Correlations of magnetic resonance, perfusion-weighed imaging parameters and microvessel density in meningioma

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Summary

Purpose: To investigate the correlations of magnetic resonance, perfusion-weighed imaging (PWI) parameters and microvessel density (MVD) in meningioma.

Methods: 48 patients with pathologically confirmed meningioma (grade I, 38 cases; grade II+III, 10 cases) completed preoperative routine magnetic resonance imaging (MRI) and PWI. The cerebral blood volume (CBV) map of solid tumor region and the mean of maximum relative cerebral blood volume (rCBV) were then calculated. Immunohistochemical staining was performed in all specimens to measure the MVD.

Results: On the CBV map, benign meningiomas showed a high perfusion signal, while malignant meningiomas exhibited a slightly higher one. The rCBV of benign meningiomas was 9.61±4.76, which was significantly higher than 3.61±0.25 of malignant meningiomas (t=7.165, p=0.000). The MVD of benign meningioma strips was 21.16 ± 11.32, which was also significantly higher than 10.71 ± 5.53 strips of malignant meningiomas (t=2.325, p=0.026). The correlation analysis showed that the mean of maximum rCBV and MVD of meningiomas had significant positive correlations (r=0.718, p=0.000).

Conclusions: The CBV map of benign meningiomas is different to that of malignant meningiomas, and the mean of maximum rCBV and MVD have significant positive correlations.

Key words: magnetic resonance, microvessel density, perfusion-weighed imaging, relative cerebral blood volume

Introduction

In 2007, the WHO classification of tumors in the nervous system divided meningiomas into 3 grades; grade I was defined as benign and would not be prone to reoccur after surgical resection; grades II and III were collectively defined as malignant, with the clinical manifestations showing invasive growth and easy recurrence after surgery. The preoperative grading of benign and malignant meningiomas would influence the surgical programs and the selection of treatment methods [1,2]. MVD is closely related to tumor pathological grading and clinical staging [3]. PWI is a new technology, that evaluate the characteristics of microvascular distribution and tissue perfusion in vivo, and could contribute to tumor grading; its main index is the rCBV mean, and there were fewer reports about the value of mean rCBV in evaluating the angiogenesis in meningiomas [4-8]. In this article, 39 cases of meningiomas performed PWI and immunohistochemical MVD-quantitative study, with the aim of investigating the correlations of rCBV and MVD, and to assess the application values of cerebral PWI in diagnosing and classifying meningioma.

Methods

Subjects

Forty eight patients with meningioma, surgically and pathologically confirmed in the affiliated Beijing Chaoyang Hospital of Capital Medical University from August 2005 to July 2015, were collected, in whom the

tumor diameter was greater than 2cm, while no large-scale calcification was found. The patients consisted of 14 males and 25 females, aged 7 to 68 years, with mean age being 48 years. According to WHO pathological classification of intracranial tumors (in 2007), 38 cases were classified as grade I and 10 cases were classified as grade II and III. The patients were informed of the inspection method prior to the test, and a consent was obtained from each patient; this study was approved by the ethics committee of our hospital.

MRI method

Sigma 1.5T superconducting MR imager, equipped with quadrature head coil (GE,USA), was used to perform sagittal spin echo (SE) T1WI, axial fast spin echo (FSE) T2WI, axial SE T1WI, PWI, and enhanced SE T1WI at three directions. The scanning parameters were as follows:

Sagittal T1WI: TE 16 ms; TR 400 ms; axial T1WI: TE 12 ms, TR 400 ms; axial T2WI: TE 80 ms, TR 3800 ms; axial fluid-attenuated inversion recovery sequence (FLAIR): TE 125 ms, TR 8500 ms, TI 2200 ms.

