Original Article

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Diagnostic Efficacy of Proton Magnetic Resonance Spectroscopy and Diffusion Weighted Imaging in Cerebral Gliomas

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Abstract

Context: Gliomas account for nearly 50 to 60% of primary brain tumors. Pre-operative diagnosis and grading of cerebral gliomas aids in prognostication and forecasting treatment. MRI alone has been suboptimal for pre-operative evaluation of gliomas and advance sequences like Proton Magnetic Resonance Spectroscopy (MRS) and Diffusion Weighted Imaging (DWI) have abetted to improve characterization of gliomas. *Aim:* To assess the efficacy of MRS and DWI in diagnosing cerebral gliomas. *Material and Methods:* A Diagnostic Efficacy study was carried out among 31 patients presenting with neurological symptoms and suspected to have gliomas through MRI. In addition, MRS and DWI were also performed along with histopathological grading among these patients. At MRS, nCho, Cho/Cr, Cho/NAA along with lipid and lactate peaks were assessed. In DWI, minimum apparent diffusion coefficient was calculated for the tumour (ADC_T), peritumoural oedema (ADC_P) as well a ratio of ADC_T to the minimum ADC in the contralateral normal tissue (ADC_N). Tumours were graded as high grade or low grade based on MRS and DWI findings. *Results:* Twenty nine out of the 31 patients (21 male and 10 female) in the age range of 8 to 71 years were confirmed to have glioma at histopathology. Of these, glioblastoma multiforme (GBM) were most common (n=13). At histology, 4 tumours were low grade (grade I:2, grade II:2); while 25 were high grade (grade III:12, grade IV:13). Conventional MRI showed a diagnostic accuracy of 80.60% in correctly classifying the various lesions and 82.76% for grading them. At MRS, there was a significant positive correlation of nCho (p=0.006) and Cho/Cr ratio (p=0.029) for grading of gliomas. Moreover there was a significant difference between these two parameters between high (I and II) and low grades (III and IV). Lipid and lactate peaks were also significantly associated with high grade gliomas (p value was 0.042 for lipids and 0.01 for lactate). On DWI, ADC_T and ADC ratio had statistically significant negative correlation with increasing tumour grades (p value was 0.015 for ADC_T and 0.006 for ADC ratio). These two parameters were significant in differentiating high grade from low grade gliomas ($p<0.05$). Combining the findings in MRS and DWI resulted in a sensitivity, specificity and accuracy of 100%, 50% and 93.10% respectively. *Conclusion:* MR Spectroscopy, using nCho and Cho/Cr and DWI using ADC_T and ADC ratio were found to be useful in evaluating the grades of cerebral glioma. Conventional MRI, however, was indispensable because of its ability to characterize and classify gliomas into subtypes. Combination of conventional contrast enhanced MRI, MRS and DWI is most appropriate to evaluate gliomas pre-operatively.

Keywords: Brain; Gliomas; Grading; Magnetic Resonance Imaging; Magnetic Resonance Spectroscopy; Diffusion Weighted Imaging; Apparent Diffusion Coefficient.

Introduction

Cerebral gliomas are most common and devastating brain tumors. These tumors vary from grade I to IV and higher the grade exhibits rapid progression [1]. Valuating the grades of glioma aids in planning therapeutic strategy, appraising the prognosis and monitoring the response to therapy. Histopathological examination is the gold standard for glioma grading but is an invasive technique and

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sometimes may be associated with sampling error due to tumor heterogeneity [2].

Magnetic resonance imaging (MRI) has been used to grade gliomas but its sensitivity varies from 55% to 83.3% with considerable overlapping of features across the grades [2-6]. MR spectroscopy has been used to grade gliomas as it evaluates various metabolites in brain tissue and plots a graphical representation of distribution of intensity against their Larmor resonance frequencies [7,8]. Concentration of metabolites like Choline (Cho), Creatinine (Cr), N-Acetyl-L-Aspartate (NAA) and their ratios have been assessed for this purpose. Diffusion Weighted Imaging (DWI) is another MRI sequence that measures apparent diffusion coefficient (ADC) indicating tumor cell density as well as presence of necrosis, cyst, and edema.

The role of MRS and DWI in characterizing and grading of gliomas has been documented. It was evident that a few studies have demonstrated considerable overlapping of sequences and only scarce studies with encouraging results. In light of the above finding the present study was carried out to evaluate the diagnostic efficacy of both MRS and DWI individually, as well as in combination in characterizing and grading gliomas.

