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Original Research Article

Grading of Intracranial Neoplasms with MR Perfusion and MR Spectroscopy

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ABSTRACT

Purpose: To compare findings of conventional magnetic resonance (MR) imaging, MR perfusion and MR spectroscopy in grading of the primary intra-cranial neoplasms.
Materials and Methods: This prospective observational, comparative study was conducted in a tertiary care hospital. 37 consecutive patients with freshly detected primary intracranial intra-axial neoplasms were included in the study. T1 axial, T2 axial, FLAIR axial, diffusion-weighted images, Coronal T2 weighted, T1-weighted, dynamic susceptibility contrast (DSC) MR perfusion, MR spectroscopy and post contrast T1-weighted 3D images were obtained. Grading of the intracranial neoplasms was done on the basis of MR imaging. Histology specimen was obtained by surgical resection or stereotactic biopsy and graded as high-grade glioma (HGG) and low-grade glioma (LGG).
Results: On histopathological examination, 24 cases were proven to be HGG and 13 to be LGG. The mean Cho/NAA ratio for HGG was 7.3 and for LGG it was 1.7. The mean rCBV for HGG was 2.95 and for LGG was 0.92. Out of 37 intra-axial tumors, 24 histologically proven HGG were all correctly diagnosed with spectroscopy imaging, however 2 LGG were over diagnosed to be HGG. The sensitivity, specificity, PPV, and NPV for determination of a high-grade glioma with MR Spectroscopy and MR Perfusion imaging were 100%, 84.6%, 92.3%, and 100%, respectively. AUC measured 0.92.
Conclusion: Advanced neuroimaging using DSC MR perfusion and MR Spectroscopy allows accurate grading of tumor, which enables surgical planning, guiding accurate stereotactic biopsy from the most malignant part of the tumor and planning further treatment.

Keywords: Gliomas, Magnetic resonance imaging, Spectroscopy, Perfusion

INTRODUCTION

Gliomas are very heterogeneous group of central nervous system (CNS) tumors and are classified by World Health Organization (WHO) in terms of histologic grades. [1] Biopsy sampling of the brain tumors is associated with inherent limitations due to sampling error and technique. This highlights the critical role of imaging to find the part of the tumor with the highest grade, as the therapeutic approaches, response to therapy, and prognosis depend on accurate grading. Imaging also aids in presurgical planning of the brain tumors, as it helps to preserve eloquent regions of the brain and fiber tracts with reduced post-surgical morbidity. [2, 3]

Neuroimaging is a powerful primary diagnostic noninvasive tool to determine and prognosticate the management of

patients with brain tumor. Magnetic resonance imaging (MRI) is the workhorse of tumor detection and diagnosis; and has continued to evolve over time. Conventional magnetic resonance imaging, owing to its high sensitivity and exquisite delineation of anatomic relationships, is used not only for the diagnosis of brain tumors but also in their follow-up. Nonetheless, conventional MR techniques are often nonspecific and provide limited information on tumor physiology. [4, 5]

With advent of high-resolution structural imaging and development of novel therapies for patients with brain tumors, the role of imaging has shifted from anatomical imaging to functional imaging to assess microstructure of the tumor tissue, its metabolism and physiology. Malignant brain tumors are associated with increased angiogenesis and neovascularity, with an increased proportion of immature and hyper-permeable vessels, which determine biological aggressive of the neoplasm. Perfusion methods provide information regarding the tumor physiology such as microvascularity, angiogenesis, micronecrosis, and cellularity. [6,7] This can act as a guide to the surgeon for planning the stereotactic biopsy into the most aggressive portions of the tumor. It can also assist in surgical and radiation planning of the tumor as perfusion provides a better delineation of tumor margins than conventional techniques. [8]

Magnetic Resonance Spectroscopy (MRS) is also used to evaluate tumor physiology. MR spectroscopy relies on detection of metabolites within tumor tissue at the cellular level. It is able to accurately depict metabolic biomarkers, which are relevant for molecular subtyping. [9, 10]

Most of the literature available for the epidemiology, molecular features, and management of brain tumors is based on the data from the western countries. It is a well-known fact that the incidence, natural history, behavior, as well as response to treatment of various neoplasms is different for different geographical population and has variable correlation to the genotype and phenotype of different populations. There is a need for standardization of neuroimaging using conventional MRI, MRS, and perfusion weighted imaging (PWI) for overcoming diagnostic challenges in Indian population.

