Title

P10.03 Management of low-grade glioma: a systematic review and meta-analysis

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P10 OTHER GLIOMAS: CLINICAL

P10.01 EPILEPSY FOLLOWING LOW GRADE GLIOMA SURGERY

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AIMS: Our aim was to review the role of prophylactic AEDs and the effect of surgical technique (awake craniotomy versus resection under general anaesthetic) on seizure outcomes in patients undergoing surgery for low grade glioma (LGG) METHODS: In our retrospective study we included all patients aged >18 years with a confirmed diagnosis of WHO grade II glioma within a 3-year period. Seizure incidence was recorded in the early post-operative period (up to 10 days post operatively) and in the longer term (3 to 12 months). To investigate the effect of AED treatment, patients were categorised into 3 groups: patients pre-established on AEDs (minimum 2 weeks prior to surgery), those started on prophylactic AEDs prior to the surgery (within 24 hours prior to surgery) and those who were not prescribed AEDs during follow up. RESULTS: A total of 135 patients met the inclusion criteria. In the early post-operative period, out of the 24 patients suffered seizures, only 1 patient who had total tumour resection (4.1%), 5 patients (20.8%) of those who had near-total resection, 11 patients (45.8%) of who underwent subtotal/partial and 7(29.1%) of those who had biopsy (p=0.03). During long term follow up, 40(29.6%) patients had seizures, 3 (7.5%) of those who had total resection, 8 (20%) of near-total resection, 18 (45%) of subtotal/partial and 11 (27.5%) of biopsies (p=0.005). 34 (25.2%) underwent awake craniotomy, and 101 (74.8%) underwent resection under GA. 26 of them (33.3%) were in pre-established group, 6 (28.6%) in the prophylactic group and 8(22.3%) in the no AED group (p=0.41). Awake craniotomy was associated with greater extent of resection(total and near total resection) compared to the GA (67.6% v/s 45.4%; OR = 2.5, p=0.028) 78 patients (57.8%) were pre-established on AEDs, 21 (15.6%) received prophylactic AED, and 36 patients (26.7%) no AEDs during follow up. 24 (17.8%) experienced seizures in the early postoperative period (defined as 10 days post-surgery). 4 patients on prophylactic AED group (19.1%); 14 patients on pre-established AED (17.9 %); and 6 (16.7%) in the no AED groups, no statistical significant difference was found between the three groups (p=0.97).; Prophylactic AED treatment did not reduce seizures in the early post-operative period (OR 1.10, p=0.87). CONCLUSIONS: Gross resection was associated with lower seizure incidence in the immediate post-operative period, and during long term follow-up. There was no significant difference in seizure incidence between patients treated with prophylactic AEDs and those who were not.

P10.02 MALIGNANT TRANSFORMATION OF LOW-GRADE GLIOMAS. PROGNOSTIC IMPLICATIONS FROM MATHEMATICAL MODEL

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INTRODUCTION: The malignant transformation (MT) (or progression) of low-grade gliomas (LGG) into higher-grade ones is the beginning of the end for patients suffering this disease. The MT has been discussed to be either due to the acquisition of new mutations for LGG cells leading to more aggressive phenotypes and genotypes, or due to an irreversible damage to the tumour microenvironment that leads to hypoxia and the growth of increasingly aggressive tumour cells. Since therapeutic decisions depend on the tumour grade, many efforts have been devoted to the radiological identification of signatures of the transformation using different imaging techniques. Our goal was to study if mathematical predictive models were able to predict the time to MT in advance on the basis of imaging data. MATERIALS & METHODS: An evolutive mathematical model based on partial differential equations describing the growth of LGG cells and their transformation to a high grade tumour cells was developed using a minimal number of biological parameters. The model was fitted to longitudinal imaging data (T2 and/or FLAIR) of LGG patients and used to predict the evolution of the disease. RESULTS: Patient-specific parameters where found for each tumour. Using these parameters we computed the tumour volumetric dynamics, velocity of growth and predicted the time to malignant transformation. Both the average proliferation rate of LGG cells and the maximal initial tumour cell density were found to be strongly correlated with the time to MT. We found several quantitative measures from imaging data which could be used as imaging biomarkers indicative of increased risk of progression. The mathematical model were also used to test if novel chemotherapy schedules could be used to delay the time to MT. CONCLUSIONS: The combination of standard imaging techniques and mathematical modelling could predict the risk of progression of LGGs. Further mathematical studies aimed at improving the understanding of the evolution of these tumours around the onset malignant transformation and revising the impact of optimised therapeutical schedules on the tumour progression are under way.

