Original Article

Predictive Value of Preoperative MRI Sequences in Successful Endoscopic Endonasal Transsphenoidal Pituitary Macroadenoma Removal

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Background: Endoscopic endonasal transsphenoidal surgery is a minimally-invasive technique that is suitable for treatment of most pituitary macroadenomas, which can be easily and effectively removed using a combination of endoscopic techniques such as suction, cauterization, and curettage. However, some pituitary macroadenomas are not easy to remove via the endoscopic approach, if they are firm, highly vascularized, or fibrous in consistency. In such cases, further transcranial surgery either by keyhole supraorbital or conventional craniotomy may be needed.

Objective: To assess the benefits of conventional magnetic resonance imaging (MRI) techniques in predicting outcomes of endoscopic surgery.

Materials and Methods: Thirty-nine cases of pituitary macroadenomas with preoperative conventional MRI sequences (T1W, T2W, T1W+Gd, and FLAIR) were included in the present study. The authors compared the difference in signal intensity (SI) between the tumor area and pons. All operations were performed using standard endoscopic transsphenoidal techniques in combination with neuro-navigators. All operations were performed by the same team of neurosurgeon and otolaryngologist. The outcomes were categorized into three groups, "Satisfactory", "Fair", and "Unsatisfactory", according to the amount of tumor left after the operations. Finally, statistical tests with binary logistic regression model, ROC, and AUC were used to study the relationship between the four MRI sequences and the outcomes of the operations.

Results: The present study included 39 cases of pituitary macroadenomas. The tumor to pons SI ratios of T2W sequence were significant indicators of the probability of success with endoscopic surgery. The ROC analysis suggested that the cutoff point should be set at a T2W ratio of less than 1.971 for female patients and 1.515 for males. The sensitivity, specificity, and accuracy were 92.31%, 73.08%, and 79.49%, respectively.

Conclusion: Scrutiny of preoperative MRI analysis using SI ratio (macroadenomas versus pons) in T2W MRI is useful in predicting the success of the endoscopic endonasal transsphenoidal approach in removal of pituitary macroadenomas.

Keywords: Pituitary macroadenoma, Endoscope, Transsphenoid, MRI, Outcome, Prediction, Selection

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Nowadays, the endoscopic endonasal transsphenoidal approach (EETA) is the least-invasive technique for treatment of pituitary macroadenomas. There is no doubt that EETA is an invaluable technical adjunct to the conventional armamentarium of any operative theatre; however, not all pituitary macroadenomas are amenable to resection using the endoscopic technique. Although, most are easily removed with the suction technique because they are usually soft in consistency, some presents with more fibrous consistency and harder components. In such cases, total tumor removal using endoscopic resection carries more risks than either conventional or keyhole craniotomy.

In the past decade, many surgeons have tried to look for preoperative means of predicting which pituitary macroadenomas can be easily and safely

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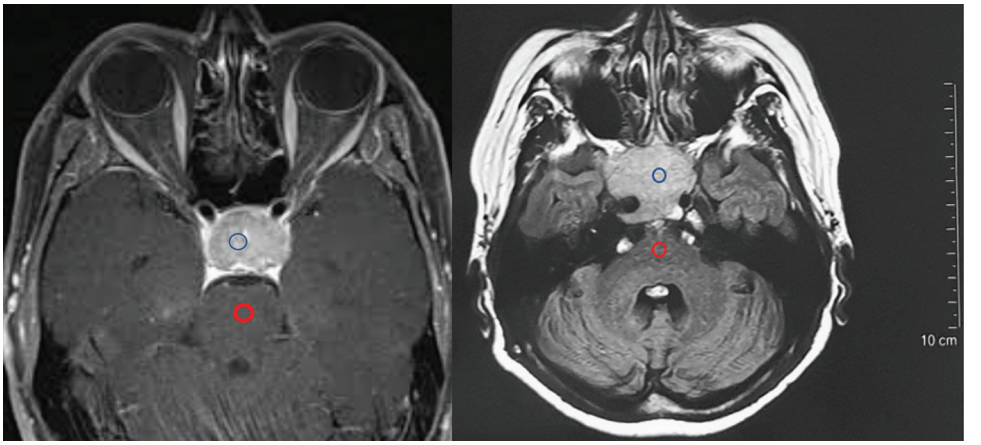

Figure 1.Representation of the region of interest (ROI) between macroadenoma area (blue thin circle) and pons (red thick circle).

removed via endoscopic technique. One such method is preoperative magnetic resonance imaging (MRI) in variable sequences. At present, MRI is commonly used for preoperative imaging of most pituitary tumors especially in evaluating the type and extension of the tumor. This concept is based on the fact that there are differences between the histological cell types of the tumor components and normal brain tissue, so that different cell types will show different images after each MRI sequence.

