Predicting progression of enhancing non-measurable disease in high-grade glioma by using dynamic contrast-enhanced MR imaging

Haimei Cao [a] [1], Zhousan Huang [a] [1], Ruowei Qiu [a], Xiang Xiao [a], Zhiyong Li [b], Jay J. Pillai [c] [d] [e], Jun Hua [f] [g], Guanglong Huang [b], Yikai Xu [a], Wen Liang [h], Yuankui Wu [a] ✉

- [a] Department of Medical Imaging, Nanfang Hospital, Southern Medical University, Guangzhou, China
- [b] Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou, China
- [c] Division of Neuroradiology, Mayo Clinic, Rochester, MN, USA
- [d] Radiology, Mayo Clinic College of Medicine and Science, Rochester, MN, USA
- [e] Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA
- [f] Neurosection, Division of MRI Research, Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, MD, USA
- [g] F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, MD, USA
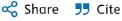- [h] Department of Radiology, Zhujiang Hospital, Southern Medical University, Guangzhou, China,

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Highlights

- Enhancing non-measurable diseases persisting after standard treatment in HGG patients pose a huge diagnostic challenge.

- The histogram models based on DCE-MRI may predict the progression of enhancing non-measurable diseases.

- The histogram models might be used to identify HGG patients requiring early treatment modification during follow-up.

Abstract

Objectives

To investigate the potential of histogram models derived from dynamic contrast-enhanced (DCE) MR imaging in predicting the progression of enhancing non-measurable disease (NMD) persisting after chemoradiotherapy in patients with high-grade glioma (HGG).

Materials and methods

A total of 97 glioma patients (mean age±standard deviation, 46.7 years ±12.1; 73 men) who underwent temozolomide-based chemoradiation following gross total resection were enrolled retrospectively, including 55 (57%) in the progression group and 42 (43%) in the non-progression group. The histogram features of K^{trans} (volume transfer constant between the plasma and extravascular extracellular space) and Ve (extravascular volume) for enhancing NMDs were extracted and compared between the two groups. Histogram features with significant differences were included in binary logistic regression to construct models to predict progression within 2 to 3 months. The models were constructed based on K^{trans} and Ve alone or combined. Receiver operating characteristic curves were used to evaluate the prediction performance of the different models. The models were testified in a prospective cohort consisting of 15 patients with HGG.

Results

The histogram model of K^{trans} showed an area under the curve (AUC) of 0.900 in predicting progression. The model of Ve had an AUC of 0.879. When combining K^{trans} and Ve, the model achieved an AUC of 0.927. These models showed excellent predictive performance in the prospective study.

Conclusion

The histogram models based on DCE MRI can predict the progression of enhancing NMDs in HGG following chemoradiotherapy 2 to 3 months in advance.

Introduction

Glioma is the most common type of primary malignant brain tumor among adults, of which WHO grade 3 and grade 4 glioma are referred to as high-grade glioma (HGG) and account for about 70% of gliomas [1]. The most widely accepted treatment for HGG is maximal safe tumor resection followed by radiation therapy with concurrent temozolomide (TMZ) and adjuvant TMZ [2]. However, the prognosis of HGG patients remains poor in spite of these treatments, with a high recurrence rate [3] and rapid disease progression leading to death [4]. Therefore, a burning question in the management of HGG patients is the optimal follow-up after chemoradiation and accurate assessment of response, in order to detect tumor recurrence early and even more to anticipate it [5]. There is no doubt that early identification or prediction of tumor recurrence may extend the survival time of patients by allowing early treatment modification [6].

