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Full Length Article

The relationship between MRI quantitative parameters and the expression of hypoxia inducible factor-1 alpha in cerebral astrocytoma

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ABSTRACT

Objective: Astrocytoma is the common type of glioma. But the MRI scanning for astrocytoma preoperation pathological diagnosis is not exact. The purpose of this study was to use the MRI multi quantitative parameters to improve the diagnosis of astrocytoma and exploit their molecular mechanism related to the expression of HIF-1α.

Methods: Superconducting MR scanner and its work station were used to calculate the MRI multi quantitative parameters of the selected patients in this experiment. Scion Image Beta4.03 software was used to get the cellular density of tumor tissue. The expression of HIF-1α in astrocytoma specimens was detected by immunohistochemistry method. The correlation of MRI multi quantitative parameters and the expression of HIF-1α was analyzed by statistical software.

Result: The values of ADC, RSIGd, EP, EI, cellular density and the expression of HIF-1α were changed with the malignant degree of astrocytoma to some extent, but not every quantitative parameter was related to the expression of HIF-1α.

Conclusion: The MRI multi quantitative parameters binding with conventional MRI imaging can significantly raise the diagnostic accuracy of astrocytoma preoperatively. MRI features could indirectly reflect the biological behavior of astrocytoma. The peritumoral edema can't be explained by only one theory.

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1. Introduction

Astrocytoma is the commonest primary cranial malignant tumor. The pathogenesis of which is not still absolutely understood for us. There is no radical cure for astrocytoma. A clinical imageology method is badly needed to precisely judge the pathological degree of the tumor and help to implement correct clinical treatment plan and prognosis judgement. The routine MRI scan has too many deficiency in diagnosis, which cannot do precisely qualitative and quantitative diagnosis of astrocytoma and cannot determine the extensive of tumor invasion,the degree of tumor proliferation and cannot judge tumor microvascular form. Recent researches showed that there were significant anoxic areas in many human tumors [1–4] .Hypoxia inducible factor-1 (HIF-1) is one of transcription factor generally existing in mammal and human beings in hypoxic conditions. Its HIF-1α subunit as a nuclear transcription factor to regular tumor cells to adapt to hypoxic conditions can adjust multiple downstream genes during transcription once activated. The purpose of this research was to explore the relationship between multi MRI quantitative parameters and the expression of HIF-1α and to raise the diagnostic accuracy of astrocytoma preoperatively.

2. Materials and methods

2.1. Clinical data

The research object was brain tumor patients who were first diagnosed in tangshan kailuan hospital. All of the thirty three patients were told the treatment condition which were in accordance with ethics principle. They were operated by the same treatment group. After operation the excisions were confirmed by pathology to be astrocytomas and kept tumor wax blocks. Among them, 18 cases were male and 15 were female. The mean age was 48.12 years old, of which 6 cases were 14–35 years old, 9 cases were

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36–50 years old and 18 cases were 50–68 years old. According to the World Health Organization (WHO) the latest classification standards 5 cases of astrocytoma were grade I, 13 cases were grade II, 11 cases were grade III, and 4 cases were grade IV that was to say glioblastoma. Because of grade I and grade IV cases' number is too small, grade I-II cases (a total of 18 cases) were classified as low grade astrocytoma (low malignant) group; grade III-IV cases (A total of 15 cases) were regarded as high-grade astrocytoma (highly malignant) group.

2.2. MRI scanning

All of the thirty three patients were perform MRI scanning by our 1.5T superconducting MRI scanner. The scanning order was conventional scan, diffusion-weighted imaging (DWI) and enhanced scan.

2.2.1. Image data analysis

All cases of MRI data were introduced to SUN ADW4.0 workstation. All eligible data were analyzed and processed by the corresponding software package operated on Console. All cases of image were read and compared by double-blind method. First we found and determined abnormal signal intensity area of DWI, and then compared with the number of lesions, morphology, signal intensity (SI) and lesion range through the sequence of T1WI, T2WI, T1WI + C(contrast-enhanced) and FLAIR. After that we done imaging data analysis by choosing each sequence mentioned above among which we chose the representative axial image of the same slice as sample layer. Imaging data analysis contained peritumorous brain edema (PTBE) data analysis, contrast-enhanced imaging data analysis and ADC values of DWI data analysis. We chose the PTBE index (EI) as the criteria for the assessment of PTBE. The method of computation EI value was performed as describe previously [5]. The SI of the most obvious part of the substantial part of the tumor contrast-enhanced and the corresponding white matter of the contralateral brain was measured respectively on workstation using T1WI + C sequence "sample layer". And then we got the SI of the substantial part of the tumor on T1WI. Each side according to the size of the substantial part of tumor take 3–5 circular Region of interest (ROI) and then got the average SI of each part. For contrast-enhanced imaging data analysis we chose two indices: Relative signal intensity on Gd-enhanced T1WI (RSIGd) and Enhancement percentage (EP). RSIGd value was the ratio of The SI of the most obvious part of the substantial part of the tumor contrast-enhanced and the corresponding white matter of the contralateral brain. EP value was the ratio of the difference SI of the substantial part of tumor before and after enhance and the corresponding white matter of the contralateral brain. In order to let the ROI (size = 20–40 mm^2) place within the substantial part of the tumor and keep the ROI shape,size and anatomic location in line we made the T1WI + C sequence, FLAIR sequence or T2WI FRFSE sequence of "sample layer" substitute for the eADC map generated by workstation. For ADC values of ROI multiple measurements may be averaged.

