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Clinical value of magnetic resonance spectroscopy in assessment of early curing impact of concurrent chemoradiotherapy after high-grade glioma surgery

Klinička vrednost spektroskopije magnetnom rezonancom u proceni uticaja konkurentne hemioradioterapije na rano lečenje posle operacije glioma visokog stepena

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Abstract

Background/Aim. High-grade glioma (HGG) is an interstitial cell-derived primary tumor of the nervous system. The current guidelines for the diagnosis and treatment of glioma recommend the maximum safe range of tumor resection for treatment methods. Adjuvant concurrent chemoradiotherapy is recommended after surgery, followed by six cycles of single-drug chemotherapy, temozolomide. Evaluation of the early efficacy of concurrent chemoradiotherapy after HGG surgery, especially for patients with a high risk of recurrence, is a crucial step in enhancing the treatment efficiency for patients diagnosed with HGG. In this study, we investigated the clinical utility of magnetic resonance (MR) spectroscopy (MRS) in assessing the early curing impact of concurrent chemoradiotherapy following HGG surgery. **Methods.** A total of 50 patients with incomplete resection or suspected residual postoperative HGG, treated in the radiotherapy department of our hospital between January 2016 and June 2021, were selected for routine concurrent chemoradiotherapy. Conventional MR imaging and MRS were performed one week prior to treatment and one month after treatment to assess changes in specific brain metabolites. All 50 patients were followed up for 6 to 12 months. Based on the follow-up results, the patients were divided into two groups: the tumor recurrence group and the tumor suppression group. One month after the end of the treatment, the differences in levels of brain metabolites between the two groups were analyzed using MRS. **Results.** The levels of N-acetylaspartate (NAA) and creatine (Cr) increased after radiotherapy, while choline (Cho) peak value, and Cho/Cr, NAA/Cr, and Cho/NAA ratios decreased compared to pre-treatment levels. There were statistically significant differences in the NAA peak value, and Cho/Cr, and Cho/NAA ratios in the tumor enhancement area before and after treatment ($p < 0.05$). There were also statistically significant differences in Cho/Cr ratio in the peritumoral edema area before and after treatment ($p < 0.05$). **Conclusion.** After concurrent chemoradiotherapy, MRS can be used to detect early metabolic changes in the tumor enhancement and peritumoral edema areas of HGG.

Key words:
biomarkers; chemoradiotherapy; chemotherapy, adjuvant; glioma; magnetic resonance spectroscopy; prognosis; surgery.

Apstrakt

Uvod/Cilj. Gliom visokog stepena (GVS) je primarni tumor nervnog sistema koji potiče od intersticijalnih ćelija. Aktuelne smernice za dijagnozu i lečenje glioma preporučuju maksimalan bezbedan opseg resekcije tumora kao metodu lečenja. Nakon operacije se preporučuje adjuvantna konkurentna hemioradioterapija praćena primenom šest ciklusa hemioterapije jednim lekom, temozolomidom. Procena rane efikasnosti konkurentne hemioradioterapije posle operacije GVS, posebno kod bolesnika sa visokim rizikom od recidiva, je ključni korak u poboljšanju efikasnosti lečenja bolesnika sa dijagnozom GVS. U ovoj studiji smo istražili kliničku vrednost spektroskopije magnetnom rezonancom (MR) – (SMR) u proceni ranog uticaja konkurentne hemioradioterapije na proces izlečenja, nakon operacije GVS. **Metode.** Ukupno 50 bolesnika sa nekompletnom resekcijom ili sumnjom na rezidualni postoperativni GVS, koji su lečeni na Odeljenju za radioterapiju naše bolnice u periodu od januara 2016. do juna

