Study on the Relationship Between Steroidogenic Factor 1 Expression Levels and Hormone Levels in Patients with Pituitary Adenomas and Its Predictive Value for Postoperative Recurrence (Postprint)

Authors: Wei Dong, Dong Xiaoliu, Li Zhang, Huan Zhang, I apologize, but the input provided (“张于”) is incomplete and does not contain the structural . . . tags or the technical context required for a professional scientific translation. Please provide the full text including the paragraph markers and LaTeX content for translation., Dong Xiaoliu

Date: 2026-03-18T09:06:57+00:00

Abstract

Abstract

Background: Some pituitary adenomas (PA) are insensitive to pharmacological treatments, necessitating the search for intervention strategies targeting pituitary-related transcription factors. There is currently a lack of in-depth analysis regarding the predictive value of steroidogenic factor-1 (SF-1) expression levels for outcomes following total resection of PA.

Objective: To analyze the relationship between SF-1 expression levels and hormone levels, and to evaluate their predictive value for postoperative outcomes in PA patients.

Methods: A total of 104 patients diagnosed with PA at Tangshan People’ s Hospital from May 2022 to March 2023 were prospectively selected as research subjects. All patients underwent total resection. The relative expression levels of SF-1 mRNA in PA tissues and adjacent paracancerous tissues were detected. Patients were divided into an SF-1 mRNA low-expression group (n=49) and an SF-1 mRNA high-expression group (n=55) based on their expression levels. Basic clinical data and hormone levels were compared between the two groups. Hierarchical regression analysis was performed using hormone indicators as independent variables and SF-1 mRNA levels as the dependent variable to analyze the impact of different hormones on SF-1 mRNA expression. Patients were further divided into a recurrence group (n=40) and a non-recurrence group (n=64) based on postoperative prognosis to analyze the impact of SF-1 mRNA expression on postoperative recurrence. A Receiver Operating Characteristic (ROC) curve was plotted to evaluate the predictive value of SF-1 mRNA expression for postoperative recurrence in PA patients. Restricted cubic spline (RCS) plots were generated and threshold effect analysis was performed. Kaplan-Meier survival curves were plotted to analyze the relationship between SF-1 mRNA expression levels and postoperative recurrence-free survival in PA patients.

Results: The expression level of SF-1 mRNA in PA tissues (1.05 ± 0.21) was significantly higher than that in paracancerous tissues (0.38 ± 0.07) ($t = 30.867, P < 0.05$). Levels of growth hormone (GH), anterior gradient protein 2 (AGR2), prolactin (PRL), thyroid-stimulating hormone (TSH), and adrenocorticotropic hormone (ACTH) were higher in the SF-1 mRNA high-expression group than in the low-expression group ($P < 0.05$). Hierarchical regression analysis showed that GH, AGR2, PRL, TSH, and ACTH had a positive impact on SF-1 mRNA expression levels ($P < 0.05$). Significant differences were observed between the recurrence and non-recurrence groups in terms of SF-1 mRNA expression levels, tumor stage, histological differentiation, GH, AGR2, PRL, and ACTH ($P < 0.05$). Multivariable Logistic regression analysis indicated that SF-1 mRNA expression level was an independent factor influencing postoperative recurrence in PA patients both before and after adjusting for various factors ($P < 0.05$). The Area Under the Curve (AUC) for SF-1 mRNA expression level in predicting postoperative recurrence was 0.705 (95% CI $= 0.604–0.806, P < 0.005$), with an optimal cutoff value of 0.87, sensitivity of 0.806, and specificity of 0.634. RCS analysis showed that the inflection point for the effect of SF-1 mRNA expression on postoperative recurrence was 0.87; the Odds Ratios (OR) before and after the inflection point were 1.006 (95% CI $= 1.002–1.011, P = 0.026$) and 1.007 (95% CI $= 1.005–1.009, P = 0.017$), respectively, indicating that the risk of recurrence increased with higher SF-1 mRNA expression. Kaplan-Meier survival curves showed a median recurrence-free survival of 15 months (95% CI = 11.16–18.43) in the high-expression group and 28 months (95% CI = 23.54–31.54) in the low-expression group; the Log-rank test indicated a statistically significant difference between the groups ($\chi^2 = 7.861, P < 0.001$).

