal	316 (31.1%)	257 (33.6%)	36 (25.4%)	23 (21.1%)
Gross total	521 (51.3%)	369 (48.2%)	88 (62.0%)	64 (58.7%)
No postoperative imaging	68 (6.7%)	54 (7.1%)	9 (6.3%)	5 (4.6%)
Unknown	6 (0.6%)	4 (0.5%)	1 (0.7%)	1 (0.9%)

More patients in LLMICs (87.0%) were in communities with low SARS-CoV-2 risk than in UMICs (35.5%) and HICs (16.9%). Of the 10 patients who were tested positive using preoperative swab test, 1 and 9 patients were in UMIC and HICs, respectively. Preexisting respiratory conditions were more common in patients from HICs (9.4%) than in those from UMICs (4.9%) or LLMICs (1.8%). Patients in UMICs and LLMICs had worse WHO performance status and better ASA grade, and those in LLMICs were younger (Table 1). Tumor types of the patients were similar between the 3 income groups. Gross total resection was achieved in 48.5% in HIC, 62.4% in UMIC, and 59.3% in LLMIC.

Pathology

There were 436 patients with a histopathologically confirmed glioma and most (76.1%) had a grade 4 glioma. Overall, 41.7% patients had gross total resection of the glioma (Table 2). There were 1 oligoastrocytoma (not otherwise specified), 52 diffuse astrocytoma, 28 oligodendrogliomas, 18 anaplastic astrocytoma, and 336 glioblastoma. Of the 28 patients with oligodendroglioma, 17 (60.7%) had their gliomas tested for both 1p/19q co-deletion and IDH mutation. In patients with a glioblastoma, 79.5% (*n*/*N* = 267/336) had IDH mutation tested and 52.7% (*n*/*N* = 177/336) had MGMT promoter methylation status determined. Clinical and molecular characteristics by income countries are presented in Supplementary Tables 1–3.

Planned Treatment and Postoperative Outcomes

There was a change from the usual oncological care for 20.8% (*N* = 211) patients (Figure 1). The most common change of care was a delay in surgical treatment (14.4%) though 2.7% patients had their surgery expedited. There were 26 (2.6%) patients who had a change to their planned oncological treatment (Supplementary Table 4).

Within 30 days postoperatively, there were 44 (4.3%) patients who had a respiratory complication and 14 (1.4%) patients who had a COVID-19 diagnosis. The 30-day postoperative mortality was 3.8%, which was higher among patients in LLMICs (9.2%) than those in UMICs (2.8%) and HICs (3.3%) (Figure 1). Of the 10 who tested positive for Covid preoperatively, 2 patients died within 30 days postoperatively. The 30-day mortality of patients with and without a change to care was 3.0% and 4.0%, respectively. There was no difference in postoperative complications between income groups (Supplementary Table 5).

Income Groups and 30-day Mortality

Excluding 6 (0.6%) patients with incomplete data, we performed our multivariable analyses on 30-day mortality using data from 1010 patients. Patients in LLMICs had higher mortality within 30 days after surgery compared to patients in HICs (odds ratio [OR] 2.83, 95% CrI 1.37–5.74) (Figure 2). There were no concerns with model convergence. A model with the same covariates using weakly informative priors centered on zero generated an OR of 2.68 (95% CrI 0.88–7.76), indicating our informative prior regularized the variance of the estimate without inflating the parameter estimate. There was no evidence of higher mortality in UMICs (OR 1.24, 95% CrI 0.32–4.62). We fitted a model with interaction between income groups and WHO performance status. When comparing the leave-one-out cross validation of the models, there was no evidence of better performance of the interaction model (expected log pointwise predictive density difference [ELPD] was 0.5, standard error of ELPD difference was –1.7).

Discussion

This study showed that in the first wave of the COVID-19 pandemic, about 1 in 5 neuro-oncology patients had a change to their treatment plan from standard practice. These changes were mostly related to the timing of surgery rather than postsurgical oncological treatment. The low SARS-CoV-2 risk in participating hospitals located in LMICs allowed us to examine the characteristics and outcomes of their patients with a relatively smaller impact of the pandemic. This revealed that postoperative 30-day mortality was higher in LLMICs compared to HICs.