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2021. godine, odabrano je za rutinsku konkurentnu hemioradioterapiju. Konvencionalna MR i SMR urađene su nedelju dana pre i mesec dana nakon lečenja da bi se procenile promene u izmerenim nivoima specifičnih metabolita mozga pre i posle lečenja. Svih 50 bolesnika praćeno je tokom 6 do 12 meseci. Na osnovu rezultata praćenja, bolesnici su bili podeljeni u dve grupe: grupu kod koje je došlo do relapsa tumora i grupu kod koje je došlo do supresije tumora. Mesec dana nakon završetka lečenja, primenom SMR analizirane su razlike u nivoima metabolita mozga između dve grupe. **Rezultati.** Nivoi N-acetilaspartata (NAA) i kreatina (Kr) povećali su se nakon radioterapije, dok su najveća izmerena vrednost holina (H), i odnosi H/Kr, NAA/Kr i H/NAA bili smanjeni u poređenju sa nivoima pre lečenja. Postojale su statistički značajne razlike u najvećoj izmerenoj vrednosti NAA, i odnosima H/Kr i H/NAA u području povećanja tumora, pre i posle lečenja ($p < 0,05$). Postojale su i statistički značajne razlike u vrednostima odnosa H/Kr u području peritumorskog edema pre i posle lečenja ($p < 0,05$). **Zaključak.** Nakon konkurentne hemioradioterapije GVS, MRS se može koristiti za otkrivanje ranih metaboličkih promena u područjima povećanja tumora i peritumorskog edema.

Ključne reči:
biomarkeri; radiohemioterapija; lečenje lekovima, adjuvantno; gliom; magnetska rezonanca, spektroskopija; prognoza; hirurgija.

Introduction

High-grade glioma (HGG) is an interstitial cell-derived primary tumor of the nervous system. It is the most prevalent type of central nervous system tumor, accounting for approximately 60% of all cases [1]. The 2018 edition of the "Guidelines for the Diagnosis and Treatment of Glioma" recommends the maximum safe range of tumor resection for treatment methods. This includes intracranial tumor resection for tumors occupying obvious space and requiring pathological biopsy due to invasive diffuse growth in the dominant hemisphere and invasion of both hemispheres. Adjuvant concurrent chemoradiotherapy is recommended after surgery, followed by six cycles of temozolomide single-drug chemotherapy. Evaluation of the early efficacy of concurrent chemoradiotherapy after HGG surgery, especially for patients with a high risk of recurrence, is a crucial step in enhancing the treatment efficiency for patients diagnosed with HGG. Currently, magnetic resonance (MR) imaging (MRI) with or without contrast is primarily used to determine whether the tumor is under control or has progressed after radiotherapy and chemotherapy for HGG. This is determined by evaluating the size of the tumor and the changes in the degree of enhancement. If the tumor metabolism can be monitored using advanced imaging technology and the efficacy of simultaneous chemoradiotherapy can be predicted prior to any change in the tumor morphology, this would be the optimal outcome for clinicians. Amin et al. [2] proposed that the change in metabolite concentration occurs always before the morphological change in HGG. Therefore, the purpose of this study was to examine the correlation between the changes in HGG metabolites before and after radiotherapy in the residual lesions and peritumoral edema areas using MR spectroscopy (MRS) and their correlation with prognosis, as well as to investigate the clinical utility of MRS in determining the early curing efficacy of concurrent chemoradiotherapy following HGG surgery.

Methods

General data

A total of 50 patients with HGG who were treated in the Radiotherapy Department of our Hospital between January 2016 and June 2021 were selected for the study. This study was approved by the Ethics Committee of the Affiliated Hospital of Inner Mongolia Medical University, China (No. WZ 2023062, from September 1, 2019).

The study included patients with incomplete or complete resection of the tumor but with significant enhancement of the operative cavity margin, as shown by MRI. Patients who, due to the anatomic location of the tumor, were unable to undergo surgical resection and only underwent pathological biopsy were also included.

