Original Investigation

# Added Value of Dynamic Contrast-Enhanced Magnetic Resonance Imaging in Predicting Response to Somatostatin Analogs in Acromegaly Patients

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## ABSTRACT

**AIM:** To investigate the added value of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) sequences in predicting somatostatin analog (SSA) responses in patients with acromegaly.

**MATERIAL and METHODS:** This study included 55 active acromegaly patients with macroadenoma. Mean and maximum signal intensities were measured using region of interests in T2-weighted (T2W) and DCE-MRI sequences. Semi-quantitative values indicating relative signal intensity ratios and contrast-enhanced kinetics were obtained. Bivariate and multivariate analyses were used to determine whether the pathological granulation pattern of adenomas (dense versus others) was associated with patients' demographic variables and semi-quantitative MRI parameters.

**RESULTS:** Three parameters formed the logistic model, $\chi2(3)=23.278$, p<0.0001: age (odds ratio [OR]=1.08), hypointensity of adenomas in T2W images (OR=15.45), and high maximum enhancement ratio in the second interval ($ER2_{max}$) values (OR=2195.74). The overall accuracy of this model was 85.45% with an area under the curve of 0.880. Sensitivity, specificity, positive predictive, and negative predictive values of the model were 68.75%, 92.31%, 78.58%, and 87.8%, respectively.

**CONCLUSION:** In patients with newly diagnosed acromegaly, the model created based on the relative T2W signal intensity, patient's age, and $ER2_{max}$ parameter from DCE-MRI sequences might be used to more accurately predict SSA responses.

**KEYWORDS:** Acromegaly, Pituitary gland, Adenoma, Somatostatin, Magnetic resonance imaging

## ■ INTRODUCTION

Although the first-line treatment option for acromegaly is trans-sphenoidal resection of the adenoma, complete cure rate is achieved in approximately 70% of cases even at experienced and high volume centers (17,20). Conversely, the complete cure rate is <70% when the adenoma is invasive in nature. Medical therapy is recommended in patients with a persistent disease postoperatively or in those who are at high risk for surgery (22). The standard option among medical therapies is first-generation somatostatin analogs (SSA). In the majority of patients, tumor size and growth hormone (GH) levels decrease after SSA treatment (1,6,18,23). In patients

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who are highly at risk for surgery, preoperative treatment with SSA may decrease the tumor size and eliminate or decrease tumor invasion to adjacent tissues. As a consequence, these favorable results may reduce the surgical risk. Furthermore, anesthetic complications are less likely to occur in patients preoperatively treated with SSA (3,7,30). However, one-third of patients are resistant to the first-generation SSAs (21).

Factors predicting the responses to the first-generation SSA treatment are highly important in patients who are planning to undergo medical treatment due to the high economic cost of SSA treatment. Although the granulation pattern of surgically resected tumors, somatostatin receptors, and aryl hydrocarbon receptor-interacting protein expression predict the responses to SSA treatment, these parameters were derived from surgical materials (8,14–16,31). Because these parameters are not available in patients newly diagnosed with acromegaly, magnetic resonance imaging (MRI) findings have a great potential to predict the responses to SSA treatment. Current literature involves strong evidence that T2-weighted (T2W)-hypointensity in GH-secreting pituitary adenomas have better responses to either primary or postoperative SSA treatment (13,25,26,29). The granulation pattern of GH-secreting adenomas is also correlated with signal intensities on T2W images. Dense granulation pattern has been demonstrated as a strong predictor of better responses to SSA treatment (4).

To the best of our knowledge, no conventional MRI data were available in the literature, which suggest the predictors of treatment response other than low signal intensity on T2W images. Therefore, this study aimed to investigate the added value of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) in predicting the response to SSA treatment in patients with acromegaly.

## ■ MATERIAL and METHODS

### Patients

This study was approved by the local ethical committee that waived the requirement of obtaining an informed consent.

This study included 55 patients with newly diagnosed acromegaly according to clinical findings and biochemical analyses from 2009 to 2017 in our institution. Exclusion criteria were as follows: (i) the absence of pituitary DCE-MRI performed in our center at the time of diagnosis; (ii) radiologically diagnosed microadenomas (maximum diameter of<10 mm); (iii) radiological or clinical diagnosis of pituitary apoplexy or bleeding; (iv) radiologically purely cystic adenomas; (v) absence or focal immunohistochemical staining in pathologic examination; and (vi) patients without pure GH-secreting adenomas.