Material and Methods

Study Setting & Subjects

Hospital based Diagnostic efficacy study was conducted from Nov'2013 to June'2015. Symptomatic patients with suspected diagnosis of intracranial space occupying lesions were evaluated using MR imaging along with MR spectroscopy (MRS) and Diffusion weighted imaging (DWI). A sample of 30 patients was studied during the study period. Ethical clearance was obtained from Institution Board and informed consent was obtained from patients. Patients with history of surgery, chemo or radiotherapy and lesion close to skull base or calvarium were excluded due to technical difficulty to obtain MRS data.

Study Tool

Subjects underwent MRI brain scan with 1.5T MR scanner (Magnetom Avanto TIM, Siemen, Erlangen, Germany). Gadolinium, at a dose of 0.1mg/ kg was used, whenever feasible. MRI images were evaluated for presence or absence of various characteristics and if present, these were graded from 0 to 2 [Table 1]. A score was assigned based on summation of these parameters. Using criteria suggested by Chisty et al [2] and Batra et al [3], tumors were classified as low grade or high grade. Location of tumor and presence or absence of calcification was also noted with an attempt to predict the histology of tumors at MRI.

The DWI measurement were done using echo planar imaging (EPI) sequence in axial plane modified by addition of bipolar gradient on both sides of the refocussing radiofrequency pulse (TR 3600/ TE 102; 5 mm thick slices and 230 x 230 mm FOV). Three different magnitudes of diffusion encoding gradients with a b value of 0 and 1000 mm^2/ sec in x, y and z directions. Post processing of ADC values was performed and standard ADC values were calculated automatically and expressed in 10^{-3} mm^2/ sec.

In all cases normal, tumoral and peritumoral areas were identified based on the following imaging features:

- Normal tissue was defined as an area with normal T2 and DWI signal intensities, no contrast enhancement (CE) and normal spectroscopic ratios.
- Tumoral area was defined as that with abnormal T2/DWI signal, increased spectroscopic ratios and CE. If the lesion showed no CE, tumoral area was assumed to be at the centre lesion as seen on T2/FLAIR and T1WI.
- Peritumoral was then identified as that with increased T2/DWI signal with normal spectroscopic ratios and without CE.

A region of interest (ROI) was then manually drawn on the ADC maps corresponding as closely as possible to the "tumoral", "peritumoral" and "normal" area as defined above and the minimum ADC value was obtained in 10^{-3} mm^2/sec for both the ROIs. The ROI size varied from 0.2 to 0.3 cm^2. The cases were graded on DWI based on cut off threshold value (1.07×10^{-3} mm^2/sec) proposed by Server A et al [12]. All gliomas showing minimum ADC value <1.07 were graded as high grade and > 1.07 as low grade on DWI. Also ratio of the ADC values: ADC tumour / ADC normal, i.e. normalized ADC ratio for tumour, was calculated for each case.

Proton MR Spectroscopy was performed using a 2D technique and water suppression with chemical shift imaging (Chemical Shift-selective excitation). The volumes were localized using point resolved spectroscopy. After deciding the region of interest (tumoral region as defined above for diffusion weighted imaging), voxel grid was kept and 2D multivoxel proton spectroscopy (TR 1500/TE 135/ 128-256 matrix) was performed and spectra were obtained. Post processing of the voxels was done

manually and baseline and phase shift correction was applied. The resonances assigned included NAA at 2.0 ppm, Cho at 3.2 ppm, Cr at 3.03 ppm, lipid at 0.8 to 1.5 ppm. Lactate at 1.3 ppm as an inverted doublet peak due to J-coupling of lactate bound protons at an intermediate TE value was also assigned.

Metabolite values were calculated automatically from the area under curve for each metabolite peak by the standard commercial software program provided by the manufacturer. For analysis purpose, the parameters evaluated on MRS included (1) Normalized Cho ratio, (2) Cho/ Cr and (3) Cho/ NAA ratios in the tumoral region and presence or absence of (4) lipid and/ or (5) lactate peaks. To ensure quality control and obtain acceptable quality of spectroscopic data normalized Choline value (nCho) was obtained by dividing the Choline value within the tumour by that within an exactly contralateral and symmetrical 'normal' region of interest (ROI), when possible, or within a contralateral representative normal ROI. Attempt was made to grade each lesion based on a semi-quantitative grading system for assessment of metabolite concentrations in the tumour, and spectroscopic ratios and the normalized Choline values as proposed by Bulik et al [Table 2] [21].

