




Impact of the COVID-19 pandemic on neuro-oncology outcomes

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Abstract

Introduction The Coronavirus disease 2019 (COVID-19) pandemic has uprooted healthcare systems worldwide, disrupting care and increasing dependence on alternative forms of health care delivery. It is yet to be determined how the pandemic affected neuro-oncology patient outcomes, given that the majority of even “elective” neurosurgical oncology procedures are time-sensitive. This study quantifies changes in neuro-oncological care during the height of the pandemic and investigates patient outcomes in 2020 compared to a historical control.

Methods We performed a retrospective review of patients with malignant brain tumor diagnoses who were seen at our institution between March 13 and May 1 of 2020 and 2019. Alterations in care, including shift from in-person to telehealth, delays in evaluation and intervention, and treatment modifications were evaluated. These variables were analyzed with respect to brain tumor control and mortality.

Results 112 patients from 2020 to 166 patients from 2019 were included. There was no significant difference in outcomes between the cohorts, despite significantly more treatment delays ($p = 0.0160$) and use of telehealth ($p < 0.0001$) in 2020. Patients in 2020 who utilized telehealth visits had significantly more stable tumor control than those who had office visits ($p = 0.0124$), consistent with appropriate use of in-person visits for patients with progression.

Conclusions Our study showed that use of telehealth and selective alterations in neuro-oncological care during the COVID-19 pandemic did not lead to adverse patient outcomes. This suggests that adaptive physician-led changes were successful and may inform management during the ongoing pandemic, especially with the emergence of the Delta variant.

Keywords COVID-19 pandemic · Neuro-oncology · Outcomes · Telehealth

Introduction

The Coronavirus disease 2019 (COVID-19) was declared to be a pandemic on March 11, 2020 [1], giving rise to an unprecedented public health emergency and leaving devastation and destruction in its wake. The medical community was heavily hit, with physicians and other medical professionals rising to the occasion and caring for sick patients in overburdened hospitals. In order to meet the extraordinary demand of caring for COVID-19 patients while simultaneously continuing care of non-COVID patients, all while minimizing unnecessary exposure risks for vulnerable patients,

adaptive physician-led changes catalyzed a transformation of patient care. A cornerstone of this transformation was the incorporation of telehealth visits and selective deferrals in care.

Telemedicine was one of the most important strategies employed during the height of the pandemic, with hospitals using this modality for “forward triage”—sorting patients based on symptoms, travel history, and potential exposures before they arrived at the Emergency Department [2]. Furthermore, utilization of telehealth provided the unique opportunity to continue medical care of patients while reducing the risk of both nosocomial and community spread of COVID-19 [3]. As the number of COVID-19 cases continued to rise, so did the United States population interest in telehealth [4]. Telemedicine, while significantly underutilized before the current pandemic as a method of delivering care (previously most commonly known for Emergency Department-based consultations about stroke), has now become an essential tool in bridging

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the gap between a patient and their providers, and contributed to “flattening the curve” [5]. A study at NYU reported a 136% increase in urgent care telemedicine visits from between March 2nd and April 14th 2020, with a remarkable 4345% increase in non-urgent care visits [6].

Even prior to the COVID-19 pandemic, telehealth was useful for differentiating patients with neurological emergencies such as intracranial hemorrhage or stroke from those who did not need urgent care [7]. During the pandemic, this tool became increasingly critical specifically in the care of neuro-oncological patients. Given concerns that COVID-19 infection could be substantially more severe in cancer patients [8], physicians involved in the care of oncological patients were forced to weigh the importance of intervention against the risk of nosocomial COVID-19 infection when determining the best plan of action for their patients [9]. Often, when the risk of nosocomial COVID-19 exposure outweighed the benefits of intervention, physicians had to consider different options. Physician-guided selective delays in care were therefore also essential during the pandemic. One large head and neck oncology group described their intricate decision-making process for choosing to delay surgery in certain patients, with all decisions reviewed via electronic consult with colleagues from a surgical review committee [10].

Overall, telehealth and selective delays in care were especially salient options for patient care during the pandemic when emergent intervention was not required. However, it has not yet been determined how these adaptations in care affected specifically neuro-oncology patients, given that the majority of even “elective” neurosurgical oncology procedures are time-sensitive.

