High grade glioma case series

Renovanz et al. used baseline data of a prospective study where High-grade glioma (HGG) patients were enrolled from 4 hospitals. Distress was measured using the distress thermometer (DT), HRQoL using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Core Questionnaire (QLQ-C30) plus brain module (BN20). We compared distress and HRQoL by age (≥ 65 vs. < 65 years), gender, performance score, and time since diagnosis using multivariate linear and logistic regressions.

A total of n = 93 (30%) out of n = 309 patients were ≥ 65 years (mean 70 years, range 65-86 years). Mean DT score of elderly patients (5.2, SD 2.6) was comparable with younger patients (4.9, SD 2.6). Elderly patients reported significantly lower global health (GHS, mean elderly vs. younger; 50.8 vs. 60.5, p = 0.003), worse physical (56.8 vs. 73.3, p < 0.001) and lower cognitive functioning (51.1 vs. 63.2, p = 0.002), worse fatigue (52.5 vs. 43.5, p = 0.042), and worse motor dysfunction (34.9 vs. 23.6, p = 0.030). KPS and not age was consistently associated with HRQoL.

Physical functioning was significantly reduced in the elderly compared with younger HGG patients, and at the same time, emotional functioning and DT scores were comparable. KPS shows a greater association with HRQoL than with calendric age in HGG patients reflecting the particular importance for adequate assessment of HRQoL and general condition in elderly patients 1).

Hwang et al. investigated the efficacy of temozolomide during and after radiotherapy in Korean adults with anaplastic gliomas without 1p/19q co-deletion.

This was a randomized, open-label, phase 2 study and notably the first multicenter trial for Korean grade III glioma patients. Eligible patients were aged 18 years or older and had newly diagnosed non-co-deleted anaplastic glioma with an Eastern Cooperative Oncology Group performance status of 0-2. Patients were randomized 1:1 to receive radiotherapy alone (60 Gy in 30 fractions of 2 Gy) (control group, n=44) or to receive radiotherapy with concurrent temozolomide (75 mg/m2/day) followed by adjuvant temozolomide (150-200 mg/m2/day for 5 days during 6 28-day cycles) (treatment group, n=40). The primary endpoint was 2-year progression-free survival (PFS). Seventy patients (83.3%) were available for the analysis of the isocitrate dehydrogenase 1 gene (IDH1) mutation status.

The two-year PFS was 42.2% in the treatment group and 37.2% in the control group. Overall survival (OS) did not reach to significant difference between the groups. In multivariable analysis, age was a significant risk factor for PFS (hazard ratio [HR], 2.08; 95% confidence interval [CI], 1.04 to 4.16). The IDH1 mutation was the only significant prognostic factor for PFS (HR, 0.28; 95% CI, 0.13 to 0.59) and OS (HR, 0.19; 95% CI, 0.07 to 0.50). Adverse events over grade 3 were seen in 16 patients (40.0%) in the treatment group and were reversible.

Concurrent and adjuvant temozolomide in Korean adults with newly diagnosed non-co-deleted anaplastic gliomas showed improved 2-year PFS. The survival benefit of this regimen needs further analysis with long-term follow-up at least more than 10 years 2).

Twenty-three patients with high grade gliomas were retrospectively analyzed. White et al., measured the perfusion at the resection area and evaluated the presence or absence of the restricted diffusion in residual tumor masses. The associations of the perfusion, diffusion and contrast enhancement...
(delayed static enhancement (DSE)) characteristics with time to tumor progression were statistically calculated. White et al., also evaluated if the location of the tumor progression was concordant to the areas of the elevated perfusion, tumor type restricted diffusion and enhancement.

Patients with >200 days to progression are more likely to have no elevated relative cerebral blood volume (rCBV) ratio (p = 0.0004), no tumor restriction (p = 0.024), and no DSE (p = 0.052). The elevated mean rCBV ratio (p<0.001) and tumor type restricted diffusion (p = 0.002) were significantly associated with a higher risk of progression. All cases with rCBV ratio of >1.5 progressed in 275 days or earlier. Tumors tended to progress at the area where patients with post-operative MRIs showed elevated perfusion (p = 0.006), tumor-type restricted diffusion (p = 0.005) and DSE (p = 0.008).

Post-operative analysis of rCBV, tumor type restricted diffusion and enhancement characteristics are predictive of time to progression, risk of progression and where tumor progression is likely to occur \(^3\).

The clinical data of 198 patients surgically treated for primary anaplastic glioma in Henan Provincial People's Hospital between Jan 2009 and Jan 2018 were reviewed. Univariate and multivariate analyses were used to identify prognostic factors with methods of Kaplan-Meier plot and Cox proportional hazards model, respectively. Based on the prognostic factors, a scoring scale was thereby proposed.