Imaging examination

The Siemens 3.0T Skyra MR imager was used for imaging one week before concurrent chemoradiotherapy and one month after treatment for all 50 patients. Routine MRI scans with and without contrast, as well as multivoxel MRS, were performed on all patients one week before concurrent chemoradiotherapy and were re-examined one month after concurrent chemoradiotherapy. MRS is based on the principle of chemical shift, which states that different chemical substances containing the same nucleus exhibit characteristic chemical shifts at resonance frequency, allowing the chemical composition of elements to be identified. This method enables the assessment of the chemical environment in tumor cells and brain tissues from the perspective of cell metabolism. Routine MRI examination included: Ax-Magnetization Prepared Rapid Acquisition Gradient Echo (MPRAGE): echo time (TE) 2.98 ms, repetition time (TR) 5,000 ms; T_2 fast spin echo (T_2FSE): TE 117 ms, TR 5,500 ms; T_2 – weighted fluid-attenuated inversion recovery (T_2FLAIR): TE 81 ms, TR 6,000 ms; axial scanning with a layer thickness of 5.5 mm, spacing of 1.1 mm; field of view (FOV) of 23 cm, and matrix size of 320 × 224. The MRS examination was conducted using the automatic MRS technique (PROBEx/S1 proton brain exam/multiple voxels), Point RESolved Spectroscopy (PRESS) sequence, with a TR of 1,700 ms, TE of 135 ms, multi-voxel phase matrix scanning, and a layer thickness of 15 mm. Voxel dimensions were 10 mm × 10 mm × 15 mm, and the FOV dimensions were 160 mm × 160 mm. The cross-sectional T_1 image after MRI enhancement was used to identify areas of interest. This included both the

enhanced area at the edge of the operative cavity and the enhanced area of the residual tumor. If the residual tumor revealed obvious enhancement, the area of interest was positioned between the enhancement area. If the residual tumor did not demonstrate contrast enhancement, the area of interest was placed within the body of the residual tumor. Due to low-grade gliomas usually not revealing contrast enhancement on T_1, an area of interest was also placed in the edema area surrounding the lesion. Metabolic maps, spectral maps, and chemical shift maps were obtained, and peak spectral values of N-acetylaspartate (NAA), choline (Cho), and creatine (Cr) were calculated. Quantification was performed using LCModel, with metabolite concentrations typically reported in institutional units, such as institutional units per unit volume or institutional units per Cr.

Concurrent chemoradiotherapy

Using a 6MV X-ray and a 3D treatment planning system, all 50 patients underwent radiation therapy. The head was secured using a plastic surface mold. Laser light was positioned, and a continuous computed tomography (CT) scan with contrast was performed with a 2.5 mm scanning layer thickness. The CT image data were then transferred to the planning system. After fusion, the treatment target area was outlined on the MRI image. For low-grade glioma, abnormal T_2 FLAIR MRI signals and all surgical cavities were delineated by the gross tumor volume (GTV), which was then extended 0.3–0.5 cm outside to form the planning GTV relative to T_1. The clinical target volume (CTV) was created by including an additional 1.0–1.5 cm outside the tumor, and it was necessary for the CTV to encompass the edema region surrounding the tumor. The planning target volume (PTV) was formed by adding a margin of 0.3 to 0.5 cm to the CTV. For HGG, the MRI abnormal T_1 and T_2 FLAIR signals, as well as surgical cavities, were delineated by the GTV, which was then extended 0.3–0.5 cm outside to form the planning GTV. The CTV1 was formed by including an additional 1.5–2.0 cm outside the tumor, while the CTV2 was formed by including an additional 2.0–2.5 cm outside the tumor. It was necessary for the CTV1 to encompass the edema area surrounding the tumor. Based on CTV1 and CTV2, a 0.3 cm margin was added to determine the PTV1 and PTV2 dimensions. The irradiation dose was 2 Gy/day, administered five times a week, with a total dose of 60 Gy for low-grade gliomas and 64 Gy for HGG. All 50 patients with HGG were treated with intensity-modulated radiation therapy and concurrent oral temozolomide at a dose of 75 mg/m^2 for sensitization chemotherapy.

Follow-up

Six cycles of adjuvant temozolomide chemotherapy (150 mg/m^2, one cycle from Day 1 to Day 5, every 28 days) were administered to all the patients. The patients were followed up for 6 to 12 months, and routine MRI scans with and without contrast were performed. The MRI images were compared to the MRI obtained one month after concurrent chemoradiotherapy. Brain positron emission tomography (PET)-CT was used to further confirm suspected cases of recurrence. Based on the follow-up results, the patients were divided into two groups: the tumor recurrence (TR) group and the tumor suppression (TS) group.