The purpose of the present study was to determine whether preoperative MRI sequences of pituitary macroadenoma patients can predict the outcomes of EETA. The authors hypothesized that pituitary macroadenomas dominated by fibrous tissue would have significantly different signal intensity (SI) from that of the brainstem. If the researchers could find some correlation between the SI ratio of macroadenomas and brainstems preoperatively, then they could probably predict the likely outcomes of the surgery.

Materials and Methods

The present study retrospectively reviewed 39 pituitary macroadenoma patients treated with EETA in Rajvithi Hospital. All cases were sent for preoperative investigation by MRI with at least four different sequence techniques of T1-weighted (T1W), T2-weighted (T2W), T1W with gadolinium (Gd) contrast enhancement, and fluid attenuated inversion recovery (FLAIR) technique. The inclusion criteria were patients with histologically confirmed pituitary adenoma of a maximum diameter greater than 10 mm. The exclusion criteria were those who had had hormonal treatment such as bromocriptine or had been surgically treated with other means (craniotomy or radiosurgery). Patients who initially presented with pituitary apoplexy were excluded from the study.

The 1.5 Tesla MRI was used to investigate all patients in the present study. The MRI protocol for pituitary adenomas consisted of 3 mm coronal and sagittal pre-and post-Gd T1W of the pituitary fossa, 3 mm coronal and sagittal T2W of the pituitary fossa, and 5 mm axial T1W, T2W, FLAIR for the whole brain. Both sagittal and axial planes were used to measure the SI of the macroadenomas and the brainstem (pons). The coronal plane was excluded in the study because the authors could not obtain both pons and tumor images at the same time. The authors used three random 3-mm circular areas to represent regions of interest (ROI) (Figure 1). The values from ROI of macroadenomas and pons were calculated and converted to macroadenoma to pons SI ratios of four different MRI sequences.

The authors classified the outcomes of the operations into three categories: “Satisfactory”, “Fair”, and “Unsatisfactory” depending on the percentage of macroadenoma removal after post-operative MRIs. “Satisfactory” was defined as more than 80% removal, while less than 40% removal was classified as “Unsatisfactory”, and the rest were considered “Fair”.

Statistical analysis

Sample size: Based on the study by Wayne (1995), the sample size of the present study was computed using the following formula:

Table 1. Patients' age categorized by gender

	Cases	Age				
		Mean	Median	Standard deviation	Min	Max
Female	19	47.4	50.0	13.9	22	71
Male	20	48.0	47.5	10.4	34	68
Total	39	47.7	48.0	12.1	22	71

$$n = \frac{Z^2_{\alpha/2}\, p(1-p)}{d^2}$$

where: n=number of samples; p=sample proportion which was based on neurosurgery standard which suggested that sensitivity should be 80%; d=margin of error which was set at 10%; $Z_{\alpha/2}$=standardized normal value of the confidence level which was set at 0.05 significance level, then, $Z_{\alpha/2} = Z_{0.05} = 1.96$

Required sample size was equal to

$$n = \frac{1.96^2 \times 0.8(1-0.8)}{0.15^2} = 27$$

Therefore, the sample used in the present study was 39 cases.

Data analysis: All data were collected and analyzed using Stata version 15. Bivariate statistical analysis was performed using the parametric tests one-way ANOVA and independent-sample t-test, together with the nonparametric Kruskal-Wallis test, in order to preliminarily determine whether mean and median of MRI sequences (T1W, T2W, T1W+Gd, and FLAIR) were significantly different among varying levels of success of the operation (Satisfactory, Fair, and Unsatisfactory) and different gender of patients.

To fulfil the objectives of the study, the authors used multivariate analysis using ordered logit model for ordinal measurement of the level of success of the operation (Satisfactory, Fair, or Unsatisfactory) and binary logistic regression model for binary measurement of level of success of the operation (Satisfactory and Fair-Unsatisfactory).