Univariate analysis results showed age, tumor location, tumor diameter, preoperative KPS, extent of resection, radiotherapy, chemotherapy, pathology with oligodendroglial components, 1p/19q, IDH, MGMT were significantly correlated with survival (P<0.05). Multivariate analysis results showed age \(\geq 45\) years old, tumor diameter \(\geq 6\) cm, preoperative KPS<70, without radiotherapy, 1p/19q intact, MGMT promoter unmethylation were independent prognostic risk factors (P<0.05). Patients were scored with 0-6 points based on the formulation that each independent prognostic risk factor was assigned with 1 point. Then patients were further grouped according to the score. Those with less than 2 points were low-risk group, equal to 2 points were medium-risk group, equal to 3 points were high-risk group, more than or equal to 4 points were extremely high-risk group. There were significant differences in survival between the different groups (P<0.000 1).

The higher score, the shorter survival time. This prognostic scoring scale can provide a theoretical basis for the prognosis estimation of patients with anaplastic glioma and help to carry out personalized clinical treatment \(^4\).

Wu et al., retrospectively evaluated intraoperative data obtained from 16 patients diagnosed with high grade glioma (HGG).

Overall, 18 nodules observed in 15 patients were examined. HGG images from ultrasound and contrast-enhanced ultrasound (CEUS) were compared to those from preoperative reconstructive coplanar enhanced T1-weighted MRI using automatic V Nav fusion image technology.

All HGG tumours were detected. Images of 13 of 18 tumours (72.2%) with obscure margins using B-mode ultrasound were improved with clear tumour boundaries using CEUS imaging. The relative difference in tumour area between CEUS and enhanced MRI modalities in 14 mainly solid component lesions was considered statistically significant (p-value < 0.05). There was a perfect correlation of the enhanced area (EA) between coplanar CEUS and enhanced MRI.
The V Nav fusion image system combining intraoperative real-time ultrasound imaging with reconstructive preoperative coplanar MRI is valuable for image-guided HGG resection. It is suitable for neurosurgeons who lack the expertise in ultrasound technology to discern the brain structure and allows better recognition of tumour and oedema tissues compared with reconstructive preoperative coplanar-enhanced MRI in real-time and in multiplane from different angles. In addition, CEUS combined with B-mode ultrasound could improve tumour detection and resection control in neurosurgery, even in single ultrasound-guided operations.

In a study of Senders et al. from Boston and Utrecht, patients were extracted from the National Surgical Quality Improvement Program registry (2005-2015) and analyzed using multivariable logistic regression.

A total of 7376 patients were identified, of which 948 (12.9%) experienced a major complication. The most common major complications were reoperation (5.1%), venous thromboembolism (3.5%), and death (2.6%). Furthermore, 15.6% stayed longer than 10 d, and 11.5% were readmitted within 30 d after surgery. The most common reasons for reoperation and readmission were intracranial hemorrhage (18.5%) and wound-related complications (11.9%), respectively. Multivariable analysis identified older age, higher body mass index, higher American Society of Anesthesiologists (ASA) classification, dependent functional status, elevated preoperative white blood cell count (white blood cell count WBC, >12 000 cells/mm³), and longer operative time as predictors of major complication (all P < .001). Higher ASA classification, dependent functional status, elevated WBC, and ventilator dependence were predictors of extended length of stay (all P < .001). Higher ASA classification and elevated WBC were predictors of reoperation (both P < .001). Higher ASA classification and dependent functional status were predictors of readmission (both P < .001). Older age, higher ASA classification, and dependent functional status were predictors of death (all P < .001).

This study provides a descriptive analysis and identifies predictors for short-term complications, including death, after craniotomy for primary malignant brain tumors.

Preibisch et al. performed a study in 12 patients with high-grade glioma, where they directly compared the two currently most promising techniques, namely the MR-based relative oxygen extraction fraction (MR-rOEF) and the PET hypoxia marker H-1-[18 F]-fluoro-2-hydroxypropyl)-2-nitroimidazole ([18 F]-FMISO). MR-rOEF was determined from separate measurements of T2, T2 * and relative cerebral blood volume (rCBV) employing a multi-parametric approach for quantification of the blood-oxygenation-level-dependent (BOLD) effect. With respect to [18 F]-FMISO-PET, besides the commonly used late uptake between 120 and 130 min ([18 F]-FMISO120-130 min ), we also analyzed the hypoxia specific uptake rate [18 F]-FMISO-k3 , as obtained by pharmacokinetic modeling of dynamic uptake data. Since pharmacokinetic modeling of partially acquired dynamic [18 F]-FMISO data was sensitive to a low signal-to-noise-ratio, analysis was restricted to high-uptake tumor regions. Individual spatial analyses of deoxygenation and hypoxia-related parameter maps revealed that high MR-rOEF values clustered in (edematous) peritumoral tissue, while areas with high [18 F]-FMISO120-130 min concentrated in and around active tumor with disrupted blood-brain barrier, i.e. contrast enhancement in T1-weighted MRI. Volume-of-interest-based correlations between MR-rOEF and [18 F]-FMISO120-130 min as well as [18 F]-FMISO-k3 , and voxel-wise analyses in individual patients, yielded limited correlations, supporting the notion that [18 F]-FMISO uptake, even after 2 h, might still be influenced by perfusion while [18 F]-FMISO-k3 was severely hampered by noise. According to these results, vascular deoxygenation, as measured by MR-rOEF, and severe tissue hypoxia, as measured by [18 F]-FMISO, show a poor spatial correspondence. Overall, the two methods...
appear to rather provide complementary than redundant information about high-grade glioma biology.

