DIAGNOSTIC ACCURACY OF DIFFUSION WEIGHTED MRI IN DIFFERENTIATING WHO GRADE-1 FROM HIGH-GRADE MENINGIOMAS

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ABSTRACT

BACKGROUND

The aim is to study the diagnostic accuracy of diffusion weighted magnetic resonance imaging in differentiating WHO Grade-1, from high-grade meningiomas and comparing with histopathology as the gold standard.

MATERIALS AND METHODS

100 patients with intracranial meningiomas referred to the Department of Radiodiagnosis for imaging were included in the study after applying inclusion and exclusion criteria. MR imaging of the head with diffusion weighted imaging was done. ADC was calculated with B value of 0 - 1000. Cut-off was obtained after drawing ROC for ADC values.

RESULTS

Using ADC value as the diagnostic test, present study shows a sensitivity of 90.48% and specificity of 98.73% ($p < 0.0001$) for differentiating Grade-1 and high-grade meningiomas.

CONCLUSION

Diffusion weighted imaging in the tumour can reliably differentiate between WHO Grade-1 and high-grade meningiomas.

KEYWORDS

MRI, ADC, Differentiation of Grade-1 and High-Grade Meningiomas, Diffusion Weighted Imaging.

HOW TO CITE THIS ARTICLE: Joseph RA, Pujar AL, Pillai MT. Diagnostic accuracy of diffusion weighted MRI in differentiating who grade-1 from high-grade meningiomas. J. Evolution Med. Dent. Sci. 2017;6(38):3097-3102, DOI: 10.14260/Jemds/2017/668

BACKGROUND

Meningioma is the most common primary non-glial benign intracranial neoplasm and arise from the arachnoid cap cells. Meningiomas are the most common of all brain tumours, accounting for one-quarter to one-third of all primary intracranial neoplasms.¹

Although most meningiomas are benign, they show a broad spectrum of clinical characteristics, and histologically distinct subsets are associated with high risk of recurrence, even after seemingly complete resection. In rare instances, meningiomas are invasive and malignant. The WHO classification helps to better predict the divergent clinical characteristics of meningioma with a histological grading system based on statistically significant clinicopathological correlations. There are three types of meningiomas according to malignancy grades: benign (WHO Grade I), atypical (WHO Grade II) and anaplastic (malignant; WHO Grade III) meningiomas.²

Magnetic Resonance (MR) imaging is the imaging modality most commonly used to evaluate intracranial meningiomas. In addition to conventional MR imaging techniques, a variety of advanced techniques are also commonly used in clinical practice.

These advanced MR imaging techniques help in demonstrating more than the anatomic information provided by the conventional magnetic resonance imaging sequences. Diffusion Weighted Imaging (DWI) is used to assess the biological and histological characteristics of brain tumours and may distinguish brain tumour grades, presumably due to differences in tumour cellularity and biochemical properties of extra-cellular space. Grade-2 and Grade-3 meningiomas are seen to have lower apparent diffusion coefficient than Grade-1 meningiomas, considered to be a consequence of high cellularity and restricted motion in the extracellular space.³

The present study was carried out to assess the accuracy of measurement of ADC values by diffusion weighted MRI in differentiating Grade-1 from high-grade meningiomas, while taking histopathological findings as the gold standard.

MATERIALS AND METHODS

This cross-sectional study was carried out in the Department of Radiodiagnosis, Government Medical College, Thiruvananthapuram for eighteen months from May 2014 to October 2015; 100 patients referred to the Department of Radiodiagnosis for MRI brain for the evaluation of suspected meningiomas diagnosed by CT brain and being planned for an incisional or excisional biopsy were included in the study.

Patients with pacemakers, cochlear implants, ferromagnetic foreign bodies or metallic implants, patients not willing to participate in the study and those patients with recurrent or residual meningioma following surgery were excluded from the study.

Name, age and relevant details of the patient was recorded on a proforma. Patients were informed that data collected would be used in a study and that issues related to confidentiality and anonymity would be taken due care of.