In the United States, New York City was especially hard-hit after its first confirmed COVID-19 case in the beginning of March and its emergence as a virus epicenter [11]. By April 2020, due to its high population density, New York had exceeded every other state with its rate of infections [12]. Our study is the first of our knowledge to quantify changes in neuro-oncological outpatient care and subsequent patient outcomes at a major academic center in New York City during the height of the COVID-19 pandemic. We hypothesize that adaptive changes due to the pandemic (such as delays in care and virtual visits) did not lead to adverse patient outcomes, when compared to a historical control. We also hypothesize that these selective modifications, tailored to individual patients, did not lead to adverse patient outcomes within the 2020 cohort itself.

Methods

Design

We performed an IRB-approved (Weill Cornell Medical College # 20-04021852) retrospective chart review of patients

with diagnoses of malignant brain tumors (primary or secondary) who presented to the Weill Cornell Brain and Spine Center for outpatient care between March 13, 2020 and May 1, 2020. A corresponding control cohort from the same time period in 2019 was analyzed for comparison. Total number of inpatient consults for new brain tumor diagnoses were also evaluated during these time periods. Patient demographics (e.g. age, sex, new brain tumor diagnosis, primary cancer) and COVID-19 status were evaluated.

Treatment variables including delays in care, use of telehealth, treatment alterations, treatment cessations, and loss to follow-up were retrospectively reviewed and compared. Outcomes including death, tumor control, and loss of follow-up through August of the study cohort year were analyzed. These were both quantitatively and qualitatively determined via manual chart review, using specific search phrases such as “progression of disease,” “stable,” and “improvement.” Detailed analysis of neuro-oncology, radiology, and neurosurgical notes was performed, searching for the above-mentioned keywords. Concordance between all 3 types of notes was required for determining disease stability or progression. Standards were applied to all charts, with discrepant cases re-reviewed in a blinded fashion by a single faculty neurosurgeon. However, discrepancies were few and were addressed on a case-by-case basis.

Statistics

A 2 sample, two-tailed independent t-test was used to assess statistical significance (alpha of 0.05) for the number of inpatient consults each year. This t-test was performed using Microsoft Excel 2016 (version 16.16.26). For all the remaining data, Fisher’s exact test was utilized to assess statistical significance (with an alpha of 0.05), and these analyses were performed using the R programming language (version 3.6.3 GUI 1.70 El Capitan build).

The 2020 cohort was then further stratified into 3 sub-groups: patients who experienced deviations from treatment plan, telehealth, and delays in care. Deviation from treatment plan was defined as patients who experienced treatment alteration or treatment cessation. Statistical analyses were then performed on each of the 3 sub-groups individually to assess the impact of deviations in care, telehealth, and delayed care on patient outcomes within the 2020 cohort (Fisher’s exact test, alpha of 0.05).

Results

The 2020 cohort and 2019 cohort did not differ significantly in regards to demographic features, including mean age, sex, new brain tumor diagnosis, and primary cancer (Table 1).

Table 1 Cohort Demographics

Demographics	2020 Cohort n = 112	2019 Cohort n = 166	Total n = 278
Mean age (years)	54.18	55	54.63
Std. Dev	15.54	15.48	15.48
<i>Sex</i>			
Male	57 (50.9%)	85 (51.2%)	142 (51.1%)
Female	55 (49.1%)	81 (48.8%)	136 (48.9%)
<i>New brain tumor diagnosis</i>			
New brain tumor diagnosis	7 (6.3%)	11 (6.6%)	18 (6.5%)
<i>Primary cancer</i>			
Brain	90 (80.4%)	133 (80.1%)	223 (80.2%)
Lung	13 (11.6%)	18 (10.8%)	31 (11.2%)
Renal	1 (0.9%)	2 (1.2%)	3 (1.1%)
Colon	0 (0%)	2 (1.2%)	2 (0.7%)
Endometrial	0 (0%)	1 (0.6%)	1 (0.4%)
Prostate	0 (0%)	2 (1.2%)	2 (0.7%)
Breast	6 (5.4%)	5 (3.0%)	11 (4.0%)
Cervical	1 (0.9%)	0 (0%)	1 (0.4%)
GE junction	1 (0.9%)	0 (0%)	1 (0.4%)
Duodenal	0 (0%)	1 (0.6%)	1 (0.4%)
Skin	0 (0%)	1 (0.6%)	1 (0.4%)
Bladder	0 (0%)	1 (0.6%)	1 (0.4%)
<i>COVID status during study period</i>			
PCR Positive	0 (0%)	–	0 (0%)
PCR Negative	11 (9.8%)	–	11 (4.0%)
PCR not tested	101 (90.2%)	–	101 (36.3%)
Serology Positive	0 (0%)	–	0 (0%)
Serology Negative	0 (0%)	–	0 (0%)
Serology not tested	112 (100%)	–	112 (40.3%)

Both cohorts were comprised of all malignant tumors, consisting predominantly of primary brain malignancy (80.4% primary brain in 2020, 80.1% in 2019). The remaining portions of each cohort were metastatic, most commonly lung and breast. Regarding COVID-19 status in the 2020 cohort, 9.8% of patients were COVID-19 negative, 90.2% of patients were not PCR-tested, and 100% were not serology tested for COVID-19 antibodies (Table 1).