Histopathological Examination

Histology was obtained during surgery in 30 cases and by brain biopsy in one case. Sections from formalin fixed, paraffin embedded blocks for all the selected cases were stained with Hematoxylin-Eosin stain. Histopathological diagnosis along with grade was confirmed. The salient features noted in each tumour were cellular polymorphism, nuclear atypia, mitotic activity, microcystic changes, vascular proliferation and necrosis. Confirmation of microscopic examination was done with immunohistochemistry.

Statistical Analysis

Validity of tumour grading on conventional MRI, MRS and DWI alone was analysed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy. The combined sensitivity and specificity on combining the sequences using parallel combination ('AND" and 'OR' method) was also assessed. Non-parametric tests, i.e. Fishers exact test, Mann Whitney test and Kruskal Wallis tests of significance were used to assess the diagnostic performance of imaging parameters on MRI, MRS and DWI as compared to histopathology. Receiver Operating Characteristic (ROC) analysis was performed to determine optimal thresholds for various parameters for prediction of tumour grades. Area under curve (AUC) were taken as a criteria for the success of the ROC analysis.

Results

A total of 31 patients in the age group range of 8 t0 71 years were studied. The mean age was 47.5 years and maximum subjects (21nos) belong to males. The histopathological examination (HPE) revealed 29 patients with gliomas. As per WHO criteria 25 gliomas were classified as high grade (Grade IV:13, Grade III:12) and 4 as low grade (Grade II: 2, Grade I:2) [32].

MRI revealed 20 tumors belonging to high grade and 9 to low grade. The Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and diagnostic accuracy of MRI in respective to HPE was 80%, 100%, 100%, 40.4% and 82.8% respectively. This was statistically significant ($p = 0.005$, Fisher's exact test).

MRS characterized all 29 histologically confirmed gliomas as tumors, but could not identify non – glioma lesions in 2 subjects. Parameters evaluated on MRS included nCho, Cho/ Cr ratio, Cho/ NAA ratio in the tumoral region and presence of absence of lipids and / or lactate peaks. As shown, there was a significant difference between high grade glioma and low grade in respect to nCho value and Cho/ Cr ratio. However, the difference was not significant for Cho/ NAA ratio [Table 3]. ROC curve with AUC and asymptotic significance are also in line with these findings [Figure 1].

There was a greater tendency of the higher grade gliomas to have lipid and lactate peaks than low grade gliomas. Association of lipid and lactate peaks with high grade gliomas was statistically significant with a p value of 0.01 for lactate and 0.042 for lipid (Fisher's exact test). In addition, even between grade III and IV tumours, there was significant tendency of lipids to occur in grade IV gliomas ($p=0.0001$, Fisher's Exact test) [Table 4].

The correlation between histological and MRS grade was statistically significant ($p = 0.001$, Fisher's exact test). Overall sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRS was 88%, 100%, 100%, 57.14% and 89.66% respectively [Table 5].

DWI did not add any diagnostic value to MRI with respect to exclusion of non – gliomas or classification of gliomas. Parameters evaluated at ADC maps included minimum ADC value of tumor (ADC_T), minimum ADC value in peritumoral area (ADC_P) and

normalized ADC ratio for tumor i.e. ration of ADC_T and minimum ADC of contralateral normal area i.e ADC_N expressed in the unit of 10^{-3} mm/sec. As shown, there was a significant difference between high grade glioma and low grade in respect to ADC_T value and ADC_T/ ADC_N ratio. However, the same was not significant in respect to ADC_P Value [Table 6].

As suggested by Server et al [12], tumors at DWI were graded as high grade if ADC_T value was < 1.07 and low grade if ADC_T was >1.07. Twenty seven tumors were correctly graded by this parameter (high grade 25, low grade 2), while two with grading as high grade at DWI turned out to be low grade at histology. Overall sensitivity, specificity, PPV, NPV, and diagnostic accuracy of DWI to correctly identify high grade gliomas was 100%, 50%, 92.60%, 100% and 93.1% respectively. The result was statistically significant (p = 0.015, Fisher's exact test).

The threshold values for classifying a tumor as high grade or low grade was calculated observing the trends with increase in HPE grading and the proposed cut off values for various MRI and DWI parameters was formulated [Table 7].