Patient's age, GH levels, insulin-like growth factor-1 (IGF-1) levels, tumor size at the time of diagnosis, preoperative medical treatment history, histopathological examinations, and biochemical remission status were obtained from the patient's archive files.

Acromegaly diagnosis was biochemically made based on elevated age-adjusted IGF-1 levels and GH nadir of >1μg/L on an oral glucose tolerance test.

### MRI Technique

MRI scans were performed with a 1.5 Tesla MRI unit (Siemens, Magnetom Avanto) using a 12-channel head coil.

For conventional MRI, coronal T2-weighted (T2W; repetition time [TR]: 2090 ms, echo time [TE]: 104 ms, slice thickness [ST]: 2.5 mm, field of view [FOV]: 180×180 mm, number of excitation [NEX]: 4, and matrix: 224×320), sagittal T1-weighted (T1W; TR: 350 ms, TE:10 ms, ST: 3 mm, FOV: 190×190 mm, NEX: 2, and matrix: 224×320), coronal T1W (TR: 300 ms, TE:10 ms, ST: 2.5 mm, FOV: 190×190 mm, NEX: 3, and matrix: 192×192) were used.

Dynamic contrast-enhanced MRI was performed after the administration of gadopentetate dimeglumine (0.1 mmol/kg) intravenously. After administering the contrast medium, coronal and sagittal T1W images were taken (TR: 448 ms, TE:10ms, ST: 3 mm, FOV: 190×190 mm, NEX: 2, and matrix: 224×320). Post-contrast T1W images were obtained in three phases at 40-s intervals.

### Image Analysis

Preoperative and pretreatment MRI scans were assessed by one radiologist and a four-year radiology resident. The mean and maximum signal intensities were measured using manually drawn region of interests (ROI) in two consecutive slices in T2W, pre-contrast T1W, and all three phases of DCE-MRI. The ROIs were placed onto (i) the largest solid portion of macroadenomas in all sequences; (ii) in the normal white and gray matters of the temporal lobe in a coronal T2W sequence; and (iii) in the normal white matter of the temporal lobe in pre and post-contrast T1W sequences (Figure 1A-E). The normal pituitary gland was not used for measurements because it is not visible in all patients due to large tumors. The semi-quantitative values of DCE-MRI were calculated from formulas defined in Table I and Figure 2. Based on the measurements, relative T2W signal intensity (rSI) in the adenomas were grouped as follows: (i) hypointense (n=12), if the adenoma is equal or less than the mean signal intensity in the white matter; (ii) hyperintense (n=29), if it is equal or higher than the mean signal intensity in the gray matter; and (iii) isointense (n=14), if the mean signal intensity value is between the white and gray matters (13).

### Biochemical Response

The SSA treatment was initiated in patients with GH levels of >1 μg/l or elevated age-adjusted IGF-1 levels after the third month of surgery. Patients were considered resistant to SSA treatment when GH levels are >1 μg/l or elevated age-adjusted IGF levels after 6 months of octreotide (40 mg per 28 days) or lanreotide (120 mg per 28 days) therapy.