The parameters of PWI gradient echo-echo planar imaging (GRE-EPI) T2 * WI: TR 2000 ms, TE 80 ms, flip angle 90°, bandwidth 62.50, matrix 128×128, vision field 24×24 cm, slice thickness 10.0 mm, interlayer spacing 0 mm, and Nex 1. Before scanning, automatic shimming was performed. A single 18 or 20G needle was used for venipuncture through the median cubital vein; the puncture needle was then fixed and connected to the MR-specific syringe (SPECTRIS); after location, the 4 phases were initially scanned, then injected with contrast agent gadolinium-DTPA injection (Gd –DTPA, Beilu, Beijing, China) during the scanning, with a dose of 0. 2 mmol/kg and a flow rate of 3-4 ml/s; after that, 20 ml of saline was bolus-injected at the same speed; 10 layers, which could cover the entire tumor tissue, were acquired; the imaging time was set at 80s to complete the acquisition of 40-phase images; a total of 400 original images of PWI were obtained; finally, the routine-enhanced scanning was performed.

MVD

Streptavidin-biotin-peroxidase (SBP) method was used for immunohistochemical staining, and the staining results were observed under an optical microscope.

The measurement of MVD with films, referred to by Weidner et al. [9], was read by double-blind method: firstly, comprehensive observation of the slice at low magnification (×100) to determine the site with the highest MVD, then recording MVDs within 5 vision fields at high magnification (×200). The endothelial cells and tiny blood vessels were also counted and the mean was then used as the MVD value of this sample.

Analysis of images and data

The collected raw data was exported to a Sun ADW4.1 workstation (GE Medical Systems, Milwaukee, USA). FuncTool software was used to build a pseudo-color image of each scanning layer, namely the CBV map; in this map, the typical layer was selected, while avoiding the cystic degeneration, necrosis and calcified areas, and setting the region of interest (ROI) at 16-20 pixels; ROI was placed inside the maximum perfusion area of tumor parenchyma, and measured 4 times; the mean was then obtained and used for that of maximum CBV; the CBV ratio of the lesion and the contralateral normal white matter were calculated, which was the midpoint of the maximum rCBV of this tumor.

Statistics

SPSS 11.0 software package was used for the single-factor analysis of variance (ANOVA) for the rCBV ratios, at different grades, between the 2 groups; the range of MVD was counted in all cases, the mean and standard deviation was calculated and the data of MVD and rCBV went through linear correlation analysis (Pearson's correlation test), to observe the correlations between the two groups.

Results

Maximum rCBV ratios of benign and malignant meningiomas

The rCBV means of benign and malignant meningiomas were 9.61±4.76 and 3.61±0.25, respectively; the rCBV ratio of benign meningiomas was significantly higher compared to malignant meningiomas, and the difference was statistically significant (t=7.165, p=0.000); on the CBV map, the tumor parenchyma showed a high perfusion signal, while that of malignant meningiomas exhibited a slightly higher perfusion (Figure 1A, 2A).

Correlations of maximum rCBV ratio and MVD in benign and malignant meningiomas

MVD of benign and malignant meningiomas showed 22.23±11.65 and 10.83± 5.49 strips, respectively; MVD of benign meningiomas were much higher compared to malignant meningiomas, difference being statistically significant (t=2.325, p=0.026). Linear correlation analysis showed that MVD was notably positively correlated with rCBV (r=0.718, p=0.000), indicating that the higher the rCBV value the more abundant the tumor blood vessels and vice versa. Namely, benign meningiomas had a greater abundance of blood vessels (Figure 1B, Figure 2B).
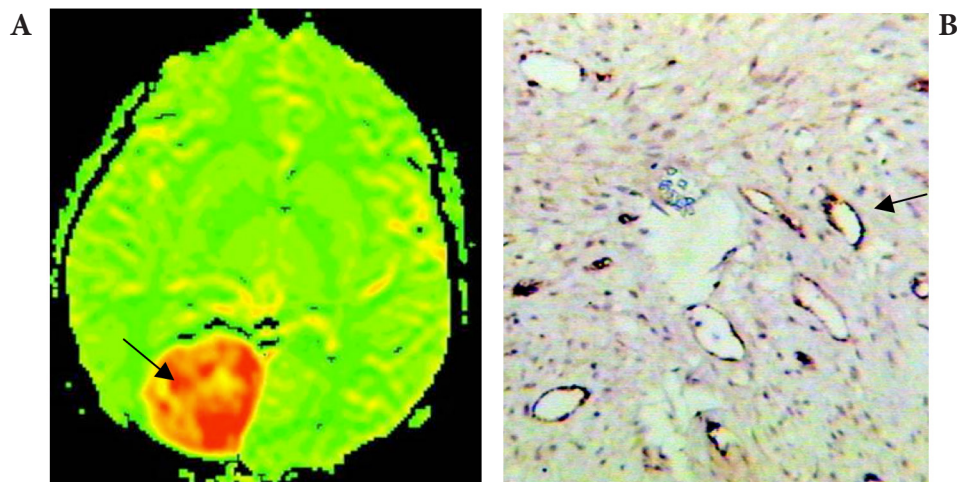
Discussion