The Index function of the ordinal logit model can be stated as:

$$I_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i}$$

Then,

$$Y_{1i} = 0 \text{ if } -\infty < I_i \leq \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \tau_1$$

$$Y_{1i} = 1 \text{ if } \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \tau_1 < I_i \leq \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \tau_1 + \tau_2$$

$$Y_{1i} = 2 \text{ if } \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \tau_1 + \tau_2 < I_i \leq \infty$$

where: Y_{1i}=0 for Unsatisfactory, 1 for Fair, and 2 for Satisfactory; X_{1i}=MRI sequences (T1W, T2W, T1W+Gd, or FLAIR); X_{2i}=gender of patient (equal 0 for female and 1 for male)

Similarly, the index function of the binary logistic regression model can be defined as:

$$I_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i}$$

$$\text{Then, } \text{Prob}(Y_i=1) = \frac{1}{1+e^{-I_i}}$$

where: Y_{2i}=0 for Fair or Unsatisfactory, and 1 for Satisfactory

The predictability power of the binary logistic regression model was then determined by area under receiver operating characteristic (ROC) curve, and the cutoff point of the prediction decision was determined based on ROC. Significance level in the present study was set at the 0.05 level.

Results

Descriptive statistical indices of age of patients categorized by gender are shown in Table 1. The authors enrolled a total of 39 patients, of whom 19 were males and 20 were females. Their ages ranged from 22 to 71 years old (mean age of 47.7±12.1 years; median age 48 years). The age range of the men was from 34 to 68 years (mean, 48±10.4 years) and that of the women was between 22 and 71 years (mean, 47.4±13.9 years).

Bivariate analysis

Operation level of success, as a dependent variable, was classified into three groups, "Satisfactory" where there was tumor removal of more than 80%, "Fair" for 40% to 80% tumor removal, and "Unsatisfactory" for less than 40% removal.

MRI sequences (T1W, T2W, T1W+Gd, or FLAIR)

Table 2 illustrates the group-mean difference tests using one-way ANOVA of MRI sequences (T1W, T2W, T1W+Gd, or FLAIR) categorized by level of success. Table 3 shows the group-median difference test using Kruskal-Wallis test of MRI sequences (T1W, T2W, T1W+Gd, or FLAIR) categorized by level of success. Endoscopic transsphenoidal hypophysectomy was successful and classified as "Satisfactory" in 13 of 39 (33%) cases of macroadenoma while 48% (19

Table 2. Parametric test of group-mean differences categorized by level of success using one-way ANOVA

	Cases	T1W	T1WGD	T2W	FLAIR
	n (%)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Unsatisfactory	19 (48.7)	0.9282 (0.1082)	1.6631 (0.4380)	1.9152 (0.3727)	1.4819 (0.2654)
Fair	7 (18.0)	0.9104 (0.1895)	1.6344 (0.2159)	1.8120 (0.3572)	1.6231 (0.2366)
Satisfactory	13 (33.3)	0.9908 (0.1467)	1.4305 (0.5981)	1.4902 (0.5495)	1.4400 (0.3458)
Total	39 (100)	0.9459 (0.1381)	1.5804 (0.4720)	1.7550 (0.4677)	1.4943 (0.2920)
ANOVA F-test		1.0800	0.9900	3.720*	0.9200
p-value		0.3515	0.3806	0.0341	0.4100

T1W=T1-weighted; T1WGD=T1W with gadolinium; T2W=T2-weighted; FLAIR=fluid attenuated inversion recovery; SD=standard deviation

* Statistically significant at 0.05

Table 3. Nonparametric test of group-median differences categorized by level of success using Kruskal-Wallis test

	Cases	T1W	T1WGD	T2W	FLAIR
		Median	Median	Median	Median
Unsatisfactory	19	0.909	1.539	1.924	1.538
Fair	7	0.872	1.670	1.640	1.710
Satisfactory	13	0.951	1.441	1.504	1.386
Total	39	0.909	1.569	1.684	1.497
Kruskal-Wallis test		3.091	1.372	7.116*	2.084
p-value		0.2133	0.5035	0.0285	0.3528

T1W=T1-weighted; T1WGD=T1W with gadolinium; T2W=T2-weighted; FLAIR=fluid attenuated inversion recovery

* Statistically significant at 0.05

Table 4. Number of patients categorized by level of success and gender

Gender	Outcome, n (%)			
	Unsatisfactory	Fair	Satisfactory	Total
Female	6 (31.6)	4 (21.1)	9 (47.4)	19 (100)
Male	13 (65.0)	3 (15.0)	4 (20.0)	20 (100)
Total	19 (48.7)	7 (17.9)	13 (33.3)	39 (100)
	Pearson chi-squares (2)=4.6223, p=0.099			

of 39 cases) were deemed "Unsatisfactory", and the remaining 7 of 39 (17%) cases were classified as "Fair". In both tests, group-mean and median tests (Table 2, 3), T2W sequence showed that the lower the SI ratio value, the higher the chance of success (being in the "Satisfactory" group).