### Immunohistochemistry

Our reference standard was the official institutional immuno-histochemistry report. According to the staining characteristics using monoclonal cytokeratin antibody, the adenomas were
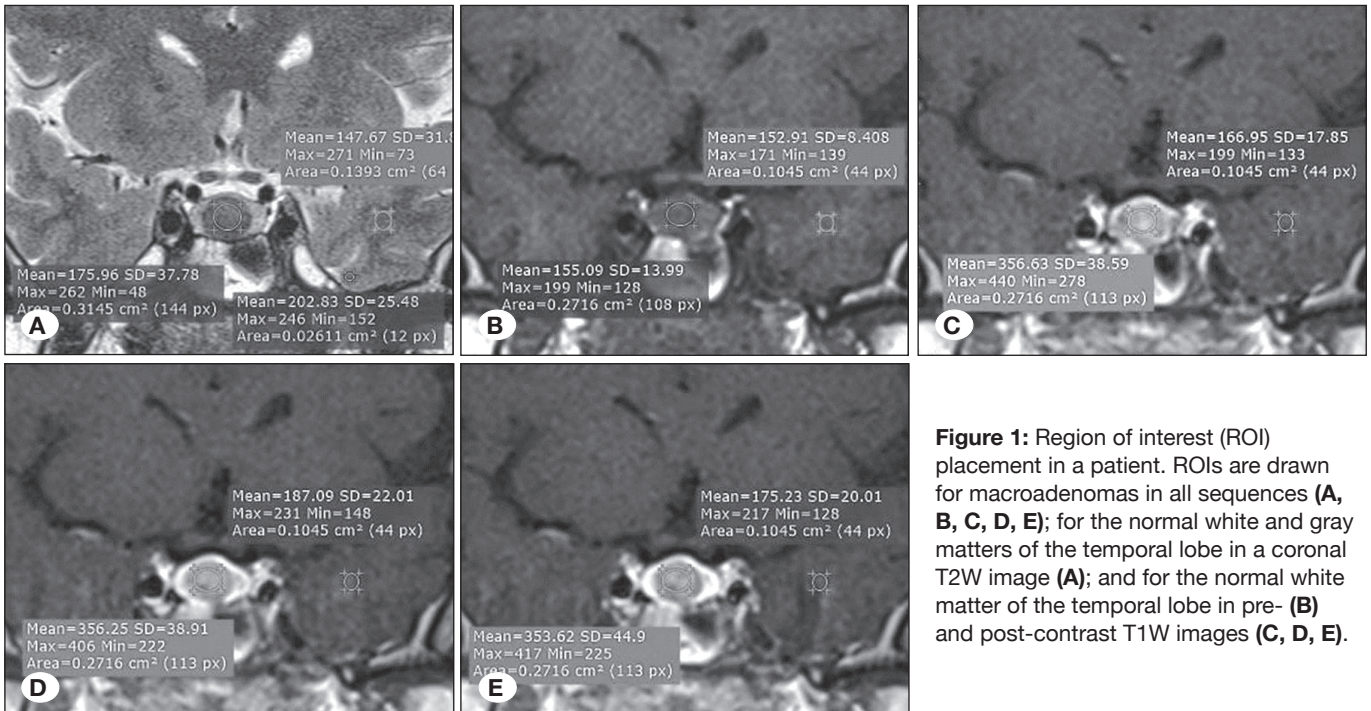
**Figure 1:** Region of interest (ROI) placement in a patient. ROIs are drawn for macroadenomas in all sequences **(A, B, C, D, E)**; for the normal white and gray matters of the temporal lobe in a coronal T2W image **(A)**; and for the normal white matter of the temporal lobe in pre- **(B)** and post-contrast T1W images **(C, D, E)**.
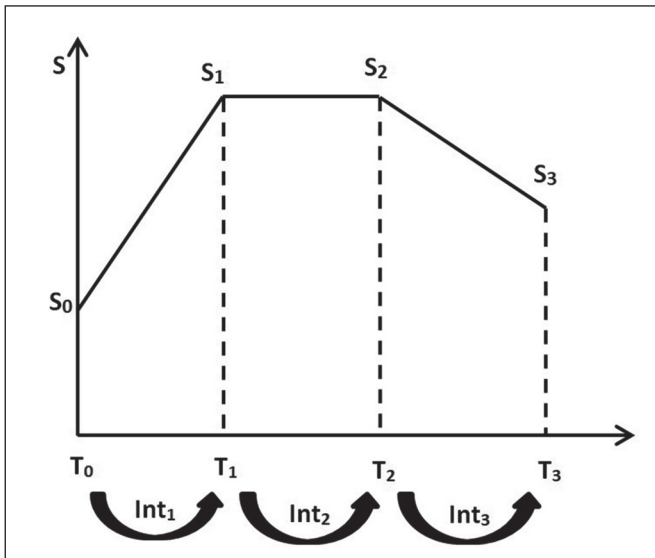


**Figure 2:** Simplified drawing showing a representative contrast-enhanced kinetics in pituitary DCE-MRI. **S**, signal intensity; $S_0$, pre-contrast signal intensity; $S_{1-2-3}$, signal intensity at the consecutive contrast-enhanced phases; $T_{0-1-2-3}$, timing of the phases; $Int_{1-2-3}$; time intervals between post-contrast phases.

divided into three groups as densely, transitional and sparsely granulated (24). For the following statistical classifications, the adenomas were then grouped as densely granulated and others (transitional and sparse).