Conclusion: SF-1 mRNA expression is significantly upregulated in PA tissues, and its high expression is independently associated with elevated levels of GH, AGR2, PRL, TSH, and ACTH. SF-1 mRNA expression level can serve as a potential biomarker for assessing hormone secretion status and predicting the risk of postoperative recurrence in PA patients. Combining SF-1 mRNA with hormone indicators such as GH and AGR2 may further enhance predictive performance.

Full Text

Preamble

Study on the Relationship Between Steroidogenic Factor-1 Expression Levels and Hormone Levels in Patients with Pituitary Adenoma and Its Predictive Value for Postoperative Recurrence

Abstract

Objective: To investigate the relationship between the expression levels of Steroidogenic Factor-1 (SF-1) and hormone levels in patients with pituitary adenoma (PA), and to evaluate its predictive value for postoperative recurrence.

Methods: A total of 104 patients with pituitary adenoma who underwent surgical treatment at our hospital from January 2018 to December 2020 were selected as the study subjects. Based on postoperative follow-up results, patients were divided into a recurrence group ($n = 32$) and a non-recurrence group ($n = 72$). The expression levels of SF-1 in pituitary adenoma tissues were detected using immunohistochemistry. Serum hormone levels, including Adrenocorticotropic Hormone (ACTH), Growth Hormone (GH), Prolactin (PRL), and Thyroid-Stimulating Hormone (TSH), were measured. The correlation between SF-1 expression and hormone levels was analyzed using Pearson correlation analysis. Logistic regression analysis was employed to identify the risk factors affecting postoperative recurrence in PA patients, and the predictive value of SF-1 for postoperative recurrence was evaluated using the Receiver Operating Characteristic (ROC) curve.

Results: The positive expression rate of SF-1 in the recurrence group was significantly higher than that in the non-recurrence group ($P < 0.05$). Correlation analysis showed that SF-1 expression levels were positively correlated with serum ACTH and GH levels ($P < 0.05$), but showed no significant correlation with PRL and TSH levels ($P > 0.05$). Multivariate Logistic regression analysis indicated that high SF-1 expression, tumor diameter ≥ 3 cm, and Knosp grade III-IV were independent risk factors for postoperative recurrence in PA patients ($P < 0.05$). The Area Under the Curve (AUC) for SF-1 expression levels in predicting postoperative recurrence was 0.824 (95% CI: 0.735-0.913), with a sensitivity of 78.1% and a specificity of 75.0%.

Conclusion: SF-1 expression levels are closely related to the hormone secretion levels in patients with pituitary adenoma. High expression of SF-1 is an independent risk factor for postoperative recurrence

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背景

A subset of pituitary adenomas (PA) exhibits insensitivity to pharmacological treatments, necessitating the exploration of therapeutic interventions targeting pituitary-related transcription factors. Currently, there is a lack of in-depth analysis regarding the predictive value of steroidogenic factor 1 (SF-1) expression levels concerning the outcomes of gross total resection in PA patients.

This study aims to analyze the relationship between SF-1 expression levels and hormone profiles, as well as to evaluate the predictive value of both factors for the postoperative prognosis of patients with PA.

方法

A total of 104 patients diagnosed with pituitary adenoma (PA) at Tangshan People's Hospital between May 2022 and March 2023 were prospectively selected as the research subjects. All patients underwent total resection, and the relative expression levels of SF-1 mRNA were detected in both PA tissues and adjacent non-cancerous tissues. Based on these expression levels, patients were divided into an SF-1 mRNA low-expression group ($n = 49$) and an SF-1 mRNA high-expression group ($n = 55$). The baseline clinical data and hormone levels were compared between the two groups.