Tumor angiogenesis is essential for the

Figure 1. Female, 43 years old, diagnosed with right anterior, para-sickle benign meningioma. **A:** the CBV map; the tumor parenchyma exhibited a high perfusion signal (arrow), and the rCBV value was higher. **B:** the staining image of immunohistochemical factor VIII-related antigen, in which a lot of brown-stained tumor microvessels could be seen (arrow).
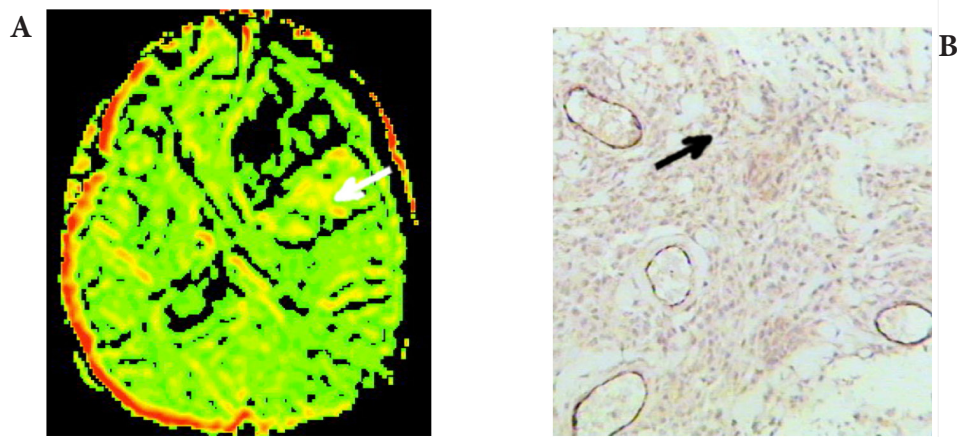

Figure 2. Female, 53 years old, with left frontal malignant meningioma. **A:** the CBV map; the tumor parenchyma (ROI 1) exhibited a slightly higher perfusion signal (arrow), while the rCBV value was low; the necrotic area had no perfusion. **B:** the staining image of the immunohistochemical factor VIII-related antigen; the microvessels are stained brown (arrow), while their number was relatively small.

growth and metastasis of cancer cells, and the gold standard, most commonly used to evaluate tumor blood vessels, is microscopic MVD counting. rCBV, one of the important indicators commonly used by PWI, can also be used for effective evaluation of angiogenesis in meningioma [10-12]. rCBV is related to the amount of contrast agent inside ROIs, during the first-pass period, and positively proportional to the vascular volume. Theoretically, reflecting on the activities of tumor angiogenesis, PWI is much more sensitive than immunohistochemical methods. Because the rCBV ratio contains factors, such as contralateral white matter CBV, and excludes the differences

in individual blood flow, the clinical evaluation could be much easier. Because rCBV is particularly sensitive in the appearance of microvessels, it would exhibit greater advantages in evaluating tumor angiogenesis.