### Statistical Analysis

MedCalc Statistical Software version 18 (MedCalc Software bvba, Ostend, Belgium) and SPSS version 20 (SPSS inc.,

Chicago, IL, USA) were used for data analysis. A *Chi-square test along with Phi (φ) coefficient (mean square contingency coefficient)* was performed in 24 patients who were not in biochemical remission at 3 months postoperatively to validate whether our patient population is consistent with the literature regarding the positive relationship between the responses to SSA treatment (or remission) and pathological dense granulation pattern. The analysis revealed the substantial relationship, p<0.05.

*Intra-class correlation (ICC) coefficient* was used to determine interobserver variability of ROI measurements. Only variables with ICC of>0.81 that represents very good to excellent agreement were included for further analyses. Consensus data were used for further analyses, which was the average of two consecutive measurements by both observers.

The *Kruskal–Wallis test* was used to analyze group differences between continuous variables based on the granulation pattern. The *Chi-square test* was used to identify group differences in proportions between categorical variables based on the granulation pattern.

To determine whether preoperative SSA treatment is associated with granulation pattern or not, *a Chi-square test* was used to test the homogeneity of granulation pattern between patients who underwent preoperative SSA treatment and those who directly underwent surgery. This was also further supported by the *rank-biserial correlation* analysis.

To create a predictive model for responses to preoperative SSA treatment using the granulation pattern (dense versus others), the multivariate analysis was conducted with *logistic regression*. All variables with p<0.10 in the bivariate analyses were included in the *logistic regression* analysis to ascertain

**Table I:** T2W MRI and DCE-MRI Parameters

| Parameter from T2W MRI | |
|---|---|
| rSIR T2 | $T2S_{adenoma}/T2S_{twm-tgm}$ |
| **Parameters from DCE-MRI** | |
| *First interval parameters:* | |
| ER1 | $S_1-S_0/S_0$ |
| Slope1 | $S_1-S_0/T_1-T_0$ |
| *Second interval parameters:* | |
| ER2 | $S_2-S_1/S_1$ |
| Slope2 | $S_2-S_1/T_2-T_1$ |
| *Third interval parameters:* | |
| ER3 | $S_3-S_2/S_2$ |
| Slope3 | $S_3-S_2/T_3-T_2$ |
| *Peak parameters:* | |
| $T_{peak}$ | Time point at which the signal intensity achieves its maximum value first |
| $rSIR_{peak}$ | $S_{peak}/S_{twm}$ |
| $ER_{peak}$ | $S_{peak}-S_0/S_0$ |
| $Slope_{peak}$ | $S_{peak}-S_0/T_{peak}$ |
| *Wash-out parameters* | |
| $ER_{wash}$ | $S_{peak}-S_3/S_{peak}$ |
| $Slope_{wash}$ | $S_{peak}-S_3/T_3-T_{peak}$ |

*Each parameter in the table was calculated using both mean and maximum signal intensity ratios.* ***rSIR,*** *relative signal intensity ratio;* ***ER,*** *enhancement ratio;* ***T2 S,*** *signal intensity in T2 weighted images;* ***TWM,*** *white matter of temporal lobe;* ***TGM,*** *temporal grey matter;* ***$S_0$,*** *initial signal intensity of the adenoma before contrast medium administration;* ***$S_1$,*** *signal intensity of the adenoma at the first post-contrast scan;* ***$S_2$,*** *signal intensity of the adenoma at the second post-contrast scan;* ***$S_3$,*** *signal intensity of the adenoma at the third post-contrast scan;* ***$T_1$,*** *time from the start of the contrast medium administration to the completion of the first scan (40sec);* ***$T_2$:*** *time from the start of the contrast medium administration to the completion of the second scan (80sec);* ***$T_3$,*** *time from the start of the contrast medium administration to the completion of the third scan (120sec).*

their possible effects on the likelihood that participants respond to the preoperative SSA treatment. An *automatic stepwise selection* method in combination with forward selection and backward elimination was used to create the final model.