Financial or Other, Competing Interest: None.

Submission 06-04-2017, Peer Review 30-04-2017,

Acceptance 06-05-2017, Published 11-05-2017.

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DOI: 10.14260/Jemds/2017/668

After obtaining informed consent, MR examinations were performed on a 1.5T Siemens Magnetom system. Axial T1-weighted spin-echo, axial fluid attenuated inversion recovery (FLAIR) sequences, sagittal, axial and coronal T2WI and diffusion weighted axial images were performed.

Parameters	T1WI	T2WI	DWI	FLAIR
TR (ms)	409	4000	3000	9000
TE (ms)	8.4	94	89	89
No. of Excitations	1	3	4	1
FOV (cm x cm)	23 x 23	23 x 23	23 x 23	23 x 23
Slice Thickness (mm)	5	5	5	5
Interslice gap (%)	30	30	30	30

Table 1. Parameters used in MR Imaging of Brain

From the diffusion weighted images, ADC values were calculated for each image.

ADC was calculated by the formula,

$$D = \frac{1}{(b_1 - b_2)} \ln \left[\frac{S(TE, b_2)}{S(TE, b_1)} \right]$$

Where D is the ADC, b1 and b2 the two b values, S (TE, b1) and S (TE, b2) the signal intensities in the respective diffusion weighted images.

After undergoing incisional or excisional biopsy in the Department of Neurosurgery, the histopathology report of the specimens was collected from the Department of Pathology.

Statistical analysis was performed with commercially available software (IBM SPSS statistics 22; MedCalc 15.10). The ADC values were then correlated with the results of histopathological examination. The means of the ADC values of Grade-1 and high-grade meningiomas were expressed as mean $\pm$ standard error of the mean. The differences between the means of Grade-1 and high-grade meningiomas were compared using an independent samples t-test. With histopathology as gold standard, the receiver operating characteristic curves (ROC) and suitable cut-off values were generated. Using the cut-off value, statistical parameters like sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were calculated.

RESULTS

Magnetic resonance imaging with diffusion weighted imaging and ADC mapping was done for the patients to image meningiomas. The observations are as follows. Over a period of 18 months, total of 100 patients were included in the study. In these patients, post-operative histopathological report was obtained; 21 (21%) of the 100 meningiomas studied were WHO Grade-2 meningiomas and 79 (79%) were WHO Grade-1 meningiomas. None of the meningiomas studied were Grade-3 meningiomas.

Figure 1. Distribution of Grade-1 and High-Grade Meningiomas

Age Distribution of Patients

Figure 2- Histogram showing Age Distribution of Patients Studied

Of the 100 patients studied, 21 patients had high-grade meningiomas and 79 patients had Grade-1 meningiomas. The commonest age group of meningiomas in the study was 51 - 60 years (33 patients) followed by 61 - 70 years (29 patients). The oldest patient was 84 years and the youngest patient was 36 years of age. Most of the atypical meningiomas were found in the age group of 51 - 60 years; 13 (61%) of the atypical meningiomas were noted in 51 - 60 years.

Figure 3. Age Distribution of Grade-1 Meningiomas

Figure 4. Age Distribution of High-Grade Meningiomas

Sex Distribution of Patients in the Study

Of the 100 patients in the study, 76 were females (76%) and 24 were males (24%).

Figure 5. Sex Distribution of Patients in the Study

Figure 6. Sex Wise Distribution of Grade-1 and High-Grade Meningiomas

Of the 76 females studied, 16 (21%) of them had high-grade meningiomas and 60 (79%) patients have Grade-1 meningiomas. Of the 24 males studied, 5 (20.8%) of them had high-grade meningiomas and 19 patients (79%) had Grade-1 meningiomas.

Evaluation of ADC Values of Meningiomas

Diffusion weighted axial images of the brain were obtained at a 'b' value of 1000. ADC maps were created for 'b' value of 1000.