The aim of this study was to compare the value of advanced MR imaging techniques, including T2*-dynamic susceptibility contrast PWI (DSC-PWI) and proton magnetic resonance spectroscopy (1HMRS) in the evaluation and grading of the brain tumors.

MATERIALS AND METHODS

The study was conducted in the department of Radiodiagnosis of a tertiary care hospital and was a prospective observational, comparative study. 37 consecutive patients with freshly detected primary intracranial intra-axial neoplasms who underwent MR imaging between Aug 2016 and May 2018 were included in the study. Post-operative patients, patients with metastasis and patients with recurrence were excluded from the study.

After informed consent, all patients selected for the study underwent pre-operative conventional contrast enhanced, MR perfusion and MR spectroscopic imaging.

Scanning Technique:

MR data was acquired using a PHILIPS MR ACHIEVA 1.5 T machine equipped with a quadrature head coil. T1 axial, T2 axial, FLAIR axial, diffusion-weighted images, Coronal T2 weighted and pre-contrast T1-weighted images were acquired.

DSC-PWI first-pass image acquisition was obtained after rapid intra-venous bolus administration of gadolinium (Gd-DTPA, 0.1 mmol/kg; Magnevist, Bayer HealthCare, Berlin, Germany). The gadolinium-contrast agent was injected with a power injector (Medrad, Indianola, PA) at a rate of 2.5 ml/s after two cycles of dynamic scan. Immediately afterward, 20 ml of saline was injected at the same

rate. Using T2* gradient echoplanar perfusion weighted imaging; signal change was recorded during the passage of the contrast agent through the cerebral vasculature.

Data processing was done using the workstation with analytic program software. CBV maps were computed on basis of the first–pass data. After construction of CBV color map, four regions of interest (ROI) measurements of approximately 2-3 sq mm were drawn manually over the area of interest and maximal CBV was recorded. The CBV values were normalized by drawing a reference ROI in the contralateral normal appearing white matter to generate relative CBV (rCBV) values. The ROI were positioned carefully to ensure it lies completely within the apparent margins of the tumor while avoiding contamination from the cerebral blood vessels, calcification, hemorrhages, CSF spaces, the scalp, skull base, or sinuses. Tumoral micro-vascularity parameters of CBF and TTP were also measured corresponding to the areas with abnormal rCBV.

After dynamic studies, post contrast T1-weighted 3D images were obtained and MR spectroscopy was done. Post contrast multiplanar T1 imaging was done to see the contrast enhancement pattern and was classified as present/ absent, focal, rim or patchy. Single-slice two-dimensional (2D) multivoxel 1HMRS was done using a point-resolved spectroscopy (PRESS) spin echo sequence. Metabolic peak positions were assigned as follows: Cho 3.22 ppm; Cr 3.02 ppm; NAA, 2.02 ppm; Lip, 0.5-1.5 ppm. Lac (1.33 ppm) was identified as an inverted doublet at 144 ppm. The maximum values of Cho/Cr , NAA/Cr and Cho/NAA ratios and presence or absence of Lip or Lac peaks were measured by MRS at long TE. The 1HRMS data were analyzed from voxel that exhibited increased rCBV values within the selected ROI. MRI was interpreted by a radiologist with >10 years of experience who was blinded to the clinical data and other imaging results.

Grading of neoplasms on imaging:

Grading of the intracranial neoplasms was done on the basis of three techniques of MRI imaging. The radiological classification of the brain neoplasm into high-grade glioma (HGG) or low-grade glioma (LGG) was based on:

1. Provisional diagnosis 1 - Conventional contrast enhanced MRI was used to give provisional diagnosis as PD1. On contrast enhanced MRI the lesion was considered HGG on the basis of presence of contrast enhancement and restriction of diffusion on DWI. It was labelled as LGG in absence of contrast enhancement or restriction of diffusion on DWI.
2. Provisional diagnosis 2- MR Spectroscopy was based on Cho/NAA ratio to give provisional diagnosis as PD2. On MR Spectroscopy, the lesion was considered HGG on the basis of increased Cho/NAA peak of >1.18. It was labelled as LGG if the Cho/NAA ratio was <1.18.
3. Provisional diagnosis 3- MR perfusion study based on rCBV was used to give a provisional diagnosis as PD3. On MR perfusion, the lesion was considered HGG on the basis of increased rCBV >1.07. It was labeled as LGG if the rCBV ratio was <1.07.

The pre-operative radiological provisional diagnosis by each MRI modality were assessed individually and compared with histopathological diagnosis in patients after surgical resection or stereotactic biopsy. The primary diagnosis given for the intracranial neoplasms was the highest grade given by the combination of the three imaging modalities.