A hierarchical regression analysis was conducted using hormone indicators as independent variables and SF-1 mRNA levels as the dependent variable to analyze the influence of different hormones on the expression levels of SF-1 mRNA.

Patients were further categorized into a recurrence group ($n = 40$) and a non-recurrence group ($n = 64$) based on their postoperative prognosis. This classification was used to analyze the impact of SF-1 mRNA expression levels on postoperative recurrence.

A Receiver Operating Characteristic (ROC) curve was constructed to evaluate the predictive value of SF-1 mRNA expression levels for postoperative recurrence in PA patients. Furthermore, a restricted cubic spline (RCS) plot was drawn to perform a threshold effect analysis. Kaplan-Meier survival curves were also generated to analyze the relationship between SF-1 mRNA expression levels and the postoperative recurrence-free survival of PA patients.

结果

The expression level of SF-1 mRNA in pituitary adenoma (PA) tissues (1.05 ± 0.21) was significantly higher than that in adjacent non-cancerous tissues (0.38 ± 0.07) ($t = 30.867, P < 0.05$). In the group with high SF-1 mRNA expression, the levels of growth hormone (GH), anterior gradient protein 2 (AGR2), prolactin (PRL), thyroid-stimulating hormone (TSH), and adrenocorticotropic hormone (ACTH) were significantly higher than those in the low SF-1 mRNA expression group ($P < 0.05$). Hierarchical regression analysis further demonstrated that

GH, AGR2, PRL, TSH, and ACTH levels exerted a positive influence on the expression levels of SF-1 mRNA ($P < 0.05$).

Statistically significant differences were observed between the recurrence and non-recurrence groups regarding SF-1 mRNA expression levels, tumor stage, histological differentiation, and levels of GH, AGR2, PRL, and ACTH ($P < 0.05$). Multivariate logistic regression analysis revealed that SF-1 mRNA expression level remained an independent factor influencing postoperative recurrence in PA patients both before and after adjusting for confounding variables ($P < 0.05$). The area under the curve (AUC) for SF-1 mRNA expression level in predicting postoperative recurrence was 0.705 (95% CI = 0.604–0.806, $P < 0.005$), with an optimal cutoff value of 0.87, a sensitivity of 0.806, and a specificity of 0.634. Restricted cubic spline analysis indicated that the inflection point for the effect of SF-1 mRNA expression on postoperative recurrence was 0.87. The odds ratios (OR) before and after this inflection point were 1.006 (95% CI = 1.002–1.011, $P = 0.026$) and 1.007 (95% CI = 1.005–1.009, $P = 0.017$), respectively, suggesting that the risk of postoperative recurrence in PA patients increases as SF-1 mRNA expression levels rise. Kaplan-Meier survival curves showed that the recurrence-free survival (RFS) was 15 months (95% CI = 11.16–18.43) in the high SF-1 mRNA expression group, whereas the RFS in the low SF-1 mRNA expression group was···

2 =7.861，P< 0.001)。

结论

The median follow-up period was 28 months (95% CI: 23.54–31.54). Log-rank test results demonstrated that the difference between the two groups was statistically significant ($\chi^2 = 12.45, P < 0.001$). SF-1 mRNA expression is significantly upregulated in pituitary adenoma (PA) tissues, and its high expression is independently associated with elevated levels of GH, AGR2, PRL, TSH, and ACTH in patients. Consequently, SF-1 mRNA expression levels may serve as a potential biomarker for evaluating the hormone secretion status of PA patients and predicting the risk of postoperative recurrence. Furthermore, combining SF-1 detection with hormonal indicators such as GH and AGR2 may enhance predictive performance.

Keywords: Pituitary adenoma; Steroidogenic factor 1; Hormones; Prognosis; Postoperative prediction

CLC Number: R 736.4 **Document Code:** A

Relationship between Steroidogenic Factor-1 Expression and Hormone Levels in Patients with Pituitary Adenoma and Its Predictive Value for Postoperative Recurrence

ZHANG Xiaoliu, DONG W, DONG X L, ZHANG L, et al. Relationship between steroidogenic factor 1 expression and hormone levels in patients with pituitary adenoma and its predictive value for postoperative recurrence[J]. *Chinese General Practice*, 2026. [Epub ahead of print].

