Original Investigation

Orbital Indeterminate Lesions in Adults: Combined Magnetic Resonance Morphometry and Histogram Analysis of Apparent Diffusion Coefficient Maps for Predicting Malignancy

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Rationale and Objectives: The aim of this study was to evaluate the added value of histogram analysis of apparent diffusion coefficient (ADC) maps in differentiating indeterminate orbital malignant tumors from benign tumors, compared to using magnetic resonance (MR) morphological features alone.

Materials and Methods: We retrospectively evaluated 54 patients with orbital tumors from March 2013 to February 2015. All the patients were assessed by both routine MR and diffusion-weighted imaging, and divided into benign group and malignant group. Routine MR imaging features and histogram parameters derived from ADC maps, including mean ADC (ADC_{mean}), median ADC (ADC_{median}), standard deviation, skewness, kurtosis, and 10th and 90th percentiles of ADC (ADC_{10} and ADC_{90}), were compared between two groups. Univariate and multivariate logistic regression analyses were used to identify the most valuable variables in predicting malignancy. Receiver operating characteristic (ROC) curve analysis was used to determine the diagnostic value of significant variables.

Results: Multivariate logistic regression analysis indicated that two or more quadrants involved, iso-intense on T2-weighted imaging (T2WI), and ADC_{10} were significant predictors for orbital malignancy. By using model 2 (iso-intense on T2WI + two or more quadrants involved + $ADC_{10} < 0.990$) as the criterion, higher AUC and specificity could be achieved than by using model 1 (iso-intense on T2WI + two or more quadrants involved) alone, (model 2 vs model 1; area under curve (AUC), 0.827 vs 0.793; sensitivity, 65.4% vs 69.2%; specificity, 100% vs 89.3%).

Conclusions: Iso-intense on T2WI, two or more quadrants involved, and ADC_{10} are risk factors for orbital malignancy. Histogram analysis of ADC map might provide added value in predicting orbital malignancy.

Key Words: Orbital tumor; Differential diagnosis; Magnetic resonance imaging; Diffusion-weighted imaging; Histogram analysis.

INTRODUCTION

Orbital space occupying lesions represent a broad spectrum of benign and malignant disease (1). Accurate differentiation of orbital benign and malignant tumors is very important for the pre-treatment plan (2). Although viewed as the gold standard, open or fine-needle aspiration biopsy is sometimes technically challenging or not feasible, especially for orbital apex lesions (3). Therefore, several previous imaging-related studies have tried to use the imaging features of routine computed tomography or magnetic resonance (MR) images to help differentiate malignant orbital tumors from benign mimics (3,4). Although some imaging features, including involvement of anterior orbit, irregular shape, ill-defined margin, and iso-intensity on T2-weighted imaging (T2WI), were indicated as potentially discriminating features for the malignant orbital tumors, their overall diagnostic performance was still limited.

Diffusion-weighted imaging (DWI) has been used increasingly to distinguish malignant orbital tumors from benign

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mimics (1,5–8). Although malignant orbital tumors usually show as high signal intensity on DWI and low apparent diffusion coefficient (ADC) value, the ADC value showed a substantial overlap between benign and malignant orbital tumors, which limited its clinical value for individual patients. Only the mean ADC value was used as the differentiating index in previous studies, which would underestimate the heterogeneity of the tumor, and might be the reason for the obvious overlap. Currently, histogram analysis of the ADC map based on pixel distribution has been proven useful to provide quantitative information about tumor heterogeneity, to differentiate and grade tumors, or to predict the treatment response in various organs (9–17). However, to the best of our knowledge, no study to date has applied the histogram analysis of ADC maps in differentiating benign and malignant orbital tumors.

Therefore, the purpose of this study was to evaluate the added value of histogram analysis of ADC maps, compared to routine MR imaging morphological features alone, in differentiating malignant tumors from benign orbital tumors.

MATERIALS AND METHODS

Study Population

Ethic approval for our retrospective study was granted by the institutional review board, and written informed consent was waived because of the retrospective nature of the study. Between March 2013 and February 2015, 102 consecutive patients underwent DWI scan as part of pretreatment MRI evaluation for orbital tumors. First, according to the definition of orbital indeterminate lesions proposed in previous studies (1,4), patients of cavernous malformation ($n = 25$), lymphangioma ($n = 1$), venous varix ($n = 4$), and epidermoid cyst ($n = 7$) were also excluded because of their characteristic findings on routine MR imaging. Then, five patients were excluded for having lesions whose largest diameter was less than 1 cm, and six patients were excluded because of poor image quality of DWI. Finally, the remaining 54 patients (30 males and 24 females; mean age, 49.9 years; range, 18–90 years) constituted the study population.

The study cohort was composed of 28 benign and 26 malignant tumors. Detailed histological composition of the two groups is shown in Table 1. The final diagnosis was made based on the surgical pathological results in 49 patients, on the typical imaging features and long-term follow-up in 2 patients with optic nerve sheath meningioma, and on follow-up after steroid treatment in 3 patients with inflammatory pseudotumor.

MRI Techniques

MRI was performed with a 3 Tesla MRI scanner (Verio; Siemens, Erlangen, Germany) with a 12-channel head coil. Routine imaging protocols contained an unenhanced axial T1-weighted imaging (repetition time [TR]/echo time [TE], 600/10 ms), axial T2WI (TR/TE, 4700/79 ms) with fat saturation, coronal T2WI (TR/TE, 3500/79 ms), and contrast-enhanced axial T1-weighted imaging (TR/TE, 500/10 ms). For contrast-enhanced axial T1-weighted imaging, a standard dose of 0.1 mmol/kg of gadolinium-diethylene triamine pentaacetic acid (Magnevist; Bayer Schering Pharma AG, Berlin, Germany) was administrated at a rate of 4 mL/s, followed by a 20-mL bolus of saline at the same injection rate.

In all cases, a single-shot spin-echo echo-planar DWI sequence was performed in the transverse plane with three orthogonal diffusion gradients of b value = 0 and 800 s/mm^2. The other detailed imaging parameters involved a 4-mm section thickness without intersection gap, a repetition time/average echo time of 4000/85 ms, a flip angle (FA) of 150°, number of averages of 6, field of view of 200 × 200 mm, matrix of 384 × 384, and number of sections of 10. The total acquisition time of DWI was 4 min and 14 s.

Imaging Processing

We performed the qualitative image assessment focusing on the tumors' laterality, shape, margin, location, number of involved quadrants, internal signal architecture, and enhancement pattern. The laterality was divided as unilateral or bilateral. The tumor location was classified as intraconal, extraconal, lacrimal fossa, and anterior orbit preseptal. The shape was described as regular or irregular. The margin was classified as well defined or ill defined. Similar to previous studies, to make

TABLE 1. Demographic and Histological Information of Two Groups

Demographic Data	Benign Group ($n = 28$)	Malignant Group ($n = 26$)	*P* Value
Mean age	44.8 ± 13.5	55.3 ± 16.2	0.012
Gender (F/M)	12/16	12/14	0.808
Diagnosis	Inflammatory pseudotumor (9)	Lymphoma (18)	—
	Pleomorphic adenoma (8)	Adenoid cystic carcinoma (2)	
	Schwannoma (6)	Metastases (2)	
	Optic nerve sheath meningioma (4)	Basocellular carcinoma (1)	
	Solitary fibrous tumor (1)	Lymphoepithelial carcinoma (1)	
		Ewing's sarcoma (1)	
		Melanoma (1)	

F, female; M, male. Data in parentheses indicate the number of the corresponding patients in our study.