Histological diagnosis:

Histology specimen was obtained by surgical resection or stereotactic biopsy in all 37 cases. The samples were analyzed by a pathologist with more than 10 years of experience, blinded to radiological assessment. Brain tumors were classified as

a) HGG (WHO grade III and IV) in 24 Cases and

b) LGG (WHO grade I and II) in remaining 13 patients.

The further subtype of tumor was determined by histopathological examination of sample.

Statistical methods:

Statistical Package for Social Sciences (SPSS) Software Version 23.0 was used for statistical analysis. Chi square test was used for comparison of pre-operative radiological findings of Conventional MRI with MR Perfusion and MR spectroscopy (nominal variables) with each other and with histopathological diagnosis.

Student t-test was used for comparison of mean values for rCBV and Cho/NAA ratios for various grades of tumors and p-value was calculated. p-value <0.05 was considered significant between the mean values of two groups at 95% confidence interval and p-value < 0.01 was considered significant at 99% confidence interval. p-value > 0.05 was considered not significant.

Kappa was used as a measure of agreement for comparison of results using different methods. Sensitivity, specificity, Positive predictive value and Negative predictive value were calculated to assess the reliability of results in comparison with the gold standard i.e., HPE.

OBSERVATIONS AND RESULTS

In the study population, there were 21 (57%) males and 16 (43%) females. the youngest patient was 6 years old and the oldest was 78 years old. The mean age was 49.16 years (±17.2). Majority of the patients were in the age group of 50-70 yrs.

The intra-axial lesions were graded as HGG or LGG by three MRI modalities:

1. Conventional contrast enhanced MRI (PD1)
2. MR spectroscopy (PD2) and
3. MR perfusion (PD3)

On histopathological examination, 24 lesions were proven to be HGG and 13 to be LGG. The mean Cho/NAA ratio for HGG was 7.3 and for LGG 1.7. The mean rCBV for HGG was 2.95 (with SD±2.04) and for LGG the mean rCBV was 0.92 (with SD ±0.49).

Out of 24 histologically proven HGG, contrast enhanced MRI was able to detect 17 cases correctly. One LGG case was overdiagnosed as HGG. Out of 13 LGG cases, all LGG were diagnosed correctly by contrast enhanced MRI but 7 cases were incorrectly graded as LGG proved to be HGG on histology (Figure 1). This shows the inefficacy of contrast enhanced MR imaging alone in pre-operative diagnosis. The kappa value measured 0.57, suggestive of poor correlation. The sensitivity, specificity, PPV and NPV for determination of a high-grade glioma with conventional MR imaging were 70.8%, 92.3%, 94.4%, and 63.1%, respectively. AUC measured 0.82.

Out of 37 intracranial neoplasms, 24 histologically proven HGG were all correctly diagnosed with spectroscopy imaging (Figure 2), however 2 LGG were over diagnosed to be HGG. Out of 13 histologically proven LGG, 11 cases were correctly diagnosed as LGG. By using Chi-square test p-value <0.05, therefore there was significant association. There was a strong correlation seen with MR spectroscopy with Kappa values ~87%. The sensitivity, specificity, PPV, and NPV for determination of a high-grade glioma with MR Spectroscopy imaging were 100%, 84.6%, 92.3%, and 100%, respectively. AUC measured 0.92.

Out of 37 intracranial neoplasms, 24 histologically proven HGG were all correctly diagnosed with perfusion imaging, however two LGG were misdiagnosed to be HGG (Figure 3). Out of 13 histologically proven LGG, all were correctly diagnosed as LGG. By using Chi-square test p-value <0.05, therefore there was significant association. The kappa value measured 0.87, suggestive of moderate correlation. The sensitivity, specificity, PPV, and NPV for determination of a high-grade glioma with MR Perfusion imaging were 100%, 84.6%, 92.3%, and 100%, respectively. AUC measured 0.92.

The findings of conventional MRI (PD1) were compared with MR spectroscopy (PD2). Out of 26 HGG, 18 enhancing brain tumors also showed increased Cho/NAA ratio, while 8 non-enhancing brain tumors also showed increased Cho/NAA ratio. The 11 non-enhancing low-grade gliomas did not show increased metabolite ratio. By using Chi-square test p-value < 0.05, therefore there is significant association. The Kappa value measured 0.57 suggestive of poor correlation between the two variables. The comparison of sensitivity, specificity, PPV, and NPV of Cho/NAA ratio obtained from MR Spectroscopy for determination of a high-grade glioma with conventional MR imaging were 69.2%, 100%, 100%, and 57.8 %, respectively. The AUC measured 0.85.