The above findings imply that patients with lower SI ratio values of T2W had a higher chance of being in the "Satisfactory" group. T1W, T1WGD, and FLAIR revealed insignificant differences in the mean among different levels of success, and thus had no significant impact on the level of success.

Gender

Table 4 presents the number and percentage of patients categorized by level of success and gender. Table 5 illustrates the group-mean differences test of MRI sequences (T1W, T2W, T1W+Gd, or FLAIR) categorized by gender using independent-sample t-test. Table 4 shows that the proportion of patients

Table 5. Parametric test of group-mean differences categorized by gender using independent sample t-test

Gender	Cases n (%)	T1W Mean (SD)	T1WGD Mean (SD)	T2W Mean (SD)	FLAIR Mean (SD)
Female	19 (48.7)	0.9941 (0.1569)	1.5042 (0.4521)	1.6511 (0.5109)	1.4549 (0.2664)
Male	20 (51.3)	0.9000 (0.1015)	1.6528 (0.4906)	1.8537 (0.4113)	1.5295 (0.3162)
Total	39 (100)	0.9459 (0.1381)	1.5804 (0.4720)	1.7550 (0.4677)	1.4943 (0.2920)
Independent sample t-test		2.234*	0.9798	1.3675	0.7616
p-value		0.0316	0.3325	0.1797	0.4522

T1W=T1-weighted; T1WGD=T1W with gadolinium; T2W=T2-weighted; FLAIR=fluid attenuated inversion recovery; SD=standard deviation

* Statistically significant at 0.05

Table 6. Estimated results of ordered logit models

Variable	M1	M2	M3	M4
T1W	0.8876			
T1WGD		–0.9099		
T2W			–1.9414**	
FLAIR				–0.0341
Male	–1.2612*	–1.2688**	–1.1832*	–1.5863**
Cut1	0.1340	–2.1445	–4.1177**	–1.1339
Cut2	0.9650	–1.2898	–3.1867**	–0.2119
Number of patients	39	39	39	39
Log-likelihood	–37.547	–36.926	–34.725	–34.676
Chi-squares test	4.8441*	6.0858**	10.4871***	6.0070**
Pseudo R-squares	0.0606	0.0761	0.1312	0.0797

T1W=T1-weighted; T1WGD=T1W with gadolinium; T2W=T2-weighted; FLAIR=fluid attenuated inversion recovery

* Statistically significant at 0.1, ** Statistically significant at 0.05, *** Statistically significant at 0.01

Dependent variable (Y_{1i}) of 0 for Unsatisfactory, 1 for Fair, and 2 for Satisfactory

in different groups categorized by level of success and gender were statistically significantly different at the 0.1 significance level (Pearson chi-squares test of 4.6223 with p-value 0.09 less than 0.1), which implied that gender had a slightly significant impact on level of success. Table 5 demonstrates that female and male patients did not have different means of MRI sequences (T1WGD, T2W, and FLAIR), with the exception of T1W (means of females and males were significantly different at the 0.05 significance level). These results showed no correlation between gender and MRI sequences (T1WGD, T2W, and FLAIR), helping to confirm that both variables can be appropriately used together in multivariate analysis of level of success as dependent variables (ordered logit model and binary logistic regression model).

Multivariate analysis

To determine the predictability power of MRI sequences (T1W, T2W, T1W+Gd, or FLAIR) on level of success of the operation, the authors utilized ordered logit models and binary logistic regression models using each MRI sequence (T1W, T2W, T1W+Gd, or FLAIR) as predictors and gender (equal to 0 for female and 1 for male) as the control variable.

Table 6 shows the estimated results of ordered logit models of level of success of operation (classified into three levels, 0, 1, 2) using T1W (M1), T1WGD (M2), T2W (M3), and FLAIR (M4) as predictors. Table 7 illustrates the estimated results of binary logistic regression models of the probability of success of operation (quantified as binary choice variable 0 or 1) using T1W (P1), T1WGD (P2), T2W (P3), and FLAIR (P4) as predictors.