Receiver operating characteristic (ROC) curve was plotted to determine cut-off values for the predictive variables (for each one and then combined) obtained in the *logistic regression* model. *Youden indices* were calculated and used to determine

the optimal cut-off values of diagnostic accuracy parameters. Furthermore, pairwise comparisons of ROC curves were also performed in order to further assess and compare the possible predictive contributions of parameters and final model.

A p<0.05 indicated statistical significance for all of the above-mentioned tests in all data analysis levels.

■ **RESULTS**

A total of 55 patients were included in the study, with the mean age of 39.8 (min-max, 19–65) years, female-to-male ratio of 36/19, and mean tumor volume of 3287 mm³ (median, 1389.1 mm³; 25th–75th percentile, 738.6–4673.7 mm³). The mean GH and IGF-1 levels and IGF-1 ratio (IGF-1/age-adjusted upper limit of normal IGF-1 level) were 24.2 µg/l (median, 24.2 µg/l; 25th–75th percentile, 6.7–33.8 µg/l), 814.8 mmol/l (median, 814.8 mmol/l; 25th–75th percentile, 671.3–945 mmol/l), and 3 (median, 2.7; 25th–75th percentile, 2.3–3.4), respectively. Among the 55 adenomas, 30 (54.5%) were classified as sparsely, 9 (16.4%) as transitional, and 16 (29.1%) as densely depending on the granulation pattern.

The ICC coefficients for the mean and maximum signal intensities measured in non-enhanced T1W and DCE-MRI images ranged between 0.91 and 1. In T2W images, ICC coefficients for maximum signal intensities measured from white and gray matters ranged between 0.81 and 0.90. Conversely, other measurements on T2W images were within the range of 0.91 to 1. Because both readers had very good to excellent agreement (ICC coefficient of >0.81), all of the signal intensity measurements were included in calculating the parameters presented in Table I.

As assessed using the *Chi-square test*, the granulation pattern distribution between the patients preoperatively treated with SSA (n=19) and those directly operated was not significantly different, $\chi2(2)=0.726$, (p=0.696). This was also supported by the *rank-biserial correlation* analysis, $r_{rb}(53)=-0.0174$, (p=0.899).

No statistically significant difference was found in gender distribution $\chi2(2)=1.813$, (p=0.404), tumor volume (p=0.365), IGF-1 level (p=0.391), and IGF-1 ratio (p=0.05) between the three granulation groups. A statistically significant difference was found in age (p=0.036) and GH level (p=0.040) between the groups. In pairwise comparisons, no statistically significant difference was noted in age between the pairs (p>0.05). Conversely, GH level differences between sparse and transitional groups were statistically significant (p=0.036). Regarding the parameters calculated from the T2W data, a statistically significant difference was observed in T2W intensity of adenomas, $\chi2(4)=15.794$, (p=0.003). Figure 3 shows the frequency chart for T2W intensity of adenomas based on the granulation pattern for pairwise comparisons. With regard to the dynamic contrast-enhanced T1W image data, the parameter of enhancement ratio in the second interval ($ER2_{max}$) was statistically significantly different between the groups (p=0.035). In pairwise comparisons, differences in $ER2_{max}$ between transitional and dense groups were also statistically significant (p=0.038).

**Table II:** Results from Logistic Regression Analysis

| Variables | Coefficient | Std. Error | Wald | Odds ratio | 95% CI | p |
|---|---|---|---|---|---|---|
| Age | 0.075877 | 0.038438 | 3.8967 | 1.0788 | 1.0005 to 1.1632 | **0.0484** |
| T2 hypointensity | 2.73775 | 0.87754 | 9.7333 | 15.4522 | 2.7670 to 86.2910 | **0.0018** |
| $ER2_{maximum}$ | 7.69428 | 3.40359 | 5.1105 | 2195.7423 | 2.7822 to 1732895.4206 | **0.0238** |
| Constant | -5.47751 | 1.85802 | 8.6909 | - | - | **0.0032** |