The findings of conventional MRI (PD1) were compared with MR perfusion (PD3). Out of 26 HGG, 18 enhancing brain tumors also showed increased rCBV, while 8 non-enhancing brain tumors also showed increased rCBV values. The 11 non-enhancing low-grade gliomas did not show increased metabolite ratio. By using Chi-square test p-value < 0.05, therefore there is significant association. The Kappa value measured 0.57, suggestive of poor association between the enhancing gliomas and the increased rCBV ratio. The comparison of sensitivity, specificity, PPV, and NPV of rCBV obtained from MR Perfusion for determination of a high-grade glioma with conventional MR imaging were 69.2%, 100%, 100%, and 57.8%, respectively. AUC measured 0.85.

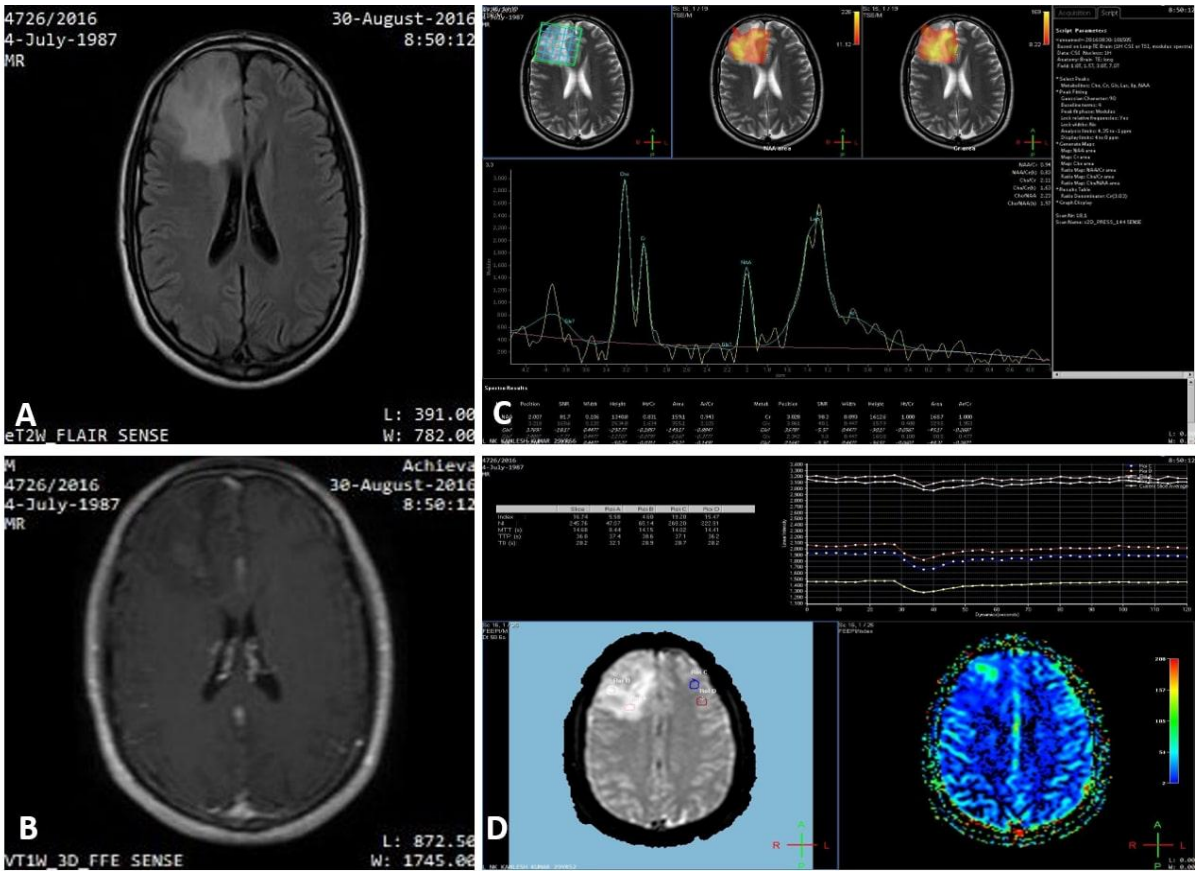

Figure 1: Histopathologically proven case of grade III anaplastic astrocytoma.