Statistical methods

The statistical analysis of all experimental data was done using the SPSS 23.0 statistical software. The measurement data are expressed as mean ± standard deviation. The differences in metabolite concentration and ratio before and after concurrent chemoradiotherapy were analyzed using a paired sample *t*-test following a normality test. One month after concurrent chemoradiotherapy, a *t*-test was used to analyze the differences in metabolite concentration and ratio between the TR group and the TS group. The differences were considered statistically significant when $p < 0.05$.

Results

Table 1 demonstrates the baseline characteristics of the patients. The age range was between 19 to 70 years, with an average age of 46.62 ± 12.14 years.

NAA and Cr levels increased after radiotherapy, while the Cho peak value, and Cho/Cr, NAA/Cr, and Cho/NAA ratios decreased compared to pre-treatment levels.

In the intensive area, the levels of NAA and Cr were higher after concurrent chemoradiotherapy than before treatment, while the peaks of Cho were lower. There were changes in the NAA peak level before and after treatment, and the difference was statistically significant ($p < 0.05$). After concurrent chemoradiotherapy, the Cho/Cr, NAA/Cr, and Cho/NAA ratios were lower than before treatment. There were statistically significant changes in Cho/Cr and Cho/NAA ratios before and after treatment ($p < 0.05$) (Table 2).

In the edema region, the levels of NAA and Cr peaks were higher after concurrent chemoradiotherapy than before treatment, while the peaks of Cho were lower. However, there was no statistically significant difference between the changes in the three observation indicators before and after treatment ($p > 0.05$). After concurrent chemoradiotherapy, the Cho/Cr, NAA/Cr, and Cho/NAA ratios were all lower than before treatment, and there was a statistically significant difference in the Cho/Cr ratio before and after treatment ($p < 0.05$) (Table 3).

The peak values of Cho and Cho/Cr, NAA/Cr, and Cho/NAA ratios in the TR group were higher, while the peak values of NAA and Cr were lower in the TR group compared to the TS group. Seventeen out of the 50 patients who underwent HGG surgery experienced tumor recurrence after 6 to 12 months of follow-up. Among these cases, 7 patients had newly enhanced lesions in the brain tissue, while 10 patients had residual lesions that were larger than before. These larger lesions had an occupying impact resulting in a worsening of clinical symptoms. Additional brain PET-CT examinations confirmed the recurrence of the tumor in 16 of the 17 cases mentioned above. The re-

maining case was confirmed as a recurrence of the tumor through a second surgery and pathology. All 17 cases belonged to the TR group. In the remaining 33 patients, the residual tumor lesions continued to decrease or remained stable during follow-up, and the occupying impact and clinical symptoms were alleviated. These 33 patients were included in the TS group. One month after concurrent chemoradiotherapy, the spectral peak value and ratio of brain metabolites related to the enhancement and edema regions on MRS were compared between the two groups.

In the enhancement region, the peak value of Cho in the TR group was higher than that in the TS group. In addition, the peak values of NAA and Cr were lower in the TR group compared to the TS group. Furthermore, there was a significant difference in the peak value of Cho between the two groups ($p < 0.05$). The Cho/Cr, NAA/Cr, and Cho/NAA ratios were higher in the TR group compared to the TS group. The Cho/Cr and Cho/NAA ratios exhibited statistically significant differences between the two groups ($p < 0.05$) (Table 4).

Table 1

Participant demographic and baseline characteristics

Characteristics	n (%)
Gender	
male	30 (60)
female	20 (40)
KPS score	
60	4 (8)
70	10 (20)
80	28 (56)
90	8 (16)
Pathological diagnosis and grading	
astrocytoma (WHO Grade II)	7 (14)
oligodendroglioma (WHO Grade II)	6 (12)
ependymoma (WHO Grade II)	2 (4)
anaplastic astrocytoma (WHO Grade III)	21 (42)
glioblastoma (WHO Grade IV)	14 (28)
Type of surgery	
partial excision	13 (26)
pathological biopsy	6 (12)
complete resection with active lumen margin	31 (62)

WHO – World Health Organization; KPS – Karnofsky Performance Scale.