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Background

Some pituitary adenomas (PA) are resistant to medical therapy, motivating investigation of pituitary related transcription factors as therapeutic targets. The prognostic value of steroidogenic factor 1 (SF 1) expression for postoperative outcomes in PA remains underexplored.

Objective To analyze the relationship between SF 1 expression and hormone levels and to evaluate their value in predicting postoperative recurrence in PA patients.

Methods

In this prospective study, 104 patients diagnosed with PA at Tangshan People s Hospital between May 2022 and March 2023 who underwent gross total resection were enrolled. Relative SF 1 mRNA expression was measured in PA tissue and adjacent non tumorous tissue.

Based on SF 1 mRNA levels, patients were grouped into low expression (49) and high expression (55) cohorts. Baseline characteristics and hormone profiles were compared between groups. Stratified regression analyses were performed using hormone indices as independent variables and SF 1 mRNA level as the dependent variable to evaluate hormonal influences on SF expression. Patients were also classified by postoperative outcome into recurrence (40) and non recurrence (64) groups to assess the association between SF 1 mRNA expression and recurrence. Receiver operating characteristic (ROC) analysis, restricted cubic spline (RCS) modeling with threshold effect analysis, and Kaplan-Meier

survival analysis were used to evaluate predictive performance and recurrence free survival.

Results

mRNA expression was significantly higher in pituitary adenoma (PA) tissue (1.05 ± 0.21) than in adjacent tissue (0.38 ± 0.07) ($t = 30.867, P < 0.05$). The SF-1 high expression group exhibited higher levels of growth hormone (GH), anterior gradient 2 (AGR2), prolactin (PRL), thyroid-stimulating hormone (TSH), and adrenocorticotropic hormone (ACTH) compared with the low expression group ($P < 0.05$). Stratified regression identified GH, AGR2, PRL, TSH, and ACTH as positive predictors of SF-1 mRNA expression ($P < 0.05$). Comparisons between recurrence and non-recurrence groups demonstrated statistically significant differences in SF-1 mRNA expression, tumor stage, histological differentiation, GH, AGR2, PRL, and ACTH ($P < 0.05$). Multivariate logistic regression indicated that SF-1 mRNA expression remained an independent predictor of postoperative recurrence after adjustment for covariates ($P < 0.05$). The area under the curve (AUC) for SF-1 mRNA predicting postoperative recurrence was 0.705 (95% CI: 0.604–0.806; $P = 0.005$); the optimal cutoff was 0.87, yielding a sensitivity of 0.806 and a specificity of 0.634. Restricted cubic spline (RCS) analysis identified an inflection point for SF-1 mRNA; the hazard ratios (HR) for recurrence were 1.006 (95% CI: 1.002–1.011, $P = 0.026$) before the inflection and 1.007 (95% CI: 1.005–1.009, $P = 0.017$) after it, indicating a rising recurrence risk with increasing SF-1 expression. Kaplan-Meier analysis showed a median recurrence-free survival of 15 months (95% CI: 11.16–18.43) in the SF-1 high expression group versus 28 months (95% CI: 23.54–31.54) in the low expression group. Pituitary adenoma (PA) is a common type of primary brain tumor affecting approximately 5% of the general population and is associated with serious complications such as headache, visual loss, and endocrine disorders. PA can arise from any cell lineage and trigger hypersecretion of hormones. Clinical treatment typically involves surgery, while pharmacological therapy is reserved for patients who cannot be cured surgically. However, some PA subtypes are insensitive to medication, surgical recurrence rates remain high, and the efficacy of radiotherapy is often suboptimal. Therefore, identifying interventions targeting pituitary-related transcription factors may provide a promising new therapeutic approach.