A – FLAIR axial image showing heterogeneously hyperintense lesion in right frontal lobe with mild peri-lesional edema.
B - Post contrast T1 axial image showing minimal enhancement of the lesion.
C- MRS showing raised Choline peak with reduced NAA peaks (Cho/NAA ratio of 2.33) and elevated lipid-lactate peaks within the lesion.
D – MR perfusion (MRP) showing increased perfusion in the lesion with rCBV max measuring 3.2. With MRP and MRS, radiological diagnosis was high-grade glioma.

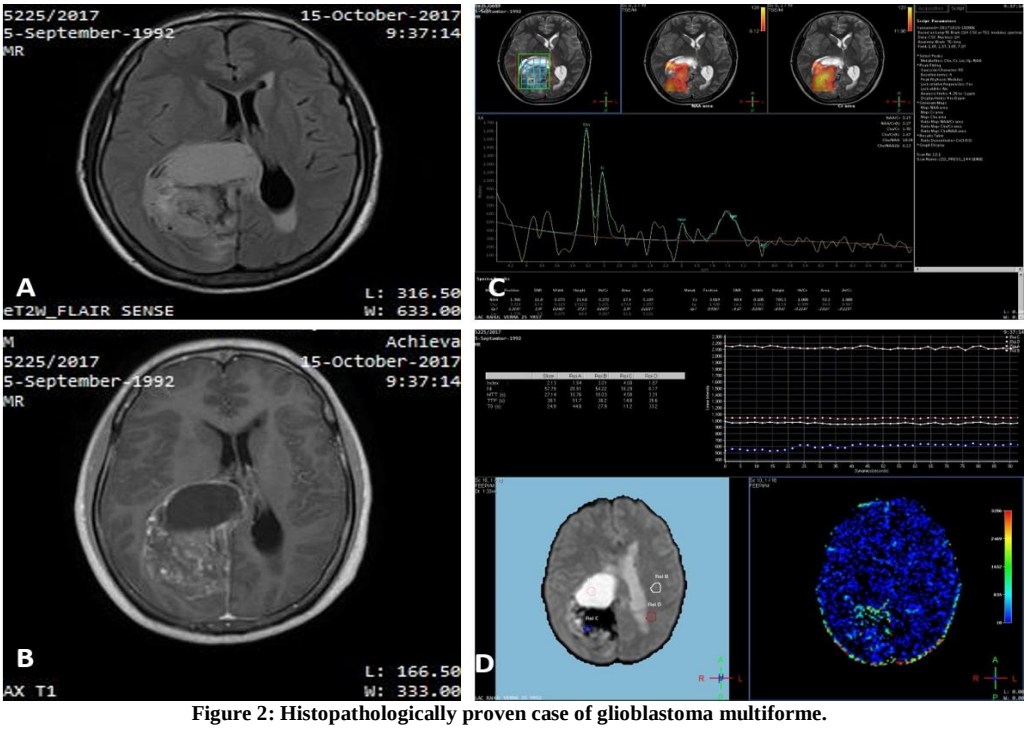

Figure 2: Histopathologically proven case of glioblastoma multiforme.

A – FLAIR axial image showing heterogenous solid-cystic lesion in parasagittal location of the right parieto-occiptal lobes. The lesion is associated with peri-lesional edema causing effacement of the sulcal spaces and compression of the occipital horn of the right lateral ventricle.

B - Post contrast T1 axial image showing heterogenous enhancement of the solid component. Conventional MRI showed features of high-grade glioma.

C - MRS showing raised Choline peak with reduced NAA peak (Cho/NAA ratio of 2.03) and elevated lipid-lactate peaks (1.3ppm) within the lesion.

D – MR perfusion showing increased perfusion with rCBV max measuring 10.2. After MR perfusion and MRS, radiological diagnosis was high-grade glioma.