The following ten variables were included in the multivariate analysis: age (p=0.036), GH level (p=0.040), IGF-1 ratio (p=0.05), T2W intensity of the adenoma (p=0.003), $rSIR-T2_{mean}$ (p=0.054), $rSIR-T2_{max}$ (p=0.056), $ER2_{max}$ (p=0.035), $Slope2_{max}$ (p=0.078), $ER3_{mean}$ (p=0.069), and $Slope3_{mean}$ (p=0.059). The final *logistic regression* model was statistically significant, $\chi2$ (3)=23.278, p<0.0001. The model explained 49.2% (*Nagelkerke R2*) of the variance in granulation pattern and correctly classified 85.45% of cases. The model's sensitivity, specificity, positive predictive value, and negative predictive value were 68.75%, 92.31%, 78.58%, and 87.8%, respectively. Among the ten predictor variables, only three were statistically significant: age, T2W-hypointensity of the adenoma, and $ER2_{max}$. Increasing age (odds ratio [OR]=1.08; 95% confidence interval [CI]=1.0005–1.1632), having T2W-hypointensity in the adenomas (OR=15.45; 95%CI=2.76–86.29), and higher $ER2_{max}$ (OR=2195.74; 95%CI=2.78–1732895.42) were associated with an increased likelihood of dense granulation that indicates better response to the SSA treatment. Table II presents the results of the *logistic regression* analysis. Table III shows the cut-off values determined using *Youden indices* and its relevant diagnostic parameters in detail. Figure 4 presents the *ROC curves* of age, $ER2_{max}$, T2W-hypointensity of the adenomas, and the final *logistic regression* model. The area under the curve (AUC) of the model was 0.880 (p<0.0001). Pairwise comparison of *ROC curves* revealed statistically significant differences between *(i)* age and *logistic regression* model (difference between AUC=0.159 [95%CI=0.027–0.0292], p=0.018) and *(ii)* T2W-hypointensity and *logistic regression* model (difference between AUC=0.167 [95%CI=0.005–0.330], p=0.431). No statistically significant difference was observed between the $ER2_{max}$ and *logistic regression* model (difference between AUC=0.184 [95%CI=0.001–0.370], p=0.051), indicating that $ER2_{max}$ alone can potentially predict the response to SSA treatment with a performance as high as the model does.

■ **DISCUSSION**

The main finding in this study is a semi-quantitative evaluation of DCE-MRI as the additive value to T2W signal intensity evaluation in predicting the response to SSA treatment in patients with acromegaly. The model created using the T2W hypointensity of the adenoma, $ER2_{max}$ parameter, and patient's age together may predict the granulation pattern of GH-secreting adenomas with rather high overall accuracy.

Current literature indicates that in acromegaly patients with macroadenoma (>10 mm), preoperative SSA treatment
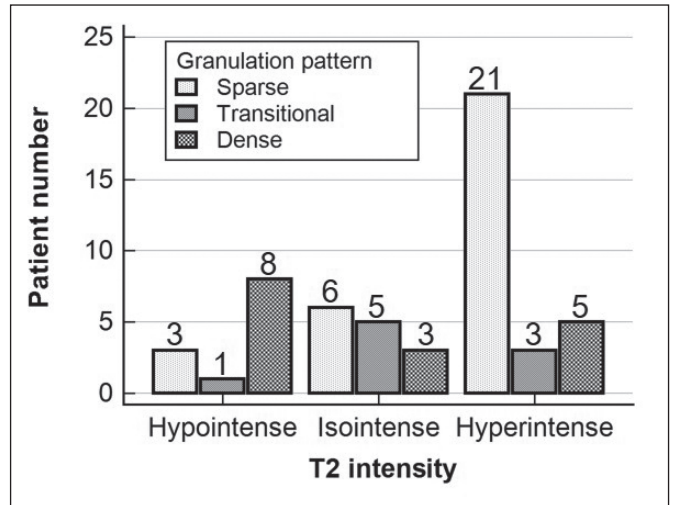


