Neuro-Oncology Practice

10(5), 429–436, 2023 | https://doi.org/10.1093/nop/npad015 | Advance Access date 24 March 2023

Neurosurgical care for patients with high-grade gliomas during the coronavirus disease 2019 pandemic: Analysis of routine billing data of a German nationwide hospital network

Ruediger Gerlach, Julius Dengler, Andreas Bollmann, Michael Stoffel, Farid Youssef, Barbara Carl, Steffen Rosahl, Yu-Mi Ryang, Jorge Terzis, Rudolf Kristof, Thomas Westermaier, Ralf Kuhlen, Andreas Steinbrecher, Vincent Pellissier, Sven Hohenstein, and Oliver Heese

All author affiliations are listed at the end of the article

Corresponding Author: Ruediger Gerlach, MD, Department of Neurosurgery, Helios Klinikum Erfurt, Nordhäuser Str. 74, 99089 Erfurt, Germany (ruediger.gerlach@helios-gesundheit.de).

Abstract

Background. Little is known about delivery of neurosurgical care, complication rate and outcome of patients with high-grade glioma (HGG) during the coronavirus disease 2019 (Covid-19) pandemic.

Methods. This observational, retrospective cohort study analyzed routine administrative data of all patients admitted for neurosurgical treatment of an HGG within the Helios Hospital network in Germany. Data of the Covid-19 pandemic (March 1, 2020—May 31, 2022) were compared to the pre-pandemic period (January 1, 2016—February 29, 2020). Frequency of treatment and outcome (in-hospital mortality, length of hospital stay [LOHS], time in intensive care unit [TICU] and ventilation outside the operating room [OR]) were separately analyzed for patients with microsurgical resection (MR) or stereotactic biopsy (STBx).

Results. A total of 1763 patients underwent MR of an HGG (648 patients during the Covid-19 pandemic; 1115 patients in the pre-pandemic period). 513 patients underwent STBx (182 [pandemic]; 331 patients [pre-pandemic]). No significant differences were found for treatment frequency (MR: 2.95 patients/week [Covid-19 pandemic] vs. 3.04 patients/week [pre-pandemic], IRR 0.98, 95% CI: 0.89–1.07; STBx (1.82 [Covid-19 pandemic] vs. 1.86 [pre-pandemic], IRR 0.96, 95% CI: 0.80–1.16, $P > .05$). Rates of in-hospital mortality, infection, postoperative hemorrhage, cerebral ischemia and ventilation outside the OR were similar in both periods. Overall LOHS was significantly shorter for patients with MR and STBx during the Covid-19 pandemic.

Conclusions. The Covid-19 pandemic did not affect the frequency of neurosurgical treatment of patients with an HGG based on data of a large nationwide hospital network in Germany. LOHS was significantly shorter but quality of neurosurgical care and outcome was not altered during the Covid-19 pandemic.

Key words

glioblastoma | oligodendroglioma | astrocytoma | neurosurgery | Covid-19 pandemic

The coronavirus disease 2019 (Covid-19) pandemic had a global disruptive effect on health care in terms of capacity and resources and has a severe socioeconomic impact worldwide. Official authorities, professional societies and various institutions published management guidelines and position papers with recommendations of treatment prioritization for neurosurgical and neurooncological care with the objective of not compromising the delivery of care in terms of safety, compassion, efficiency, and effectiveness.[1–9] Recommendations were based on clinical presentation, type of tumor, expected prognosis, and relevance of immediate therapy. Declining numbers of neurosurgical emergencies[10] and oncological admissions[11] have been reported but only a very limited number of publications addressed the problem whether reduced health care resources during Covid-19 pandemic had an impact on the number and neurosurgical treatment quality of patients with high-grade glioma (HGG). Administrative data, which are used to bill insurance companies, may be helpful to analyze the actual utilization of health care resources during the pandemic compared to the pre-pandemic control period.[12–14] Since patients with newly diagnosed HGG have a rather dismal prognosis, urgent treatment is required. We therefore analyzed those administrative routine data of neurosurgical care in a nationwide network of neurosurgical departments in Germany to assess the number of treated patients with an HGG, their outcome and periprocedural complications related to existing comorbidities for either microsurgical resection (MR) or stereotactic biopsy (STBx) during the Covid-19 pandemic compared to a pre-pandemic control group.

Material and Methods

This large observational retrospective multicenter cohort study includes administrative data of all patients hospitalized for neurosurgical treatment of high-grade gliomas (WHO grade III and IV) at 10 neurosurgical departments within the Helios network in Germany between March 1, 2020 and May 31, 2022 (pandemic period) and January 1, 2016 and February 29, 2020 (pre-pandemic control period). Periods of different Covid-19 virus variants were defined as follows (wild type: February 4, 2020 to March 7, 2021; Alpha variant: March 8, 2021 to June 25, 2021, Delta variant: June 26, 2021 to January 2, 2022 and Omicron variant from 2022-01-03 onward).