Table 1: Characteristics evaluated at MRI and their grading

Characteristics	Score		
	0	1	2
Mass effect	Absent/minimal	Moderate	Significant
Midline crossing	Absent	Equivocal	Definitive
Perilesional edema	Minimal	Moderate	Severe
Signal heterogeneity	Homogenous	Equivocal	Heterogenous
Hemorrhage	Absent	Small/focal	Large/multiple
Tumor margins	Well defined	Infiltrating	-
Necrosis/Cystic changes	Absent	Equivocal	Definitive
Contrast enhancement	Absent/homogenous	Rim enhancing heterogenous	-

Table 2: Semi-quantitative assessment of metabolite concentrations and grading in gliomas

	NAA	Cho	Cr	MLNS	Lip	Lac	Cho/NAA	Cho/CR
Grade I	0	+	0	+	0	0	+	+
Grade II	-/--	0/+	-	++	0	0/+	++	0/+
Grade III	--	++	-/--	0	0/+	++	+++	++
Grade I	---	-/+++	---	---	+++	+++	+++*+++*	+++

* including necrosis / excluding necrosis
0= No significant change; '- / - - / - - -' = degree of relative decrease of metabolite concentration in the tumour; '+ /++ / +++' = degree of relative increase of metabolite concentration in the tumour.

Table 3: Association of MRS Criteria with Histopathological Grading

MRS Criteria	Histopathological Examination						P value
	Low Grade			High Grade			
	Gr I (n=2)	Gr II (n=2)	Total (n=4)	Gr III (n=12)	Gr IV (n=13)	Total (n=25)	
N Cho range	0.70- 1.00	1.02- 1.47	0.70- 1.47	1.08- 4.30	1.16- 15.8	1.08- 15.8	0.004
mean ± SD	0.85 ± 0.21	1.24 ± 0.32	1.05 ± 0.32	2.38 ± 1.14	6.30 ±5.14	4.42 ±4.22	
Cho/Cr range	0.90-1.4	1.20-1.57	0.90- 1.57	1.00- 8.30	1.40- 12.00	1.00- 12.00	0.006
mean ± SD	1.15 ± 0.35	1.38± 0.26	1.27 ± 0.29	3.67± 2.42	5.75± 3.86	4.75± 3.36	
Cho/NAA range	0.95- 1.80	1.03- 2.20	0.95- 2.20	1.20- 5.80	0.70- 13.20	0.70-13.20	0.195
mean ± SD	1.38 ± 0.60	1.62 ± 0.83	1.50 ± 0.61	2.60 ± 1.80	4.02 ± 4.35	3.34 ± 3.39	

*Mann- Whitney test
+ nCho value was significantly lower (p=0.030) in grade (II) compared to grade IV

Table 4: Association of MRS lactate and lipid peaks with Histopathological grading of gliomas

HPE Grade	No.	MRS – Lactate		MRS – Lipid		p value (Fisher Exact test)
		Present	Absent	Present	Absent	
Low (I + II)	4	1	3	0	4	>0.05
High (III+IV)	25	23	2	16	9	< 0.01

Table 5: Comparison of MRS grading in relation to HPE grading

Grade on MRS	HPE		Total	p value (Fisher Exact test)
	High grade (I+II)	Low grade (III+IV)		
High	22	0	**22**	<0.001
Low	3	4	**7**	

Table 6: Association of DWI ADC Criteria with Histopathological Grading

ADC Criteria	Histopathological Examination						p value Mann-Whitney test
	Low Grade			High Grade			
	Gr I (n=2)	Gr II (n=2)	Total (n = 4)	Gr III (n=12)	Gr IV (n=13)	Total (n = 25)	
ADCT Range	0.80 – 1.22	0.92-1.47	0.80- 1.47	0.40- 0.98	0.25- 0.74	0.25- 0.98	0.004
mean ± SD	1.01 ± 0.30	1.20 ± 0.39	1.1 ± 0.30	0.67 ± 0.19	0.54 ± 0.15	0.60 ± 0.18	
APC_P Range	0.85- 1.32	1.13- 1.60	0.85- 1.60	0.80- 1.93	0.96- 1.86	0.80- 1.93	0.899
mean ± SD	1.08 ± 0.33	1.36 ± 0.33	1.22 ± 0.32	1.16 ± 0.28	1.41 ± 0.23	1.29 ± 0.28	
ADCT / ADC_N ratio	1.1- 1.5	1.5- 2.0	1.1- 2.0	0.7- 1.4	0.40- 0.97	0.40- 1.14	0.003
range mean ± SD	1.3 ± 0.28	1.75 ± 0.35	1.52 ± 0.37	0.98 ± 0.22	0.74 ± 0.21	0.86 ± 0.24	