Conventional MRI is the basic technology for diagnosing brain tumors, although it has some limitations, such as grading tumors inaccurately. MRI enhancement indicates the extent of contrast agent accumulation among tissue gaps, after the blood brain barrier (BBB) is damaged, while it cannot display the changes of the tumor vascular bed. The mechanism of BBB damage is that the tumor damages the capillaries or the blood

vessels of lesion tissues, which are composed by abnormal capillaries. No matter whether T1WI is enhanced or not, there are limitations in reflecting tumor angiogenesis; the degree of abnormal perfusion in PWI could directly show the extent of vascular proliferation, and the region with significantly increased perfusion would usually be the one with the highest grade of malignancy. Studies had shown that important correlations existed between rCBV and the pathological grade of tumors, and the rCBV value of high-grade tumors was significantly higher than that of low-grade ones [13,14].

Studies have also shown that angiogenesis was an important indicator of histological grading in brain tumors. Because of high growth speed, angiogenesis in high-grade gliomas and metastatic tumors would be significant. Meningioma has rich blood vessels, though different from brain tumors, yet it has almost no BBB, in order for the contrast agent to leak into the interstitial space through the capillaries, so that the meningioma could be significantly enhanced, and this makes the perfusion characteristics of meningioma different to other brain tumors [12].

This study found that the mean rCBV was influenced by a cystic necrotic region inside the tumor tissue, so it could not accurately indicate the density of tumor blood vessels. Therefore, selecting the maximum rCBV is very important.

Yang et al. analyzed the preoperative PWI characteristics of a group of meningiomas (12 benign and 5 malignant cases) and found that the mean of maximum rCBV of malignant meningiomas (11.8±2.5) was higher than that of benign meningiomas (9.2 ± 6.8), without remarkable difference [15].

Previous studies also found that the mean of maximum rCBV of benign meningiomas was higher compared to malignant meningiomas (7.16 ± 4.08 vs 5.89 ± 3.86, p>0.05), and the difference also had no statistical importance [16,17].

Partial results of this study did not match the ones above. In this study, the mean of maximum rCBV of benign meningiomas was higher compared to their malignant counterparts. This might occur because the meningioma itself has rich blood vessels, so the mean of maximum rCBV of benign meningiomas was higher. Also, because malignant meningiomas grew faster, the tumor blood supply would be relatively low, therefore microscopic necrosis may exist in a certain re-

gion. As a result, rCBV measured from the rCBV map would be lower; however, the results of immunohistochemical staining showed that MVD of the benign group was greater than that of the malignant group, indicating that MVD and rCBV had consistency in presenting tumor angiogenesis.

Ginat et al. [18] retrospectively analyzed a group of meningiomas (24 high-grade and 24 low-grade) and found that the midpoint of high-grade meningiomas (12.6±5.2) was higher compared to low-grade meningiomas (8.2±5.2), and rCBV was significantly correlated with the expression of vascular endothelial growth factor (VEGF) (r=0.37, p=0.01), prompting that rCBV could accurately display the expression of VEGF and the classification of benign and malignant meningiomas. Therefore, rCBV could be used as a valuable indicator to reflect the characteristics of meningiomas [18]. Several studies reported that the expression of VEGF was positively correlated with MVD in meningioma [19-21]. These studies confirmed, from another aspect, the consistency of rCBV and MVD in reflecting tumor angiogenesis.

The value of PWI in evaluating tumor angiogenesis has been recognized, although the universal indicators in evaluating tumor angiogenesis are currently VEGF protein expression and MVD [14]. No research exists about the consistency of rCBV and MVD in evaluating tumor angiogenesis in meningiomas. This study revealed that rCBV and MVD in meningiomas were positively related and the tumors with richer blood vessels exhibited higher rCBV, indicating that rCBV could be used as a reliable indicator for the preoperative evaluation of angiogenesis in meningiomas. Malignant tumors might be included in the status of relative ischemia and hypoxia because of their rapid growth, so that the number of tumor microvessels would be less. rCBV would also be lower, and additionally, it was negatively correlated with the pathologic grade of meningiomas.

In conclusion, PWI could not only provide intuitive diagnostic information in meningiomas, but also semi-quantitatively provide the hemodynamic information of microcirculation in these tumors. Therefore, it might be a very important means of guidance for the selection of clinical treatment options and evaluation of prognosis.

Conflict of interests

The authors declare no confict of interests.

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