Inclusion Criteria

The diagnosis of an HGG was made according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10-GM, German Modification) codes using the main codes C71.x. According to the ICD-10 classification, a discrimination between grade III and IV tumors of the WHO 2016 classification is not possible. Therefore, patients with anaplastic astrocytoma, anaplastic oligodendroglioma and glioblastoma were included. Procedures and treatment paths for neurosurgical interventions e.g. microsurgical resection [MR] (5-015.0) and stereotactic biopsy [STBx] (1-511.x) were identified via the Operations and Procedures codes (OPS (German adaptation of the International Classification of the Procedures in Medicine of the World Health Organization, version 2017). Patients were included if they were coded as in-hospital patients with an HGG and the codes for MR or STBx between January 1, 2016 and May 31, 2022. Patients coded as an HGG without operative procedures were excluded.

Data Extraction

Outcome measures were defined within 30 days of the procedure as in-hospital mortality, postoperative infection (5-013.5), postoperative hemorrhage (5-013.4 [intracerebral] and 5-013.1 [subdural]) and cerebral ischemia (I63.x).

Relevant comorbidities such as coronary artery disease (I 25.x), arterial hypertension (I10.x; I11.x; I12.x; I13.x; I15.x), diabetes mellitus (E10.x; E11.x; E12.x; E13.x; E14.x), previous or current anticoagulation (Z92.1), chronic obstructive pulmonary disease (COPD, J44.x) renal insufficiency (N18.x; N19) or symptomatic epilepsy (G40.x; G41.x) were identified from encoded secondary diagnoses at hospital discharge.

To assess the amount of resources allocated to treatment of HGG patients we used the following variables: length of hospital stay (LOHS [days]), time in intensive care unit stay (TICU [days]), mechanical ventilation outside the operating room [OR] (OPS 8-70x, 8-71x, or duration of ventilation > 0). Moreover, the total numbers of computed tomography (CT; 3-200; 3-220) and magnetic resonance tomography (MRI, 3-800; 3-820) during 30 days after the procedure were analyzed. We were not able to differentiate pre- and postoperative time periods contributing to TICU or with ventilation outside the OR. Thus, it can be possible, that some patients required already preoperative ICU care or ventilation, while some of the patients needed prolonged postoperative ventilation or ICU care.

All data were stored in pseudonymized form, and data use was in accordance with national data protection standards. Informed consent was waived due to the retrospective nature of this study. The study was approved by the ethics committee of the University of Leipzig on January 28, 2021 (490/20-ek) and the ethics committee of the State Medical Association Thuringia (22748/2021/140).

Surgical Treatment

Decision about surgical treatment (MR or STBx) was at the discretion of the treating neurosurgical department following internal guidelines developed by the "Helios Neurooncology Working Group". Microsurgical resection was performed in a standardized state of the art procedure, using ultrasonic aspirators, 5-ALA fluorescence, image guided surgery, frameless neuronavigation and whenever indicated intraoperative evoked potentials, cranial nerve monitoring and cortical/subcortical mapping including awake surgery for intraoperative language monitoring. Postoperative MRI was performed for resection control and exclusion of complications within 72 hours after MR. A postoperative CT within 24 hours after completing surgery was performed according to the discretion of the respective centers. All patients were intended to be observed in the ICU/intermediate care unit (IMCU) overnight, and referred to the peripheral ward the following day depending on patient´s condition and clinical findings.

Stereotactic biopsy was performed in general anesthesia with preoperative CT and MRI guided trajectory planning. Patients were monitored in the post anesthesia care unit for at least 4 hours and had a routine CT scan before transfer to the neurosurgical ward to exclude relevant hematoma. If a hematoma was detected patients were referred to the ICU or IMCU for further monitoring and control CT was done according to the center's policy.

Statistical Analysis

Administrative data were extracted using QlikView (QlikTech, Radnor, Pennsylvania, USA). Inferential statistics were based on generalized linear mixed models (GLMM) specifying hospitals as random factor.[15] Effects were estimated with the lme4 package (version 1.1-21)[16] in the R environment for statistical computing (version 4.0.2, 64-bit build) (https://www.R-project.org/). In all models, we specified varying intercepts for the random factor. For all tests we apply a two-tailed 5% error criterion for significance.

For the description of the patient characteristics of the cohorts (before and during the Covid-19 pandemic), Wilcoxon tests for continuous variables and Chi-squared tests for categorical variables were used. Proportions or mean (SD) and *P* values are reported.

The comparison of weekly admissions, LOHS, TICU, number of cCT and number of cMRT between cohorts (either Covid-19 pandemic vs. pre-pandemic or Covid-19 waves) was carried out with GLMM) with a Poisson distribution and a log–link function. Mean (SD), ratios (computed as the exponential of the regression coefficients) along with 95% CI and *P* values are reported.

