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CROSSLINKING MRI WITH HISTOPATHOLOGY: CROSS-SECTIONAL ANALYSIS TO ASSESS THE EFFECTIVENESS IN THE IDENTIFICATION OF BENIGN AND MALIGNANT TUMORS

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Abstract

Background: *Orbital masses including benign and malignant tumors are still an important diagnostic and therapeutic problem. Magnetic Resonance Imaging MRI has played a crucial role in the non-invasive assessment of these lesions, on account of its better soft tissue resolution and planar detail. The association between MRI and histopathological characteristic is still vital in reaching the correct management decisions.*

Objective: In this study, MRI was assessed for its ability to diagnose the location of orbital masses specifically distinguishing between malignant and benign forms of tumors histopathological results were used as a standard of reference.

Methods: *After study approval, this cross-sectional prospective study (June- November 2022) was done inter-collaboratively at Teaching Hospital, University of Lahore, Shalimar Hospital Lahore in affiliation with private medical diagnostic centers in Lahore. Using non-probability sequential sampling technique, 145 patients diagnosed with clinical symptoms pointing at orbital mass, who were to undertake surgery or biopsy, were selected. MRI scans were done using a 1.5 enhanced MR machine. The overall accuracy of MRI in diagnosing the orbital masses was assessed using the following parameters; sensitivity, specificity, PPV, NPV, and diagnostic accuracy all in comparison to histopathological prognostications.*

Results: *While 145 admitted patients were involved in the study, 55.2% of the patients were females while the remainder (44.8%) were male, and the patient ages were mostly 18-30 years (87.6%). MRI successfully detected 77.2 percent of cancer cases as malignant, and 22.8 percent as benign, whereas histopathological examination revealed 83.4 percent as malignant, and 16.6 percent as benign. Diagnostic performance assessment of MRI for benign masses revealed 81.82% sensitivity, 96.43% specificity, 87.10% of PPV, 94.74% of NPV, and an overall 93.10% accuracy. MRI in malignant masses showed sensitivity 90.16%, specificity 86.90%, PPV 83.33%, NPV 92.41% and diagnostic efficiency 88.28%.*

Conclusion: *In this study, high diagnostic accuracy is shown for MRI in distinguishing benign from malignant orbital masses, but this study is limited by its single center design and a relatively homogeneous patient population, not allowing generalization of these results. These findings need further studies across different centers with different demographics to be confirmed and the applicability of MRI diagnostics to further be improved in the settings of other clinical teams.*

Keywords: *Benign pathology on the orbit, Diagnostic reality, Histopathological examination, Magnetic resonance imaging, Orbital masses*

INTRODUCTION

Orbital masses include a wide range of both malignant and benign lesions, and present different clinical challenges requiring distinct treatment modalities. Achieving an accurate and timely diagnosis of these masses is critically important because it directly determines appropriate selection of treatment and directly impacts patient outcome (1). Because of its unparalleled ability to differentiate between different types of soft tissues, and offer detailed anatomical insight, magnetic resonance imaging (MRI) has evolved as a critical diagnostic tool in this context. Because of its better soft tissue resolution, MRI, thanks to the availability of this capability, has become a necessary technique in the evaluation of eye disorders, particularly in the characterization of orbital lesions (1-3).

Among those of the orbital lesions which span a broad spectrum of clinical signs and symptoms which normally make the diagnosis and treatment difficult, there is the need for accurate diagnostic means, both during diagnosis and in the clinical setting. The superior soft tissue characterization of MRI becomes critical in the diagnostic process where clinical evaluation and medical history are not definitive (4, 5). However, histopathological examination remains the standard by which the defining tissues and appropriate diagnosis of diseases are interpreted. The reliability and effectiveness of MRI in diagnosing orbital masses is assessed by way of the correlation of MRI findings with histopathology data (6). In this realm, the diagnostic accuracy of MRI is influenced by an innumerable number of factors: The lesion nature, the modalities used in imaging and of course, the radiologist's experience.

A review shows that MRI has a sensitivity of 83% and specificity of 97% for diagnosis of the benign orbital lesion. Diagnostic accuracy of 95% was also achieved, including positive and negative predictive values of 83% and 97%, respectively (7).

