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Diffusion-Weighted Magnetic Resonance Imaging in the Evaluation of Non Traumatic Orbital Lesions

Kawther Attia Gad a*, Mohammed Mahmoud Dawoud ^a , Mohammed Ashraf Eldesouky ^b and Manal Fathy Hemisa ^a

^a Diagnostic Radiology Department, Faculty of Medicine, Tanta University, Tanta, Egypt. ^b Ophthalmology Department, Faculty of Medicine, Tanta University, Tanta, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Magnetic Resonance Imaging (MRI) Scans are better than high-resolution computed tomography (CT) scans. They are frequently used to discover tumors, infections and chronic diseases that affect the structures in and around the orbits. This study's aim was to evaluate the contribution of diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) measurements to MRI in the assessment of non-traumatic orbital lesions.

Methods: This prospective research involved 30 cases with clinical and radiological non-traumatic orbital lesions. All patients underwent clinical assessment, ocular examination, laboratory investigations, radiological assessment (Conventional MRI, DW-MRI)) and histopathological analysis.

Results: There was substantial agreement between the magnetic resonance and pathologic diagnosis, k=0.722, p<0.001. The cut-off value of ADC for orbital lesions was $\leq 1.0 \times 10^{-3}$ to be considered malignant lesions. Diffusion-weighted MRI and ADC had a sensitivity of 87.5 %, specificity 100%, and positive predictive value of 100 %, and a negative predictive value of 94.92 % to distinguish among benign and malignant orbital lesions.

Conclusions: MRI alone can detect orbital lesions, but they couldn't distinguish among benign and malignant lesions. The ADC value is non-invasive imaging technique that may be utilized to characterize orbital lesions and distinguish among benign and malignant ones.

**Corresponding author;*

E-mail: thesismses@gmail.com;

Keywords: Magnetic resonance imaging; diffusion-weighted MRI; non-traumatic orbital lesions; apparent diffusion coefficient.

1. INTRODUCTION

Orbital lesions in adults and children comprise a range of benign and malignant lesions that may be difficult to identify and treat. Due to the limitations of clinical examination and the hazards involved with biopsy, imaging plays an essential role in diagnosis [1]. Imaging of the orbit is essential to validate the lesion's diagnosis and features. However, owing to intrinsic similarities, it is usually difficult to discriminate between particular diseases based just on image characteristics. Magnetic resonance imaging (MRI) is a potent imaging technique for the orbit; because it offers better tissue contrast [1, 2].

MRI scans are better than high-resolution computed tomography (CT) scans. They are frequently used to discover tumors, infections and chronic diseases that affect the structures in and around the orbits [3].

Using conventional MRI methods, it is sometimes hard to determine if a cystic lesion is a tumor or an abscess. Imaging approaches for imaging brain and orbital disease continue to grow and advance. Clinicians today have access to an extensive assortment of diagnostic tests. With the advent of diffusion-weighted imaging (DWI), further noninvasive MR tumors characterization is possible [4, 5].

Diffusion weighted MRI depends on assessment of random water proton movement within tissues and reflects cellular density and tissue architecture, offering imaging techniques that does not require the use of ionizing radiation or MR contrast agents and can be easily incorporated into a standard MRI protocol. DWI can monitor changes in water molecule diffusion in vivo. This assessment of the water's selfdiffusion coefficient reveals water movement inside tissue and is known as the apparent diffusion coefficient (ADC) [6].

When used in combination with clinical and conventional MRI results, DWI may assist identify ambiguous orbital lesions and considerably helps in tissue characterization with high accuracy, giving an additional noninvasive predictor of histological type and tool for directing treatments [1].

Numerous previous researches suggested that DWI and ADC values have a role in predicting

malignancy in orbital tumors, differentiating orbital lymphoma from pseudotumor, and evaluating orbital cellulitis, identifying orbital abscesses, optic nerve lesions, and infarcts [7].

Malignant lesions are more cellular and have lower ADC values in comparison with benign lesions. New post-processing techniques with automated ADC calculation improved the diagnostic performance of DWI MRI and made it more precise and simple to conduct [8].

This study's aim was to evaluate the contribution of DWI and ADC values to MRI in the assessment of non-traumatic orbital lesions.

2. PATIENTS AND METHODS

This prospective study was conducted on 30 cases of all ages and with clinical and radiological findings of non-traumatic orbital lesions referred to Radio-diagnosis and Medical Imaging department from ophthalmology department at Tanta University Hospitals throughout period extending from July 2018 to August 2020.