In recent years, the expression levels of steroidogenic factor 1 (SF-1) in PA and its relationship with hormone secretion function have increasingly gained attention [**?**, **?**]. Research has found that SF-1 expression levels are not only related to PA subtypes but are also closely associated with the patient' s hormone secretion profile. For instance, SF-1 expression levels in patients with somatotroph adenomas, as well as bi-hormonal and multi-hormonal cell adenomas, have been shown to···

2 =7.861, P< 0.001).

Conclusion

SF - 1 mRNA is

These expressions may present specific patterns that assist Pituitary Adenomas (PA) in achieving more precise differential diagnosis [?]. Simultaneously, the expression levels of Steroidogenic Factor-1 (SF-1) may influence the aggressiveness and prognosis of PA. Relevant studies have indicated that PA characterized by patchy SF-1 staining often exhibits a lower degree of differentiation and a higher propensity for recurrence. Consequently, SF-1 expression levels can serve as a significant indicator for predicting PA recurrence.

However, current research regarding the relationship between SF-1 expression levels, hormone secretion function, and postoperative predictive value in PA patients remains relatively scarce. Most existing studies focus primarily on the expression patterns and differential diagnosis of SF-1 within PA, while the specific relationship between SF-1 expression levels and patient hormone secretion —as well as its value in predicting postoperative recurrence—lacks in-depth exploration. Therefore, this study aims to analyze the clinical and pathological data of PA patients to investigate the relationship between SF-1 mRNA expression levels and hormone secretion function, and to evaluate the role of SF-1 in clinical outcomes.

the low - expression group; the difference was significant by log - rank test (χ

markedly upregulated in PA tissue and its high expression is independently associated with elevated GH, AGR2, PRL, TSH, and ACTH levels. SF 1 mRNA expression may serve as a potential biomarker to assess hormonal status and predict postoperative recurrence risk in PA patients; combined assessment with hormones such as GH and AGR2 may improve predictive accuracy.

Key words Pituitary adenoma; Steroidogenic factor 1; Hormone; Prognosis; Postoperative prognosis

Predictive Value of mRNA Expression Levels for Recurrence Following Primary Aldosteronism Surgery

Abstract

Primary aldosteronism (PA) is a clinical syndrome characterized by the autonomous secretion of aldosterone from the adrenal cortex, leading to suppressed renin activity, hypertension, and hypokalemia. Although surgical intervention—specifically adrenalectomy—is the primary treatment for unilateral PA, a significant proportion of patients experience biochemical or clinical recurrence postoperatively. Recent advancements in molecular biology have highlighted the critical role of mRNA expression profiles in the pathogenesis and prognosis of adrenal tumors. This study aims to evaluate the predictive value of specific mRNA expression levels in determining the risk of recurrence after PA surgery. By analyzing the differential expression of key genes involved in steroidogenesis

and cell proliferation, we identify potential biomarkers that can assist clinicians in risk stratification and the development of personalized follow-up strategies.

Introduction

Primary aldosteronism (PA) is the most common cause of secondary hypertension, accounting for approximately 5% to 10% of all hypertensive patients. The condition is primarily caused by aldosterone-producing adenomas (APA) or unilateral/bilateral adrenal hyperplasia. For patients with confirmed unilateral disease, laparoscopic adrenalectomy is the gold standard treatment, often resulting in the normalization of aldosterone levels and significant improvement in blood pressure.

However, clinical outcomes vary. While many patients achieve complete clinical success, others suffer from persistent or recurrent hypertension and hyperaldosteronism. Predicting which patients are at a higher risk for recurrence remains a challenge. Traditional predictors, such as age, duration of hypertension, and preoperative imaging, often lack sufficient sensitivity and specificity. Consequently, there is an urgent need to explore molecular markers, specifically mRNA expression levels, to enhance the accuracy of postoperative prognosis.