The sensitivity and specificity for malignant orbital lesions were 91% and 83% respectively, positive and negative predictive values were 87% and 88% respectively, resulting in an overall diagnostic accuracy of 88% (8). This allows the early initiation of appropriate treatments including pharmacological and surgical modalities, knowing well which orbital disorder there is, by their expert imaging techniques that can identify and characterize them perfectly. In addition to preserving the patient's visual acuity, it also reduces the risks that are associated with adverse outcomes, including progressive infiltration or destruction of surrounding tissues. Radiologists must comprehend the common orbital lesions, their unique imaging patterns, and their appearances on computed tomography, MRI and ultrasound. High resolution MRI of the orbit is particularly used for diagnosis of a multitude of orbital diseases and malignancies. In fields of ophthalmology and radiology histopathology is the best method to make a precise diagnosis of orbital masses when they are necessary (9-11).

Despite its high diagnostic potential, no report of a consistent and comprehensive evaluation of the sensitivity, specificity, and predictive value of orbital masses by MRI in the presence of histological evidence is available in the current literature. This gap calls for the need for robust, evidence-based data on MRI’s diagnostic accuracy to help clinicians make fully informed decisions. Therefore, this study attempts to provide a measure of the sensitivity, specificity, PPV, and NPV of MRI of orbital tumors in differentiating such tumors as benign or malignant. The study will fill this gap by improving MRI’s noninvasive identification of orbital diseases, thereby optimizing ophthalmological care to meet individual patient needs and advancing practice at the ophthalmology field.

MATERIALS AND METHODS

This cross-sectional prospective study (June-November 2022) was done inter-collaboratively at Teaching Hospital, University of Lahore, and Shalimar Hospital Lahore in affiliation with private medical diagnostic centers in Lahore after getting permission from Head of departments. The purpose of this research was to assess the diagnostic accuracy of magnetic resonance imaging (MRI) for diagnosing the orbital mass, with histopathology as reference standard. A non-probability sequential sampling technique was used to enroll 145 patients scheduled for surgical operations or biopsies in the study. Participants were included if they were adults aged 18 years or older, of any gender, with a diagnosis of suspected orbital masses that persisted for longer than a few weeks. Clinical symptoms, such as pain, proptosis or a lesion suggestive of an orbital mass, were present in these individuals but they did not have a confirmed diagnosis.

The recruitment process included a very thorough clinical evaluation that included medical history review, physical exam and diagnostic imaging. Imaging checks were performed on a 1.5 Tesla MRI scanner. Hypersensitivity to contrast agents or claustrophobia, or insufficient renal function was indicated by blood creatinine levels >1.5 mg/dL, were exclusion criteria for MRI. In addition, subjects who were unwilling to undergo histological testing were not included in the study. Gold standard histological examinations were obtained on admission and a three month follow up. Correlations were established between biopsy data and MRI findings using this approach to distinguish benign from malignant orbital tumors. The study was adhered rigorously to all ethical guidelines throughout to ensure patients' safety and data confidentiality. All the participants were informed consented for our study according to the ethical principles of the Declaration of Helsinki.

Statistically significant data were analyzed using SPSS version 26, and with a 95% confidence interval adopted for statistical significance. Mean ± standard deviation and the frequency and proportion of observed characteristics were calculated. The study also examined the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of MRI in detection of orbital masses.

Diagnostic accuracy metrics (sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV)) were calculated using standard formulas and the histopathology result as a reference standard. MRI was evaluated for sensitivity which was the proportion of true positive cases correctly identified out of all cases histopathologically confirmed. Specificity was the proportion of true negative cases correctly identified among all confirmed non-cases. True positive results were defined as PPV, which was also the ratio of true positive cases to all MRI positive cases; true negative results were designated as NPV, which was the ratio of true negative cases to all MRI negative cases. The overall diagnostic accuracy was computed as the number of correctly identified cases (i.e. both positive and negative cases) over the total number of cases.

This methodological approach represents a significant contribution to the field of diagnostic radiography and is intended to help guide informed clinical decision making for the patient with suspicion of an orbital mass.

RESULTS

Study conducted at Jinnah Postgraduate Medical Centre (JPMC), Karachi included 145 participants; in the distribution of gender in the study population the participants slightly preferred female over males with a total of 55.2 % (n=80) female participants and 44.8 % (n=65) male participants. The range of age of participants was very broad, with a mean age of 26.63 years and a standard deviation of 11.92 years. The majority of the study population, 87.0% (n=127), was between 18 and 30 years of age, and 12.5% (n=18) were older than 30 years. Table I shows that the left side of orbital tumor is more commonly affected, 57.9% (n=84) versus right side 42.1% (n=61).