The comparison of binary outcome (in-hospital mortality, infection, postoperative hemorrhage, cerebral ischemia and additional ventilation outside the OR) between cohorts was carried out with a logistic GLMM and a logit-link function. Proportions, OR (95% CI) and *P* values are reported. Furthermore, we analyzed the binary outcomes with multivariable logistic GLMMs using the predictor variables coronary heart disease, arterial hypertension, diabetes mellitus, previous or current anticoagulation, chronic obstructive pulmonary disease, renal insufficiency, symptomatic epilepsy, period (pandemic vs. pre-pandemic), age, and sex. Dichotomous predictors entered the analyses as 0.5 vs. −0.5 contrasts, and age was centered on its mean and scaled to unit variance.

Results

Baseline Characteristics

About 2276 patients with HGG were treated in 10 neurosurgical departments of the Helios Clinics Network between January 1, 2016 and May 31, 2022. Accordingly, the mean number of patients with HGG admitted to the Helios network was 355 patients per year. 1763 patients underwent microsurgical resection of their HGG (648 patients during the Covid-19 pandemic period and 1139 patients in the pre-pandemic period). 513 patients underwent stereotactic biopsy (182 patients during the Covid-19 pandemic and 331 patients during the pre-pandemic period, respectively). Table 1 delineates baseline characteristics and co-morbidities of patients with HGG, who underwent MR during the Covid-19 pandemic period and the pre-pandemic control period, while Table 2 shows the same data for patients with STBx.

There were significantly more female patients with MR in the Covid-19 pandemic period (42%) compared to pre-pandemic period (40%; $P < .05$). Patients, who underwent STBx during the Covid-19 period were significantly younger compared to the pre pandemic period (62 ± 17 years vs. 66 ± 14 years ($P < .05$). Patients treated with their HGG during Covid-19 pandemic had significantly lower coding of renal insufficiency (7.4% vs. 13%, $P < .01$ for MR and 8.2% vs. 15% for STBx, $P < .05$, respectively). Symptomatic epilepsy was significantly lower in the Covid-19 pandemic compared to the pre-pandemic control period (35% vs. 40%, $P < .05$ for MR and 21% vs. 29% for STBx; $P < .05$).

Treatment Frequency

During the Covid-19 pandemic the weekly average microsurgical treatment rate within the network of 10 institutions for patients with an HGG was 2.95 (±1.94) patients and therefore not different to the pre-pandemic control group with 3.04 (±1.73) operated patients/week (IRR 0.98 [0.88; 1.07]; $P = .61$). A mean of 1.82 (±1.24) patients/week underwent STBx during the Covid-19 period compared to 1.86 (±1.24) patients/week in the pre-pandemic control group (IRR 0.96 [0.80; 1.16]; $P = .694$).

Outcome Analysis

Tables 3 and 4 present the results of patient's outcome following MR or STBx, respectively. 22 (3.4%) patients died during hospital stay after MR during the Covid-19 period

Table 1. Baseline Characteristics (Demographics, Co-morbidities) are Presented as Mean (SD) per Patient or Number of Cases (%) for Microsurgical Resection. The Covid-19 Pandemic Period and the Pre-pandemic Control Period are Compared Using a Wilcoxon Test (continuous variable) or a Chi-squared Test (Categorical Variables). COPD Chronic Obstructive Pulmonary Disease

	Total	Covid-19 pandemic group	Pre-pandemic Control Group	*P*
Number of patients	1.763 (100%)	648 (100%)	1.115 (100%)	
Age	56 (18)	55 (19)	57 (18)	.45
Female	736 (42%)	293 (45%)	443 (40%)	<.05
Diabetes mellitus	244 (14%)	80 (12%)	164 (15%)	.17
Coronary heart disease	96 (5.4%)	35 (5.4%)	61 (5.5%)	.95
Arterial hypertension	718 (41%)	270 (42%)	448 (40%)	.54
Anticoagulation	116 (6.6%)	38 (5.9%)	78 (7.0%)	.36
COPD	24 (1.4%)	8 (1.2%)	16 (1.4%)	.73
Renal insufficiency	196 (11%)	47 (7.4%)	148 (13%)	<.01
Symptomatic epilepsy	680 (39%)	230 (35%)	450 (40%)	<.05

Table 2. Baseline Characteristics (Demographics, Co-morbidities) are Presented as Mean (SD) per Patient or Number of Cases (%) for Stereotactic Biopsy. The Covid-19 Pandemic Period and the Pre-pandemic Control Period are Compared Using a Wilcoxon Test (Continuous Variable) or a Chi-Squared Test (Categorical Variables). COPD Chronic Obstructive Pulmonary Disease

	Total	Covid-19 Pandemic Group	Pre-pandemic Control Group	*P*
Number of patients	513 (100%)	182 (100%)	331 (100%)	
Age	64 (15)	62 (17)	66 (14)	<.05
Female	237 (46%)	82 (45%)	155 (47%)	.70
Diabetes mellitus	103 (20%)	36 (20%)	67 (20%)	.90
Coronary heart disease	43 (8.4%)	15 (8.2%)	28 (8.5%)	.93
Arterial hypertension	237 (46%)	86 (47%)	151 (46%)	.72
Anticoagulation	38 (7.4%)	11 (6.0%)	27 (8.2%)	.38
COPD	10 (1.9%)	5 (2.7%)	5 (1.5%)	.34
Renal insufficiency	64 (12%)	15 (8.2%)	49 (15%)	<.05
Symptomatic epilepsy	135 (26%)	38 (21%)	97 (29%)	<.05

