miRNA arrays to measure the expression of exosomal miRNAs in the plasma from glioblastoma patients (n = 24) and healthy volunteers (n = 7) as control. In addition, we performed global miRNA profiling of exosomal miRNAs in the CSF from glioblastoma patients (n = 5) and non-tumoral patients (n = 3; hydrocephalus patients) as control. In plasma derived exosomes, 80 miRNAs were altered by >2-fold in glioblastoma patients compared to controls. In CSF, 92 miRNAs were altered by >2-fold in glioblastoma patients compared to controls. Combined analysis of plasma and CSF revealed a similar fold difference in eight miRNAs. Next, we measured these eight miRNAs expression in in the plasma from pre- and post-operative glioblastoma patients (n = 9). Among these eight miRNAs, we identified only one miRNA (miR-34b-3p) that was upregulated in exosomes from pre-operative glioblastoma patients. Our results suggest that miR-34b-3p might have a potential as a novel diagnostic marker or a therapeutic tool for glioblastoma patients.

Key words: glioblastoma | icroRNA | exosome

COT-6

BODY MASS INDEX AND HEIGHT IN RELATION TO BRAIN TUMOR RISK IN A JAPANESE POPULATION

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Purpose: Because the prognosis of the malignant brain tumor including glioblastoma is extremely worse than other cancer, it is important to clarify the preventive factors of the brain tumor in the prospective cohort study. In the Japanese epidemiologic study of the brain tumor, the report of the prospective cohort study has not been accomplished. Therefore, we have reported the study in recent years from a multipurpose cohort study (Japan Public Health Center-based Prospective Study: JPHC study) that the national cancer center was mainly conducted. This prospective study investigated the association between height and BMI (Body mass index) and brain tumor risk in an Asian population, whose distribution of anthropometric data differs from Westerners. Methods: A total of 106,324 subjects (50,438 men and 55,886 women) enrolled in JPHC Study, was followed from 1990. We divided participants into 5 categories based on the distribution of BMI as <18.5, 18.5- <23, 23- <25, 25- <27.5, and >-27.5 Kg/m2. We used the Cox proportional hazards regression model and estimated brain tumor incidence by gender and tumor subtype, with adjustment for potential confounding variables; age, sex, pack-years of cigarette smoking, alcohol intake, coffee intake, green tea intake, past history of allergy and past history of diabetes mellitus.Results: During an average follow-up of 18.1 years, 157 incident cases of brain tumor were newly identified, included glioma (n=60), meningioma (n =51), lymphoma(n=9), schwannoma(n=3), pituitary adenoma(n=2), and others(n=32). Higher BMI was significantly positively associated with the risk of brain tumor. This positive association of BMI was stronger in men and for meningioma in subgroup analyses. In contrast, height showed no clear association with brain tumor risk. Conclusion: Higher BMI was associated with an increased risk of brain tumor, in particular of meningioma, and among men.Full article has been published annals of epidemiology.

Key words: JPHC study | Body mass index | Prospective study

COT-7

ONLINE SUPPORTS FOR OPENING OF THE TUMOR TREATING FIELD

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Background: EF-14 trial showed the efficacy of tumor treating fields (TTF), and TTF was approved as a standard therapy for glioblastoma in Japan. In TTF opening, Device Support Specialist (DSS) explains how to use it for the patient and the family. Because there is no DSS in Yamaguchi prefecture, DSS has to come to our hospital across other prefectures. On the other hand, COVID-19 is still spreading and it is sometimes tough to move from a big city to countryside. Here, we would present the experiences of TTF opening with online DSS support. Method: From June 2020, Zoom was used for 4 patients, and from June 2021, iPad/Face-Time was used for one patient. TTF was introduced via online DSS support with direct support from our nurse in our out clinic. After that, initial times of TTF change were performed via online DSS support in patient's home. Two patients who used Zoom had trouble to connect to internet, however finally completed with relative helps.Conclusion: Online medicine should be absolutely spreading in country sides. Now, we change from Zoom to iPad, because the old patients in country sides were hard to use internet utility. We should make efforts to provide patients more brief methods of online support.