Data of 47 consecutive patients with HGG have been collected in our study (25 males, 22 females; mean age: 60.3 years, range: 27-86 years). Fluorescein (5 mg/kg of body weight) was injected intravenously right after the induction of general anesthesia. A YELLOW 560 filter was used on an OPMI Pentero 900 microscope (Carl Zeiss Meditec, Oberkochen, Germany) to complete a microsurgical tumor removal. Glioma resection and quality of life were evaluated preoperative and postoperatively.

Gross total resection (GTR) was achieved in 53.2% (n = 25) of patients. A subtotal resection (STR) (>95%) was achieved in 29.8% (n = 14), while a partial resection (PR) (<95%) was obtained in 17% (n = 8) of patients. Overall, in 83% (n = 39) of patients who underwent fluorescence-guided surgery the resection rate achieved was >95%. No adverse effects correlated to fluorescein have been recorded.

Fluorescein seems to be safe and effective in the resection of HGGs, allowing a high rate of gross total removal of contrast enhanced areas.

2015

A retrospective study of 125 HGG patients used three different classification standards of age-groups (≤50 and >50 years old, ≤60 and >60 years old, ≤45 and 45-65 and ≥65 years old) to evaluate the impact of age on prognosis. The primary end-point was overall survival (OS). The Kaplan Meier method was applied for univariate analysis and Cox proportional hazards model for multivariate analysis. Univariate analysis showed a significant correlation between OS and all three classification standards of age-groups as well as between OS and pathological grade, gender, location of glioma, and regular chemotherapy and radiotherapy treatment. Multivariate analysis showed that the only independent predictors of OS were classification standard of age-groups ≤50 and >50 years old, pathological grade and regular chemotherapy. In summary, the most appropriate classification standard of age-groups as an independent prognostic factor was ≤50 and >50 years old. Pathological grade and chemotherapy were also independent predictors of OS in post-operative HGG patients.

Malignant glioma, ie, anaplastic astrocytoma and glioblastoma, is the most common type of primary malignant brain tumor in the People's Republic of China, and is particularly aggressive.

The median survival of patients with newly diagnosed glioblastoma is only 12-14 months despite advanced therapeutic strategies.

Treatment of malignant glioma consists mainly of surgical resection followed by adjuvant radiation and chemotherapy. Temozolomide (TMZ), a second-generation oral alkylating agent, is playing an increasingly important role in the treatment of malignant glioma in Chinese patients. Since the publication of a study by Stupp et al in 2005, which used a protocol of conventional fractionated irradiation with concomitant TMZ followed by standard TMZ for six cycles, many clinical studies in the People's Republic of China have demonstrated that such a treatment strategy has significantly improved efficacy with limited side effects for newly diagnosed glioblastoma after surgery as compared with strategies that do not contain TMZ. However, as a relatively new agent, the history and development of TMZ for malignant glioma is not well documented in Chinese patients. Multicenter, randomized controlled trials including appropriately sized patient populations investigating multiple aspects of TMZ therapy and related combination therapies are warranted in
patients with malignant glioma\textsuperscript{10}).

The Nationwide Inpatient Sample (NIS) database was queried from 2002 to 2011. All adult patients who underwent elective brain surgery for a malignant brain tumor were included. Surgical complications included wrong side surgery, retention of a foreign object, iatrogenic stroke, meningitis, hemorrhage/hematoma complicating a procedure, and neurological complications. A regression model was conducted to estimate the odds ratios (OR) with their 95% confidence intervals (95% CI) of in-hospital mortality for each surgical complication.

A total of 16,530 admissions were analyzed, with 601 (36.2 events per 1000 cases) surgical complications occurring in 567 patients. Over the examined 10-year period, the overall incidence of surgical complications did not change (\textit{P}=0.061) except for iatrogenic strokes, which increased in incidence from 14.1 to 19.8 events per 1000 between 2002 and 2011 (\textit{P}=0.023). Patients who developed a surgical complication had significantly longer lengths of stay, total hospital costs, and higher rates of other complications. Patients who experienced an iatrogenic stroke had a significantly increased risk of mortality (OR 9.6; 95% CI 6.3-14.8) and so were patients with a hemorrhage/hematoma (OR 3.3; 95% CI 1.6-6.6).

In this study of an administrative database, patients undergoing surgery for a malignant brain tumor who suffered from a surgical complication had significantly longer lengths of stay, total hospital charges, and complication rates. Having a surgical complication was also an independent risk factor for in-hospital mortality. Nonetheless, it is unclear whether all surgical complications were clinically relevant, and further research is encouraged \textsuperscript{11}).

References