2.3. Tumor specimens histological analysis

The medical image software Scion Image for Windows 4.0.3.2 was used to determine the tumor cell density of pathological picture.

2.4. Immunohistochemical staining of HIF-1α

The immunohistochemical method was performed as described previously [6]. Each section was chose a high power lens field randomly in the up and down or so in order to calculate positive cell rate. Five fields of Lis (labeling index) were averaged as the result of the experiment, which was described by "mean ±standard deviation".

2.5. Statistic process

The values of ADC, RSIGd, EP and EI were calculated by the software named Excel. SPSS for windows 13.0 statistical software package was used to assess the data processed by Excel. All quantitative data were expressed as the means ± SD. Statistically significant differences were determined by using Independent Sample T test; Correlative studied of quantitative data values were made using "Bivariable Correlations". P value of less than 0.05 was considered to indicate statistical significance.

3. Result

(1) ADC: ADC value of low grade(grade I-II) astrocytoma is 1619.24 ± 376.22 $(10^{-6}mm^2/s)$ higher than that of high grade(grade III-IV) astrocytoma: 954.29 ± 80.63 $(10^{-6} mm^2/s)(t = 7.300, p < 0.05)$. (2) RSIGd, EP: The value of RSIGd and EP were significantly different between the low grade astrocytoma $1.29 \pm 0.26,(52.29 \pm 18.9)\%$ and high grade astrocytoma $1.62 \pm 0.25,(82.61 \pm 22.48)\%$ $(t = -3.669, p < 0.05; t = -4.212, p < 0.05)$. (3) EI: There were significantly different between the low grade astrocytoma 1.93 ± 1.60 and high grade astrocytoma 3.73 ± 2.05. $(t = -2.839, p < 0.05)$. (4) Cellular density: The astrocytoma cellular density value was significantly higher in the low grade astrocytoma $(9.36 \pm 5.38\%)$ than that in high grade astrocytoma $(20.13 \pm 0.1)\%(t = -3.845, p < 0.05)$. (5) HIF-1α: There was no expression of HIF-1α in normal brain organization. The HIF-1α LIs is: low grade astrocytoma: $(20.08 \pm 10.01)\%$, high grade astrocytoma: $(47.91 \pm 19.03)\%$. They were significantly different between the two group $(t = -5.104, p < 0.05$. (6) Pearson correlation analysis showed that: (1) ADC and HIF-1α LIs $r = -0.756$ $(p < 0.05)$, cellular density $r = -0.617(p < 0.05)$ showed significantly negative correlation. (2) The ADC value for the solid tumor component was negatively correlated with the value of RSIGd $r = -0.483$ $(p<0.05)$, EP $r = -0.514$ $(p<0.05)$ and EI $r = -0.458$ $(p < 0.05)$. (3) There was no obvious significant correlation existed between the value of HIF-1α LIs and EI $r = 0.317$ $(p > 0.05)$; The value of HIF-1α LIs was positively correlated with the value of RSIGd $r = 0.431$ $(p < 0.05)$. The value of HIF-1α LIs was significantly positively correlated with the value of cellular density and EP $r = 0.622$ $(p < 0.05)$, $r = 0.661$ $(p < 0.05)$. (4) There was no obvious significant correlation existed between the value of Cellular density and RSIGd, $r = 0.320$ $(p > 0.05)$. Cellular density value was positively correlated with the value of EP $r = 0.400$ $(p < 0.05)$ and EI $r = 0.457$ $(p < 0.05$. (5) There were significantly positive correlation between the value of RSIGd and EP $r = 0.651$ $(p < 0.05$. (6) The value of EI was significantly positively correlated with the value of RSIGd $r = 0.554$ $(p < 0.05)$ and no significantly correlation existed with the value of EP $r = 0.327$ $(p > 0.05)$.

4. Discussion

4.1. The relationship between ADC value and tumor cell density

DWI has made MR go into a more micro level for human body research. Water molecules diffusion can provide more information about organization's spatial composition more accurately and reliably. The more cellular components, the less interstitial components, the weaker the diffusion movement of water molecules in the tissue and vice versa. The result of this study has shown that the ADC value of low grade