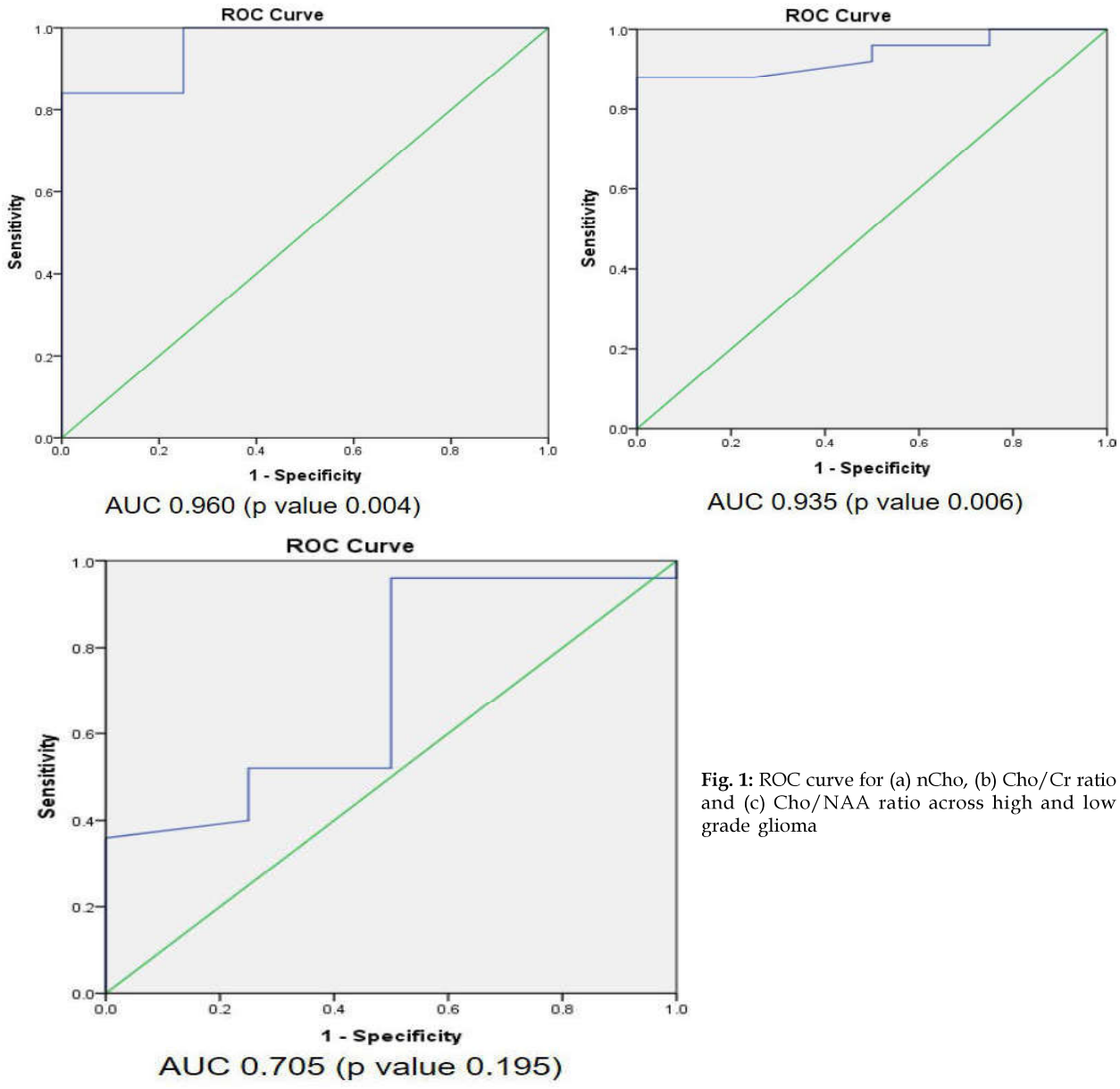

Fig. 1: ROC curve for (a) nCho, (b) Cho/Cr ratio and (c) Cho/NAA ratio across high and low grade glioma