In January–April of 2019 and January–February of 2020 (pre-pandemic time period), there were an average of 22.8 brain tumor consults per month on the inpatient service. In March–April (pandemic time period), this number dropped by half to 10.5 per month ($p=0.0003$) (Table 2). When evaluating outpatient visits, compared to 2019, the 2020 cohort had significantly more delays in care ($p=0.0160$) and use of telehealth ($p<0.0001$) (Table 3). There was no significant difference between the two cohorts with respect to treatment alteration, treatment cessation, and proportion of patients lost to follow-up (Table 3). Furthermore, when patient outcomes for 2020 were compared to 2019, there were no significant differences in mortality or tumor control, including no differences in unknown outcomes/loss to follow-up (Table 4). Of the 20 total outpatient deaths reported

Table 2 Number of brain tumor inpatient/emergency room consults per month for 2020 and 2019, as a percentage of the total number of neurosurgical consults per month

Month	Number of consults in 2020 (% of total)	Number of consults in 2019 (% of total)
January	22 (13.2)	24 (14.1)
February	22 (14.7)	20 (15.1)
March	10 (10.5)	27 (17.4)
April	11 (15.1)	22 (13.9)

Table 3 Changes in care for the 2020 and 2019 cohorts

Variable	2020 Cohort n = 112	2019 Cohort n = 166	p value
Treatment alteration	0 (0%)	3 (1.8%)	0.2757
Treatment cessation	7 (6.3%)	4 (2.4%)	0.1251
Delay in care	9 (8.0%)	3 (1.8%)	0.0160
Telehealth	92 (82.1%)	0 (0%)	<0.0001
Lost to follow-up	9 (8.0%)	16 (9.6%)	0.8312

in Table 4, only one death was unexpected (due to cardiac arrest), while the other 19 deaths were attributable to progression of disease or transition to hospice.

Upon further stratification of the 2020 cohort, there was no significant difference in death, stable tumor control, improved tumor control, or lost to follow-up outcomes for 2020 patients who experienced deviations in care (defined as treatment alteration or treatment cessation) compared to other 2020 patients who did not experience deviations in care (Table 5). However, patients in 2020 who experienced deviations in care did have significantly more tumor recurrence/progression compared to other 2020 patients ($p=0.0014$) (Table 5).

Patients in 2020 who utilized telehealth encounters did not have significantly different rates of death, tumor recurrence, improved control, or unknown outcomes/loss to follow-up when compared to 2020 patients who had only in-person encounters (Table 5). Of note, patients with telehealth encounters had significantly higher rates of stable brain tumor control ($p=0.0124$) compared to patients who had only in-person encounters (Table 5). Finally, upon comparative analysis, there were no significantly different outcomes (death, tumor recurrence/progression, stable tumor

control, improved tumor control/response to treatment, or unknown/loss to follow-up) between 2020 patients who experienced delays in care and 2020 patients who did not have delayed care (Table 5).

Discussion

The COVID-19 pandemic wreaked havoc across the world and affected patient care in every medical specialty. The impacts of the pandemic are especially of interest in the field of neuro-oncology, where even “elective” procedures are time-sensitive and delays could potentially derail patient outcomes. Our study is the first of our knowledge to quantify changes in neuro-oncological care at a major academic center in New York City during the height of the pandemic, and to investigate patient outcomes in 2020 compared to a historical control. We also performed sub-group analysis of the 2020 cohort to determine the effects of adaptive changes in care during the pandemic on 2020 patient outcomes, with an additional evaluation of total number of inpatient consults for brain tumors during matched periods of time in 2019 and 2020. Due to the practice patterns at our institution,

