DIAGNOSTIC ACCURACY OF MAGNETIC RESONANCE SPECTROSCOPY AND DIFFUSION WEIGHTED IMAGING IN GRADING OF INTRACRANIAL GLIOMAS TAKING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Background: MRI is the modality of choice for characterization of intracranial space occupying lesions. However, a sizeable proportion of non-enhancing gliomas turn out to be malignant and conversely, some low-grade gliomas, show avid enhancement. Significant overlap for imaging features on conventional MRI, therefore, limit it as a definitive predictor of grade in clinical practice. Advanced MRI techniques such as Diffusion weighted imaging (DWI) and Magnetic Resonance Spectroscopy (MRS) offer a promising alternative for the purpose.

Objectives: To determine diagnostic accuracy of magnetic resonance spectroscopy and magnetic resonance diffusion in grading of gliomas with histopathology as gold standard.

Methods: It is a cross sectional study conducted at Department of Radiology, Mayo Hospital, Lahore in 06 months. One hundred patients fulfilling selection criteria were enrolled in the study. Then all patients underwent MRI including conventional sequences as well as DWI and MRS using a spin echo sequence (SE) with short TE (35 mm/s) and long TE (144 mm/s). Patients were labeled as positive or negative (as per operational definition). Subsequently patients underwent biopsy under general anesthesia. Reports were assessed and patients were confirmed as positive or negative according to operational definition. All of this information was recorded in a predesigned Performa.

Results: Total number of patients in the study were one hundred. Mean age of the patients were 38.61(years) $\pm$11.40 whereas there were 43 (43.0) male and 57 (57.0) female patients included in the study. The diagnostic accuracy, sensitivity, specificity, PPV and NPV of magnetic resonance spectroscopy was 84.00%, 89.86%, 70.97%, 87.32% and 75.86% respectively whereas diagnostic accuracy, sensitivity, specificity, PPV and NPV of diffusion weighted imaging was 75.00%, 78.26%, 67.74%, 84.38% and 58.33% respectively.

Conclusion: Diagnostic accuracy of MRS is more helpful and reliable than DWI in grading of gliomas taking histopathology as gold standard. Future studies at multiple setups must be conducted which could help in deciding whether to rely on MRS or DWI for determination of gliomas grading.

Keywords: Magnetic Resonance Spectroscopy, Magnetic Resonance Diffusion, Gliomas, Diffusion Weighted MRI.

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INTRODUCTION

Central nervous system tumors are global health problem with an increasing trend over the past two decades[1]. Out of these, gliomas are the most common

primary brain tumor. They are graded according to World Health Organization along a continuum from grade I which includes pilocytic astrocytoma to grade IV which is glioblastoma multiforme. Tumor grading is important for deciding management as it helps decide appropriate treatment strategies[2].

MRI is the modality of choice for characterization of intracranial space occupying lesions. Conventional MRI has not only been traditionally used for differentiating primary brain neoplasms from metastasis and infective processes, but also predict the grade of tumor. Features of contrast enhancement like heterogeneity and degree of enhancement, amount of edema and mass effect and amount of necrosis, as seen on conventional MRI, are usually associated with grade of the tumor[3]. However, a sizeable proportion of non-enhancing gliomas turn out to be malignant and conversely, some low-grade gliomas, show avid enhancement. Significant overlap for imaging features on conventional MRI, therefore, limit it as a definitive predictor of grade in clinical practice[4].

Advanced MRI techniques such as Diffusion weighted imaging (DWI) and Magnetic Resonance Spectroscopy (MRS) offer a promising alternative for the purpose. Diffusion weighted MRI (DWI) is frequently performed in routine clinical practice to image changes in cellular density and motion of the molecules[5]. A meta-analysis showed high sensitivity and specificity of ADC values at b-values of 1000 s / mm^2 as well as 3000 s / mm^2 in differentiating low grade and high-grade gliomas[6]. MRS is a technique that relies on changes in biochemical activity of pathological tissue. Low grade primary tumors depicted low lactate and lipid peaks and high-grade tumors depicted increasing levels of lipid & lactate peaks (indicating necrosis) with marked difference[7].

However, different studies have shown variable results for the purpose of grading gliomas. A study showed MRS as having better PPV, NPV, sensitivity, specificity and accuracy compared to DWI[8]. One study reported that the specificity and sensitivity of MRS in grading gliomas were 60% and 75%, respectively[9] but another study showed that the specificity and sensitivity of MRS in grading gliomas were 86% and 86%, respectively[10]. The sensitivity and specificity of DWI in grading gliomas were 71% and 87%[11]. While another study showed specificity and sensitivity of DWI in grading gliomas were 90% and 90%[12].