Table 2. Clinical and Molecular Characteristics of 436 Patients With a Glioma

	Glioma *N* (%)				
	Overall *N* = 436	**Grade 1** *N* = 20	**Grade 2** *N* = 42	**Grade 3** *N* = 42	**Grade 4** *N* = 332
Extent of resection					
Biopsy	72 (16.5%)	7 (35.0%)	8 (19.0%)	7 (16.7%)	50 (15.1%)
Subtotal	167 (38.3%)	4 (20.0%)	13 (31.0%)	6 (14.3%)	144 (43.4%)
Gross total	182 (41.7%)	7 (35.0%)	18 (42.9%)	27 (64.3%)	130 (39.2%)
Unknown	15 (3.4%)	2 (10.0%)	3 (7.1%)	2 (4.8%)	8 (2.4%)
1p/19q co-deletion					
Intact	24 (5.5%)	0 (0.0%)	4 (9.5%)	3 (7.1%)	17 (5.1%)
Deleted	26 (6.0%)	1 (5.0%)	12 (28.6%)	9 (21.4%)	4 (1.2%)
Not tested/unknown	386 (88.5%)	19 (95.0%)	26 (61.9%)	30 (71.4%)	311 (93.7%)
IDH mutation					
Wildtype	263 (60.3%)	3 (15.0%)	4 (9.5%)	12 (28.6%)	244 (73.5%)
Mutated	63 (14.4%)	2 (10.0%)	23 (54.8%)	15 (35.7%)	23 (6.9%)
Not tested/unknown	110 (25.2%)	15 (75.0%)	15 (35.7%)	15 (35.7%)	65 (19.6%)
MGMT promoter methylation					
Unmethylated	103 (23.6%)	1 (5.0%)	4 (9.5%)	6 (14.3%)	92 (27.7%)
Methylated	94 (21.6%)	0 (0.0%)	3 (7.1%)	7 (16.7%)	84 (25.3%)
Not tested/unknown	239 (54.8%)	19 (95.0%)	35 (83.3%)	29 (69.0%)	156 (47.0%)

Impact of COVID-19 Pandemic

Two studies from the United Kingdom with overlapping recruitment periods but both reflecting the first wave of the pandemic reported 8.6–10.7% of patients who had their management changed.[5,6] However, there were variations between neurosurgical centers from 0% to 28% that appeared to correlate with the volume of neuro-oncology patients.[5] These studies also included all neuro-oncology patients without restriction to those undergoing surgery. Together with different hospital management strategies adopted,[13,14] these would explain the higher proportion of patients with a change to their treatment plan in this study. It is difficult to assess the impact of general surgical care guidance[15] and specific guidance for the management of neuro-oncology patients during the pandemic.[16–18] The decision to alter usual care is a dynamic process that depends on the volume of people with COVID-19 requiring hospitalization and the capacity of the hospitals for carrying out medical and surgical oncological treatment in this context. The effect of guidelines is likely to make decision-making more similar between neuro-oncology services rather than reducing the number of patients receiving non-routine management.

Since the end of this study, there has been new evidence about surgical care during the pandemic. The COVIDSurg-Cancer study demonstrated that COVID-19-free surgical pathways were associated with lower postoperative pulmonary complications within 30 days.[19] Planned delay of surgery for 7 weeks in patients with preoperative SARS-CoV-2 infection can mitigate the increased risk of short-term pulmonary complication and perioperative mortality,[20] though may not be possible or safe for patients with brain tumors and raised intracranial pressure. Targeted use of preoperative nasopharyngeal swab testing in areas with high SARS-CoV-2 risk can be a strategy in lower resource settings to implement measures to reduce the risk of postoperative pulmonary complications.[21] Although not reflected in our results, these findings can help reduce the need to change routine care where possible.