Table 7. Estimated results of binary logistic regression models

Variable	P1	P2	P3	P4
T1W	2.4260			
T1WGD		–1.0765		
T2W			–2.2372**	
FLAIR				–0.8314
Male	–1.0717	–1.2048*	–1.0718*	–1.3974*
Constant	–2.5152	1.5222	3.6029*	1.3286
Number of patients	39	39	39	39
Log-likelihood	–22.755	–22.365	–20.313	–21.327
Chi-squares Test	4.1386	4.9180*	9.0216**	4.4374
Pseudo R-squares	0.0834	0.0991	0.1817	0.0942

T1W=T1-weighted; T1WGD=T1W with gadolinium; T2W=T2-weighted; FLAIR=fluid attenuated inversion recovery

* Statistically significant at 0.1, ** Statistically significant at 0.05, *** Statistically significant at 0.01

Dependent variable (Y_{2i}) of 0 for Unsatisfactory or Fair, and 1 for Satisfactory

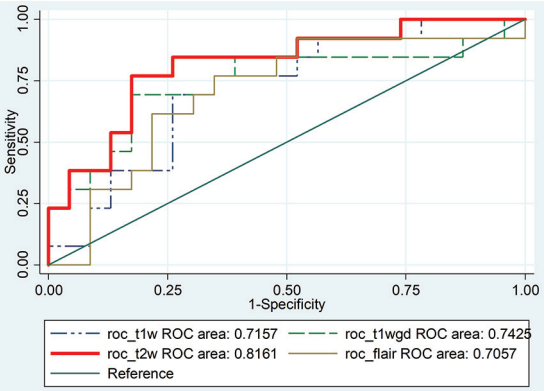

Figure 2. ROC curves and AUC comparison.

Tables 6 and 7 shows that the estimated results of both models indicating that T2W significantly influenced the probability of success of the operation, as the estimated coefficients of T2W (in M3 and P3) were significantly different from zero at 0.05 while those of other MRI sequences (T1W (M1 and P1), T1WGD (M2 and P2), and FLAIR (M4 and P4) were not significant. These findings were in line with the results of bivariate analysis indicating that the SI ratio of T2W sequence can be used as a predictor in determining the probability of success of the operation: the lower the value of the SI ratio of T2W, the higher the chance of success of the operation. Additionally, gender had a significant effect on the probability of success, with females having a higher chance of successful outcomes than males.

The high predictive power of T2W was also confirmed by ROC curve comparison among T1W, T1WGD, T2W, and FLAIR. Figure 2 illustrates the ROC curves and area under ROC curve (AUC) of binary logistic regression models of T1W, T1WGD, T2W, and FLAIR (model P1, P2, P3, and P4, respectively in Table 7). AUC of T2W (0.8161) was the highest of the four predictors, indicating that T2W had the highest predictive power in determining the probability of success of the operation.

Figure 3 illustrates the ROC analysis of T2W model (P3 in Table 7). ROC analysis (Figure 3), showed that AUC was equal to 0.8161 and the optimal cutoff (threshold) should be 0.3 to obtain optimal levels of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with lower levels of false positive for predict positive (FPPP) and false negative for predict negative (FNPN). To reach the cutoff point of 0.3, T2W for female patients should be less than 1.971 while for males it should not be higher than 1.515.

Table 8 shows the validity of the prediction of operation success at SI ratio of T2W of less than 1.971 for females and SI ratio of T2W of less than 1.515 for males. The validity of T2W in predicting operation success using the suggested threshold revealed accuracy of 79.49%, sensitivity of 92.31%, specificity of 73.08%, PPV of 63.16%, and NPV of 95.00%. FPPP of 36.84% indicated that 9 out of 21 cases for which endoscopic surgery were suggested would have had "Unsatisfactory" outcomes. FNPN of 5% revealed that only one out of 18 cases not recommended for

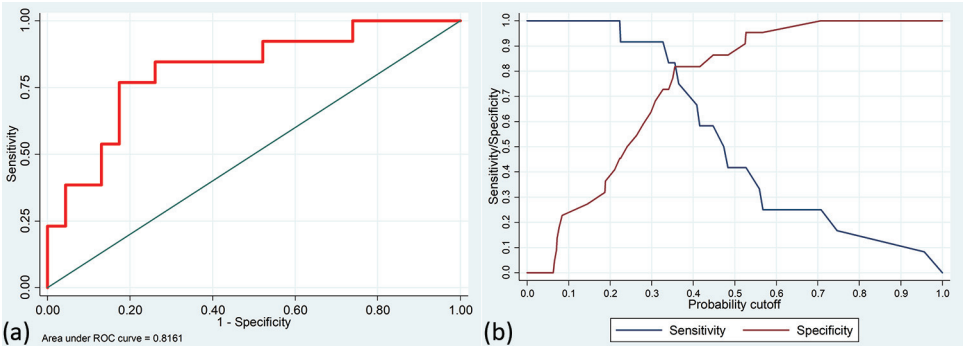

Figure 3. ROC curves and AUC comparison.