**Figure 3:** Frequency chart for T2W intensity of the adenoma based on the granulation pattern.
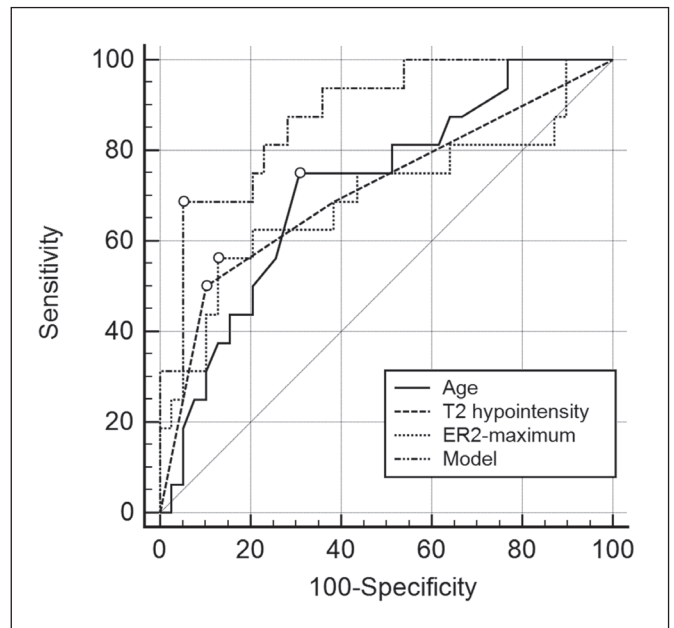


**Figure 4:** Receiver operating characteristic (ROC) curves of age, $ER2_{max}$, T2W-hypointensity of the adenomas, and the final logistic regression model.

**Table III:** Data from Receivers Operating Characteristic (ROC) Curve Analyses

| Variables | AUC | 95% CI | p | Cut-off* | Youden Index | SEN | 95% CI | SPE | 95% CI | PLR | 95% CI | NLR | 95% CI | PPV | 95% CI | NPV | 95% CI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age | 0.720 | 0.583 to 0.833 | 0.0035 | >43 | 0.4423 | 75.00 | 47.6 - 92.7 | 69.23 | 52.4 - 83.0 | 2.44 | 1.4 - 4.2 | 0.36 | 0.2 - 0.9 | 50.0 | 36.6 - 63.4 | 87.1 | 73.8 - 94.2 |
| T2 hypointensity | 0.712 | 0.574 to 0.826 | 0.0073 | ≤1 | 0.3974 | 50.00 | 24.7 - 75.3 | 89.74 | 75.8 - 97.1 | 4.88 | 1.7 - 13.9 | 0.56 | 0.3 - 0.9 | 66.7 | 41.2 - 85.1 | 81.4 | 72.6 - 87.8 |
| ER2$_{max}$ | 0.696 | 0.557 to 0.812 | 0.0310 | >0.091 | 0.4343 | 56.25 | 29.9 - 80.2 | 87.18 | 72.6 - 95.7 | 4.39 | 1.7 - 11.1 | 0.50 | 0.3 - 0.9 | 64.3 | 41.6 - 82.0 | 82.9 | 73.3 - 89.6 |
| Model | 0.880 | 0.764 to 0.952 | <0.0001 | >0.534 | 0.6362 | 68.75 | 41.3 - 89.0 | 94.87 | 82.7 - 99.4 | 13.41 | 3.3 - 53.8 | 0.33 | 0.2 - 0.7 | 84.6 | 57.8 - 95.7 | 88.1 | 78.1 - 93.9 |

*ER2$_{max}$: Enhancement ratio within the second interval of the DCE-MRI based on the maximum signal intensity measured, **Model:** Statistically significant final logistic regression model, **AUC:** Area under the curve, **CI:** Confidence interval, **SEN:** Sensitivity, **SPE:** Specificity, **PLR:** Positive likelihood ratio, **NLR:** Negative likelihood ratio, **PPV:** Positive predictive value, **NPV:** Negative predictive value.*

improves the surgical outcomes (2,5,19,28). Response to SSA treatment is highly variable among patients with acromegaly. Some patients respond quite well to SSA treatment with a full biochemical remission and reduction of tumor volume (1,6,18,23). In contrast, some patients are resistant to SSA treatment, which may delay the surgery and deteriorate surgical outcomes. For this reason, creating and developing the preoperative predictive models for the response to SSA treatment is of supreme importance because they may guide the treatment strategy and improve patients' prognosis. Although all evidential data is based on histological variables obtained from surgically resected adenomas, MRI, particularly the T2W sequence, appears to be a potential tool in predicting the preoperative response to SSAs (11,12,25,26,29). To the best of our knowledge, no other study evaluated GH-secreting macroadenomas with the dynamic enhancement characteristics.