Materials and Methods

Patient Selection and Data Collection This study included patients diagnosed with unilateral PA who underwent adrenalectomy at our institution. Diagnosis was confirmed according to the Endocrine Society clinical practice guidelines, including screening via the aldosterone-to-renin ratio (ARR) and confirmatory testing. Postoperative follow-up was conducted to monitor for recurrence, defined by the reappearance of biochemical abnormalities or the need for antihypertensive medication after an initial period of remission.

mRNA Expression Analysis Adrenal tissue samples were collected during surgery and preserved. Total RNA was extracted, and the expression levels of target mRNAs—including those related to the CYP11B2 (aldosterone synthase) pathway and markers of cellular turnover—were quantified using quantitative real-time PCR (qRT

1.1 研究对象

A total of 104 patients diagnosed with pituitary adenoma (PA) at Tangshan People' s Hospital between May 2022 and June 2023 were prospectively selected for this study. The cohort consisted of 56 males and 48 females, with ages ranging from 34 to 57 years and a mean age of (45.2 ± 7.0) years. This study was approved by the Medical Ethics Committee of Tangshan People' s Hospital (Ethics Approval No.:

RMYY-LLKS-2022-021), and all included patients provided signed informed consent. The inclusion criteria were as follows: (1) patients undergoing total resection; (2) no prior relevant treatment before surgery; (3) not currently pregnant or breastfeeding; and (4) voluntary participation in the study with a signed informed consent form. The exclusion criteria were: (1) presence of other neoplastic diseases in addition to functional PA; (2) comorbid psychiatric disorders, major organ dysfunction, or hematological diseases; and (3) incomplete clinical data.

1.2.1 资料收集

Inclusion criteria: (1) Patients must meet the diagnostic criteria for functional pituitary adenoma (PA). Clinical and pathological data collected included age, sex, BMI, disease duration, and comorbidities such as hypertension and diabetes. Additionally, tumor-specific characteristics were recorded, including pituitary gland type, tumor stage, histological differentiation, tumor diameter, depth of invasion, and lymphovascular space invasion (LVSI), alongside patient prognosis. On the day following admission, 4 mL of fasting venous blood was collected from each patient. Serum levels of growth hormone (GH), anterior gradient protein 2 (AGR2), prolactin (PRL), thyroid-stimulating hormone (TSH), and adrenocorticotropic hormone (ACTH) were measured using enzyme-linked immunosorbent assay (ELISA).

1.2.2 SF-1 mRNA 表达水平检测

Approximately 10 mg of pituitary adenoma (PA) tissue and adjacent noncancerous tissue specimens were collected from patients. Total cellular RNA was extracted using a one-step method, and cDNA was synthesized via reverse transcription. The resulting cDNA served as a template for qPCR analysis. The PCR amplification conditions were as follows: initial denaturation at 95 ℃ for 10 min; followed by 40 cycles of 95 ℃ for 10 s and 60 ℃ for 1 min. The forward primer for SF-1 was 5’ -TCTGAGTACCCGGAGCCTGAGTA-3’ , and the reverse primer was 5’ -TGGAGATGAAGGTCTGGTCG-3’ . For the internal control gene GAPDH, the forward primer was 5’ -CCAAGGAGTAAGACCCCTGG-3’ and the reverse primer was 5’ -TGGTTGAGCACAGGGTACTT-3’ . The relative mRNA expression levels of the target gene in the specimens were calculated using the $2^{-\Delta\Delta Ct}$ method.

Patients were divided into two groups based on the median expression level of SF-1 mRNA: the low SF-1 mRNA expression group (fold change ≤ 0.87, $n = 49$) and the high SF-1 mRNA expression group (fold change > 0.87, $n = 49$).

1.2.3 随访

Follow-up was conducted every three months until November 2024. Patients underwent magnetic resonance imaging (MRI) examinations during these visits to evaluate their postoperative prognosis.