Table 8. Validity of T2W in predicting success of operation at 1.971 for females and 1.515 for males

	Satisfactory	Unsatisfactory	Total
Positive prediction	12	9	21
Negative prediction	1	17	18
Total	13	26	39

Index	Percent
Sensitivity	92.31
Specificity	73.08
Positive predictive value	63.16
Negative predictive value	95.00
False positive for true positive	26.92
False negative for true negative	7.69
False positive for predict positive	36.84
False negative for predict negative	5.00
Accuracy	79.49

surgery cases would have had successful endoscopic procedures.

Discussion

In patients with visual acuity problems resulting from mass effect after pituitary macroadenoma, tumor removal via EETA should be the first-line treatment of choice in every case. However, not all macroadenomas can be easily and safely removed. Even in the hands of experienced EETA neurosurgeons, there are risks such as conchal non-pneumatized sphenoid, dumbbell tumor, tumor extension out of sellar turcica especially the lateral and retrosellar extension, small hiatus of diaphragmatic sella, invasion of the circle of Willis arteries, and encasement of optic apparatus[1]. Firm and fibrous adenoma consistency may be the most challenging obstacle for such a deep narrow-corridor approach as EETA, and even when performed by well-trained and expert surgeons, it still carries high risks in cases of removal of firm adenomas. Consequently, if the authors can pre-operatively predict the consistency of pituitary macroadenomas, the authors will be better equipped to choose the best surgical approach for our patients. For such firm and highly vascularized macroadenomas, the transcranial approach, either with conventional pterional craniotomy or keyhole supraorbital approach, is safer[2-7].

A study by Yun et al[8], included 50 patients with pituitary macroadenomas. They calculated the ratio between the SI of the adenoma and that of pons, and a non-parametric Kruskal-Wallis test was performed to determine the correlation of MRI images and surgical outcomes. It was found that only pre-operative T2W MRI was useful in helping to predict the intraoperative consistency of macroadenomas. Adenomas with T2W ratios of less than 1.49 were more likely to be fibrotic and more difficult to resect easily, while FLAIR sequence was not correlated with the consistency of macroadenoma.

To pre-operatively predict the tumor consistency of pituitary macroadenoma using MRI, Smith et al[9] retrospectively evaluated T2W MRI of 36 non-secreting macroadenoma patients. ROI were sampled from the adenoma and cerebellar peduncle, and the ratio was calculated. Using unpaired t-test for these ratios, they finally concluded that soft macroadenomas were associated with ratios greater than 1.5 (sensitivity 100%, specificity 66.7%) while firm tumors were associated with ratios of less than 1.8 (sensitivity 100%; specificity 42.9%).

Another study by Boxerman et al[10] aimed to determine whether the pre-operative MRI findings of enhanced diffusivity in pituitary macroadenomas were predictive of successful transsphenoidal hypophysectomy. A neuropathologist, who was

blinded to the clinical and MRI data, graded reticulin content in tumor specimens. For MRI studies, they calculated the apparent diffusion coefficient (ADC) and the SI of T2W between macroadenoma and pons. They concluded that solid tumors with enhanced diffusivity (greater than 1.1) were more likely to be successfully managed with transsphenoidal hypophysectomy whereas those of solid, enhancing tumors with restricted diffusion were more likely to fail because of the greater reticulin content of the tumor.