Table 2

Peak value and ratio of metabolites in enhancement area before and after concurrent chemoradiotherapy (CC)

Phase	NAA	Cho	Cr	Cho/Cr	NAA/Cr	Cho/NAA
Before CC	3.362 ± 1.202	5.809 ± 2.129	3.362 ± 1.331	1.874 ± 0.738	1.120 ± 0.477	1.801 ± 0.575
After CC	3.773 ± 1.174	5.319 ± 1.922	3.570 ± 0.956	1.581 ± 0.683	1.109 ± 0.399	1.474 ± 0.535
t-value	-2.349	1.863	-1.079	2.320	0.141	3.220
p-value	0.023	0.068	0.286	0.025	0.889	0.002

NAA – N-acetylaspartate; Cho – choline; Cr – creatine; Cho/Cr – choline/creatine ratio; NAA/Cr – N-acetylaspartate/creatine ratio; Cho/NAA – choline/N-acetylaspartate ratio. Results are shown as mean ± standard deviation.

Table 3

Peak value and ratio of metabolites in edema area before and after concurrent chemoradiotherapy (CC)

Phase	NAA	Cho	Cr	Cho/Cr	NAA/Cr	Cho/NAA
Before CC	5.788 ± 1.364	8.447 ± 2.902	5.410 ± 1.681	1.614 ± 0.454	1.150 ± 0.345	1.502 ± 0.556
After CC	5.824 ± 1.498	7.794 ± 2.615	5.821 ± 1.616	1.380 ± 0.448	1.041 ± 0.273	1.369 ± 0.393
t-value	-0.172	1.931	-1.546	3.042	1.999	1.847
p-value	0.864	0.059	0.124	0.004	0.051	0.071

For abbreviations, see Table 2. Results are shown as mean ± standard deviation.

Table 4

Peak value and ratio of related metabolites in the tumor recurrence (TR) and tumor suppression (TS) groups in the enhancement area

Group	NAA	Cho	Cr	Cho/Cr	NAA/Cr	Cho/NAA
TR	3.736 ± 0.926	6.433 ± 1.800	3.505 ± 1.133	1.985 ± 0.754	1.168 ± 0.477	1.791 ± 0.506
TS	3.792 ± 1.296	4.745 ± 1.743	3.603 ± 0.868	1.373 ± 0.547	1.079 ± 0.357	1.312 ± 0.478
t-value	-0.160	3.209	-0.341	3.286	0.739	3.289
p-value	0.874	0.002	0.735	0.002	0.463	0.002

For abbreviations see Table 2. Results are shown as mean ± standard deviation.

Table 5

Peak value and ratio of related metabolites in the tumor recurrence (TR) and tumor suppression (TS) groups in the edema region

Group	NAA	Cho	Cr	Cho/Cr	NAA/Cr	Cho/NAA
TR	5.555 ± 1.379	8.629 ± 2.570	5.461 ± 1.418	1.649 ± 0.465	1.057 ± 0.265	1.565 ± 0.322
TS	5.963 ± 1.558	7.364 ± 2.570	6.006 ± 1.700	1.254 ± 0.415	1.032 ± 0.280	1.268 ± 0.392
t-value	-0.911	1.648	-1.134	3.062	0.307	2.690
p-value	0.367	0.106	0.262	0.004	0.760	0.010

For abbreviations, see Table 2. Results are shown as mean ± standard deviation.

In the edema area, the peak value of Cho was greater in the TR group than in the TS group, whereas the peak values of NAA and Cr were lower than that in the TS group. The three observation indices did not differ significantly between the two groups ($p > 0.05$). The Cho/Cr, NAA/Cr, and Cho/NAA ratios were higher in the TR group than in the TS group. In addition, there were statistically significant differences between the two groups in the Cho/Cr and Cho/NAA ratios ($p < 0.05$) (Table 5).

