low-grade glioma malignant transformation

The process of malignant transformation (MT) of low-grade glioma (LGG) to HGG is poorly understood but likely involves the activation of signaling programs that suppress apoptosis.

In a comparative study one favoured a biopsy followed by a “wait-and-see” strategy, delaying further therapy until malignant progression while other preferred to perform maximal safe resection whenever possible. Outcome comparison between two hospitals revealed that patients of the surgery-preferring hospital had a significantly better survival rate, suggesting that a proactive and aggressive treatment plan improves survival of low-grade glioma patients. Moreover, the rate of malignant transformation was twice as high in the “wait-and-see” cohort. Taken together, these findings support a proactive and radical surgical approach for low-grade gliomas rather than a “wait-and-see” strategy [1)].

However, heterogeneity within the LGG entity warrants investigation in a homogenous subgroup. Astrocytoma represents the largest subgroup of LGG, and is characterized by diffuse growth and inferior prognosis.

Patient data was retrospectively reviewed in two neurosurgical departments with regional referral practice. In one hospital, initial diagnostic biopsies and watchful waiting was favored, while early resections guided with three-dimensional (3D) ultrasound were advocated in the other hospital. This created a natural experiment with patient management heavy influenced by residential address. In the hospitals' histopathology databases, all adult patients diagnosed with supratentorial LGG from 1998 through 2009 were screened (n = 169) and underwent blinded histopathological review. Histopathological review concluded with 117 patients with grade II astrocytomas that were included in the present study. The primary end-point was overall survival assessed by a regional comparison. RESULTS:

Early resections were performed in 51 (82 %) versus 12 (22 %) patients in the respective hospitals ($p < 0.001$). The two patient populations were otherwise similar. Median survival was 9.7 years (95 % CI 7.5-11.9) if treated in the hospital favoring early resections compared to 5.6 years (95 % CI 3.5-7.6) if treated at the hospital favoring biopsy and watchful waiting ($p = 0.047$). No difference in surgical-related neurological morbidity was seen ($p = 0.843$).

Early 3D ultrasound guided resections improve survival, apparently without increased morbidity, compared to biopsy and watchful waiting in patients with diffuse World Health Organization (WHO) grade II astrocytomas [2)].

Forty-seven patients underwent brain magnetic resonance imaging follow-up between 2006-2014 after gross-tumor resection of intra-axial WHO II glioma. Axial/Mean/Radial diffusivity maps (AD/MD/RD) were generated from DTI data. ADmin/MDmin/RDmin values were quantified within tumor regions-of-interest generated by two independent readers including tumor contrast-to-noise (CNR). Sensitivity/specificity and area-under-the-curve (AUC) were calculated using receiver-operating-characteristic analysis. Inter-reader agreement was assessed (Cohen's kappa).

Eighteen patients demonstrated malignant transformation (MT) confirmed in 8/18 by histopathology and in 10/18 through imaging follow-up. Twelve of 18 patients (66.6%) with MT showed diffusion restriction timely coincidental with contrast-enhancement (CE). In the remaining six patients (33.3%), the diffusion restriction preceded the CE. The mean gain in detection time using DTI was (0.8±0.5

years, p = 0.028). Compared to MDmin and RDmin, ROC-analysis showed best diagnostic value for ADmin (sensitivity/specificity 94.94%/89.7%, AUC 0.96; p<0.0001) to detect MT. CNR was highest for AD (1.83±0.14), compared to MD (1.31±0.19; p<0.003) and RD (0.90±0.23; p<0.0001). Cohen's Kappa was 0.77 for ADmin, 0.71 for MDmin and 0.65 for RDmin (p<0.0001, respectively).

MT is detectable at the same time point or earlier compared to T1w-CE by diffusion restriction in diffusion-tensor-derived maps. AD demonstrated highest sensitivity/specificity/tumor-contrast compared to radial or mean diffusivity (= apparent diffusion coefficient) to detect MT [3].

1)
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