Reported in the Egyptian journal of radiology and nuclear medicine, a study by Alashwah et al[11], assessed the role of diffusion weighted (DW)-MRI as a non-invasive imaging modality in predicting the tumor consistency of pituitary macroadenomas. Twenty patients underwent conventional MRI sequence including pre- and post-contrast DW-MRI with ADC map. The tumor consistency was determined both macroscopically by neurosurgeons and microscopically by histopathologists. The correlation between macroscopic findings and histological findings were evaluated using SPSS version 20.0 software and the statistical tools Kolmogorov-Smirnov test, F-test (ANOVA, and post hoc test (LSD)) to detect the cutoff value and accuracy of ADC maps in order to determine macroadenoma consistency and resectability. The final conclusions were that a cutoff value of ADC 1×10^{-3} mm²/s can be used to identify pituitary macroadenomas liable to aspiration (soft and intermediate consistency). The ADC values of the hard consistency were more than 1×10^{-3} mm²/s. They were very difficult to handle using the transsphenoidal approach and needed further transcranial procedures. Another finding from the present study was that the hypointense signal from T2W was not related to the tumor cellularity. Therefore, it was proposed that DW-MRI was a useful tool for predicting pituitary macroadenoma consistency and selecting the most suitable surgical approach for resection.

Another study by Mohamed and Abouhashem[12] of pre-operative assessment of macroadenoma consistency for proper surgical planning sought to find the correlation between DW-MRI and ADC value measurement. They concluded that DWI correlation with ADC value should be a routine pre-operative assessment of macroadenoma consistency to ensure proper planning of the surgical approach. The ADC value measurement had a high sensitivity and specificity in assessing pituitary macroadenomas. The cutoff ADC value in differentiating the soft versus intermediate consistency adenoma types from firm adenomas was 0.6×10^{-3} mm²/s. This value can be confidently used to detect soft or intermediate consistency adenoma, which shows low ADC values with the lowest ADC value in the soft consistency group due to high cellularity rendering them liable for endoscopic suction.

Yamamoto et al[13] studied the consistency of pituitary macroadenomas and the obtained image (contrast-enhanced 3D FIESTA) from three Tesla MRI. They found that there was a significant correlation between tumor consistency and contrast-enhanced FIESTA findings after MRI. They concluded that tumors with high SI ratio in CE-FIESTA would be easily removed via EETA using simple suction and curettage techniques.

A study by Taghvaei et al[14], which studied 45 pituitary macroadenoma patients, found that only 26.7% of macroadenomas were classified as soft, 66.6% as intermediate, and 6.7% as of hard consistency. These intraoperative findings were not correlated with pre-operative DW-MRI and they surmised that the DWI technique and the ADC values were not useful for pre-operative prediction of tumor consistency, collagen content of pituitary macroadenomas.

In summary, surgical teams (neurosurgeons, otolaryngologists, and radiologists) have utilized all efforts in pre-operative pituitary planning to find the safest and most effective approach. Correlation of difficulty of surgery with the MRI findings seems to be the most efficacious tool, but there is still some debate regarding which MRI sequence is the best predictor. A few studies have demonstrated that a lower signal on T2W correlated with a fibrous component in the tumor[15]. One study showed a relationship between ADC ratio and the success rate of surgery[10]; however, others have found no distinct correlation between MRI findings and tumor consistency[16,17].

The results of the present study are in line with those of several previous ones that found significant impacts of SI ratio after some MRI sequences in predicting the success of pituitary macroadenomas. The differences in SI ratio between the macroadenoma and pons of T2W can significantly determine the probability of the success of the surgery; however, the authors found no significant impacts of the SI ratio of T1W, T1WGD, and FLAIR MRI on surgery outcomes. Therefore, the present study suggested T2W cutoff values of less than 1.971 for females and 1.515 for male patients. The validity of SI ratio from T2W in predicting operation success using the suggested

threshold revealed an accuracy of 79.49%, sensitivity of 92.31%, and specificity of 73.08%.

The limitations of the present study included its small sample size (39 patients), the use of a 1.5 Tesla MRI machine (poor quality compared with the 3.0 Tesla), and the presence of predominant-cystic content or massive extension out of sella turcica in some macroadenomas. The authors recommend further research using a larger prospective series with more exclusion criteria under higher MRI resolution.

Conclusion

The authors determined that the T2W sequence from conventional MRI can be used in predicting the surgical outcomes of pituitary macroadenoma removal using EETA. SI ratios between macroadenoma to pons in T2W value are a good screening tool for pituitary macroadenoma surgery by EETA. The values of SI ratio in T2W of less than 1.971 for females and 1.515 for males can be used as the cutoff value in order to achieve high predictive values for successful EETA.

What is already known on this topic?

Although several studies have reported that MRI is a useful tool in predicting the consistency of pituitary adenomas, it is still debatable whether MRI sequences are accurate in terms of specificity and sensitivity in predicting outcomes.

What this study adds?