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P10.03 MANAGEMENT OF LOW-GRADE GLIOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Low-grade gliomas (LGG, WHO grade I-II) account for 16.9-22% of all primary brain tumors. Management of these tumors consists of surgery, sometimes followed by radiation and/or chemotherapy. A rigorous, quantitative evaluation of the literature investigating the management of LGG has never been published. METHODS: We conducted an exhaustive, PRISMA-compliant systematic review of the literature from January 1966 to September 2016 comparing the association of chemotherapy, radiation, or extent of resection with survival and progression-free survival at 2, 5, and 10 years in LGG. Included studies were graded for quality using AAN criteria. Pre-specified data were extracted and summary statistics were calculated using the inverse variance method and random effects model. RESULTS: Five studies (n=567) report on LGG patients treated with chemotherapy. The relative risk (RR) and 95% confidence intervals [95% CI] for death (chemotherapy vs. no chemotherapy) at 2, 5, and 10 years was 1.34 [0.85-2.12], 0.83 [0.64-1.09], and 0.77 [0.58-1.03]. RR for progression at 2, 5, and 10 years was 0.92 [0.64-1.33], 0.69 [0.55-0.87, p=0.001], and 0.58 [0.39-0.87, p=0.008]. A sensitivity analysis of OS including only class I and II studies showed a RR of death (chemotherapy vs. no chemotherapy) at 2, 5, and 10 years of 1.23 [0.72-2.08], 0.78 [0.58-1.05, p=0.1], and 0.69 [0.56-0.86, p=0.0006]. Among only IDH1-mutated patients, the RR of progression with chemotherapy compared to control at 2, 5, and 10 years was 0.48 [0.06-4.1], 0.27 [0.08-0.84, p=0.02], and 0.21 [0.03-1.59]. Ten studies (n=1918) provide data regarding the effect of post-operative radiation vs. delayed or no radiation. RR and 95% CI for death at 2, 5, and 10 years was 0.92 [0.53-1.58], 0.93 [0.60-1.43], and 0.99 [0.69-1.41]. RR for progression at 2, 5, and 10 years was 0.66 [0.51-0.86, p=0.002], 0.73 [0.61-0.88, p=0.0008], and 0.74 [0.60-0.91, p=0.005]. Twenty-three studies (n=3891) compare gross total resection (GTR) vs. subtotal resection (STR) in LGG. RR and 95% CI of death at 2, 5, and 10 years (GTR vs. STR) was 0.29 [0.17-0.52, p<0.0001], 0.39 [0.29-0.51, p<0.00001], and 0.50 [0.35-0.70, p<0.0001]. RR of progression (GTR vs. SR) at 2, 5, and 10 years was 0.37 [0.24-0.57, p<0.0001], 0.50 [0.39-0.64, p<0.0001], and 0.67 [0.53-0.84, p=0.0005]. Relevant prognostic factors were also analyzed. For all three treatment subsets combined, only 6 studies provided class I or II evidence, and then only for the OS endpoint. CONCLUSIONS: This analysis, the largest systematic review and only quantitative systematic review performed on these questions, suggests that early post-operative radiation and chemotherapy may improve PFS in patients with LGG. Chemotherapy may also improve OS. GTR (compared with STR) is associated with substantially improved OS and PFS. Due to the lack of high quality prospective trials, additional rigorous studies are needed.

P10.04 ANTI-ANGIOGENETIC THERAPY WITH BEVACIZUMAB FOR GLIOMAS WITH A GLIOMATOSIS CEREBRI GROWTH PATTERN

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Anti-angiogenetic therapy is widely used in patients with glioma in the relapse situation. In glioblastoma and glioma, bevacizumab has been shown to have an impact on progression-free survival and neurologic function, but not on overall survival. However, its use on patients with gliomas showing a gliomatosis cerebri growth pattern is still more controversial. Due to the mainly diffuse infiltrative growth of these tumors, it may appear question-