



CLINICAL OUTCOMES BASED ON INTRA OPERATIVE CONSISTENCY OF TUMORS AND APPARENT DIFFUSION COEFFICIENT VALUE IN PITUITARY MACROADENOMA POST ENDOSCOPIC TENTS EXCISION

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ABSTRACT

Aim: Pre operative evaluation of tumor consistency of pituitary adenomas is important and is being routinely evaluated radiologically. We have evaluated pre-operatively ADC value derived from MRI and consistency of tumors intraoperatively as per Neurosurgeon and correlated with the different post operative outcomes in pituitary adenoma. We have evaluated the outcomes post surgery in relation to the tumor consistency assessed intraoperatively and ADC values.

Materials and Methods: 33 cases of Pituitary adenoma had been divided into three groups, according to the intra operative assessment of the consistency of the tumor. Tumors which were easily suckable with suction were grouped as "soft" and the tumors which were fibrous and could not be removed despite fragmentation and manipulation, and required CUSA (Cavitron Ultrasonic Surgical Aspirator) for resection were grouped as "firm" consistency. Contrast MRI in 3T with diffusion weighted sequences with ADC values was done. All surgeries were performed by a single experienced neurosurgeon. Finally, Fisher probability tests and unpaired t tests were used to compare predictions on the basis of the MR imaging findings with the tumor consistency discovered peroperatively.

Results: Statistical analysis revealed that there was no correlation between consistency of tumor with the age, sex, durations of symptoms, tumor size and extension, endocrine dysfunction and post op visual recovery. Findings in this study suggest a predictability between preoperative radiological assessment of consistency and per op tumor consistency of Pituitary macroadenomas at a clear cut off value at $0.681 \times 10^{-3} \text{ mm}^2/\text{s}$.

Conclusion: Our conclusion is that preoperative ADC values can predict tumor consistency but consistency per se have no statistical relation with different outcomes post surgery.

KEYWORDS : Pituitary macroadenoma; consistency; Apparent diffusion coefficient

INTRODUCTION

Pituitary tumors believed to comprise 10–15 % of all primary brain tumors (7). 10% macroadenomas with increased fibrosis are hard and difficult to be removed by the endoscopic technique and may require more extensive surgery (1). Tumor consistency is one of the main pre operative predictive factor in deciding the post operative outcomes since soft tumors are easily removable but firm, fibrous consistency tumors which compromise about 10% are not easily amenable. Measurements of the ADC would be expected to be useful in tumor assessment because variations in water content, which can be found within tumor for various reasons (eg, necrosis, variation in cellularity) and adjacent to tumors (eg, vasogenic edema), likely provide information that is not readily available from conventional MRI (11). DTI and fiber tractography are new DWI methods that can demonstrate the orientation and integrity of white matter fibers in vivo. Various studies had been done on the consistency of tumors, but very less study done particularly on the pituitary macroadenomas with nowadays available advanced MRI sequences. There are few other studies about the utility of DW MRI in prediction of the consistency of pituitary adenoma that have yielded conflicting results (8, 3, 12). The purpose of this study was to evaluate the ability of preoperative DW, ADC and DTI MRI to predict the tumor consistency and correlation between consistency of tumor and resection rate, the clinical outcome in patients with pituitary macroadenomas operated through an endoscopic transsphenoid approach.

MATERIALS AND METHODS :

All 33 cases of Pituitary Macroadenoma reporting to Neurosurgery OPD at this centre underwent Contrast MRI in 3T with diffusion weighted sequences with ADC values. The patients had been divided into three groups, according to the intra operative assessment of the consistency of the tumor. Tumors which were easily suckable with suction were grouped as "soft" and the tumors which were fibrous and could not be removed despite fragmentation and manipulation, and required CUSA (Cavitron Ultrasonic Surgical Aspirator) for resection were grouped as "firm" consistency. All surgeries were performed by a single experienced neurosurgeon. Finally, Fisher probability tests and unpaired t tests were used to compare predictions on the basis of the MR imaging findings with the tumor consistency discovered peroperatively. The relationship to the outcome of surgery in terms of

totality of resection or otherwise was also assessed in cases of soft, intermediate and firm tumour groups.