The objective of this study is to determine diagnostic accuracy of MRS and DWI in grading of gliomas taking histopathology as gold standard. Literature has showed contradictory results regarding accuracy of MRS and DWI in differentiating high- and low-grade gliomas. Moreover, there is a dearth of local data on this subject. This data will surely help to improve our practice and guide about further management.

METHODS

It is a Cross Sectional Study conducted at Department of Radiology, Mayo Hospital, Lahore in 06 months (Sep, 2018 to February 2019). Sample Size **of** 100 cases was calculated with 95% confidence level, taking expected percentage of high-grade glioma i.e., 59% with MRS sensitivity 86% with 9% margin of error and MRS specificity 86% with 11% margin of error taking histopathology as gold standard. One hundred patients of age 20-60 years, presenting with suspicion of SOL brain and showing suspicion of glioma on CT scan were selected by non-probability consecutive sampling. Recurrent cases (medical record), Post-chemotherapy or radiotherapy (on medical record), Claustrophobic patients not willing to undergo MRI, Patients not willing to undergo biopsy were excluded. Informed consent was taken. Demographic detail (name, age, gender, duration of symptoms) was noted. Then all patients underwent MRI including conventional sequences as well as DWI and MRS using a spin echo sequence (SE) with short TE (35 mm/s) and long TE (144 mm/s). Patients were labeled as positive or negative (as per operational definition).

Then patients underwent biopsy under general anesthesia. All intervention was performed by a senior neurosurgeon and samples were sent to the histopathology department. Reports were assessed and patients were confirmed as positive or negative as per operational definition. All this information was recorded in pre designed proforma (attached).

The data was organized, and analyzed using SPSS. Age of the patient and duration of symptoms was presented as mean ± SD. Gender of the patient and grade of glioma (on MRS, DWI and histopathology) was presented as frequency and percentage. Data were stratified for age, gender and duration of symptoms. Post-stratification, 2x2 tables was generated to calculate the PPV, NPV, sensitivity, specificity and accuracy of MRS & DWI taking histopathology as gold standard.

RESULTS

Mean age of the patients was 38.61 years with standard deviation of 11.40. 43 % of the patients were male and 57 % were female. According to MRS findings, 71 % of the lesions had Cho/Cr ratio of greater than 2.0 and categorized as high-grade gliomas. According to DWI, 64 % of the tumors had ADC value more than $1.0x10^{-3}/mm^2$ and therefore fell into the category of high-grade gliomas. Tables 1-4

show sensitivity, specificity and diagnostic accuracy of MRS and DWI for grading gliomas and the effect of modifiers on them.

Table. No. 01 2 x 2 table showing Diagnostic Accuracy of MRS findings in gliomas keeping Histopathology as Gold Standard

MRS Findings	Histopathology Findings		Total
	Positive	Negative	
Positive	62	9	71
	89.9%	29.0%	71.0%
Negative	7	22	29
	10.1%	71.0%	29.0%
Total	69	31	100

Sensitivity:	89.86 %
Specificity:	70.97 %
PPV:	87.32 %
NPV:	75.86 %
Diagnostic Accuracy:	84.00 %

Table. No. 02 2 x 2 table showing Diagnostic Accuracy of DWI findings in detecting in gliomas keeping Histopathology as Gold Standard

DWI Findings	Histopathology Findings		Total
	Positive	Negative	
Positive	54	10	64
	78.3%	32.3%	64.0%
Negative	15	21	36
	21.7%	67.7%	36.0%
Total	69	31	100

Sensitivity:	78.26%
Specificity:	67.74 %
PPV:	84.38%
NPV:	58.33%
Diagnostic Accuracy:	75.00%

Table. No. 03 Effect modifier like Age stratification and comparison with diagnostic Accuracy of MRS findings in detecting in gliomas keeping Histopathology as gold Standard

Age Group	MRS Findings	Histopathology Findings		P-value	Diagnostic Accuracy
		Positive	Negative		
20 - 40 years	Positive	42 93.3%	7 41.2%	0	Sensitivity: 93.33% Specificity: 58.82 % PPV:85.71 % NPV:76.92 % Accuracy: 83.87 %
	Negative	3 6.7%	10 58.8%		
40 - 60 years	Positive	62 89.9%	9 29.0%	0	Sensitivity: 89.86% Specificity: 70.97 % PPV: 87.32 % NPV: 75.86 % Accuracy: 84.00 %
	Negative	7 10.1%	22 71.0%		

Table. No. 04 Effect modifier like Age stratification and comparison with diagnostic Accuracy of DWI findings in detecting in gliomas keeping Histopathology as Gold Standard