Postoperative Mortality

Our 30-day mortality after surgery for a brain tumor in UMICs and HICs was consistent to those in the published literature.[10–12,22,23] There is limited reporting of short-term mortality in LLMIC. One study in Egypt—an LLMIC at the time of writing—included 193 craniotomies for tumor resection over a 3-month period before the pandemic.[24] They reported a mean length of hospital stay of 9 days and an in-hospital mortality of 10.5%. This supports the association between LLMICs and higher 30-day mortality observed in our study. It also suggests that this association did not result from the COVID-19 pandemic since the community SARS-CoV-2 risk was low in LLMICs.

Surgical mortality is a leading cause of death globally and 1 in 4 cancer patients receive a form of surgery as a part of their cancer treatment. However, the quality of evidence available on LLMICs is suboptimal due to selective and poor reporting, thereby limiting comparisons.[25] The GlobalSurg initiative reported on the disparity in perioperative mortality in LLMICs compared to HIC.[26] This collaborative study included 15 958 surgical patients with primary colorectal, gastric, or breast cancer, of which 4131 were in LLMIC. In their multivariable analyses, 30-day

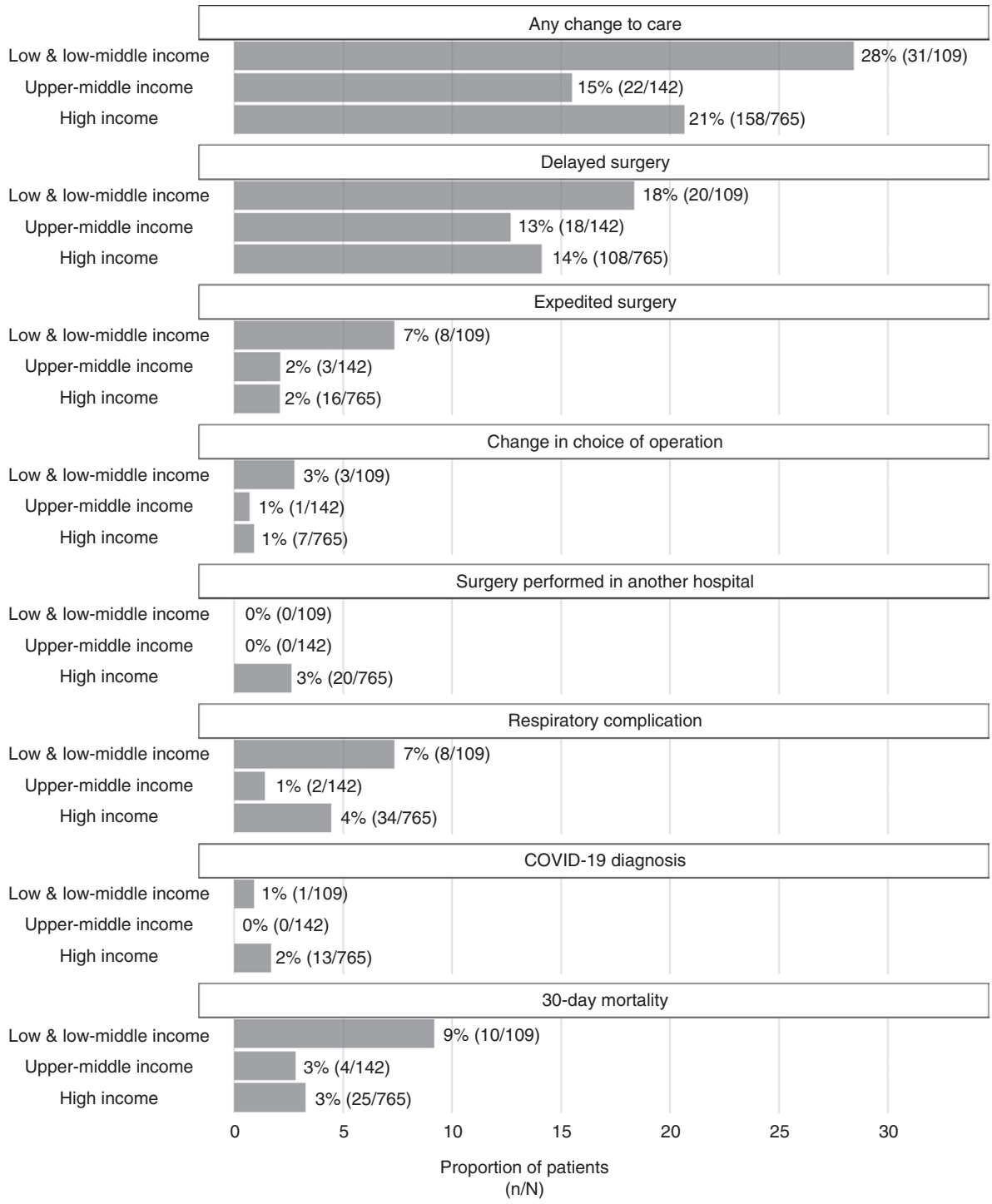