Table 3. Outcomes are Presented as Number of Cases (%) for Patients With Microsurgical Resection. The Covid-19 Pandemic Period is Compared to the Pre-pandemic Period Using Logistic GLMMs

	Total	Covid-19 Pandemic Group	Pre-pandemic Control Group	*P*	OR (95% CI)
In-hospital mortality	51 (2.9%)	22 (3.4%)	29 (2.6%)	.35	1.32 (0.74; 2.31)
Infection	7 (0.6%)	1 (0.2%)	6 (0.8%)	.19	0.24 (0.03; 2.04)
Postoperative Hemorrhage	44 (3.9%)	16 (4.0%)	28 (3.8%)	.57	1.2 (0.62; 2.26)
Cerebral Ischemia	45 (2.6%)	18 (2.8%)	27 (2.5%)	.55	1.2 (0.64; 2.20)

Table 4. Outcomes are Presented as Number of Cases (%) for Patients With Stereotactic Biopsy. The Covid-19 Pandemic Period is Compared to the Pre-pandemic Period Using Logistic GLMMs. CHD Coronary Heart Disease

	Total	Covid-19 Pandemic Group	Pre-pandemic Control Group	*P*	OR (95% CI)
In-hospital mortality	32 (6.3%)	10 (5.5%)	22 (6.7%)	.60	0.81 (0.36; 1.71)
Infection	3 (0.9%)	0 (0.0%)	3 (1.4%)	.98	0
Postoperative Hemorrhage	1 (0.3%)	0 (0.0%)	1 (0.5%)	1.0	0
Cerebral Ischemia	4 (0.8%)	3 (1.6%)	1 (0.3%)	.098	7.81 (0.68; 89.19)

compared to 29 patients (2.6%) in the pre-pandemic period. 10 patients (5.5%) died after STBx during the hospital stay in the Covid-19 period compared to 22 patients (6.7%) in the pre-pandemic period. In-hospital mortality for surgical treatment of HGG was therefore not statistically different between treatment periods, neither for MR (OR 1.32 [0.74–2.31]; $P = .34$) nor for STBx (OR 0.81 [0.36–1.71]; $P = .59$, Covid-19 pandemic compared to the pre-pandemic control period). Using multivariable analyses including demographic factors, comorbidities and periods, we also did not find significant differences between pre- and Covid-19 pandemic cohorts.

No further statistically significant differences were found for perioperative complications e.g., infection, postoperative hemorrhage or cerebral ischemia for patients with an HGG and MR or STBx during Covid-19 pandemic compared to the pre-pandemic control period. No significant differences were detected for all outcome parameters during the different waves of the Covid-19 pandemic (Wildtype, Alpha, Delta or Omicron variant).

Table 5. Perioperative Resources Used for Patients With Microsurgical Resection Presented as Mean (SD) or Number of Cases (%). The Covid-19 Pandemic Period is Compared to the Pre-pandemic Period Using Poisson GLMMs (Binary Variables) or Logistic GLMMs (Continuous Variables), CT Computed Tomography, MRI Magnetic Resonance Tomography, LOHS Length of Stay

	Covid-19 Pandemic Group	Pre-pandemic Control Group	Ratio	*P*
LOHS (days)	**14.52 (14.04)**	**15.58 (12.39)**	**0.95 (0.93; 0.98)**	**<.01**
Time in ICU (days)	**5.47 (32.19)**	**4.68 (29.69)**	**1.32 (1.26; 1.38)**	**<.01**
Number of patients required ventilation outside the operating room	54 (8.4%)	98 (8.9%)	0.97 (0.69; 1.38)	.883
CT	0.76 (0.78)	0.78 (0.72)	1.00 (0.87; 1.15)	.986
MRI	**0.77 (0.7)**	**0.55 (0.63%)**	**1.37 (1.18; 1.59)**	**<.01**

Table 6. Perioperative Resources Used for Patients With Stereotactic Biopsy Presented as Mean (SD) or Number of Cases (%). The Covid-19 Pandemic Period is Compared to the Pre-pandemic Period Using Poisson GLMMs (Binary Variables) or Logistic GLMMs (Continuous Variables), CT Computed Tomography, MRI Magnetic Resonance Tomography, LOHS Length of Stay.

	Covid-19 pandemic group	Pre-pandemic control group	Ratio	*P*
LOHS (days)	**14.71 (16.06)**	**18.47 (16.06)**	**0.82 (0.79; 0.86)**	**<.01**
Time in ICU (days)	1.82 (11.86)	2.35 (12.5)	0.98 (0.86; 1.11)	.713
Number of patients required ventilation outside the operating room	10 (5.5%)	13 (4.0%)	1.41 (0.61; 3.29)	.422
CT	1.02 (0.42)	1.04 (0.28)	0.98 (0.78; 1.22)	.837
MRI	**0.34 (0.63)**	**0.19 (0.47%)**	**1.79 (1.15; 2.77)**	**<.01**

No difference in hospital mortality, infection, postoperative hemorrhage, cerebral ischemia and additional ventilation in ICU was found with respect to institutional caseload, neither for MR nor STBx, when compared at different institutional neurosurgical departments.