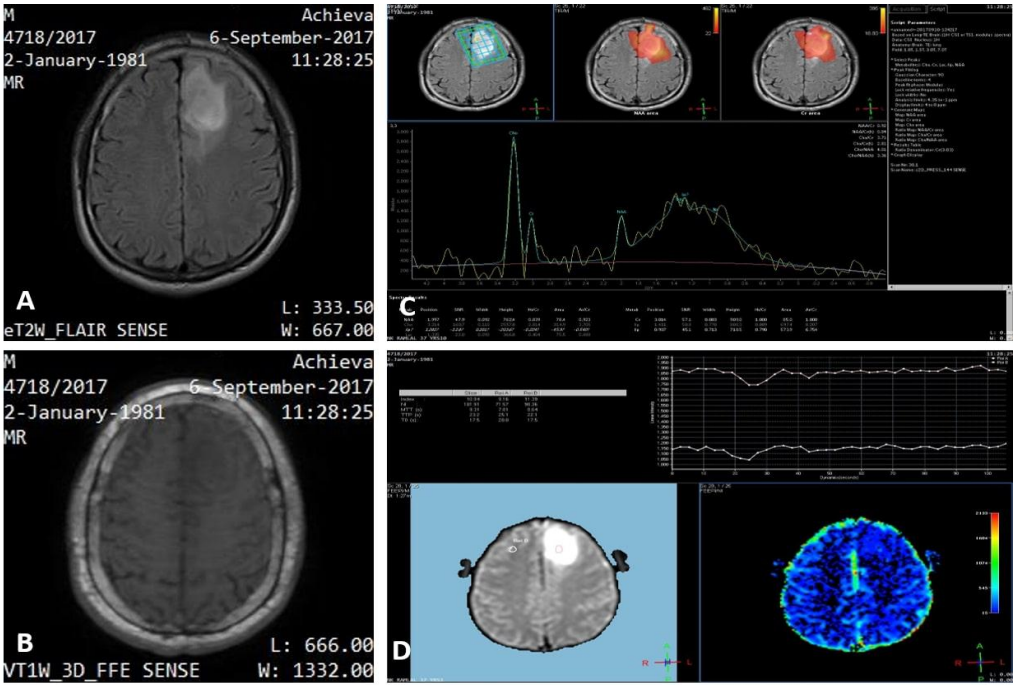

Figure 3: Histopathologically proven case of low-grade glioma - grade II diffuse fibrillary astrocytoma.

A – FLAIR axial image showing focal hyperintense lesion in the left frontal lobe with associated peri-lesional edema causing effacement of the sulcal spaces.

B - Post contrast T1 axial image showing no enhancement of the lesion. Conventional MRI showed features of low-grade glioma.

C - MRS showing raised Choline peak and reduced NAA peak with Cho/NAA ratio of 4.2 within the lesion.

D – MR perfusion showing increased perfusion with rCBV max measuring 3.7. After MR perfusion and MRS, radiological diagnosis was of high-grade glioma.

TABLES 1 AND 2 GRADING OF INTRACRANIAL NEOPLASMS BY MR SPECTROSCOPY.

TABLE 1:

Intra-axial		N	Mean	Std. Deviation	Std. Error Mean
Cho/Cr	HGG	26	3.6450	3.03722	.59565
	LGG	11	1.1273	.40998	.12361
Cho/NAA	HGG	26	6.9988	4.09759	.80360
	LGG	11	1.5191	.38865	.11718
NAA/Cr	HGG	26	.7396	1.02990	.20198
	LGG	11	.9727	.58104	.17519

Out of 37 intra-axial brain tumors, 26 were classified as HGG and 11 were classified as LGG on the MR spectroscopy.

TABLE 2:

Intra-Axial	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% CI of the Difference	
						Lower	Upper
Cho/Cr	4.139	27.074	.000	2.51773	.60834	1.26968	3.76577
Cho/NAA	6.748	26.045	.000	5.47976	.81210	3.81060	7.14891
NAA/Cr	-.701	35	.488	-.23311	.33241	-.90794	.44171

The MRS Cho/Cr and Cho/NAA ratio show significance value <0.05, suggestive of significant association. The NAA/Cr ratio shows significance value >0.05, suggestive of no significant association.

TABLES 3 AND 4 GRADING OF INTRACRANIAL NEOPLASMS BY MR PERFUSION.

TABLE 3:

intra-axial		N	Mean	Std. Deviation	Std. Error Mean
rCBV	HGG	26	2.8731	1.98807	.38989
	LGG	11	.7545	.16306	.04916
CBF	HGG	26	23.6323	22.98883	4.50848
	LGG	11	15.7536	15.56866	4.69413
TTP	HGG	26	28.3881	8.20945	1.61001
	LGG	11	23.0455	7.86173	2.37040

Out of 37 intraaxial brain tumors, 26 were classified as HGG and 11 were classified as LGG. The mean rCBV for HGG was 2.87 for HGG (with SD ±1.98) and 0.75 for LGG (with SD ±0.16).

TABLE 4:

INTRA-AXIAL	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
						Lower	Upper
rCBV	5.391	25.785	.000	2.11853	.39298	1.31042	2.92664
CBF	1.036	35	.307	7.87867	7.60233	-7.55487	23.31221
TTP	1.831	35	.076	5.34262	2.91760	-.58042	11.26566

The rCBV value is 0.00 i.e, <0.05 , suggestive of significant association. The CBF and TTP values are 0.30 and 0.076 i.e, <0.05, suggestive of no significant association.