This research demonstrated that patients who had pituitary macroadenomas benefited from having an MRI study to predict the probability of successful outcomes after EETA. However, from this study, T2W has a strong correlation with the outcome of EETA, while T1W, T1W+Gd, and FLAIR do not. Proper selection of cases of pituitary macroadenoma for EETA can be achieved using T2W with the conventional 1.5 Tesla MRI.

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Conflicts of interest

The authors declare no conflict of interest.

References

1. Di Maio S, Cavallo LM, Esposito F, Stagno V, Corriero OV, Cappabianca P. Extended endoscopic endonasal approach for selected pituitary adenomas: early experience. J Neurosurg 2011;114:345-53.
2. Wongsirisuwan M, Ananthanandorn A, Prachasinchai P. The comparison of conventional pterional and transciliary keyhole approaches: pro and con. J Med Assoc Thai 2004;87:891-7.
3. Wongsirisuwan M. What is the better minimally invasive surgery in pituitary surgery: endoscopic endonasal transsphenoidal approach or keyhole supraorbital approach? J Med Assoc Thai 2011;94: 888-95.
4. Wongsirisuwan M, Karnchanapandh K. Comparative outcomes of keyhole supraorbital approach (KSA) and endonasal endoscopic transsphenoidal approach (EETA) in pituitary surgery. J Med Assoc Thai 2014; 97:386-92.
5. Naganuma H, Satoh E, Nukui H. Technical considerations of transsphenoidal removal of fibrous pituitary adenomas and evaluation of collagen content and subtype in the adenomas. Neurol Med Chir (Tokyo) 2002;42:202-12.
6. Couldwell WT. Transsphenoidal and transcranial surgery for pituitary adenomas. J Neurooncol 2004;69:237-56.
7. Youssef AS, Agazzi S, van Loveren HR. Transcranial surgery for pituitary adenomas. Neurosurgery 2005; 57:168-75.
8. Yun JJ, Johans SJ, Borys E, Patel CR, Reddy S, Germanwala AV. Prediction of intraoperative pituitary adenoma consistency by preoperative MRI evaluation. J Neurol Surg B 2018;79(S 01):S1-188.
9. Smith KA, Leever JD, Chamoun RB. Prediction of consistency of pituitary adenomas by magnetic resonance imaging. J Neurol Surg B Skull Base 2015;76:340-3.
10. Boxerman JL, Rogg JM, Donahue JE, Machan JT, Goldman MA, Doberstein CE. Preoperative MRI evaluation of pituitary macroadenoma: imaging features predictive of successful transsphenoidal surgery. AJR Am J Roentgenol 2010;195:720-8.
11. Alashwah MA, Moharram MA, Allakany AS. Role of diffusion weighted magnetic resonance imaging DW-MRI in choice of the surgical approach for pituitary macroadenoma resection. Egypt J Radiol Nucl Med 2017;48:983-9.
12. Mohamed FF, Abouhashem S. Diagnostic value of apparent diffusion coefficient (ADC) in assessment of pituitary macroadenoma consistency. Egypt J Radiol Nucl Med 2013;44:617-24.
13. Yamamoto J, Kakeda S, Shimajiri S, Takahashi M, Watanabe K, Kai Y, et al. Tumor consistency of pituitary macroadenomas: predictive analysis on the basis of imaging features with contrast-enhanced 3D FIESTA at 3T. AJNR Am J Neuroradiol 2014;35:297-303.

14. Taghvaei M, Tajik F, Zeinalizadeh, Ardalan FA, Ghanaati H. Is there any congruity between tumor consistency in Pituitary macroadenomas and preoperative diffusion weighted imaging and apparent diffusion coefficient (ADC) map? Arch Neurosci 2017;4:e14553.
15. Iuchi T, Saeki N, Tanaka M, Sunami K, Yamaura A. MRI prediction of fibrous pituitary adenomas. Acta Neurochir (Wien) 1998;140:779-86.
16. Chakrabortty S, Oi S, Yamaguchi M, Tamaki N, Matsumoto S. Growth hormone-producing pituitary adenomas: MR characteristics and pre- and postoperative evaluation. Neurol Med Chir (Tokyo) 1993;33:81-5.
17. Hagiwara A, Inoue Y, Wakasa K, Haba T, Tashiro T, Miyamoto T. Comparison of growth hormone-producing and non-growth hormone-producing pituitary adenomas: imaging characteristics and pathologic correlation. Radiology 2003;228:533-8.