Exclusion criteria were traumatic lesion, cases with impaired renal function, electronically, mechanically, and magnetically activated implants, electronically or ferromagnetic operated active devices like automatic cardioverter, cardiac pacemakers, defibrillators, metallic splinters in the eye and ferromagnetic haemostatic clips in the central nervous system.

All cases underwent clinical evaluation by ophthalmologist (meticulous history taking, ocular examination, assessment of corrected visual acuity, ocular movements, visual fields and fundoscopy, laboratory investigations (total and differential leucocytic counts, erythrocytic sedimentation rate, tumor markers and thyroid function test), radiological assessment (conventional MRI and DW-MRI) and histopathological analysis.

2.1 Radiological Assessment

MRI for all patients, conventional MRI, MRI with contrast for selected patients, diffusion weighted MRI and ADC, MRI of the orbit performed in 1.5 tesla super conducting magnet system (Signa Explorer, GE health care) in Radio-diagnosis and Medical Imaging department. The technique involved the use of standard quadrature head coil. The patients examined in supine position. The patient instructed to remove all metallic items such as cloths contain metal also, earrings, ferromagnetic material within the patient before entering the examination room or any personnel entering the scan environment were also prohibited such as cardiac pacemaker, ferromagnetic aneurysm clips, metallic fragment in the eye, cochlear implants, prosthetic heart valve.

2.2 Conventional MRI

All the patient were evaluated by MRI orbit with diffusion in radio-diagnosis and medical imaging using a 1.5 Tesla MRI scanner (Signa Explorer, GE health care). The total time of the scan is about half an hour. All cases were investigated in supine position with standard circularly polarized head coil utilizing the following sequences: Axial T1-weighted images (TR/TE= 400-600/15-20 ms), Axial T2-weighted images (TR/TE= 4000- 5000/100-110 ms), axial and/or coronal T1WI with fat suppression were done (TR/TE= 500-600/5 ms), sagittal T1WI (TR/TE =400-600/10 ms) and post contrast MRI was also done following intravenous administration of 0.1 mmol/kg body weight of (Gd-DTPA). After contrast, T1WI images were obtained in the axial, sagittal, and coronal planes.

The lesions were evaluated in CMRI as regard: the number of the lesions, signal behavior on T1 and T2 (iso, hypo and hyper intense compared to muscles), existence of intratumoral necrotic or hemorrhagic components and bone destruction and degree of enhancement (no, minimal or avid) and pattern (homogenous or heterogenous).

2.3 MR Diffusion Imaging

Using a multi-section single-shot echo planar imaging sequence (TR/TE= 5200/84 ms), section thickness of 4 mm, and b values of 0 and 1000 s/mm², diffusion-weighted MRI was acquired. On DWI ($b = 0$ and 1000), the signal intensity of the lesion was categorised as either hypointense (free diffusion) or hyperintense (restricted diffusion). The ADC maps were automatically computed by the MRI software. The ADC values were expressed 10^{-3} mm²/s. The regions of interest (ROIs) were drawn manually from all slices displaying the lesion on the ADC images. ROIs were generally $3-10$ mm² in size depending on the extent of the lesions (and not the cystic, necrotic, and hemorrhagic tumor areas).

2.4 Statistical Analysis

SPSS v26 was used to do statistical analysis (IBM Inc., Chicago, IL, USA). Using the Shapiro-Wilks test and histograms, the normality of the data distribution was determined. As mean and standard deviation (SD), quantitative parametric data were given. Non-parametric quantitative data were given as the median and interquartile range (IQR). The qualitative characteristics were provided in terms of frequency and percentage (%).

3. RESULTS

Table 1 shows demographic characteristics, distribution of the orbital lesions according to the histopathologic diagnosis, clinical presentation of orbital lesions and side of the lesions of the studied cases.

Table 2 shows the conventional MRI findings, comparison among the benign and malignant lesions regarding the ADC values and the agreement between DWI, MRI diagnosis, and histopathological diagnosis in the different studied lesions. ADC values of benign-looking lesions by diffusion MRI were ranged between $1.30 - 1.90 \times 10^{-3}$ mm²/sec detected in 16 cases, on histopathology 14 of them were benign and 2 of them were malignant. While ADC values of malignant looking lesions ranged between 0.50 – 1.80×10^{-3} mm²/sec detected in 14 cases on histopathology all of them were malignant with statistically significant results. Restricted diffusion (high signal intensity at DWI and low at ADC maps) was found in 14 cases with ranged ADC values from 0.5- 0.90 \times 10⁻³ mm2/sec; on histopathology, all of them were malignant lesions. No restricted diffusion was detected within benign lesions in this study.