Magnetic resonance images were evaluated by two experienced neuroradiologists who were blinded to the clinical and imaging outcomes of the study population. Recurrence was defined as the appearance of a new tumor on contrast-enhanced T1WI or the enlargement of a residual postoperative tumor during the follow-up period. The threshold for recurrence was defined as an increase of more than 2 mm in at least one dimension of the residual tumor compared to the postoperative MRI study. Based on the follow-up results, patients were divided into a recurrence group ($n = 40$) and a non-recurrence group ($n = 60$). Statistical analysis was performed using SPSS 25.0 software. Quantitative data following a normal distribution are expressed as ($\bar{x} \pm s$), and comparisons between the two groups were conducted using independent samples t-tests. Categorical data are expressed as [n (%)] and were analyzed using the χ^2 test.

2 检验。采用分

Hierarchical regression analysis was employed to investigate the influence of hormonal indicators on SF-1 mRNA expression levels. Multivariate Logistic regression analysis was conducted to evaluate the impact of SF-1 mRNA expression levels on the recurrence of patients with Pituitary Adenoma (PA). To assess the predictive performance of SF-1 mRNA expression levels regarding PA recurrence, a Receiver Operating Characteristic (ROC) curve was constructed. Furthermore, a restricted cubic spline (RCS) was plotted to analyze the threshold effect of SF-1 mRNA expression levels on PA recurrence. Finally, Kaplan-Meier survival curves were utilized to analyze the association between SF-1 mRNA expression and the recurrence-free survival of PA patients.

2.1 SF-1 mRNA

Expression levels in pituitary adenoma (PA) tissues and adjacent normal tissues: The expression level of SF-1 mRNA in PA tissues was (1.05 ± 0.21), which was significantly higher than that in adjacent tissues (0.38 ± 0.07). This difference was statistically significant ($t = 30.867$, $P < 0.05$).

Comparison of clinical data according to SF-1 mRNA expression levels: The recurrence rate in the high SF-1 mRNA expression group was higher than that in the low SF-1 mRNA expression group, and the difference was statistically significant ($\chi^2 = 10.037$, $P = 0.002$). There were no statistically significant differences between the two groups regarding gender, age, BMI, disease duration, proportion of hypertension, proportion of diabetes, pituitary gland type, tumor stage, histological differentiation, tumor diameter, depth of invasion, or proportion of vascular space invasion ($P > 0.05$). Regarding the comparison of hormone indicators between the SF-1 mRNA expression groups, the levels of GH, AGR2, PRL, TSH, and ACTH in the high SF-1 mRNA expression group were higher than those in the low SF-1 mRNA expression group, with differences being statistically significant ($P < 0.05$), as shown in Table 2 .

Hierarchical regression analysis of the influence of hormone indicators on SF-1 mRNA expression levels.

分析

Layer 1: A linear regression analysis was conducted using GH as the independent variable (measured values) and SF-1 mRNA expression levels as the dependent variable (measured values). The results demonstrated that GH exerts a positive influence on SF-1 mRNA expression levels ($\beta = 1.763$, $P = 0.005$).

Layer 2: Building upon Layer 1, AGR2 was incorporated as an independent variable. While the F-value decreased, the R^2 increased from 0.495 to 0.683. The analysis indicated that AGR2 has a positive effect on SF-1 mRNA expression levels ($\beta = 2.292$, $P = 0.008$).

Layer 3: Building upon Layer 2, PRL was added as an independent variable. The F-value decreased further, while the R^2 increased to 0.816. The results showed that PRL exerts a positive influence on SF-1 mRNA expression levels ($\beta = 1.910$, $P = 0.017$).

Layer 4: Building upon Layer 3, TSH was incorporated as an independent variable. The F-value decreased, and the R^2 increased to 0.943. The analysis revealed that ACTH exerts a positive influence on SF-1 mRNA expression levels.

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Comparison of clinical characteristics between SF - 1 mRNA low - and high - expression groups

Gender [n (%)] Note: SF-1 = Steroidogenic Factor 1;

The results showed a positive impact on expression levels ($\beta = 3.072$, $P = 0.006$). In Layer 5, ACTH was included as an independent variable based on Layer 3. The F-value decreased while the R^2 increased to 1.206. ACTH was found to exert a positive influence on SF-1 mRNA expression levels ($\beta = 2.051$, $P = 0.005$), as shown in .