Discussion

HGG is a primary tumor of the central nervous system with a relatively high level of malignancy. The epidemiological characteristics of the disease include a high incidence, high disability rate, and a high mortality rate, and pose a serious threat to human health. Surgical resection within the maximum safe range remains the preferred initial treatment option for HGG. In the early stages of the disease, however, the highly invasive growth of HGG cells causes them to spread to the surrounding normal brain tissue and develop into highly irregular lesions. This makes complete surgical resection extremely difficult [3]. Postoperative concurrent chemoradiotherapy is, therefore, an important adjunctive treatment for HGG, and accurate monitoring of the early response to concurrent chemoradiotherapy is essential for determining prognosis. In the early stages of treatment, MRS can be used to detect the microscopic infiltration of HGG cells and determine their aggressiveness [4] and is effective in evaluating the early efficacy of concurrent chemoradiotherapy. In this study, the spectral peaks of NAA and Cr were found to be higher in both the enhancement and edema regions after treatment, than before treatment, and there was a statistically significant difference between the spectral peaks of NAA in the tumor-enhanced area before and after concurrent chemoradiotherapy ($p < 0.05$), which is consistent with most reports. The increase in NAA suggests the recovery of neuronal function in the brain tissue, while the increase in Cr indicates that the level of energy metabolism in brain tissue has been restored, indicating that the treatment is effective. In addition, the results of this study revealed that the Cho spectral peaks in the enhancement area and edema area were lower after treatment compared to before treatment with no statistically significant difference between the changes in the two areas before and after treatment ($p > 0.05$). The decrease in the Cho spectral peak indicates that the proliferation of tumor cells is being inhibited, and the disease may be effectively controlled. Lotumolo et al. [5] suggested that tumorigenesis and progression are characterized by elevated levels of Cho and decreased levels of NAA. The molar concentration of Cho in the brain tissue of patients who responded positively to the treatment was reduced.

In this study, the NAA/Cr ratio in the enhancement area and the edema area was found to be lower after treatment compared to that before the treatment with no statistically significant difference before and after treatment ($p > 0.05$). Wen et al. [6] studied MRS performance in patients diagnosed with HGG after chemotherapy and discovered that the NAA/Cr ratio decreased in patients who responded to the treatment. In addition, our study revealed that the Cho/Cr and Cho/NAA ratios in the enhancement area and the edema area were lower following treatment than they were prior to treatment with no statistically significant difference between the changes in the Cho/NAA ratio before and after concurrent chemoradiotherapy in the edema area ($p > 0.05$). Zhang et al. [7] discovered a strong positive correlation between the invasion ability of glioma cells and the Cho/Cr and Cho/NAA ratios. Based on the significant changes in the ratios between the tumor enhancement area and the edema area observed in this study before and after concurrent chemoradiotherapy, it can be concluded that the aggressiveness of the tumor cells was inhibited in patients diagnosed with HGG who received concurrent chemoradiotherapy, indicating the effectiveness of the treatment. Lotumolo et al. [5] suggested that patients diagnosed with HGG who received effective treatment exhibited decreased Cho/Cr and NAA/Cr ratios post-treatment, which is consistent with our experimental findings.

After concurrent chemoradiotherapy, the peak value of the Cr spectrum increased in both groups compared to that before treatment. However, the peak value of the Cr spectrum was lower in the TR group than in the TS group. There was no statistically significant difference in the peak value of the Cr spectrum between the two groups ($p > 0.05$). Sauwen et al. [8] believe that Cr exists as a raw material for energy supply in brain HGG with active energy metabolism. They argue that the more vigorous the glioma cell metabolism, the more Cr is consumed, leading to a decrease in its content. Therefore, there is a negative correlation between the Cr level in brain tissue and the proliferation and activity of glioma cells. It is not difficult to conclude based on our experimental data, that the glioma cells in the TS group continued to proliferate and metabolize vigorously in the early stage after synchronous chemoradiotherapy, compared to the glioma cells in the TR group. This ultimately results in different tumor outcomes.