METHODOLOGY:

Data selected for analysis included patient demographics, preoperative duration of systemic and visual symptoms, preoperative presence of suprasellar tumor extension and Hardy's classification of tumor. Additionally, comparative pre- and postoperative data were obtained for tumor size, VA, and VF.

All patients underwent MRI with a 3-T MRI scanner equipped with high performance gradients. The standard imaging protocol consisted of the T1W, T2W and postcontrast T1. Breath hold DWI was done with a single-shot spin-echo echo-planar sequence (TR/TE: 2000/33–55, matrix size 128×128 , section thickness 6 mm, interslice gap 1 mm, FOV 38 cm, b values 0 and 1000 s/mm^2). DTI was performed using a single-shot echo-planar imaging technique with the following parameters: TR 10,000 ms; TE 55ms; FOV 430 430 mm; matrix 256 256; slice thickness 5 mm; gap 0 mm. Data was analyzed with the special manufacturer supplied software. ADC values were generated automatically by the software. The ROIs were then manually copied to the corresponding ADC and FA maps, from which the ADC and FA values were obtained. Findings of magnetic resonance imaging (MRI) were independently evaluated by the single neuroradiologist.

For calculation of Sample size the assumptions taken into account are minimum 80% power and 5% significance level (significant at 95% confidence level). Assuming that at 95% confidence level, 0.85 probability of success, and a margin of error (confidence interval) of $\pm 12\%$ the sample size should be minimum of 32.

Statistical analysis- Statistical analysis was done by using descriptive and inferential statistics using Pearson chi square test for categorical data and unpaired t-test to compare mean values between the two groups. ANOVA test followed by post-hoc test was applied to compare mean values between more than two groups. P-value less than 0.05 considered as significant at 95% confidence level. The statistical software SPSS version 16.0 used in the analysis. ROC curve, sensitivity, specificity, positive predictive value (PPV) and negative

predictive value (NPV) to detect validity of ADC in assessment of tumor consistency.

RESULTS

Total -33 patients
 25 men, 8 women
 mean age 37.8 years(31-50yrs)
 range, 22—58 years
 mean duration of visual loss, 3.12 months
 standard deviation 2.68.

Patients presented with different symptoms as listed. Visual disturbance, n = 33(as patients having visual symptoms was an inclusion criterion), acromegaly, n = 18; galactorrhoea, n = 1; seizure, n = 1; other like headache, n = 11.

According to Hardy classification maximum tumor was of grade B (39.4%) and grade E (30.3%).Grade C and grade A was of 15.2%.

Mean ADC value for “soft” consistency was 0.610x10(-3)mm(2)/s(SD-0.11) and for “Firm” consistency it was 989x10(-3)mm(2)/s(SD-0.04).

Correlation of tumor consistency with clinical outcomes. On comparing 2 groups with Mann-whitney U test ,there was no statistical difference in residual volume of tumor.

When we compared the visual recovery in terms of improved to normal and partial improvement in 2 groups of consistency there was no statistically difference between 2 groups.(p-value 0.957). On applying t-test to overall variables, differences in age, sex, preoperative clinical symptoms, clinical endocrine classification, maximum tumor size, extension, post op tumor size and complications rate in 2 groups of consistency was not found in respect with consistency of tumors statistically as depicted in (Table 1). In our series, out of total 33 patients of pituitary adenoma who were surgically treated; 22 (67%) were found to be non-secretory pituitary adenoma. 4 (12%) were prolactinoma, 6 (18%) were GH secreting adenoma, 1 (3%) were TSH secreting adenoma.

On statistical analysis mean tumor pre op volume was 14.098cm(3) and post op was 1.6cm(3) in “soft” consistency which was significant (p-value<.001). In “Firm” consistency on comparing pre and post op volume of tumor there is decrease in volume of tumor but not as significant as in “soft” consistency group. This difference was present because soft tumors were easily resectable intraoperatively by suction. In order to find a cut- off level of the mean ADC value that can reliably predict the tumor consistency, Roc curve was plotted(Graph 1) between the intraoperative consistency decided by the surgeon and the ADC value derived from the MRI. Area under the curve was 0.881 (0.736–1.027, SE-0.074). The ADC value 0.681x10(-3)mm(2)/s was the cut off value in differentiating the soft consistency adenoma types from firm adenoma. The sensitivity, specificity,PPV, and NPV of 80%,94.4%, 92.3%,85.7% respectively at 0.681x10(-3)mm(2)/s as depicted in (Table 2). This value detected the soft consistency adenoma(with low ADC values) and the Firm consistency adenomas.