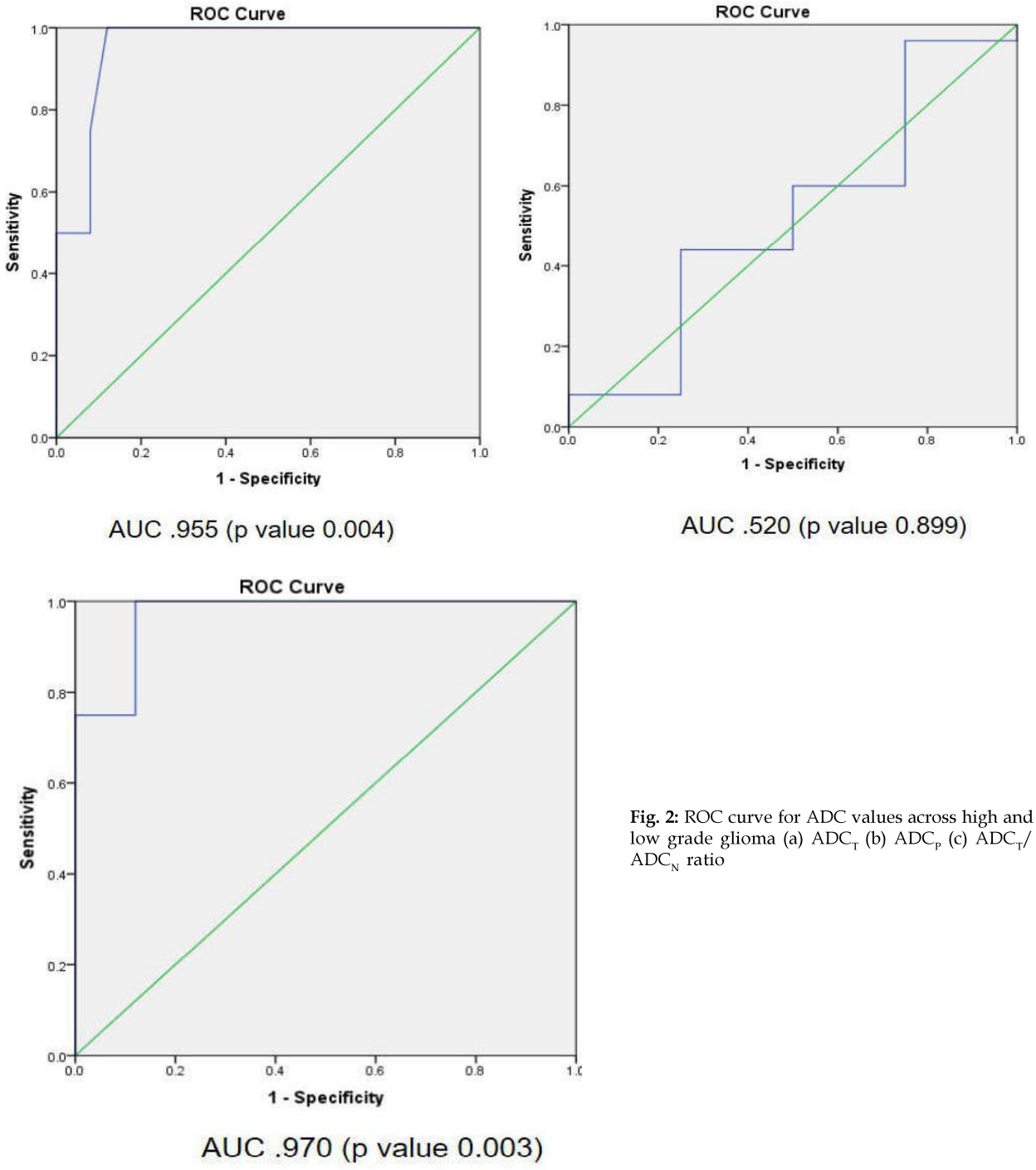

Fig. 2: ROC curve for ADC values across high and low grade glioma (a) ADC_T (b) ADC_P (c) ADC_T/ ADC_N ratio

Table 7: Trends of various MRS and DWI parameters and cut off values

Parameter	Trend with Increasing HPE Grade	Proposed cut off Value	Sensitivity (%)	Specificity (%)
nCho	↑	1.48	84	100
Cho/Cr	↑	1.58	88	100
Cho/NAA	↑	1.04	96	50
ADC(T)	↓	0.79	88	100
ADC Ratio	↓	1.05	88	100
ADC(P)	↑	0.90	96	25

Discussion

At conventional MRI, we found a high sensitivity, specificity and diagnostic accuracy (80%, 100%, 82.8% respectively) for predicting the grade of glioma. Batra et al [3] earlier had shown that the features like strong enhancement on post-contrast T1W images can be specific characteristic of high grade glioma. However, many studies have found considerable overlap of characteristics between high grade and low grade gliomas and did not find conventional MRI to be useful for this purpose [4-6].