The cut-off value of ADC for orbital lesions was ≤ 1.0 \times 10⁻³ to be considered malignant lesions. Diffusion-weighted MRI and ADC had a sensitivity of 87.5 %, specificity 100%, and positive predictive value of 100 %, and a negative predictive value of 94.92 % to distinguish among benign and malignant orbital lesions Fig. 1.

The findings of T1W1 and T2W1 showed a lack of significant association with the malignancy of the lesion. All benign lesions showed free diffusion, while most malignant lesions (87.5%) exhibited restricted diffusion (p<0.001). Compared to conventional MRI, the DWI had a higher sensitivity (68.8 vs. 87.5%, respectively),

specificity (85.7 vs. 100%, respectively), and
accuracy (76.7 vs. 93.3%, respectively). accuracy (76.7 vs.

However, these differences still not significant Table 3.

Fig. 1. ROC curve for diagnosis of malignant lesions using ADC value

Table 2. Conventional MRI findings, comparison between the benign and malignant lesions regarding the ADC value and the agreement between DWI, MRI diagnosis, and histopathological diagnosis in the different studied lesions

*Data represented as Mean ± SD, median or frequency. MRI: Magnetic resonance imaging. ADC: apparent diffusion coefficient. DWI: Diffusion-weighted imaging. T1WI: T1 weighted image. T2WI T2 weighted image *: significant as P value ≤ 0.05*

Table 3. Findings of conventional MRI, DWI, and ADC according to the malignancy and specificity, sensitivity, and accuracy of conventional MRI and DWI in diagnosing malignant lesions

*MRI: Magnetic resonance imaging. ADC: apparent diffusion coefficient. DWI: Diffusion-weighted imaging. T1WI: T1 weighted image. T2WI T2 weighted image CI: confidence interval. *: significant as P value ≤ 0.05*

Gad et al.; JAMMR, 34(22): 131-141, 2022; Article no.JAMMR.91822

(A) Axial T1WI (B) Axial T2WI

(C) Axial FLAIR (D) Coronal T1 + C

(E) Sagittal T1 + C (F) Diffusion image

(G) ADC map

Fig. 2. Axial T1(A), Axial T2(B), Axial FLAIR(C), Coronal T1 post contrast (D), Sagittal T1 post contrast(E): Diffuse enlargement of both lacrimal glands more evident on right side displayed low signal intensity at T1WI(A), high signal intensity at T2WI (B) with mild homogenous enhancement after IV contrast injection and just touching the lateral aspect of lateral rectus muscle on both sides with bilateral preseptal edema more on the right side and causing mild right eye proptosis. Axial DWI (F), Axial ADC (G): The lesion showed hyperintense signal on DWI (restricted diffusion), ADC value was 0.9 x10⁻³ mm²/sec. MRI findings consistent with **bilateral inflammatory orbital lesions versus lacrimal gland lymphoma. DW MRI showing that lesions had restricted diffusion which is consistent with bilateral lacrimal gland lymphoma**

(A) Axial T1WI (B) Axial T2WI

(C) Axial STIR (D) Coronal T1

(E) Sagittal T1 +C (F) Diffusion image

(G) ADC map

Fig. 3. Axial T1(A), Axial T2 (B), Axial STIR (C), Coronal T1 (D), Sagittal T1 post contrast (E): Diffuse enlargement of medial rectus, inferior rectus and lateral rectus muscles on right side displayed isointense signal at T1WI (A) and T2WI(B) with homogenous enhancement after IV contrast injection. Axial DWI (F), Axial ADC(G): The lesion showed hypointense signal on DWI (free diffusion), ADC value was 1.4 x10-3 mm² /sec (G). MRI findings consistent with right sided thyroid orbitopathy. DW MRI showing hypointense signal of the lesion on DWI (free diffusion) consistent with right sided thyroid orbitopathy

4. DISCUSSION

MRI is used to locate and characterize the extent of orbital tumor. However, precise diagnosis and differentiation between malignant and benign orbital diseases may be challenging due to overlapping and non-specific imaging analysis, and tumors may be misdiagnosed in situations of unanticipated uncommon tumour types [1]. DWI is a noninvasive prospective diagnostic technique for in vivo tissue characterization. This innovative approach provides a clinical help for the ophthalmologist in diagnosing some disorders in vivo [9].

