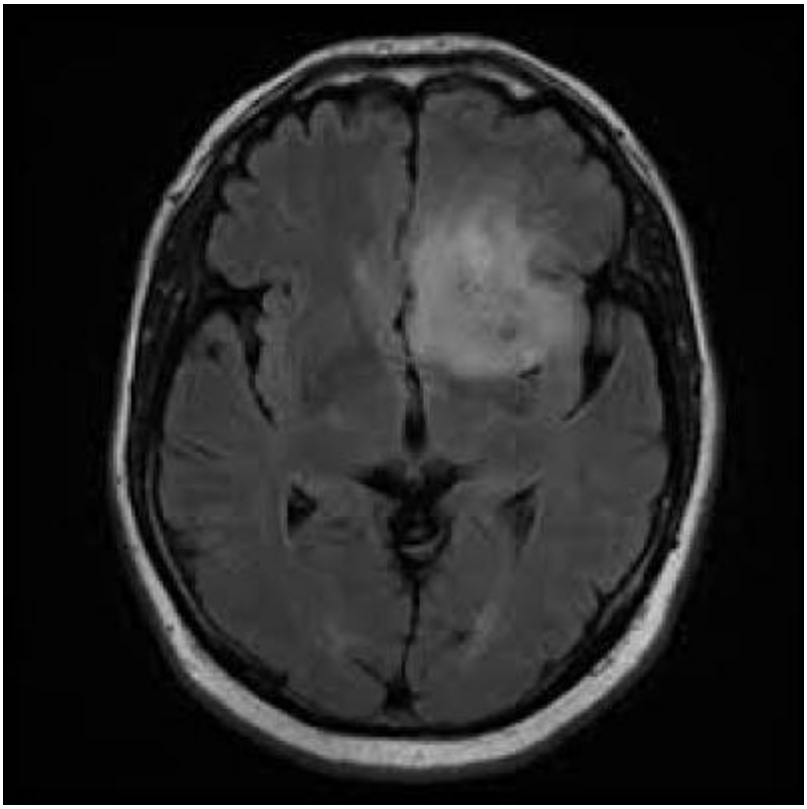
High risk low-grade glioma



On the basis of two randomized studies from the European Organization for Research and Treatment of Cancer (EORTC) [1) 2)]. and a synthesis by Pignatti et al, [3)] high-risk low-grade glioma LGG were defined by any three of five characteristics, including astrocytic histology, large tumor size (> 6 cm in diameter), midline tumor involvement, neurologic deficits ascribed to the tumor and not to surgery, and age older than 40 years.

This definition differ significantly from the definition used in the RTOG 9802 trial [4)].

Radiation Therapy Oncology Group (RTOG) 9802 has established postoperative radiation therapy (RT) and chemotherapy sequentially as the new standard of care for patients with high-risk low-grade glioma (LGG) meeting trial criteria. Although this trial investigated sequential chemoradiation therapy (sCRT) with RT followed by chemotherapy, it is unknown whether concurrent chemoradiation therapy (cCRT) may offer advantages over sCRT.

The National Cancer Database (NCDB) was queried for newly diagnosed World Health Organization (WHO) grade II glioma. Patients with unknown surgery, RT, or chemotherapy status were excluded, along with patients below 40 years old who underwent gross total resection to coincide with RTOG 9802 exclusion criteria. The χ, the Fisher exact, or Wilcoxon rank-sum tests evaluated differences in characteristics between groups. Kaplan-Meier analysis was used to evaluate overall survival (OS) between groups (sCRT vs. cCRT). Cox proportional hazards modeling determined variables associated with OS.

In total, 496 patients were analyzed (n=416 [83.9%] cCRT, n=80 [16.1%] sCRT). Sequencing or concurrency of therapy did not independently influence survival on univariable/multivariable analysis. Factors associated with worse OS on multivariable analysis included advanced age ($P<0.001$), whereas mixed glioma ($P=0.017$) and oligodendroglioma ($P=0.005$) were associated with better OS

than astrocytoma histologies.

This is the only analysis of which we are aware of cCRT versus sCRT for LGG. There is no evidence that cCRT improves outcomes over sCRT [5].

The level of evidence for adjuvant treatment of diffuse WHO grade II glioma (low-grade glioma, LGG) is low. In so-called "high risk low-grade glioma" patients most centers currently apply an early aggressive adjuvant therapy after surgery. The aim of a assessment was to compare progression free survival (PFS) and overall survival (OS) in patients receiving radiation therapy (RT) alone, chemotherapy (CT) alone, or a combined/consecutive RT+CT, with patients receiving no primary adjuvant treatment after surgery.

Based on a retrospective multicenter cohort of 288 patients (≥ 18 years old) with diffuse WHO grade II gliomas, a subgroup analysis of patients with confirmed isocitrate dehydrogenase mutation was performed. The influence of primary adjuvant treatment after surgery on PFS and OS was assessed using Kaplan-Meier estimates and multivariate Cox regression models, including age (≥ 40 years), complete tumor resection (CTR), recurrent surgery, and astrocytoma versus oligodendroglioma.

One hundred forty-four patients matched the inclusion criteria. Forty patients (27.8%) received adjuvant treatment. The median follow-up duration was 6 years (95% confidence interval 4.8-6.3 years). The median overall PFS was 3.9 years and OS 16.1 years. PFS and OS were significantly longer without adjuvant treatment ($p = 0.003$). A significant difference in favor of no adjuvant therapy was observed even in high-risk patients (age ≥ 40 years or residual tumor, 3.9 vs 3.1 years, $p = 0.025$). In the multivariate model (controlled for age, CTR, oligodendroglial diagnosis, and recurrent surgery), patients who received no adjuvant therapy showed a significantly positive influence on PFS ($p = 0.030$) and OS ($p = 0.009$) compared to any other adjuvant treatment regimen. This effect was most pronounced if RT+CT was applied ($p = 0.004$, hazard ratio [HR] 2.7 for PFS, and $p = 0.001$, HR 20.2 for OS). CTR was independently associated with longer PFS ($p = 0.019$). Age ≥ 40 years, histopathological diagnosis, and recurrence did not achieve statistical significance.

In this series of IDH-mutated LGGs, adjuvant treatment with RT, CT with temozolomide (TMZ), or the combination of both showed no significant advantage in terms of PFS and OS. Even in high-risk patients, the authors observed a similar significantly negative impact of adjuvant treatment on PFS and OS. These results underscore the importance of a CTR in LGG. Whether patients ≥ 40 years old should receive adjuvant treatment despite a CTR should be a matter of debate. A potential tumor dedifferentiation by administration of early TMZ, RT, or RT+CT in IDH-mutated LGG should be considered. However, these data are limited by the retrospective study design and the potentially heterogeneous indication for adjuvant treatment [6].

There was no significant difference in progression-free survival in patients with low-grade glioma when treated with either radiotherapy alone or temozolomide chemotherapy alone. Further data maturation is needed for overall survival analyses and evaluation of the full predictive effects of different molecular subtypes for future individualised treatment choices.

The effect of temozolomide chemotherapy or radiotherapy on HRQOL or global cognitive functioning did not differ in patients with low-grade glioma. These results do not support the choice of temozolomide alone over radiotherapy alone in patients with high-risk low-grade glioma [7].

References

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