Figure 7. Distribution of ADC Values of Meningiomas

Outcome	N	ADC		T	P
		Mean	SD		
Grade-1	79	1.31	0.51	7.546	< 0.001
High Grade	21	0.46	0.16		

Table 2. Statistical Analysis of ADC Values of Meningiomas

On DWI, the ADC values of meningiomas ranged from $0.27 \times 10^{-3} \text{ mm}^2/\text{s}$ to $2.8 \times 10^{-3} \text{ mm}^2/\text{s}$.

The mean and SD of absolute intratumoral ADC in Grade-1 meningioma was $1.31 \pm 0.51 \times 10^{-3} \text{ mm}^2/\text{s}$, and in high-grade meningiomas the mean ADC of $0.46 \pm 0.16 \times 10^{-3} \text{ mm}^2/\text{s}$ was significantly lower ($p < 0.0001$).

Receiver Operator Curve Analysis of Intratumoral ADC Values.

Criterion	Sensitivity	Specificity	+LR	-LR	+PV	-PV
< 0.27	0.00	100.00		1.00		86.4
≤ 0.47	61.90	100.00		0.38	100.0	94.3
≤ 0.5	71.43	98.73	56.43	0.29	89.9	95.6
≤ 0.6	90.48	98.73	71.48	0.096	91.8	98.5
≤ 0.85	90.48	83.54	5.50	0.11	46.4	98.2
≤ 0.86	95.24	83.54	5.79	0.057	47.7	99.1
≤ 0.87	100.00	78.48	4.65	0.00	42.2	100.0
≤ 2.8	100.00	0.00	1.00		13.6	

Table 3. Criterion Values and Coordinates of the ROC Curve

Area under the ROC curve (AUC)	0.980
Standard Error	0.0128
95% Confidence Interval	0.930 to 0.998
Z statistic	37.578
Significance Level P (Area = 0.5)	< 0.001
Youden Index J	0.8921
Associated Criterion	≤ 0.6

Table 4. Parameters obtained in ROC Analysis of Intratumoral ADC

From the graph, a cut-off value of $0.6 \times 10^{-3} \text{ mm}^2/\text{s}$ was derived. This cut-off has a sensitivity of 90.48% and specificity of 98.73%. Positive likelihood ratio with this cut-off is 71.48 and negative likelihood ratio is 0.096.

ADC	High Grade	Grade-1
≤ 0.6	19	1
> 0.6	2	78
Total	21	79

Table 5. 2 x 2 Table with 0.6 as Cut-Off for ADC

Statistical Index		95% CI
Sensitivity	90.48%	69.6 - 98.9
Specificity	98.73%	93.1 - 100
Positive predictive value	91.8%	63.9 - 99.7
Negative predictive value	98.5%	93.2 - 99.9
Positive likelihood ratio	71.48	10.1 - 503.6
Negative likelihood ratio	0.096	0.03 - 0.4

Table 6. Statistical Indices with 0.6 as cut-off for ADC

Figure 8. ROC Curve for Predicting cut-off for ADC

Figure 9. Scatter Diagram showing Distribution of Intratumoral ADC

Nagar VA et al in their study “Diffusion-Weighted MR Imaging: Diagnosing atypical or malignant meningiomas and detecting tumour dedifferentiation.” Published in 2014, an ADC cut-off of $0.8 \times 10^{-3} \text{ mm}^2/\text{s}$ was derived to differentiate benign from atypical/malignant meningiomas.⁴ With this cut-off, 2 x 2 table was constructed to assess the diagnostic power of ADC 0 - 1000 with literature cut-off value.