Perioperative Resources Used During Treatment Periods

To analyze the resources used for treatment of HGG patients during the Covid-19 period we determined the number of patients with ventilation outside the OR in the ICU, the time in ICU, the overall LOHS, the average number of computed tomography and magnetic resonance imaging and compared data to the pre-pandemic period (Tables 5 and 6).

Patients with MR and STBx of an HGG had a significantly shorter hospital stay during the Covid-19 period compared to the pre-pandemic period (14.5 ± 14 vs. 15.6 ± 12.4 days, ratio: 0.95, 95% CI: 0.93–0.98; $P < .01$ and 14.7 ± 13.9 vs. 18.5 ± 16.1, ratio: 0.82, 95% CI: 0.79–0.86; $P < .01$).

For patients, who underwent MR of an HGG theTICU was significantly longer during the Covid-19 period compared to the pre-pandemic period (5.5 vs. 4.7 days, ratio: 1.32, 95% CI: 1.26–1.38, $P < .01$).

For both MR and STBx the use of MRI was significantly more frequent during the Covid-19 period compared to the pre-pandemic period (0.8 ± 0.7 vs. 0.6 ± 0.6, ratio: 1.37, 95% CI: 1.18–1.59; $P < .01$, 0.3 ± 0.6 vs. 0.2 ± 0.5, ratio: 1.79, 95% CI: 1.15–2.77; $P < .05$).

Discussion

Frequency of Surgical Treatment of HGG Patients during the Covid-19 Pandemic

Due to the disruptive effect of the Covid-19 pandemic for the healthcare systems worldwide in terms of available operative and ICU capacities as well as other treatment resources, the care of patients with brain cancer may have been severely affected during the different waves of the Covid-19 pandemic. Moreover, patients may fear in hospital Covid-19 contagion and therefore avoid admission to the hospital with the risk of consecutive delays in diagnosis and surgical therapy. Especially patients with HGG are considered as high risk patients due to neurological compromise, age related frailty and are thus at risk for various critical events from SARS-COV-2 infection, eg, thromboembolism. Scientific data addressing the frequency and quality of care of HGG treatment during Covid-19 pandemic is pending. A review from Airth et al. aimed to summarize the early impact of the pandemic on clinical care and research within the practice of neurooncology. They described, that most adult and pediatric neurosurgical centers experienced reductions in new referrals and operations for brain malignancies, and those who did present for treatment frequently had operations cancelled or delayed.[17] Although not specifically analyzed in a reported from Egypt the number of oncological patients dropped around 39% (36 vs. 59) in the Covid-19 period.[18] A similar trend was found for patients with general oncological admissions in German hospitals, where a significant lower overall cancer admission rate was seen for the early lockdown period.[11]

We therefore first addressed the question, whether or not the total number of patients with newly diagnosed HGG differed during the Covid-19 pandemic compared to a pre-pandemic control period in a large number of patients treated in a nationwide hospital network with neurosurgical service in Germany. With respect to published guidelines of neurosurgical care for patients with HGG[1–9] the treatment aim was gross total resection, whenever safely possible. If surgery related deficits would outweigh the benefit of microsurgery, stereotactic biopsy was indicated for diagnosis and molecular tumor characteristics. To the best of our knowledge, this is the first large volume multicenter analysis, which shows that the absolute number of patients treated for an HGG did not decline significantly during the Covid-19 pandemic in Germany neither for microsurgical resection nor for stereotactic biopsy, when compared to the pre-pandemic period. This holds true also for the different waves of Covid-19 pandemic, although the numbers of patients during these periods are quite low. The Helios network of neurosurgical departments comprises hospitals in rural and urban areas in 13 of the 16 federal states of Germany and accounts for about 7% of patient hospitalizations nationwide. Patients of all health insurance funds available in Germany (public and private) were included. This improves the generalizability of our findings on healthcare processes and outcomes to the entire population of Germany, as there is no selection for insurance fund associated subpopulations with specific profiles of comorbidities and risk factors.[13]

Outcome of Surgically Treated Patients with HGG

Quality of neurosurgical care for patients surgically treatment for an HGG was maintained during the Covid-19 pandemic in general. In particular, the 30-day mortality of patients in this series with an HGG did not differ between the Covid-19 pandemic and the pre-pandemic control period. Data reporting in-house or early mortality for treated patients with glioblastoma ranges from 1[19] to 5.2%[20] in pre-pandemic series. In-house 30-day mortality rate in this analysis was 3.4% during Covid-19 and 2.6% during the pre-pandemic period for MR and 4.5% and 6.7% for patients with STBx, respectively. Therefore, our data compare well with a cross-sectional study of inpatients from a multicentric German database, which suggests that absolute in-hospital mortality for 2020 across disease groups was not higher compared with previous years.[14]

