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Machine Learning Model Using Radiomics and Clinical Parameters for the Diagnosis of Growth Hormone Deficiency

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Growth hormone deficiency (GHD) and idiopathic short stature (ISS) are the two most prevalent etiologies of pathological short stature in children. Differentiating GHD from ISS is clinically critical, as GHD is associated with significant metabolic complications—including dyslipidemia, impaired glucose metabolism, and reduced bone mineral density—and necessitates recombinant GH therapy. Currently, the gold standard for diagnosis is the GH provocation test, which requires pharmacological stimulation with at least two agents and repeated blood sampling. However, this test carries substantial limitations: an arbitrary peak GH cutoff of 10 ng/mL, poor reproducibility, and considerable invasiveness and burden for pediatric patients. Sella MRI is routinely performed to exclude structural pituitary abnormalities in GHD workup, yet conventional visual assessment cannot evaluate hormonal secretion. We hypothesized that radiomics—a technique extracting quantitative features from medical images invisible to the naked eye—could provide additional diagnostic information from normal-appearing sella MRI when combined with clinical parameters.
In this cross-sectional, multicenter study, 293 children with short stature and normal sella MRI from Severance Hospital were enrolled in the training set, and 47 children from Yongin Severance Hospital constituted the external validation set. All participants underwent GH provocation testing as the reference standard. A total of 186 radiomic features—encompassing shape, first-order, GLCM, GLRLM, GLSZM, and NGTDM features—were extracted from T2-weighted and contrast-enhanced T1-weighted sella MRI following semi-automatic pituitary gland segmentation with N4 bias correction and resampling. Clinical parameters included auxological data (height SDS, weight SDS, BMI SDS, growth velocity), IGF-I SDS, IGFBP-3 SDS, bone age, and chronological age minus bone age (CA-BA). Three XGBoost-based models were developed: a clinical model, a radiomics model, and a combined model. Model performance was assessed by the area under the receiver operating characteristic curve (AUC), and feature importance was evaluated using SHAP (Shapley Additive Explanations) analysis.

In external validation, the AUCs of the clinical, radiomics, and combined models were 0.684 (95% CI 0.590–0.778), 0.691 (0.620–0.762), and 0.830 (0.741–0.919), respectively. The combined model significantly outperformed both the clinical model ($p=0.034$) and the radiomics model ($p=0.019$). SHAP analysis identified BMI SDS and CA-BA as the top clinical predictors, while Maximum Probability and Run Length Nonuniformity Normalized from T2-weighted images were the leading radiomic contributors, reflecting pituitary gland texture heterogeneity undetectable by visual inspection. In conclusion, integrating sella MRI-based radiomics with clinical parameters significantly improves GHD prediction accuracy over either approach alone. This model demonstrates the potential of machine learning as a non-invasive screening tool to support clinical decision-making prior to GH provocation testing, and highlights an underexplored role of quantitative MRI analysis in pediatric endocrinology.

Keywords: *Radiomics, Growth hormone deficiency, Idiopathic short stature, Child*