Proton MR Spectroscopy

The parameters evaluated on MRS included nCho, Cho/ Cr, Cho/ NAA ratios in the tumoral area as well as presence or absence of lipid or lactate peaks. It has been hypothesized that aggressiveness of intracranial tumours is associated with an increase in Choline (Cho), a marker of cell membrane and myelin turnover; decrease in NAA, marker for neuronal integrity and a decrease in Cr, which provides inorganic phosphates for adenosine triphosphate production involved in cellular energetics and osmotic balance [17,18].

There was significant difference for nCho and Cho/Cr values between high and low grade gliomas. Moreover, nCho values were significantly lower (p=0.030) in grade III when compared to grade IV. With respect to Cho/NAA ratios, there was a considerable overlap seen between the different tumour grades. The difference of mean Cho/NAA ratio between the various grades individually and between high and low grade groups was not significant.

Various studies have tried to evaluate the role of MRS in grading gliomas with varied results. Gupta et al [9] correlated cellular density in 18 cases of glioma with nCho values. They found a statistically significant linear correlation, as seen in our study. Law et al [10] and Zonari et al [11], amongst many others have reported a significant increase in Cho/ Cr ratio with increasing tumour grade; while few others have failed to concur [12,13]. Cho/NAA ratio was seen to be correlating with increasing grade in a few studies [10,12,14-17]. However similar to our study, Kim et al [18] demonstrated no significant differences in Cho/NAA ratios between low grade and high grade gliomas

High grade gliomas, including malignant astrocytoma and glioblastoma multiforme have extensive areas of hypoxia and necrosis. Presence of hypoxia induces tumour angiogenesis, which in turn sets up a vicious cycle with production of immature abnormal microvasculature resulting in more hypoxia and more necrosis [19,20]. Lactate is one of the end products of anaerobic glycolysis. It's presence therefore, correlates well with hypoxia in the tumour cells. Since lipid peaks are associated with presence of necrosis, their presence correlates with higher grade gliomas [15,21]. In our study, there was a greater association of lactate (p=0.01) and lipid peaks (p=0.042) with high grade as compared to low grade gliomas. Additionally, grade IV gliomas were associated with lipid peaks, more frequently than with grade III gliomas (p=0.0001). This was in concurrence with a study by Oshiro et al [7], who noted presence of lactate and lipids predominantly in high grade gliomas. A lactate peak was identified in 50% of patients with grade III and IV gliomas compared to 10% in grade II gliomas in a study by Hsu et al [16]. However the results for presence of lactate has been inconsistent in many studies [22,23].

Further, an attempt was made to grade the gliomas at MRS using criteria proposed by Bulik et al [21]. Using this MRS had a sensitivity, specificity and diagnostic accuracy of 88%, 100% and 89.66% respectively for identifying high grade gliomas. Only three gliomas out of a total of 29 were misdiagnosed, i.e. under-graded by one grade (All these 3 cases were grade III tumours, and were graded incorrectly as grade II).

Diffusion Weighted Imaging

Minimal ADC_T value and normalised ADC ratio showed a decreasing trend with increasing tumour grade. Moreover, there was significant difference for ADC_T values and normalised ADC ratio between high and low grade gliomas. In contrast, we did not note significance difference in ADC_P value between high grade and low grade gliomas.. Server et al [12] also found almost similar results, with significant difference between high and low grade tumours for ADC_T and normalized ADC ratios and non-significant for ADC_P. We also used a cut off value of 1.07 for ADC_T as proposed by Server A et al [12] to differentiate high grade from low grade gliomas, and found a sensitivity, specificity and diagnostic accuracy of 100%, 50% and 93.1% respectively.

Tumour cellularity is one of the important parameters for WHO grading of gliomas, with higher grades associated with higher cellularity. ADC is inversely proportional to cellular density. Diffusion of free water molecules in high grade tumours is reduced because of reduction in extra cellular space

due to increased cellularity. Therefore, ADC values have a negative correlation with tumour grade. Gupta et al [9] correlated cellular density (MIB-1 index and nuclei count per high power field on immunohistochemistry) with ADC values in 18 patients of glioma. There was statistically significant inverse linear correlation between glioma ADC values and cellular density.