Figure 1. Change in treatment and postoperative outcomes by income groups. Each panel represents the proportion of patients in which the event occurred. Respiratory complications included pneumonia, acute respiratory distress syndrome, and unplanned mechanical ventilation postoperatively. The numbers to the right of each bar are the percentage and number of events over the number of patients in each income groups.

mortality was higher in LLMICs compared to HICs in patients following colorectal (OR 4.59, 95% CI 2.39–8.80) and gastric (OR 3.72, 95% CI 1.70–8.16) cancer surgery. Their findings suggested that a lower capacity to rescue major complications associated with health system factors contributed to the observed higher postoperative mortality.[26] These factors such as access to imaging facilities and critical care facilities are shared with all surgical procedures.

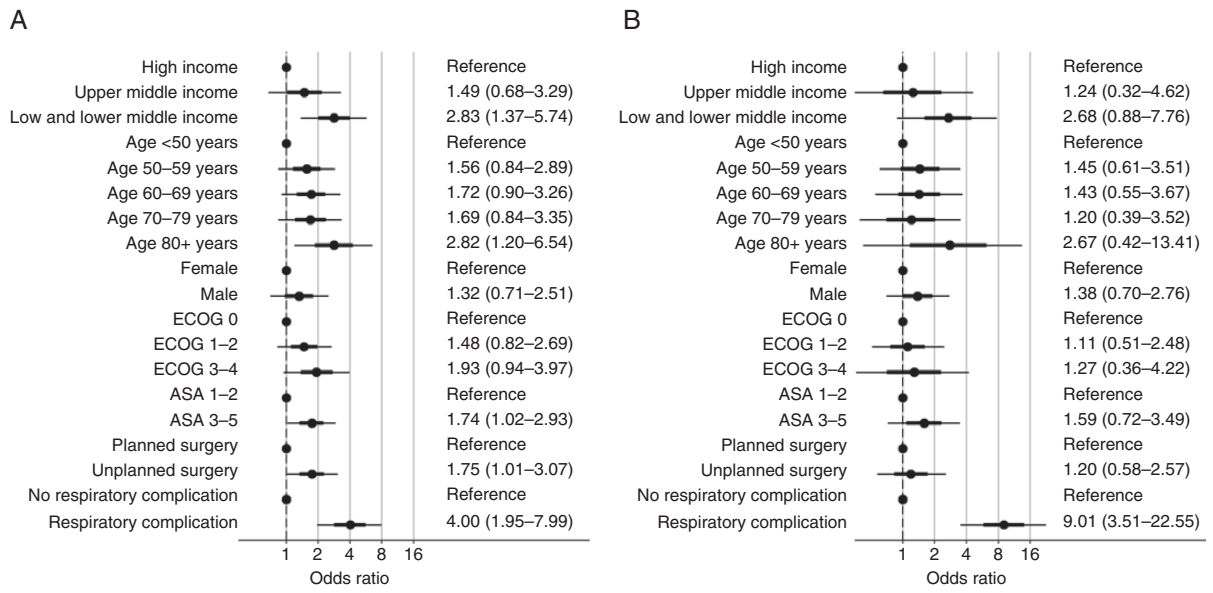

Figure 2. Bayesian multilevel logistic regression models on 30-day postoperative mortality in 1010 patients. (A) Forest plot of odds ratios from the Bayesian multilevel logistic regression on 30-day postoperative mortality using informative priors. (B) Forest plot showing odds ratios from sensitivity analysis using weakly informative priors to assess the influence of informative priors on the posterior distributions of the odds ratios.