Table 4 Outcomes for the 2020 and 2019 cohorts

Outcome	2020 Cohort n = 112	2019 Cohort n = 166	p value
Death	7 (6.3%)	13 (7.8%)	0.8136
Brain tumor recurrence or progression	30 (26.8%)	36 (21.7%)	0.3887
Stable brain tumor control	52 (46.4%)	87 (52.4%)	0.3921
Improved brain tumor control or response to treatment	14 (12.5%)	14 (8.4%)	0.3116
Unknown, lost to follow-up	9 (8.0%)	16 (9.6%)	0.8312

Table 5 Stratified 2020 outcome analysis for deviation from treatment plan (including treatment alteration or cessation), telehealth, and delay in care

Outcome	Deviation from treatment plan			Telehealth			Delay in Care		
	Deviation n=7	No deviation n=105	p value	Telehealth n=92	In-person encounters n=20	p value	Delay in care n=9	No delay in care n=103	p value
Death	0 (0%)	7 (6.7%)	1	5 (5.4%)	2 (10.0%)	0.6063	0 (0%)	7 (6.8%)	1
Brain tumor recurrence or progression	6 (85.7%)	24 (22.9%)	0.0014	21 (22.8%)	9 (45.0%)	0.0536	2 (22.2%)	28 (27.2%)	1
Stable brain tumor control	1 (14.3%)	51 (48.6%)	0.1199	48 (52.2%)	4 (20.0%)	0.0124	7 (77.8%)	45 (43.7%)	0.0789
Improved brain tumor control or response to treatment	0 (0%)	14 (13.3%)	0.5932	12 (13.0%)	2 (10.0%)	1	0 (0%)	14 (13.6%)	0.5990
Unknown, lost to follow-up	0 (0%)	9 (8.6%)	1	6 (6.5%)	3 (15.0%)	0.2001	0 (0%)	9 (8.7%)	1

the majority of patients with malignant brain tumor diagnoses followed by the neuro-oncology team carried a primary brain malignancy diagnosis, as patients with systemic metastases are typically followed by medical oncology.

Of note, none of the patients in our study were COVID-positive, and the majority of the cohort was not tested. This can be attributed to the fact that our study period was during the height of the pandemic, when testing resources were limited and patients were not routinely evaluated for COVID-19 unless they were symptomatic or undergoing surgery.

The number of inpatient neurosurgical consults in March–April 2020 was significantly lower than pre-pandemic time periods ($p=0.0003$), likely owing to fear in the community driving down the number of patients seeking medical attention. This was a trend seen across multiple specialties [13], and raised significant alarm in the cancer community in particular given the importance of a timely diagnosis. At our institution, as well as at many others, treatment for cancer was prioritized in our surgical triage system, even during the peak of the pandemic, and reductions in volume were largely patient-driven. It is essential to continue educating the public about seeking care for neurologic and oncologic conditions regardless of the state of the pandemic. While beyond the scope of this study, future studies focusing on the impact of delayed initial cancer diagnoses may be helpful in driving community education efforts during the ongoing pandemic. Fortunately, at our institution, although the total number of neurosurgical consults fell, the percentage of patients with brain tumors within these consults stayed relatively stable. This suggests that while all other types of neurosurgical patients presented less frequently during the pandemic, brain tumor patients weren't particularly more or less likely to present for care. Further, for the matched "lockdown" time period (March 13–April 30 2020), there were 8 brain tumor patients that had surgery within 7 days of the consult. During the same period in 2019, there were 19 patients that had surgery within 7 days. This represents a 57% decrease in operative brain tumors which is similar to the overall approximate 50% drop in the total number of brain tumor consults seen over this time period. Taken together, this suggests that patients were not necessarily more likely to be presenting in extremis needing urgent surgery, during the pandemic.

Our study showed that the 2020 cohort had significantly more delays in care and use of telehealth compared to the 2019 control cohort, as expected. However, there was no significant difference in outcomes (including death, tumor recurrence/progression, stable tumor control, improved control/response to treatment, or unknown/lost to follow-up) between the 2020 and 2019 cohorts. Notably, since there was no significant difference in adverse outcomes such as death or tumor recurrence/progression, our study suggests that delays in care and telehealth visits did not cause worse

outcomes for neuro-oncological patients when compared to a historical control. Furthermore, both the 2020 and 2019 cohorts were comprised of all malignant brain tumors. Therefore, it is even more significant that delays in care and telehealth visits did not cause worse outcomes, given that malignant brain tumors can often be aggressive and rapidly progressive. Taken together, these results suggest that our allocation of in-person care, telehealth visits, and physician-led delays during the 2020 pandemic were appropriate and successful.