Analysis of our data suggested a cut off value of 0.79 and 1.05 for ADC_T and ADC ratio respectively, to differentiate high grade from low grade glioma (negative correlation). Each of these 2 parameters had a sensitivity of 88% and specificity of 100%. Our results in this respect were better than that of Server et al [12], which showed a sensitivity and specificity of 79.7% and 60.0% for minimum ADC_T using a cut off value of 1.07 and 57.6% and 73.3% for ADC ratio using a cut off value of 1.41. A prospective study with larger number of patients and a 'normal' distribution of cases between various grades is however required, to determine an optimum cut off value.

A significant negative correlation between ADC and astrocytic tumours of grade II to IV was also seen in a study by Yamasaki et al [24]. A study by Balos et al [25] also showed a statistically significant difference in the ADC_T between grade II and grade III gliomas. (p=0.023). On the contrary, studies by Rollin et al [26] and Lam et al [27] failed to find a significant difference for ADC value for high grade and low grade gliomas.

With respect to peritumoural oedema, we did not find ADC_P values to be significant in differentiating high grade from grade gliomas. Lack of ability of ADC_P to differentiate high and low grade gliomas has been demonstrated in a number of previously published studies [12,28-30]. Guzman et al [31] however, did find a high ADC_P value in high grade gliomas when comparing with low grade gliomas. It should be emphasized that there may be a bias in evaluating ADC_P values because of inability to clearly distinguish tumour from oedema in some of the gliomas [12]. Moreover, peritumoural oedema consists of an unquantifiable combination of vasogenic oedema and infiltrative tumour cells causing cytotoxic oedema, with different diffusion characteristics and consequent effect on average ADC values.

Utility of Combining MRS and DWI in Grading Gliomas

We analysed the impact of combining MRS and DWI in grading gliomas by their parallel combination in an AND/OR fashion; i.e. a tumour was graded as high graded, if either of the two sequences showed it to be so, whereas the tumour was graded as low graded when both MRS and DWI showed it to be low grade. The combined sensitivity, specificity, PPV, NPV and diagnostic accuracy of this combination was 100%, 50%, 92.59%, 100% and 93.1% respectively. This is similar to that of DWI alone. However, MRS has a higher specificity. Moreover, MRS helped divide the 25 high grade gliomas into grades III and IV, correlating well with the histopathological grade. Conventional MRI remains indispensable for identifying gliomas and classifying suspected gliomas into specific subtypes.

Limited number of studies have utilized both DWI and MRS in conjunction, to look for their combined value in grading gliomas. Server et al [12] used a four factor model, combined mean ADC_T, maximum ADC ratio, peritumoural Cho/Cr and Cho/NAA metabolite ratios to differentiate high grade from low grade gliomas. The sensitivity, specificity, PPV, NPV and diagnostic accuracy were 91.5%, 100%, 100%, 100% and 92.5% respectively. They concluded that this combination of sequences increases the accuracy of image assisted grading of gliomas, when compared with individual sequence alone. These results are broadly in agreement with our results, although the method for analysis was somewhat different.

Limitations

Limitations of our study include the number of patients and distribution among various grades. Though we achieved a sample size as per the requirement of the study, the total number of cases evaluated were less than some of the other reported studies. Distribution of our patients in the various grade was non-uniform with only 4 cases in low grade, and 25 in high grade gliomas. In spite of using appropriate tests for statistical analysis to overcome this limitation (non-parametric distribution), there could be a bias.

While we evaluated multiple parameters for MRS, some of the parameters such as myoinositol levels, NAA/Cr, (Cho+Cr)/NAA, metabolites and ratios in peritumoural area were not incorporated. Similarly on DWI, we did not assess the significance of ADC_T/ ADC_P and other tumoural ADC values like mean ADC and maximum ADC. Incorporating these above parameters could have further validated the role of MRS and DWI in evaluation of gliomas as seen in other studies for MR grading of gliomas [12,33,34].

Inspite of these limitations, we can conclude that addition of MRS and DWI to conventional MRI individually and more so in combination, can help in improved characterization and grading of cerebral gliomas.

Conclusion

MR Spectroscopy, using nCho and Cho/Cr and DWI using ADC_T and ADC ratio were found to be useful in evaluating the grades of cerebral glioma. Conventional MRI, however, was indispensable because of its ability to characterize and classify gliomas into subtypes. Combination of conventional contrast enhanced MRI, MRS and DWI is most appropriate to evaluate gliomas pre-operatively.

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Nil

Conflict of Interest: Nil

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