It is plausible that these factors could explain the higher 30-day mortality of patients with a brain tumor in LLMICs.

Strengths and Limitations

This study had low levels of missing data and included common prognostic variables associated with short-term outcomes. Our findings provided data on short-term neuro-oncology surgical outcomes after operations for intracranial tumors across different countries. We were able to describe the use of molecular markers in glioma diagnosis in different settings. Importantly, our data added to the limited literature on early postoperative outcomes in LLMIC.

We were unable to include preoperative positive swab results into our model because of data sparsity, with no patients in LLMICs having a positive test. Although this may lead to an underestimation of the effect size for mortality associated with LLMIC, this does not change our narrative of the disparity in postoperative outcome. This study did not collect information on the cause of death. This would have been useful to identify preventable deaths following surgery. We accounted for variations in hospital pathways using a hierarchical model, but there was likely to be residual confounding from the healthcare system and infrastructure that can affect postoperative outcomes. However, these effects are likely to be small since our estimate is similar to larger studies examining general surgical outcomes. A quarter of the patients did not have a preoperative COVID-19 screening and postoperative SARS-CoV-2 infection may be variably reported due to testing capacity. But this was unlikely to affect our results because we used pulmonary complications as a variable in our model, which would account for the higher risk of pulmonary complications associated with preoperative SARS-CoV-2 infection. It was not possible to determine whether the delay in surgery affected the short-term postoperative mortality. Because patients with delayed surgery can have deterioration in WHO performance status, controlling for WHO performance status in our model would, at least partially, account for the delay in surgery. Lastly, we were unable to compare our results to those from an equivalent precovid dataset to determine and extrapolate the effect of the COVID-19 pandemic more confidently. Details about case-volume, case-mix, surgical preparedness[27], and background surgical outcomes can help to interpret differences in postoperative mortality.

Conclusions

The impact of the COVID-19 pandemic on neurosurgical services for patients with intracranial tumors mainly affected surgical care and there was a low (0.3%) proportion of patients having SARS-CoV-2 infection within 30 days after surgery in the participating centers during the pandemic's first wave. Postoperative mortality was higher in LLMICs than in UMICs and HIC, which was not explained by patient characteristics and postoperative pulmonary complications. As the pandemic evolves and new evidence becomes available for the management of surgical patients, neuro-oncology centers can adopt the safest surgical pathways for their patients and audit their performances against the findings presented in this study.

Disparity in 30-day postoperative mortality between different income countries should become a focus of global neurosurgery and warrants further examination to identify any modifiable factors that could be addressed.

Supplementary material

Supplementary material is available online at *Neuro-Oncology* (http://neuro-oncology.oxfordjournals.org/).

Keywords

collaborative research | global neurosurgery | neuro-oncology

Acknowledgments

This research was part-funded by the National Institute for Health Research (NIHR; NIHR 16.136.79) using UK aid from the UK Government to support global health research. RS receives funding from the Economic and Social Research Council. JCG and AAB are funded by personal awards from the NIHR Academy. MTCP was funded by Cancer Research UK Brain Tumour Centre of Excellence Award (C157/A27589). HJM was funded by the Wellcome/ EPSRC Centre for Interventional and Surgical Sciences and NIHR Biomedical Research Centre at University College London. The views expressed in this publication are those of the authors and not necessarily those of the NIHR or the UK Government.

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Funding

National Institute for Health Research Global Health Research Unit, Association of Coloproctology of Great Britain and Ireland, Bowel and Cancer Research, Bowel Disease Research Foundation, Association of Upper Gastrointestinal Surgeons, British Association of Surgical Oncology, British Gynaecological Cancer Society, European Society of Coloproctology, Medtronic, Sarcoma UK, The Urology Foundation, Vascular Society for Great Britain and Ireland, and Yorkshire Cancer Research.

Conflict of Interest

All authors declare no conflict of interest.

Authorship

The writing group contributed to the writing, data interpretation, and critical revision of the manuscript. The collaborators contributed to data collection and study governance across included sites.

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