When further stratified, the 2020 cohort showed no significant difference in outcomes between patients who experienced delays in care and patients who did not experience delays in care. Of the 9 patients who experienced delayed care, 8 out of 9 delays were physician-led, and 7 out of the 9 were directly related to the pandemic. Reasons for these pandemic-related delays include delayed chemotherapy due to concern about immunosuppression, delayed radiation due to patient having a cough and needing to quarantine, and delayed surgery given the ongoing pandemic and surgical triage systems limiting non-urgent surgeries due to resource limitations.

The majority of these delays and transitions to telehealth were physician driven; our institution urged providers to limit in-person visits as much as possible and to only utilize in-office visits for those with progression of disease or worsening symptoms during the height of the pandemic. These measures were put in place for the health and safety of patients and the community at large. It was therefore at the discretion of the physicians to determine which patients necessitated an in-person visit or urgent imaging study, and which patients could be seen over telehealth or have their imaging follow-up deferred. Overall, patients were stratified based on a risk-benefit analysis of the value of an in-person visit relative to the risk of adverse outcomes from exposure to COVID. Furthermore, allocation of imaging equipment including MRIs was made based on both urgency and availability, and non-routine follow-up visits were often modestly delayed. Physicians worked to prioritize imaging for time-sensitive conditions. Our results help support the hypothesis that selective, physician-led delays in care during the pandemic did not lead to adverse patient outcomes. These adaptive and selective physician-led changes were made to optimize treatment during the pandemic, without a clear negative consequence for individual patient care.

On the other hand, 2020 patients who experienced deviations from treatment plan (defined as treatment alteration or treatment cessation) did have significantly more brain tumor recurrence or progression when compared to other 2020 patients who did not have deviations in care. However, this result can be further understood by evaluating the 7 patients who experienced deviations in care. Of the 7 patients experiencing deviations in care, only one patient had a change

in treatment plans directly attributable to the ongoing pandemic. The remaining 6 patients had cessations in care due to patient or family-driven decisions regarding hospice and advanced disease processes. Therefore, in this population, treatment deviations during the pandemic did not appear to be causative of adverse outcomes in this sub-group; in fact, the majority of patients in this group withdrew from care due to progressive disease.

The stratified 2020 cohort also showed that patients who had telehealth encounters had significantly more stable brain tumor control when compared to patients who had only in-person encounters. Further, these patients with only in-person visits trended towards having more brain tumor recurrence/progression as well. However, since patients with disease progression were more likely to be seen in-person rather than via telehealth, there is a clear confounding element of selection bias in this cohort that likely contributed to this finding. Taken together, these results are consistent with appropriate use of in-person visits for patients with progression of disease, and selective use of telehealth for patients with well-controlled disease.

Overall, our study found that there were significantly more delays in care and telehealth visits during the pandemic in 2020, and that these did not lead to adverse patient outcomes when compared to a 2019 control cohort. Stratification of the 2020 cohort showed that selective modifications (such as telehealth and delays in care) tailored to individual patients were both appropriate and efficacious.

There are several notable limitations to this study, including having a relatively small sample size and being retrospective, which limits its ability to determine causality and temporality. Further studies are needed to evaluate impact on long-term patient outcomes and survival. Given that the pandemic continues to markedly affect the practice of medicine and neuro-oncology into 2021, particularly with the emergence of the Delta variant, it is critical that we continue to analyze how COVID-19 has impacted patient care, and which changes can be made to balance individual and population-based infection risks against the need to deliver timely and effective care. Certainly, these results suggest that carefully selected adaptations in care can be accomplished without adversely affecting patient outcomes in neuro-oncology. These results may provide reassurance to patients and family members that neuro-oncologic care can be modified under pandemic constraints without an adverse effect on patient outcomes. It remains essential that patients are encouraged to seek cancer care irrespective of the status of the pandemic, necessitating studies that highlight logical treatment decision paradigms and the safety of modified care delivery models during this unprecedented time. Ongoing patient education and reassurance is critical for continuing to safely care for patients in the upcoming year.

Conclusions

This study found there were significantly more delays in care and use of telehealth for neuro-oncological patients with malignant brain tumors during the 2020 pandemic. Importantly, physician-led delays in care and transitions to telehealth did not cause adverse outcomes in patients with primary or secondary brain tumors. Longer-term patient outcomes following the pandemic still need to be evaluated in future studies.

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Declarations

Conflict of interest The authors have no relevant non-financial or financial interests to disclose.

Ethical approval This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration. The Human Investigation Committee (IRB) of Weill Cornell Medicine approved this study.

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