In this experimental study, we discovered that the Cho/Cr, NAA/Cr, and Cho/NAA ratios in the enhancement and edema areas of patients diagnosed with HGG were significantly lower after concurrent chemoradiotherapy than before treatment. However, the Cho/Cr, NAA/Cr, and Cho/NAA ratios after concurrent chemoradiotherapy at the above two sites were significantly higher in the TR group than in the TS group. There were statistically significant differences in the Cho/Cr and Cho/NAA ratios between the two groups ($p < 0.05$). As mentioned previously, patients who responded positively to chemotherapy had a lower NAA/Cr ratio, while patients in the TR group displayed a higher NAA/Cr ratio than the TS group. However, there was no statistically significant difference in the NAA/Cr ratio between the two groups ($p > 0.05$). Furthermore, it was observed that patients in the TR group exhibited relatively low sensitivity to concurrent chemoradiotherapy. Zhang et al. [7] observed the ratios of Cho/NAA > 2, Cho/Cr > 2, lactic acid (Lac)/Cr >1, and lipid (Lip)/Cr > 1 in metabolically active tumor voxels. Although no spectral peaks of Lac and Lip were observed in our study, the other indicators observed were similar to those found in the study by Zhang et al. [7].

In light of the significant differences in the spectral peaks and ratios of related metabolites between the TR and the TS group, the detection of higher Cho peak and Cho/Cr and Cho/NAA ratios using MRS in the early period after concurrent chemoradiotherapy for patients diagnosed with HGG following surgery, strongly suggests that the tumor cells are still metabolically active and pose a high risk of recurrence. This finding serves as a reminder for clinicians to enhance patient follow-up, consider increasing adjuvant drugs, and intensify late temozolomide chemotherapy, if necessary, to prevent tumor recurrence in patients.

It is difficult for conventional MRI to detect the information on the invasion of tumor cells in patients diagnosed with HGG in the early stage after the completion of concurrent radiotherapy and chemotherapy following surgery. In addition, most HGG tumor recurrences are detected during long-term follow-up after treatment. By detecting changes in the peak values and ratios of brain tissue-related metabolites, MRS can be used to accurately evaluate the efficacy of concurrent radiotherapy and chemotherapy in patients with HGG after earlier surgery than traditional MRI. This is especially advantageous for patients with a high risk of recurrence and provides clinicians with valuable reference information, enabling them to develop comprehensive follow-up and treatment strategies for patients diagnosed with HGG with varying treatment outcomes, to minimize tumor recurrence following combined radiotherapy and chemotherapy administered after surgery. This strategy aims to enhance the quality of life of patients and extend their lives.

MRS is also effective in distinguishing between HGG recurrence and radiation brain necrosis. The specificity of this technique lies in its capacity to distinguish between tumor recurrence and brain radionecrosis. This is accomplished by evaluating the extent of HGG invasion and identifying the metabolic information of the brain tissue at the tumor margin [9]. Lotumolo et al. [5] suggested that tumor recurrence following HGG treatment is linked to an increase in Cho levels. Radioactive brain necrosis on the other hand is linked to an increase in Lac or Lip concentration, whereas other brain metabolites demonstrate a decreased state in cases of radioactive brain necrosis. After HGG treatment, Chuang et al. [10] discovered significant differences in the Cho/NAA and Cho/Cr ratios between tumor recurrence and radiation-induced brain necrosis. Crain et al. [11] proposed five indicators for diagnosing HGG recurrence following treatment in their study: Cho/Cr > 1.54 (sensitivity: 66%, specificity: 79%), Cr/Cho ≤ 0.63 (sensitivity: 65%, specificity: 79%), Lac/Cho ≤ 2.67 (sensitivity: 85%, specificity: 58%), Lac/Lip ≤ 1.64 (sensitivity: 54%, specificity: 95%), and Lip/Lac > 0.58 (sensitivity: 56%, specificity: 95%). Thust et al. [12] confirmed that the Cho/NAA and Cho/Cr ratios distinguished tumor recurrence from radiation-induced brain necrosis with an accuracy of 80% to 97%. MRS has important clinical application value in differentiating long-term tumor recurrence from radiation brain necrosis after concurrent chemoradiotherapy for HGG surgery, as shown by the aforementioned data.

Conclusion

In light of the previously reported clinical trial data and the results of this experimental study, it is evident that MRS has significant clinical value for the early assessment of treatment effectiveness in patients diagnosed with HGG undergoing concurrent chemoradiotherapy after surgery, thus it is an essential imaging technique in clinical practice.

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