Age Group	DWI Findings	Histopathology Findings		P-value	Diagnostic Accuracy
		Positive	Negative		
20 - 40 years	positive	38 84.4%	7 41.2%	0.001	Sensitivity: 84.44% Specificity: 58.82 % PPV:84.44 % NPV:58.82 % Accuracy: 77.42 %
	negative	7 15.6%	10 58.8%		
40 - 60 years	positive	54 78.3%	10 32.3%	0.000	Sensitivity: 78.26% Specificity: 67.74 % PPV:84.38 % NPV:58.33 % Accuracy: 75.00 %
	negative	15 21.7%	21 67.7%		

DISCUSSION

Management of gliomas, particularly timing and use of chemotherapy and radiotherapy, depends on a number of factors including age, performance status, histopathology, molecular markers and previous therapy[13]. For low grade gliomas treatment strategies may include simple observation instead of more aggressive treatment since the potential benefits of

treatment must be weighed against the potential risks of treatment[14]. High grade gliomas require more aggressive treatment although outcomes are still usually poor with no significant change in outcome over the last decade[15]. Hence the need for accurately predicting the tumor grade before treatment. Biopsy serves the answer but is invasive. MRI serves as a non-invasive alternative.

While conventional MRI can quite accurately differentiate gliomas from other intracranial lesions, its role in further characterization as low versus high grade is limited due to overlap in tumor characteristics. Use of advanced techniques improves this weakness of MRI.

A meta-analysis done in 2014 showed moderate diagnostic performance of MRS in differentiating low- and high-grade glioma[16]. This reported sensitivity and specificity of MRS for this purpose as 80.58 % and 78.46 % respectively. The difference from our results is likely due to the fact that this meta-analysis was done on all brain neoplasms rather than gliomas alone and also did not differentiate between the various metabolite ratios in each study. Another study showed sensitivity and specificity of MRS in differentiating low grade and high-grade gliomas as 81.8 % and 51.7 % respectively and the diagnostic accuracy as 71.4% [17]. However, this study was done on pediatric population only and took a cut off value of Cho Cr ratio of 2.6 for categorizing low- and high-grade gliomas which could account for the difference. Another study also showed sensitivity and specificity of Cho/Cr for this purpose to be 83.3 % and 85.8 % respectively[18]. However, this study also used a different threshold level of 1.35. Another study done in China showed sensitivity and specificity of Cho Cr ratio to be 86.7 % and 85.7 % respectively [19].

One of the other techniques that have been explored to help determine the grade of glioma non-invasively is diffusion weighted imaging that relies on the differential Brownian motion of hydrogen in different tissues. A recent meta-analysis concluded ADC analysis of DWI to have high accuracy in differentiating low- and high-grade gliomas[6]. The pooled sensitivity and specificity of DWI in accurately categorizing the grade of glioma in this meta-analysis was 0.81 and 0.87 respectively ay b value of 1000s / mm^2 and 0.80 and 0.90 respectively at higher b value of 3000s / mm^2. This analysis however did point out various factors that could account for the heterogeneity of the data such as magnetic field strength, different b values and different cut-off values. A study done in Norway reported sensitivity of quantitative DWI for making this differentiation to be 79.7 % which is very similar to our study [18]. However, the specificity was different at 60.0 % which could be due to multiple factors pointed out in the meta-analysis, including the fact that threshold level in the study was slightly different from our study. Another study done in China has reported values of 82.1 % and 83.3 % for the sensitivity and specificity of DWI in declaring a glioma as low grade or high grade [19]. Another study on pediatric patients showed different sensitives and specificities using different cut off values of ADC, ranging from 73.4 % to 86.0 % and 80.3 % to 90.9 % [17].

This study also highlights the limitation of variable sensitivities and specificities at different ADC cut off values.

CONCLUSION

The study concluded that diagnostic accuracy of MRS is more helpful and reliable than DWI in grading of gliomas taking histopathology as gold standard. More studies with larger sample size using different metabolite peaks in MRS and different ADC values for DWI, must be conducted which could help in deciding whether to rely on MRS or DWI for determination of gliomas grading.