Currently, treatment response assessment is still mainly dependent on regular structural MRI and the determination of disease progression is based on the Response Assessment in Neuro-Oncology (RANO) criteria [7]. The RANO criteria mainly focus on measurable disease (MD), and in most cases, progressive disease (PD) is considered when the product of the perpendicular diameters of MD increases by 25% in the sum and patients have clear clinical deterioration, which mandates a change in therapy. Follow-up and continuing with current therapy are usually recommended for enhancing non-measurable diseases (NMDs), i.e., with a diameter of less than 10mm. However, tumor biological progression usually precedes the clinical onset of progression [8]. In our clinical practice, it is not infrequent that enhancing NMDs progress quickly in 2–3months. Therefore, early prediction of the outcome of enhancing NMDs is of great clinical significance. However, imaging predictors for progression of NMDs are currently unavailable in clinical practice.

Dynamic contrast-enhanced (DCE) MRI can provide quantitative information on tumor angiogenesis and microcirculation, facilitating a more accurate evaluation of treatment response. Studies have shown that DCE parameters have important diagnostic values for early tumor recurrence [[9], [10], [11]]. Yoo et al. found that DCE parameters could help predict the development trend of MD within a certain period in glioblastoma patients receiving chemoradiotherapy [12]. However, there is yet no published report on the prediction of the development trend of enhancing NMDs.

Histogram analysis is a robust method that can provide quantitative information on tissue characteristics [13]. Histogram features of DCE perfusion parameters have demonstrated great potential in glioma grading [14,15], differentiation between lymphoma and glioma [16], and predicting genetic phenotypes and prognosis [17,18].

Therefore, the purpose of this study was to investigate the potential of histogram models based on volume transfer constant (K^{trans}) between the plasma and extravascular extracellular space and extravascular volume (Ve) in predicting the progression of enhancing NMDs of HGG at the next follow-up MRI after completion of chemoradiotherapy.

Section snippets

Study participants

This study consisted of a retrospective study and a small sample prospective study, conducted from January 2016 to May 2023. The Ethics Committee of Nanfang Hospital approved the prospective study application for this study. All patients in the prospective study received written informed consent. Patient informed consent was waived in the retrospective study. All examinations were performed in accordance with local institutional review board guidelines.

A total of 195 consecutive patients with ...

Results

A total of 97 glioma patients (mean age±standard deviation, 46.7 years ±12.1; 73 men) were enrolled retrospectively, including 55 (57%) in the progression group and 42 (43%) in the non-progression group. The patients including 10 cases of WHO grade 3 astrocytoma and 87 cases of grade 4 astrocytoma or glioblastoma. In second-look operations, the pathological diagnoses included 22 PD cases and 6 non-progression cases. Table 1 summarizes the clinical characteristics of the patients. The two ...

Discussion

Early prediction of the progression of enhancing NMDs is of potential use for the management of HGG patients. Our results demonstrated that the histogram models based on K^{trans} and Ve individually or combined could accurately predict the progression of enhancing NMDs.

Previous studies have used DCE perfusion parameters to predict glioma progression [11,12]. Yoo et al. [12] found that mean K^{trans} and Ve and 5th percentile of K^{trans} could predict the progression of MD in glioblastoma patients ...

Conclusion

The present study demonstrated that histogram models based on K^{trans} and Ve can predict the progression of enhancing NMDs after completion of chemoradiotherapy in HGG patients 2–3 months in advance. Promisingly, this would assist the management of HGG patients and prompt early treatment modification in those who progress in the next follow-up. ...

CRediT authorship contribution statement

Haimei Cao: Writing – original draft, Methodology. **Zhousan Huang:** Writing – original draft, Methodology. **Ruowei Qiu:** Methodology, Investigation. **Xiang Xiao:** Supervision, Funding acquisition. **Zhiyong Li:** Conceptualization. **Jay J. Pillai:** Writing – review & editing. **Jun Hua:** Writing – review & editing. **Guanglong Huang:** Conceptualization. **Yikai Xu:** Software,

Resources. **Wen Liang:** Methodology. **Yuankui Wu:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. …

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. …

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1   Haimei Cao and Zhousan Huang contributed equally to this study and were considered co-first authors.

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