DISCUSSION:

In the present study, we evaluated whether ADC values generated from DWI/DTI sequences could predict tumor consistency in pituitary macroadenomas and whether any clinical outcomes were associated with the consistency of the tumor. Our results suggest that DWI/DTI sequences is a useful imaging sequence for tumor consistency estimation. Tumor consistency remains one of the most important, still doubtful factors in the consideration of an endonasal versus open craniotomy for skull base tumors.(2,14,5). Preoperative prediction of

tumor consistency, if possible, would be very important for planning surgical resection, biopsies, radiation therapy and avoidance of multistage surgical procedure. Tumour hardness was regarded as a prognostic factor of the visual variations caused by tuberculum sellae meningioma in view of technical difficulty in removing of adherent tumor with optic nerve(6), which become more significant in view of endoscopic surgery for pituitary adenoma as soft consistency tumor was easily suckable. This strategy may be cost effective and psychologically valuable for both the patient and the neurosurgeon [10]. We found no statistically significant correlation between tumor consistency and post surgical outcomes. There were four studies(4,13,9,6) that assessed tumor consistency, comprising 165 patients. Overall odds of improvement for soft tumor versus firm were 4.91 (95% CI = 2.27 to 10.63). In our study there was no correlation of consistency with vision improvement as suggested by t-test with no significant p-value this may due to several factors involved in consistency of tumour. Our study is in accordant with some of the previous studies but again some studies are divergent from that. Conventional MRI has little role in tumor consistency. But with DW and DTI protocols, ADC calculated are more converse with the consistency of tumor. With 'soft' consistency have lower ADC values and 'firm' consistency have higher value with clear cut cut off value at 0.681x10(-3) mm(2)/s. It have accuracy of 89% which was high but not 100% as found in study of yinping(5). Also the cut off value was little higher in Pierallini(10) study (ADC<1.077) and in Faten Fawzy Mohamed study (3) cut off value was 0.6. This variable figures may be due the various factors like variable sample size , small sample size in all study and very small samples of 'hard' consistency tumors. Our study found that there is no correlation of consistency with the post operative residual tumor volume, visual outcome and recovery in endocrinological dysfunction.

CONCLUSION:

This study results indicate that DW MR and ADC value can provide information about the consistency of macroadenomas with cut off ADC value at 0.681x10(-3) mm(2)/s-. Values less than the above were found in soft tumours(suckable) & values with higher ADC value(>1) were found in Firm tumors(not suckable but required CUSA), although one ADC value was overlapped with soft tumors and in between values were of “intermediate” consistency with some overlap values. MRI protocols should include the DW images and determination of the ADC values , as these values can help in surgical planning to some extent.

Limitations of our study was small sample size and unequal proportion of the “soft” and “firm” consistency groups (for equal proportion we need large sample size as only 15-18% pituitary adenomas are of firm consistency.

Conflict of interest: None

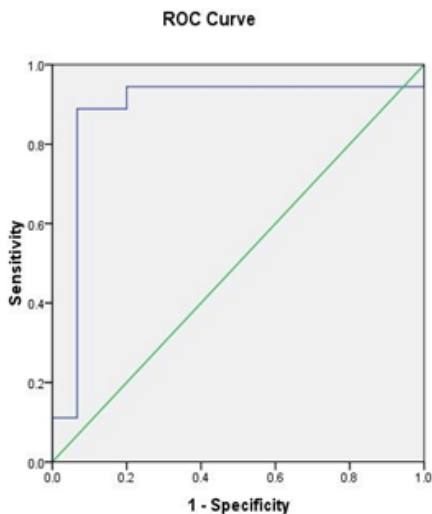
Table-1: t-test apply for all variables

	Consistency of tumor	N	Mean	Std. Deviation	t-value	p-value
Duration of visual loss	Soft	26	3.12	2.68	0.491	0.627
	Firm	7	3.63	1.11		
Size of tumor	Soft	26	13262.00	20777.30	0.123	0.903
	Firm	7	14277.00	11720.66		
Hardy Grade	Soft	26	3.04	1.93	0.978	0.336
	Firm	7	3.86	2.12		
MRI Size Pre op	Soft	25	14098.00	21389.99	0.021	0.983
	Firm	7	14277.00	11720.66		
MRI Size Post op	Soft	25	1603.00	4521.27	0.857	0.398
	Firm	7	3659.10	8687.86		