CONFLICT OF INTEREST: Authors declare no conflict of interest

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ETHICAL APPROVAL

The study was approved by the Institutional Review Board of King Edward Medical University Lahore, vide Reference No. F62/RC/KEMU Dated 12.01.2021

REFERENCES

1. Fan Y, Zhang X, Gao C, Jiang S, Wu H, Liu Z, Dou T. Burden and trends of brain and central nervous system cancer from 1990 to 2019 at the global, regional, and country levels. Archives of Public Health. 2022 Dec;80(1):1-4
2. Amin U, Ahmad A, Ather S, Ahmed A. Diagnostic Accuracy of Magnetic Resonance Spectroscopy in Diagnosing Glioblastoma by Taking Histopathology as A Gold Standard. PJR. 2019 Mar 30;29(1).
3. Asari S, Makabe T, Katayama S, Itoh T, Tsuchida S, Ohmoto T. Assessment of the pathological grade of astrocytic gliomas using an MRI score. Neuroradiology 1994; 36:308–311.
4. Upadhyay N, Waldman A. Conventional MRI evaluation of gliomas. The British journal of radiology. 2011 Dec;84(special_issue_2): S107-11.

5. van Dijken BR, van Laar PJ, Holtman GA, van der Hoorn A. Diagnostic accuracy of magnetic resonance imaging techniques for treatment response evaluation in patients with high-grade glioma, a systematic review and meta-analysis. Eur Radiol 2017;27 (10):4129-4144.
6. Wang QP, Lei DQ, Yuan Y, Xiong NX. Accuracy of ADC derived from DWI for differentiating high-grade from low-grade gliomas: Systematic review and meta-analysis. Medicine. 2020 Feb;99(8).
7. Hellström J, Zapata RR, Libard S, Wikström J, Ortiz-Nieto F, Alafuzoff I, Raininko R. The value of magnetic resonance spectroscopy as a supplement to MRI of the brain in a clinical setting. PloS one. 2018 Nov 15;13(11):e0207336.
8. Darwiesh AMN, Abd-El Maboud NM, Khalil AMR, ElSharkawy AM. Role of magnetic resonance spectroscopy & diffusion weighted imaging in differentiation of supratentorial brain tumors. Egypt J Radiol Nucl Med 2016;47(3):1037-42.
9. Weidle UH, Birzele F, Kollmorgen G, Rueger R. Dissection of the process of brain metastasis reveals targets and mechanisms for molecular-based intervention. Canc Genom Proteom 2016;13(4):245-258.
10. Hafez H, Elmoneim BA, Fawzy T, Omar SF. The role of proton magnetic resonance spectroscopy in grading of brain gliomas. Menoufia Medical Journal. 2016 Jan 1;29(1):136.
11. Lotumolo A, Caivano R, Rabasco P, Iannelli G, Villonio A, D'Antuono F, et al. Comparison between magnetic resonance spectroscopy and diffusion weighted imaging in the evaluation of gliomas response after treatment. Eur J Radiol 2015;84(12):2597-2604.
12. Jovčevska I, Kočevar N, Komel R. Glioma and glioblastoma-how much do we (not) know? Mol Clin Oncol 2013;1(6):935-941.
13. Reni M, Mazza E, Zanon S, Gatta G, Vecht CJ. Central nervous system gliomas. Critical reviews in oncology/hematology. 2017 May 1; 113:213-34.
14. Forst DA, Nahed BV, Loeffler JS, Batchelor TT. Low-grade gliomas. The oncologist. 2014 Apr;19(4):403-413.
15. Nayak L, Reardon DA. High-grade gliomas. CONTINUUM: Lifelong Learning in Neurology. 2017 Dec 1;23(6):1548-1563.
16. Wang W, Hu Y, Lu P, Li Y, Chen Y, Tian M, Yu L. Evaluation of the diagnostic performance of magnetic resonance spectroscopy in brain tumors: a systematic review and meta-analysis. PloS one. 2014 Nov 13;9(11):e112577.
17. Yao R, Cheng A, Liu M, Zhang Z, Jin B, Yu H. The diagnostic value of apparent diffusion coefficient and proton magnetic resonance spectroscopy in the grading of pediatric gliomas. Journal of computer assisted tomography. 2021 Mar;45(2):269.
18. Server A, Kulle B, Gadmar ØB, Josefsen R, Kumar T, Nakstad PH. Measurements of diagnostic examination performance using quantitative apparent diffusion coefficient and proton MR spectroscopic imaging in the preoperative evaluation of tumor grade in cerebral gliomas. European journal of radiology. 2011 Nov 1;80(2):462-470.
19. Hu X, Xue M, Sun S, Zou Y, Li J, Wang X, Liu X, Ma H. Combined application of MRS and DWI can effectively predict cell proliferation and assess the grade of glioma: a prospective study. Journal of Clinical Neuroscience. 2021 Jan 1; 83:56-63.

AUTHOR'S CONTRIBUTIONS

NR: Discussion writing, data collection
IS, AH: Result compilation, data collection
AM: Editing & formatting the manuscript
IHD: Literature review, correlation
MT: Literature review, manuscript writing