Pituitary adenoma subtypes demonstrate various vascular features. Guo et al. evaluated the DCE-MRI value to differentiate ACTH-secreting pituitary adenomas from non-functioning adenomas. In that study, they measured the enhancement time, enhancement peak, and pre-peak slope (PPS), which showed that the PPS of ACTH-secreting pituitary adenomas were statistically significantly lower than that of non-functioning adenomas (10). Romano et al. evaluated the differences in areas of consistency in macroadenomas. Their results proved that DCE-MRI can distinguish macroadenoma's consistency with good accuracy (27). In our study, DCE-MRI was semi-quantitatively assessed with additional kinetic features such as mean or maximum enhancement ratios for each interval. Nonetheless, one (ER2$_{max}$) of these additional kinetic features was included in the final multivariate logistic model. Although it is unclear, the interval kinetic parameter (ER2$_{max}$) may signify subtle differences in vascular kinetics of adenomas. Continued efforts are needed to validate these features.

In our study, T2W-hypointense macroadenomas are significantly associated with a dense granulation pattern consistent with previous studies, indicating better responses to preoperative SSA treatment. Hagiwara et al. demonstrated T2W hyperintensity is shown to be more frequently found in sparsely granulated adenomas than densely granulated (11). Several studies in the literature assessed the relationship between preoperative use of SSA and T2W signal intensity of adenomas (13,26).

In three studies, T2W signal intensity has been quantitatively evaluated. The lower signal intensity values in T2W images were correlated with higher decrease in GH and IGF-1 levels in patients with SSA treatment (12,25,29). Although the threshold of T2W signal intensity ratio to predict response to SSA treatment was measured in two different studies, these values cannot be compared due to different tissues used as reference. One of these studies did not reveal any differences in T2W signal intensity of adenomas when evaluated quantitatively or qualitatively (12).

In this study, the granulation pattern and patient's age were statistically significant in both bivariate and multivariate

analyses. Increasing age is found to be associated with dense granulation pattern, indicating that older patients respond better to SSA treatment than younger ones. This finding is also concordant with studies in the literature (29).

A number of important limitations should be considered. First, during the evaluation of response to SSA treatment, the granulation pattern was used as the reference, which may be a limitation instead of biochemical remission criteria. However, in successfully operated patients without residual tumor, biochemical remission is an expected outcome; therefore, it would not be possible to evaluate the response of SSA treatment. Therefore, the biochemical response status was correlated with the granulation pattern in 24 patients who were not in biochemical remission at 3 months postoperatively. Current literature also involves studies that demonstrate the relationship between better response to SSA treatment and dense granulation pattern (4). Second, the pituitary DCE-MRI protocol in our center includes three post-contrast phases. Using different protocols might provide new valuable parameters. Third, all patients were included regardless of their preoperative SSA treatment history. To assess whether the granulation pattern changes after the therapy or not, the distribution of granulation pattern was assessed and found no statistically significant difference between patients treated and untreated with SSA treatment preoperatively. In the literature, as far as we know, only one study analyzed the granulation pattern distribution in a few patients with available adenoma tissue from surgeries before and after SSA treatment (9). Their findings were consistent with those of our study. Fourth, a Bonferroni correction for multivariate analysis was not performed considering the potential risk of Type II error. Finally, our hospital is a referral center for pituitary surgery, although many patients had follow-up data, those who underwent MRI in different centers, with microadenomas or pure cystic adenomas, with hemorrhagic adenomas, diagnosed with pituitary apoplexy, without pure GH-secreting adenomas, and with incomplete immunohistochemically staining adenomas were excluded. Therefore, the number of included patients is rather small.

### ■ CONCLUSION

Our study demonstrated that the model created based on the relative T2W signal intensity, patient's age, and $ER2_{max}$ parameters from DCE-MRI sequences might be used to more accurately predict SSA responses in patients with newly diagnosed acromegaly.

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