ADC	High Grade	Grade-1
< 0.8	8	17
> 0.8	13	62
Total	21	79

Table 7. 2 x 2 Table in assessing Diagnostic Power of ADC using Literature Cut-Off Value⁴

The Calculated Parameters are as follows

Statistical Index		95% CI
Sensitivity	38.10%	18.11 - 61.56
Specificity	78.48%	67.80 - 86.94
Positive Predictive Value	21.79%	7.67 - 43.34
Negative Predictive Value	88.96%	79.69 - 94.98

Table 8. Statistical Parameters with Literature Cut-Off for ADC⁴

	Sensitivity	Specificity	PPV	NPV
	%	%	%	%
Literature cut-off (Nagar VA et al)	96	82.6	85.7	95
Applying in Present Study	38.1	78.48	21.79	88.96

Table 9. Comparison of ADC Cut-Off obtained in the Study and in Literature

Figure 10(A). T2WI of HPR-WHO Grade-1 Meningioma of the Falx Cerebri.
(B) FLAIR Image of HPR-WHO Grade-1 Meningioma of Falx Cerebri.

Figure 11(A). T1WI of HPR-WHO Grade-1 Meningioma of the Falx.
(B) Post-Contrast Image of WHO Grade-1 Meningioma of the Falx.

Figure 12. Diffusion Weighted Image of HPR-WHO Grade-1 Meningioma of the Falx

Figure 13. ADC Map of HPR-WHO Grade-1 meningioma of the Falx

Figure 14 (A). T2WI of Grade-2 Meningioma of Right Temporal Region.
(B) FLAIR Image of Grade-2 Meningioma of Right Temporal Region.

Figure 15(A). T1WI of Grade-2 Meningioma of Right Temporal Region.
(B) Post Contrast Image of Grade-2 Meningioma of the Right Temporal Region.

Figure 16. Diffusion Weighted Image of Grade-2 Meningioma of Right Temporal Region

Figure 17. ADC Map of Grade-2 Meningioma of the Right Temporal Region

DISCUSSION

Age and Sex Distribution

Of the 100 patients studied, 21 patients had high-grade meningiomas and 79 patients had grade-1 meningiomas. The commonest age group of meningiomas in the study was 51 - 60 years (33 patients) followed by 61 - 70 years (29 patients). The oldest patient was 84 years and the youngest patient was 36 years of age. Most of the atypical meningiomas were found in the age group of 51 - 60 years; 13 (61%) of the atypical meningiomas were noted in 51 - 60 years.

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Histopathological Results

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meningiomas studied were WHO Grade-2 meningiomas, and 79 (79%) were WHO Grade-1 meningiomas. None of the meningiomas studied were Grade-3 meningiomas.

ADC Values

On DWI, the ADC values of meningiomas ranged from $0.27 \times 10^{-3} \text{ mm}^2/\text{s}$ to $2.8 \times 10^{-3} \text{ mm}^2/\text{s}$. The mean and SD of absolute intratumoral ADC in Grade-1 meningioma was $1.31 \pm 0.51 \times 10^{-3} \text{ mm}^2/\text{s}$, and in high-grade meningiomas the mean ADC of $0.46 \pm 0.16 \times 10^{-3} \text{ mm}^2/\text{s}$ was significantly lower ($p < 0.0001$).

By ROC analysis, a cut-off value of $0.6 \times 10^{-3} \text{ mm}^2/\text{s}$ was derived. This cut-off has a sensitivity of 90.48% and specificity of 98.73%. Positive likelihood ratio with this cut-off is 71.48 and negative likelihood ratio is 0.096 (p value < 0.001).

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Limitations of the Study

1. The study sample might not be a true representative of the real world due to "sampling errors" and spectrum bias.
2. Inoperable cases of meningiomas were omitted from the study.
3. None of the meningiomas studied were Grade-3 meningiomas. Hence, the findings may not apply to Grade-3 meningiomas.

CONCLUSION

ADC values can be reliably used to differentiate Grade-1 from high-grade meningiomas. Thus, preoperative characterisation of meningiomas is possible for planning further management.

ACKNOWLEDGEMENT

We are thankful to the Department of Radiodiagnosis, Government Medical College, Thiruvananthapuram for all the help in carrying out this study.

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