TABLES 5 AND 6. COMPARISON OF CONVENTIONAL MRI PD1 vs MR SPECTROSCOPY PD2

TABLE 5:

	PD2				Total	
Intra-Axial	HGG		LGG			
PD1	Count	% within pd2	Count	% within pd2	Count	% within pd2
HGG	18	69.2%	0	0.0%	18	48.6%
LGG	8	30.8%	11	100.0%	19	51.4%
TOTAL	26	100.0%	11	100.0%	37	100.0%

Out of 26 HGG, 18 enhancing brain tumors also showed increased Cho/NAA ratio, while 8 non-enhancing brain tumors also showed increased Cho/NAA ratio. The 11 non-enhancing low-grade gliomas did not show increased metabolite ratio.

TABLE 6:

Pearson Chi-Square	df	Asymptotic Significance (2-sided)
14.830[b]	1	.000

By using Chi-square test p-value < 0.05, therefore there is significant association.

TABLES 7 AND 8 COMPARISON OF CONVENTIONAL MRI PD1WITH MR PERFUSION PD3

TABLE 7:

	PD3				Total	
Intra-Axial	HGG		LGG			
PD1	Count	% within pd3	Count	% within pd3	Count	% within pd3
HGG	18	69.2%	0	0.0%	18	48.6%
LGG	8	30.8%	11	100.0%	19	51.4%
Total	26	100.0%	11	100.0%	37	100.0%

Out of 26 HGG, 18 enhancing brain tumors also showed increased rCBV, while 8 non-enhancing brain tumors also showed increased rCBV values. The 11 non-enhancing low-grade gliomas did not show increased metabolite ratio.

TABLE 8:

Pearson Chi-Square	df	Asymptotic Significance (2-sided)
14.830[b]	1	.000

By using Chi-square test p-value < 0.05, therefore there is significant association.

DISCUSSION

Preoperative grading of brain tumors using MR imaging techniques is challenging and still requires further investigation. Currently, the histopathological diagnosis based on the WHO 2017 classification remains the gold standard for the diagnosis of intra-cranial neoplasms. In our study, we aimed to provide objective data on the clinical utility of conventional MR imaging in combination with analysis of the rCBV max ratios in advanced perfusion MR imaging and Cho/NAA max ratios on MR spectroscopy for grading of brain tumors.

MR is the primary investigation of choice and plays a crucial role in non-invasive pre-operative diagnosis, as it has the ability to analyse the lesion as well as the adjacent brain tissue. Conventional gadolinium-based contrast MR imaging provides excellent anatomic or morphologic information of brain tumors. The grading is based on the aggressiveness of brain tumor and evidence of blood-brain barrier breakdown as demonstrated by post contrast enhancement, edema, tumor infiltration, hemorrhage, necrosis, and mass effect. Unfortunately conventional contrast enhanced MR imaging alone cannot differentiate between areas of tumor infiltration from vasogenic edema, as it does not show tumor physiology, which plays a significant role in brain tumor grading. So, often a high-grade brain tumor may be labelled as a low-grade brain tumor due to poor contrast enhancement and absence of necrosis or mass effects. Conversely, low-grade brain tumor with perilesional edema, contrast enhancement, necrosis, and mass effect may be overdiagnosed for a high-grade brain tumor.

The sensitivity and specificity of the conventional MR imaging in identifying high-grade tumors in our study was 70.8% and 92.3%. Out of 24 histologically proven HGG, contrast enhanced MRI wrongly diagnosed 51.4% HGG cases as LGG. This shows the inefficacy of contrast enhanced MR imaging alone in pre-operative diagnosis. Ginsberg et al [11] demonstrated that absence of enhancement of brain tumors does not equate with low-grade brain tumors. Using conventional MRI criteria, other authors obtained lower values (sensitivity of 42.1%-92.3% and a specificity of 60%-75.0%), possibly as a result of different selection criteria for high-grade glioma MRI criteria. [12] Juan A Guzman-DeVilloria analyzed 129 patients with primary brain tumors. They concluded that when all the magnetic resonance variables were combined, necrosis and enhancement were the only predictors of HGG (sensitivity 97.6%; specificity 76%). [13]