Moreover, no statistically significant differences were found for perioperative complications eg, infection, postoperative hemorrhage or cerebral ischemia for patients with an HGG and MR or STBx during the Covid-19 pandemic compared to pre-pandemic control period. The rate of surgical infections in this series was less than 1.5% for both MR and STBx, which compares well with a reported prevalence of surgical infection of 4.3% at 3 months after standard intracranial neurosurgical procedures.[21] Postoperative hemorrhage was 3.8% in patients with MR (Covid-19 pandemic and pre-pandemic period) and less than 0.5% after STBx. Therefore, the rate of postoperative hemorrhage is comparable with previous studies[22,23] and was associated with iatrogenic anticoagulation as previously discussed elsewhere.[24] All- together we were able to demonstrate that patients with an HGG can be treated in the most effective manner without a compromise in safety. This is in concordance with single center studies,[25–27] who analyzed general neurosurgical patients. Norman et al. found no significant difference in outcomes of patients with malignant brain tumors during the Covid-19 pandemic compared to a pre-pandemic control period, despite significantly more treatment delays and use of telehealth in 2020.[28] In contrast, a single center analysis of general neurosurgical patients from Egypt found a higher 1-month mortality during the Covid-19 period compared to the pre-pandemic period, but did not discriminate patient's outcome according to the treated pathology.[18]

Another aspect of our data analysis was whether the caseload has an impact on postoperative outcome or major complications after surgery for patients with an HGG. In this series, mortality and postoperative complication such as infection, postoperative hemorrhage, cerebral ischemia was not depending on the caseloads of HGG patient's in the individual institutions participating in this study. This is in line with data from a prospective registry of the Dutch Society for Neurosurgery, which shows that institutional characteristics, overall case volume, university hospital and biopsy percentage were not associated with complication severity nor with performance decline.[29] However, other reports demonstrate, that higher case volume was related to significant lower early mortality.[20]

Treatment Resources Used to Treat HGG during the Covid-19 Pandemic

This study showed that patients with MR and STBx of an HGG had a significantly shorter hospital stay during the Covid-19 period compared to the pre-pandemic period. This result most likely reflects the attempt to effectively use all in-hospital resources and decrease the risk of contagion of patients with SARS-COV-2 infection as recommended by scientific societies and medical authorities and published guidelines for diagnostic and treatment of neurooncological patients.[1,2,5,7,8,25,30] It is important to underline, that the overall reduction in hospital stay was not associated with increased complications or adverse outcome. A recent study, analyzing general neurosurgical patients showed, that the LOHS was shorter in the Covid-19 period, although not statistically significant.[18] In contrast, other reports found, that hospitalization time, the time to wait for surgery and the time from operation to discharge was longer in patients with glioma during the pandemic compared before.[31]

Interestingly, patients, who underwent MR of an HGG during the Covid-19 period had a significantly longer TICU compared to HGG patients in the pre-pandemic period. Zou et al. found, that the tumor volume was larger and the midline shift distance was greater after the pandemic than before in neurooncological patients[31] as a result of delayed admission. Although we were not able to test this with the current data set this may explain the prolonged TICU for patients, who underwent MR of their HGG during the Covid-19 pandemic.

MRI was significantly more frequently used during the Covid-19 pandemic for all patients with an HGG. This was probably related to reduced MRI resources outside the hospital during the Covid-19 pandemic rather than to the necessity to diagnose treatment associated complications, which did not differ between the Covid-19 pandemic and pre-pandemic control period.

Limitations of the Study

There are several potential limitations to consider when interpreting our results. First, our analysis relies on ICD-10 and Operations and Procedures codes. In general, administrative data are not collected for research interests but for remuneration reasons, which could affect the encoded information. The quality of our study results depends largely on the correct encoding of procedures and diagnoses at hospital discharge.[32] However, regarding the main discharge diagnosis and the adequacy of hospitalization, as well as encoding interventions and treatment resources, there is a continuous evaluation by reimbursement and health insurance companies that supports the assumption of overall valid information. All analyses were performed on a case rather than patient level owing to data structure because neither cross-linking of patients between hospitals nor follow-up outside the investigated hospital network was possible as it was described in a large comparative analysis of in-hospital mortality per disease groups in Germany before and during the Covid-19 pandemic from 2016 to 2020.[14] Second, the database does not differentiate between grade III and IV intrinsic brain neoplasms. Therefore patients with malignant WHO°III glioma may be underrepresented since patients with glioblastoma are generally treated more frequently, are older, may have more co-morbidities and thus treatment may be associated with adverse outcome. Third, it was impossible to adjust the analyses for a number of potential confounders such as socioeconomic status owing to missing data. Because the investigation was retrospective, additional unknown factors may have influenced results. However, due to the large number of included patients it may be possible to use claims data for comparison of HGG patients treated during the Covid-19 pandemic compared to pre-pandemic control groups until prospective data are available.