Table I. Demographics summary of selected population (n=145)

Variables	Total n (%)
Gender	
Male	65 (44.8%)
Female	80 (55.2%)
Age (Mean ± SD)	26.63 ± 11.92
18-30 years	127 (87.6%)
>30 years	18 (12.4%)
Side of Orbital Tumors	
Left	84 (57.9%)
Right	61 (42.1%)

We examined gender distribution as a function of types of orbital tumors (Table II), with hemangiomas evenly distributed between genders (Table II) accounting for 9.0% (n=13) of the entire cases. On the other hand, females (7.5% or 11 of the cases) were more often responsible for meningiomas in contrast to only 2.8% (4 of the cases) in men. Distribution of pseudotumors, gliomas, and lacrimal adenomas also varied; pseudotumors were in 6.9% (10 males) and 5.5% (8 females); gliomas in 2.1 % (3 males and 6 females) and lacrimal adenomas in 3.4% (5 males and 4.1% females). A variation of how these tumors presented across the genders was observed; for instance, dermoid cysts, schwannomas, and other tumors were variously distributed and constituted the diversity of orbital tumors noted in the study population based on comparison as shown in Table III.

Table II. Distribution of Each Tumor Type (n=145)

Type of tumor	Total n (%)	Male n (%)	Female n (%)
Hemangioma	26 (18.0%)	13 (9.0%)	13 (9.0%)
Meningioma	15 (10.3%)	4 (2.8%)	11 (7.5%)
Pseudotumor	18 (12.4%)	10 (6.9%)	8 (5.5%)
Glioma	12 (8.3%)	3 (2.1%)	9 (6.2%)
Schwannoma	8 (5.5%)	3 (2.1%)	5 (3.4%)
Lacrimal Adenoma	11 (7.5%)	5 (3.4%)	6 (4.1%)
Dermoid Cyst	9 (6.2%)	6 (4.1%)	3 (2.1%)
Fibrous Dysplasia	3 (2.1%)	0 (0.0%)	3 (2.1%)
AVM	4 (2.8%)	3 (2.1%)	1 (0.7%)
Lymphoma	19 (13.1%)	9 (6.2%)	10 (6.9%)
Metastasis	14 (9.6%)	8 (5.5%)	6 (4.1%)
Choroid Melanoma	6 (4.1%)	1 (0.7%)	5 (3.4%)

The comparison between MR imaging and histopathological diagnosis of orbital masses showed a higher incidence of malignant cases diagnosed through MRI, with 77.2% (n=112) of the MRI diagnoses being malignant compared to 83.4% (n=121) confirmed through histopathology. Benign cases comprised 22.8% (n=33) of the MRI diagnoses, which slightly differed from the histopathology results at 16.6% (n=24), indicating a degree of discrepancy between the two diagnostic methods (Table III).

Table III. Comparison of MR Imaging and Histopathological Diagnosis (n=145)

Orbital masses	MRI Diagnosis n (%)	Histopathology diagnosis n (%)	P-Value
Benign Cases	33 (22.8%)	24 (16.6%)	0.313
Malignant Cases	112 (77.2%)	121 (83.4%)	

Diagnostic accuracy of MRI in detecting benign orbital masses was evaluated, showing a sensitivity of 81.82%, specificity of 96.43%, positive predictive value (PPV) of 87.10%, negative predictive value (NPV) of 94.74%, and an overall diagnostic accuracy of 93.10% (Table IV). For malignant orbital masses, MRI demonstrated a sensitivity of 90.16%, specificity of 86.90%, PPV of 83.33%, NPV of 92.41%, and a diagnostic accuracy of 88.28% (Table IV). These findings underscore the effectiveness of MRI in the diagnostic assessment of orbital masses, with high sensitivity, specificity, and diagnostic accuracy for both benign and malignant lesions, thereby reinforcing the pivotal role of MRI in the clinical evaluation and management of patients with suspected orbital masses.