Table 2 (Validity of ADC value at the cut off value of 0.681x10(-3)mm(2)/s)

	Consistency of tumor	ADC value		Total	Sensitivity	Specificity	PPV	NPV	Accuracy
		<0.681	>0.681						
	Soft	14	3	17	80.0%	94.4%	92.3%	85.7%	87.9%
	Intermediate/Firm	1	15	16					
Total	15	18	33						

Graph 1



(The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values)

REFERENCES

- Alberto P, Francesca C, Carlo F, Emanuele T, Amalia P, Alessia BC: Pituitary macroadenomas: Preoperative evaluation of consistency with diffusion-weighted MR imaging—initial experience. *Radiology*.2006;239:223–31.
- Ciric I, Mikhael M, Stafford T, Lawson L, Garces R (1983) Transsphenoidal microsurgery of pituitary macroadenomas with long-term follow-up results. *J Neurosurg* 59(3):395–401.
- Faten Fawzy Mohamed a, SafwatAbouhashem: Diagnostic value of apparent diffusion coefficient (ADC) in assessment of pituitary macroadenomaconsistency: The Egyptian Journal of Radiology and Nuclear Medicine (2013) 44, 617–624.
- Galal A, Faisal A, Al-Werdany M, El Shehaby A, Lotfy T, Moharram H: Determinants of postoperative visual recovery in suprasellarmeningiomas. *ActaNeurochir (Wien)* 2010;152:69–77.
- Iuchi T, Saeki N, Tanaka M, Sunami K, Yamaura A (1998): MRI prediction of fibrous pituitary adenomas. *ActaNeurochir (Wien)* 140(8):779–786.
- Kim T W, Jung S, Jung T Y, Kim I Y, Kang S S, Kim S H: Prognostic factors of postoperative visual outcomes in tuberculumsellae meningioma. *Br J Neurosurg.* 2008;22:231–234.
- Kontogeorgos G (2005) Classification and pathology of pituitary tumors: *Endocrine* 28:27–35.
- Lu Yiping, Xiong Jib, GengDaoyinga, Yin Boa: Prediction of the consistency of pituitary adenoma: A comparative study on diffusion-weighted imaging *Journal of Neuroradiology* (2015).
- Nozaki K Kikuta K Takagi Y Mineharu Y Takahashi J A Hashimoto N: Effect of early optic canal unroofing on the outcome of visual functions in surgery for meningiomas of the tuberculumsellae and planumsphenoidale *Neurosurgery* 2008;62:839–844., discussion 844–846.
- Pierallini A, Caramia F, Falcone C, Tinelli E, Paonessa A, Ciddio AB, Fiorelli M, Bianco F, Natalizi S, Ferrante L, Bozzao L (2006): Pituitary macroadenomas: preoperative evaluation of consistency with diffusion-weighted MR imaging—initial experience 1. *Radiology* 239(1):223–231.
- Provenzale JM, Mukundan S, Barboriak DP: Diffusion-weighted and perfusion MR imaging for brain tumor characterization and assessment of treatment response. *Radiology*.2006 Jun;239(3):632–49.
- Qing-shizeng, Chuan-Fu Li,Hong Liu, Jun-Hui Zhen, De-Chao Feng: Distinction between recurrent glioma and radiation injury using magnetic resonance spectroscopy in combination with diffusion-weighted. *int. j. radiation oncology biol. phys.*, vol. 68, no. 1, pp. 151–158, 2007.
- Suri A, Narang K S, Sharma B S, Mahapatra A K: Visual outcome after surgery in patients with suprasellar tumors and preoperative blindness. *J Neurosurg.* 2008;108:19–25.
- Zada G, Du R, Laws ER Jr (2011): Defining the “edge of the envelope”: patient selection in treating complex sellar-based neoplasms via transsphenoidal versus open craniotomy. *JNeurosurg* 114(2):286–300.