Conclusions

Despite all the inherent and well-known limitations of claims data use, these data show that the frequency of treated patients suffering from an HGG was not reduced during the Covid-19 pandemic and the quality of treatment and outcome of patients may be comparable to pre-pandemic data. This is the first study including a large number of patients, which provides data on neurosurgical care for HGG patients in a nationwide German hospital network. Mid- and long-term neurooncological outcome of patients with treatment of an HGG during Covid-19 are unknown and deserve further studies.

Funding

Grant-ID: 2021-0420 supported by Helios Kliniken GmbH, 5000,-€ to RG

Acknowledgment

We thank the nursing and medical staff and specialists in the HELIOS network for their efforts in caring for patients in these difficult times. This study was supported by Helios Kliniken GmbH, Grant-ID: 2021-0420.

Conflict of Interest

None.

Author Contribution

Idea, study design, writing the manuscript: RG, OH. Statistical analysis: VP, SH, AB, RG. Patient treatment, editing the manuscript, data collection: JD, MS, FY, BC, SR, YMR, JT, RK, TW, AS, RG, OH. Study design, national data protection standard advisory: RG, OH, RK.

Affiliations

Department of Neurosurgery, HELIOS Klinikum Erfurt, Erfurt, Germany (R.G., S.R.) ; Faculty of Health Sciences Brandenburg, Brandenburg Medical School Theodor Fontane, Campus Bad Saarow, Bad Saarow, Germany and Department of Neurosurgery, HELIOS Hospital Bad Saarow, Bad Saarow, Germany (J.D.); Helios Health Institute, Berlin and Department of Electrophysiology, Heart Center Leipzig at University of Leipzig, Leipzig, Germany (A.B.); Department of Neurosurgery, HELIOS Hospital Krefeld, Krefeld, Germany (M.S.); Department of Neurosurgery, HELIOS Vogtland-Hospital Plauen, Plauen, Germany (F.Y.); Department of Neurosurgery, HELIOS Dr. Horst Schmidt Kliniken Wiesbaden, Wiesbaden, Germany (B.C.); Department of Neurosurgery, HELIOS Klinikum Berlin-Buch, Berlin, Germany (Y-M.R.); Department of Neurosurgery; HELIOS Universitätsklinikum Wuppertal, Wuppertal, Germany (J.T.); Department of Neurosurgery, HELIOS Klinikum Meiningen, Meiningen, Germany (R.K.); Department of Neurosurgery, Helios Amper-Klinikum Dachau, Dachau, Germany (T.W.); HELIOS Health GmbH, Berlin, Germany (R.K.); Department of Neurology, HELIOS Klinikum Erfurt, Erfurt, Germany (A.S.); HELIOS Health Institute, Berlin and Department of Electrophysiology, Heart Center Leipzig at University of Leipzig, Leipzig, Germany (V.P., S.H.); Department of Neurosurgery and Spinal Surgery, HELIOS Medical Center, Campus of MSH Medical School Hamburg, Schwerin, Germany (O.H.)