Key words: glioblastoma | TT field | online support

COT-9

PROGNOSTIC IMPACT OF HYPERCOAGULATION IN GLIOBLASTOMA AND MOLECULAR MECHANISM THEREOF

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Introduction: Pathological features of glioblastoma include intravascular thrombosis, suggesting that the thrombus formation in tumor microenvironment contributes to progression of gliomas. Meanwhile, glioblastoma has been known to be high risk malignant tumor for venous thromboembolism, however, it remains unclear how the coagulation-fibrinolysis system is disrupted, which essentially grow within the cranium in a localized manner, and how the disruption contributes to the malignant transformation. Methods: Total 64 patients with glioblastoma between January 2014 and April 2021 who underwent a D-dimer test before the therapeutic intervention were divided into two groups: the high D-dimer group (D-dimer level >3.0μg/ml) and the low D-dimer group (D-dimer level <3.0μg/ml). We compared the two groups in the maximum gadolinium-enhanced MRI lesions, MIB-1 index, and gene abnormalities (IDH mutation, TERT promoter mutation, and MGMT promotor methylation). The progression-free survival (PFS) and overall survival were analyzed using the Kaplan-Meier method. Furthermore, in 23 patients who underwent a D-dimer test at recurrence, the time to death after recurrence was analyzed. Results: The PFS in high D-dimer group was significantly shorter than that in the low D-dimer group (log-rank p = 0.0075). The D-dimer increase at the time of recurrence significantly correlated with the decrease in post-recurrence survival duration (log-rank p = 0.0226). Moreover, the gadolinium-enhanced lesions in the high D-dimer group were significantly larger. Conclusion: The Pre-intervention D-dimer levels and PFS suggest that glioblastoma-induced systemic enhancement of the coagulation-fibrinolysis system plays a role in the malignant transformation. The D-dimer increase during the treatment was found to be a predictor of poor prognosis after recurrence. Furthermore, the MRI findings revealed a correlation between the D-dimer increase and the size of intratumoral necrosis. Meanwhile, no correlation with the MIB-1 index was found, suggesting that the mechanism of malignant transformation by hypercoagulation differ from enhanced cell proliferation.

Key words: glioblastoma | coagulation | D-dimer

COT-11

RELATIONSHIP BETWEEN PREOPERATIVE LIQUID BIOPSY AND PROGNOSIS OF GLIOBLASTOMA -NEXT GENERATION SEQUENCING OF SMALL NONCODING RNA-

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Background: Non-invasive biomarkers are required in clinical practice of glioblastoma (GBM). We have previously reported the liquid biopsy for differentiating glioblastoma, central nervous system primary lymphoma and healthy control. In this study, we analyzed the relationship between the preoperative serum expression of circulating small non-coding RNAs and the prognosis of GBM patients. **Methods**: Preoperative blood samples of GBM, IDH-wildtype patients (N=26) were centrifuged and collected all small RNAs in serum. The expression of small non-coding RNAs were analyzed using a next-generation sequencing system. The small non-coding RNAs that could predict short-term survivals in GBM patients were selected by the stepwise analysis. A diagnostic model was created using the combination of these RNAs and evaluated with ROC curve. **Results**: GBM patients treated with adjuvant therapy of temozolomide and radiotherapy were divided into two groups: (1) a short-term survival group (N=11) with a survival time less than 15 months and (2) a long-term survival group (N=15) with a survival time more than 15 months. In the short-term survival group, the preoperative serum expression levels of small RNA-X and small RNA-Y were high, and the expression levels of small RNA-Z and small RNA-W were low. Using these four small non-coding RNAs, a prognostic model was created. The model was able to predict the short-term survival group of GBM patients with a sensitivity of 90.9% and specificity of 93.3% (AUC: 0.969). **Conclusion**: The prognostic model developed with preoperative small non-coding RNA in GBM patients may be useful for estimating the survival of GBM patients treated with adjuvant therapy of temozolomide and radiotherapy.

Key words: Glioblastoma | liquid biopsy | small noncoding RNA