Table IV. Diagnostic accuracy of MRI in detecting benign orbital masses

Diagnostic variables	MRI Benign orbital masses	MRI Malignant orbital masses
Sensitivity	81.82%	90.16%
Specificity	96.43%	86.90%
Positive Predictive Value	87.10%	83.33%
Negative Predictive Value	94.74%	92.41%
Diagnostic Accuracy	93.10%	88.28%

DISCUSSION

The present study is in line with an extension of previously published work in the area of using magnetic resonance imaging (MRI) for identification of orbital masses. MRI was shown to be effective in diagnosing benign orbital lesions, with proved sensitivity, specificity, and overall diagnostic accuracy of 83, 97 and 95 percent respectively (12). Therefore, this also pointed out that MRI can detect orbital malignant lesions with a reported sensibility and specificity of 91% and 83%, respectively, as well as in this study (8). This is consistent with results from studies (13) measuring accuracy in noncancerous growths at 71.87% and sensitivity and specificity at 68.75 and 100% for malignant lesions respectively. In addition, two other works agree with the robustness of MRI in this setting since they also record sensitivities and specificities really close to that recorded at our place (14, 15).

However, this research shows, 9.6% prevalence of metastasis and 10.3% of meningioma tumors, and when compared to Shields JA, et al. (16), where metastatic tumors and meningioma are 7% and 4% respectively, is an interesting contrast in tumor type distribution. Furthermore, orchid cyst and schwannoma occurrence in our patient cohort contrasts with Bastola P, et al. who found occurrence at 21% and 1.7%, respectively, representing the variability in prevalence of specific orbital tumors in different study populations (17).

It has been recognized that accurate diagnostic tools are essential for the clinical management and treatment planning of patients given the critical role of MRI in the preoperative assessment of orbital and ocular lesions to distinguish benign from malignant conditions (18-20). As demonstrated in the present study's diagnostic accuracy of 88.28 %, high sensitivity of MRI in detecting true positive cases of malignant orbital masses renders the present study's significance in clinical practice. Despite the relative specificity and infrequency of false positives, interpretation of MRI findings should always be done cautiously with caution placed in either confirming or refuting suspected diagnoses when appropriate.

Its strength is likely to be the size of this sample and the balance of the subjects, making it more external, valid and applicable in a general patient population. A deeper understanding of orbital diseases is provided by inclusion of a broad spectrum of ages, especially the signal for 18 to 30 age band and the detailed assessment of tumor type incidence with respect to gender. Since the study compares MRI findings with histopathological data, it not only confirms the diagnostic accuracy of MRI but also provides precious numerical data regarding MRI's diagnostic value and critical diagnostic metrics that are not discussed in the existing literature.

Although these strengths exist, there are many limitations, especially in understanding the disagreement between MRI and histopathology results. Though MRI is highly sensitive at detecting orbital masses, it can sometimes yield false positives so as to identify the benign from the malignant. The causes of this discrepancy, including overlapping imaging characteristics between benign and malignant lesions (e.g. overlapping signal intensity or border irregularity) can cause MRI to overestimate malignancy. They may also be affected by surrounding conditions such as edema or inflammation that obscure tumor borders making it even more difficult to accurately identify (21).

One limitation of MRI is that significant experience and knowledge of particular orbital pathology is required for the radiologist to perform the studies and reduce observer’s variability and diagnostic inconsistencies. Therefore, some masses of the orbit can also be poorly represented by the specificity of MRI as a diagnostic tool, a diagnosis which may need to be further confirmed by other imaging modalities or histopathology. Additionally, this study was conducted across a wide age continuum, although a single center, and limitation in geographic and demographic diversity may limit the generalizability of these findings to other populations.

Further work could be done to explore the context of observed gender disparities in specific tumor types and how that contributes to the study’s findings with the objective of improving the diagnostic precision even further. Overall, this study sheds important light on MRI’s diagnostic ability and shortcomings and emphasizes the need for multi-center studies of different demographics and a more nuanced analysis of the diagnostic foibles of MRI in the diagnosis of orbital masses.

CONCLUSION

Overall, this study shows that the high diagnostic accuracy of MRI in differentiating malignant from benign orbital tumors and the high sensitivity for malignancies highlights the use of this technique. The results of the study emphasize MRI's usefulness in a clinical diagnosis but owing to the single center and the limited demographic range, the results are not generalizable. MRI’s potential for wider demographics, needs investigation and future research should turn to multicenter studies with diverse populations to validate its diagnostic potential across different populations. In addition, while higher positive predictive value is demonstrated by MRI, the moderate number of false positives indicates requiring the addition of complementary diagnostic tools to the MRI for more precise patient assessment.

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