The present study included thirty patients (16 females and 14 males), these results don't cope with Abdel Razek et al. [8] who stated that orbital lesions frequently affect males more than female with male to female ratio was 34:13. In the current study the commonest age incidence in patients with orbital lesions was between 40 - 60 years old (53.4%).

In the present study the most common presenting symptom was proptosis, it was the main symptom in all cases (100%). This in agreement with the findings obtained by Sultan AA et al. [10] who reported that the most common presenting symptom in 60 cases of orbital masses was proptosis.

By histopathology, 14 were benign orbital lesions and 16 were malignant orbital lesions. These results don't cope with Abdel Razek et al. [8] who revealed that benign orbital lesions were more than malignant ones with benign to malignant ratio 25:22.

In the current study we noticed no restricted diffusion detected within benign orbital lesions (14 cases). Also 14 cases with pathologically proved malignant lesions showed restricted diffusion, however 2 malignant cases; one with optic glioma and other with orbital metastasis showed free diffusion (false negative result) so the presence of free diffusion does not exclude malignancy. This was in line with research done by Sultan AA et al. [10], they involved sixty patients. Of these 60 cases, 26 were malignant cases with restricted diffusion and 1 malignant case with free diffusion, peripheral nerve sheath tumor, malignant schwannoma proved high ADC value 1.4 × 10−3 mm²/s giving false negative result. However, he reported 20 were benign cases with free diffusion and 13 benign cases with restricted diffusion. The ADC value were

high for the majority of benign lesions $(n = 20)$ but were low in 13 cases (false positives). Five cases of meningioma, one case of dermoid, five cases of cellulites, one case of cavernous hemangioma, and one case of recurrent angiofibroma were represented.

In the current research the most prevalent malignant lesions were lymphoma and metastasis (20% and 13.3% respectively). These outcomes are in accordance with Sultan AA et al. [10], who reported that lymphoma and metastasis were the most prevalent malignant tumors (25.9% and 14.8%, respectively).

All of lymphoma cases displayed hypointense signal on T1WI, while on T2WI 4 cases showed hypointense signal and the other cases showed hyperintense signal, all cases showed restricted diffusion of the lesion with low ADC value (0.7 \pm 0.13 \times 10-3 mm²/s). These findings go with the results obtained by Sepahdari, et al. [11] who reported 6 cases of orbital lymphoma T2 weighted fast spin-echo image showed infiltrating and hypointense signal. The DWI displayed hyperintense signal comparable to that of grey matter in the brain, whereas the ADC map reveals related hypointensity. Also, ADC values were $0.47 - 0.92 \times 10^{-3}$ mm²/s.

All of metastasis cases displayed hypointense signal on T1WI, while on T2WI they showed hyper intense signal, 3 cases showed restricted diffusion of the lesion with low ADC value $(0.73\pm$ 0.12×10^{-3} mm²/s) but the other case showed free diffusion of the lesion with high ADC value $(1.8 \times 10^{-3} \text{ mm}^2/\text{s})$. These outcomes in agreement with Sepahdari et al. [11] who indicated that even though there is a strong correlation among diffusion restriction and enhanced cellularity, not all orbital cancers are hypercellular.

In the current research there were 2 cases of optic nerve glioma, both of them displayed hypointense signal on T1WI and hyperintense signal on T2WI, one of them clarified restricted diffusion with low ADC value (0.8 \times 10⁻³ mm²/s). This was consistent with Sepahdari et al. [11] who indicated that as established in investigations of CNS lymphoma and high-grade glioma, lower ADC has various pathologic correlations, with increased cellularity being the most relevant.

The 2 cases of neuroblastoma displayed isointense signal on T1WI and T2WI, both of them showed confined diffusion of the lesion with low ADC value $(0.6 \times 10^{-3} \text{ mm}^2/\text{s})$.

The mean ADC value of the studied subjects of rhabdomyosarcoma was low $(0.9 \times 10^{-3} \text{ mm}^2/\text{s})$. They showed confined diffusion (hyperintense signal on DWI). They displayed isointense signal on T1WI and hyperintense signal on T2WI.