References

1. Gupta T, Singh VP, Balasubramian A, et al. ISNO position statement on treatment guidance in neuro-oncology during pandemics. *Neurol India.* 2020;68(4):769–773.
2. Bernhardt D, Wick W, Weiss SE, et al. Neuro-oncology management during the COVID-19 pandemic with a focus on WHO grade III and IV gliomas. *Neuro-oncology.* 2020;22(7):928–935.
3. Batistella GNR, Santos AJ, Paiva Neto MA, et al. Approaching glioblastoma during COVID-19 pandemic: Current recommendations and considerations in Brazil. *Arq Neuropsiquiatr.* 2021;79(2):167–172.
4. Noticewala SS, Ludmir EB, Bishop AJ, et al. Radiation for glioblastoma in the era of coronavirus disease 2019 (COVID-19): Patient selection and hypofractionation to maximize benefit and minimize risk. *Adv Radiat Oncol.* 2020;5(4):743–745.
5. Ramakrishna R, Zadeh G, Sheehan JP, et al. Inpatient and outpatient case prioritization for patients with neuro-oncologic disease amid the COVID-19 pandemic: General guidance for neuro-oncology practitioners from the AANS/CNS Tumor Section and Society for Neuro-Oncology. *J Neurooncol.* 2020;147(3):525–529.
6. Burke JF, Chan AK, Mummaneni V, et al. Letter: The coronavirus disease 2019 global pandemic: A neurosurgical treatment algorithm. *Neurosurgery.* 2020;87(1):E50–E56.
7. Mohile NA, Blakeley JO, Gatson NTN, et al. Urgent considerations for the neuro-oncologic treatment of patients with gliomas during the COVID-19 pandemic. *Neuro-oncology.* 2020;22(7):912–917.
8. Weller M, Preusser M. How we treat patients with brain tumour during the COVID-19 pandemic. *ESMO Open.* 2020;4(suppl 2):e000789.
9. Internò V, Rudà R, Sergi MC, et al. Newly diagnosed Glioblastoma Multiforme (GBM) during COVID-19 pandemic: Changes in therapeutic approach to minimize in-hospital SARS-COV-2 contagion in pre-vaccine era. *Acta Biomed.* 2022;93(3):e2022067.
10. Falter J, Schebesch KM, Schmidt NO. Declining numbers of neurosurgical emergencies at a German university medical center during the coronavirus lockdown. *J Neurol Surg A Cent Eur Neurosurg.* 2022;83(4):314–320.
11. Reichardt P, Bollmann A, Hohenstein S, et al. Decreased incidence of oncology admissions in 75 Helios hospitals in Germany during the COVID-19 pandemic. *Oncol Res Treat.* 2021;44(3):71–75.
12. Bollmann A, Hohenstein S, Pellissier V, et al. Utilization of in- and outpatient hospital care in Germany during the Covid-19 pandemic insights from the German-wide Helios hospital network. *PLoS One.* 2021;16(3):e0249251.
13. Dengler J, Prass K, Palm F, et al. Changes in nationwide in-hospital stroke care during the first four waves of COVID-19 in Germany. *Eur Stroke J.* doi: 10.1177/23969873221089152
14. König S, Pellissier V, Hohenstein S, et al. A comparative analysis of in-hospital mortality per disease groups in Germany before and during the COVID-19 pandemic from 2016 to 2020. *JAMA Netw Open.* 2022;5(2):e2148649.
15. Baayen RH, Davidson DJ, Bates DM. Mixed-effects modeling with crossed random effects for subjects and items. *J Mem Lang.* 2008;59(4):390–412.
16. Bates D, Mächler M, Bolker B, et al. Fitting linear mixed-effects models using lme4. *J Stat Softw.* 2015;67(1):1–48.
17. Airth A, Whittle JR, Dimou J. How has the COVID-19 pandemic impacted clinical care and research in Neuro-Oncology? *J Clin Neurosci.* 2022;105:91–102.
18. Azab MA, Azzam AY, Eraky AM, et al. Analyzing outcomes of neurosurgical operations performed before and during the COVID-19 pandemic in Egypt. A matched single-center cohort study. *Interdiscip Neurosurg Adv Tech Case Manage.* 2021;26:101369.
19. Gulati S, Jakola AS, Nerland US, et al. The risk of getting worse: Surgically acquired deficits, perioperative complications, and functional outcomes after primary resection of glioblastoma. *World neurosurg.* 2011;76(6):572–579.
20. De Witt Hamer PC, Ho VKY, Zwinderman AH, et al; Quality Registry Neuro Surgery glioblastoma working group from the Dutch Society of Neurosurgery. Between-hospital variation in mortality and survival after glioblastoma surgery in the Dutch Quality Registry for Neuro Surgery. *J Neurooncol.* 2019;144(2):313–323.
21. Abu Hamdeh S, Lytsy B, Ronne-Engstrom E. Surgical site infections in standard neurosurgery procedures- a study of incidence, impact and potential risk factors. *Br J Neurosurg.* 2014;28(2):270–275.
22. Palmer JD, Sparrow OC, Iannotti F. Postoperative hematoma: A 5-year survey and identification of avoidable risk factors. *Neurosurgery.* 1994;35(6):1061–1064; discussion 1064.
23. Gerlach R, Raabe A, Scharrer I, et al. Post-operative hematoma after surgery for intracranial meningiomas: Causes, avoidable risk factors and clinical outcome. *Neurol Res.* 2004;26(1):61–66.
24. Gerlach R, Krause M, Seifert V, et al. Hemostatic and hemorrhagic problems in neurosurgical patients. *Acta Neurochir.* 2009;151(8):873–900.
25. Amoo M, Horan J, Gilmartin B, et al. The provision of neuro-oncology and glioma neurosurgery during the SARS-CoV-2 pandemic: A single national tertiary centre experience. *Ir J Med Sci.* 2021;190(3):905–911.
26. Pessina F, Navarria P, Bellu L, et al. Treatment of patients with glioma during the COVID-19 pandemic: What we learned and what we take home for the future. *Neurosurg Focus.* 2020;49(6):E10.
27. Toman E, Soon WC, Thanabalasundaram G, et al. Comparison of outcomes of neurosurgical operations performed before and during the COVID-19 pandemic: A matched cohort study. *BMJ Open.* 2021;11(2):e047063.
28. Norman S, Ramos A, Giantini Larsen AM, et al. Impact of the COVID-19 pandemic on neuro-oncology outcomes. *J Neurooncol.* 2021;154(3):375–381.
29. Kommers I, Ackermans L, Ardon H, et al. Between-hospital variation in rates of complications and decline of patient performance after glioblastoma surgery in the Dutch Quality Registry Neuro Surgery. *J Neurooncol.* 2021;152(2):289–298.
30. Antony J, James WT, Neriamparambil AJ, et al. An Australian response to the COVID-19 pandemic and its implications on the practice of neurosurgery. *World Neurosurg.* 2020;139:e864–e871.
31. Zou Y, Zhang J, Zhang T, et al. Characteristics and operation outcomes of neuro-oncology patients after COVID-19 pandemic—a case series. *Interdiscip Neurosurg Adv Tech Case Manage.* 2021;25:101172.
32. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care.* 2005;43(11):1130–1139.