Despite extensive reports, preoperative grading of brain tumors using advanced MR imaging techniques still requires further investigation. MR perfusion measures tumor hemodynamics, which is an indicator of tumor aggressiveness due to endothelial hyperplasia and endothelial neovascularization. Relative cerebral blood volume (rCBV) measurements are associated with quantitative estimates of

microvascular permeability and with grade of malignancy of the brain tumor. The two most widely used methods to study and quantify brain tumor vasculature are contrast-enhanced MR imaging methods-DSC and dynamic contrast-enhanced (DCE) perfusion MR imaging. [14-16] Proton Magnetic Resonance Spectroscopy is a valuable diagnostic modality and helps in further characterization of brain lesions. It distinguishes various metabolites on the basis of their slightly different chemical shifts. MRS provides biochemical data of the brain tissue in terms of spectra reflecting cellular turnover and neuronal metabolites. [17]

The aim of our study was to provide objective data on the clinical utility of conventional MR imaging in combination with analysis of the rCBV max ratios in perfusion MR imaging and Cho/NAA max ratios on MR spectroscopy for grading of brain tumors. We also tried to distinguish low-grade from high-grade brain tumors with quantitative criteria. In our study, we chose Cho/Cr and Cho/NAA ratios for assessing tumor grade because Cho is an indicator of cellular proliferative activity and may be a strong predictor of tumor grade. [18]

Despite the low specificities, a significant difference was noted in Cho/Cr, and Cho/NAA, (P = .000, and .000 respectively) for differentiating between low- and high-grade gliomas. MRS revealed mean Cho/NAA ratio for intracranial tumors was 5.37 and mean Cho/Cr ratio was 2.9. The mean Cho/NAA ratio was 6.99 for HGG and 1.51 for LGG and mean Cho/Cr ratio was 3.64 for HGG and 1.12 for LGG. The Cho/Cr ratios were significantly higher in HGGs (1.7±0.63) than in LGGs (1.2±0.38). With the threshold value of Cho/NAA ratio of 1.18, the sensitivity, specificity, PPV, and NPV of Cho/NAA ratio obtained from MR Spectroscopy for determination of a high-grade glioma with conventional MR imaging were 69. 2%, 100%, 100%, and 57.8 %, respectively.

With the threshold value of rCBV of 1.07, the sensitivity, specificity, PPV, and NPV for determination of a high-grade glioma with MR Perfusion imaging were 100%, 84.6%, 92.3%, and 100%. The qualitative and quantitative assessments demonstrated that areas with the greatest Cho/Cr and NAA/Cr ratios on 1HMRS and areas of highest rCBV ratios on CBV maps corresponded to each other.

The nonspecific findings of non-enhancing gliomas by conventional MR imaging, in terms of lack of contrast material enhancement, no mass effect, no necrosis, and no edema should be evaluated by MR perfusion. If MR perfusion study demonstrates an rCBV value above 1.07 and Cho/NAA ratio more than 1.18, there is high sensitivity and specificity for the lesion being a high-grade glioma. This study increased our confidence in glioma grading by using these threshold values in cases that had nonspecific conventional MR imaging findings. The sensitivity and specificity of Cho/NAA and rCBV suggests that Cho levels which directly correlate with tumor cellularity, and the rCBV which correlates with increased vascularity are useful in supplementing diagnostic information in clinical management of the non enhancing gliomas. This study demonstrates that rCBV and MR spectroscopy are sensitive techniques and have a significant role in improving the preoperative grading.

Our study had a few limitations. Firstly, as we used an internal reference within the same voxel, we got semiquantification of metabolite ratios. Using Cr as a reference metabolite may increase variability and inaccuracy. Methods have been described to normalize Cho to contralateral normal Cho or contralateral normal Cr, to provide absolute quantification of metabolites in gliomas. Secondly, even with current automated techniques, one of the challenges faced in spectroscopy, is to obtain reliable and reproducible intrapatient and interpatient data. The heterogeneity of tumor may also affect the values within the same voxel.

Thirdly, we had conflicting results with some of the perfusion MRI studies. It would need further studies to investigate the threshold values of subtypes of brain tumors separately for obtaining more accurate threshold values of rCBV and Cho/NAA ratios.

CONCLUSION

To conclude, rCBV and Cho/NAA ratios are associated with optimal sensitivity and specificity in predicting the grade of brain tumor. Their assistance in diagnosing and follow up imaging will be significant in decreasing the morbidity and mortality associated with the fatal brain tumors.

Long-term studies are required to determine the superiority of the techniques and predict the outcomes on the basis of rCBV with Cho levels. Future studies are needed to validate the study in heterogeneous population of different demographic patterns. Further analysis may provide an insight into the stages of angiogenesis, which may aid in development of angiogenic-targeted therapy.

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