In the current study the most prevalent benign lesions were thyroid orbitopathy and orbital cellulitis (20% and 13.3%), respectively. These findings are in accordance with Roshdy N et al. [4] who revealed that idiopathic orbital inflammatory disease and Dysthyroid ophthalmopathy were the most prevalent benign lesions (20% and 15%), respectively. But the difference between the current research and the that done by Roshdy N et al. [4] is that the current study didn't include cases with idiopathic orbital inflammatory disease.

Most of thyroid orbitopathy cases displayed isointense signal on T1WI and hyperintense signal on T2WI. All of thyroid orbitopathy cases showed free diffusion of the lesion with high ADC value $(1.43 \pm 0.13 \times 10.3 \text{ mm2/s})$. This in agreement with the research that done by Roshdy N et al. [4] who indicated that there were two of three cases of Dysthyroid ophthalmopathy showing free diffusion of the lesion (hypointense signal on DWI).

All of orbital cellulitis cases displayed hypointense signal on T1WI, 2 of them displayed isointense signal on T2WI and the other 2 cases displayed hyperintense signal on T2WI. All of them showed free diffusion of the lesion with high ADC value (1.75 \pm 0.17 \times 10-3 mm2/s). These results don't go with the research done by Sultan AA et al. [10], who found that all of cases of

orbital cellulitis showing restricted diffusion due to abscess formation. The high ADC value was associated with the dense cellular packing and viscosity of purulent material, despite the fact that inflammatory orbital lesions have normally greater ADC values than abscesses.

In the current research all cases of cavernous hemangioma displayed isointense signal on T1WI and hyperintense signal on T2WI. They clarified free diffusion of the lesion and high ADC value (1.5 \times 10-3 mm²/s). These outcomes are in accordance with Sultan AA et al. [10], who informed that case of cavernous hemangioma showed free diffusion (hypointense signal on DWI) and high ADC value $(1.1 \times 10^{-3} \text{ mm}^2/\text{s})$.

In the current research there were 2 cases of neurofibroma. They displayed hypointense signal on T1WI and hyperintense signal on T2WI. They showed free diffusion of the lesion (hypointense signal on DWI) and high ADC value (1.8 x10⁻³ \overline{mm}^2 /s).

In the current research we reported that the mean ADC values of benign and malignant orbital lesions were $1.2 - 1.9 \times 10^{-3}$ mm²/s and 0.5- 0.90 x 10^{-3} mm²/s respectively. The average ADC measures of benign lesions was significantly increased than that of malignant orbital lesions.

In the present study we used ADC value of ≤ 1.0 $x10^{-3}$ mm²/sec as a cut off value in differentiating benign and malignant orbital lesions with sensitivity 87.5% and specificity 100 %.

This in line with Soliman AF et al. [12], they found that ADC value of 0.90 $x10^{-3}$ mm²/sec is a cut off among benign and malignant orbital lesions by sensitivity 76 % and specificity 96 %. Below the cut off value (0.90 $x10^{-3}$ mm²/sec), 1 benign & 20 malignant lesions were found, and above this cut off value, 24 benign & 5 malignant lesions were detected.

Elkhamary [2] did her study on the lacrimal gland lesions on 42 lesions of 40 cases who participated in this research, concluded that With great precision, a threshold ADC value of 0.90 x 10^{-3} mm²/sec was determined for distinguishing malignant lacrimal tumours from benign lesions.

The absolute ADC value of benign and malignant orbital lesions was significantly different confirming previous observations of benign orbital lesions and malignant tumors elsewhere in the body. The ADC value may thus be regarded a biomarker for distinguishing between malignant and benign lesions.

5. CONCLUSION

MRI alone can detect orbital lesions, but they were unable to distinguish properly between benign and malignant lesions. ADC value is noninvasive imaging technique that can be utilized to characterize orbital lesions and distinguish among benign and malignant ones. ADC value paired with MRI technique increases the diagnostic efficacy of MRI in the distinction among benign and malignant orbital lesions resulting in an increase in the overall accuracy of MRI and a decrease in the frequency of falsepositive findings and needless biopsies.

6. LIMITATIONS

Several orbital compartments were included, also the numbers of the lesions in each compartment were few. So, we are looking for extending our study to include the lesion in each compartment separately and different pathological entities. The other limitation was to include patient from all ages, so we need further study for pediatric and adult age groups separately.

ETHICAL APPROVAL AND CONSENT

Informed written consent was obtained from the case or relatives of the cases. The research was performed after approval from the Ethical Committee Tanta University Hospitals.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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