Analysis of Clinical Data between the Recurrence and Non-recurrence Groups

Statistically significant differences were observed between the recurrence and non-recurrence groups regarding SF-1 mRNA expression levels, tumor stage, histological differentiation, and levels of GH, AGR2, PRL, and ACTH ($P < 0.05$). No statistically significant differences were found between the two groups in terms of gender, age, BMI, disease duration, hypertension, diabetes, pituitary gland type, tumor diameter, invasion depth, vascular space invasion, or TSH levels ($P > 0.05$). To evaluate the impact of SF-1 mRNA expression on postoperative recurrence, a Logistic regression analysis was performed using SF-1 mRNA expression level as the independent variable (assignment: low expression = 0, high expression = 1) and postoperative recurrence as the dependent variable (assignment:

non-recurrence = 0, recurrence = 1). The results indicated that, without adjusting for any factors, high SF-1 mRNA expression is an independent risk factor for postoperative recurrence in patients with pituitary adenoma (PA) (Unadjusted Model: $OR = 0.698$, $95\%CI = 0.476–0.784$, $P < 0.001$). After adjusting for gender (assignment: male = 1, female = 0), age (assignment: ≥ 45 years = 1, < 45 years = 0), and BMI (assignment: ≥ 21.65 kg/m^2 = 1, < 21.65 kg/m^2 = 0),

disease duration (assignment: ≥ 2 years = 1, < 2 years = 0), hypertension (assignment: yes = 1, no = 0), diabetes (assignment: yes = 1, no = 0), and pituitary gland type (assignment:

functional = 1, non-functional = 0), and tumor stage (assignment: Stage III/IV = 1, Stage I/II = 0)···

2 =1，<21.65 kg/m

Pituitary gland types [n (%)] [n (%)] [n (%)] Vascular space invasion [n (%)] Stratified regression analysis of hormone indices influencing SF mRNA expression Unstandardized coefficients

2 F

Layer 1: Constant 8.945, 1.543, 5.797, $P < 0.001$, 0.495, 186.43

Layer 2: Constant 7.584, 1.687, 4.496, $P < 0.001$, 0.683, 135.14

Layer 3: Constant 7.194, 1.803, 3.990, $P < 0.001$, 0.816, 97.61

Layer 4: Constant 6.495, 1.653, 3.929, $P < 0.001$, 0.943, 68.54

Layer 5: Constant 5.842, 1.653, 3.929, $P < 0.001$, 1.206, 52.61

The variables analyzed included body mass index (kg/m^2), tumor stage [n (%)], and histological differentiation [n (%)]. [TABLE:N] presents the comparison of hormone indices between SF-1 mRNA expression groups. Note: GH = growth hormone; AGR2 = anterior gradient 2; PRL = prolactin; TSH = thyroid-stimulating hormone; ACTH = adrenocorticotropic hormone.

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After adjusting for potential confounders in Model 4—including tumor stage (Stage III = 1, Stages I/II = 0), histological differentiation (Grade III = 1, Grades I/II = 0), tumor diameter (≥ 22.80 mm = 1, < 22.80 mm = 0), GH (≥ 12.35 ng/mL = 1, < 12.35 ng/mL = 0), AGR2 (≥ 166.73 ng/mL = 1, < 166.73 ng/mL = 0), PRL (≥ 6.12 nmol/L = 1, < 6.12 nmol/L = 0), TSH (≥ 21.27 mU/L = 1, < 21.27 mU/L = 0), and ACTH (≥ 5.15 nmol/L = 1, < 5.15 nmol/L = 0)—SF-1 mRNA expression remained a significant independent predictor of recurrence in patients with pituitary adenoma (PA) ($OR = 0.768$, 95% CI = 0.525-0.882, $P = 0.001$). Furthermore, interaction testing demonstrated that these adjustment factors did not significantly modify the relationship between SF-1 mRNA expression levels and PA recurrence ($P < 0.05$).

The SF-1 mRNA expression levels were dichotomized into high expression (> 0.87) and low expression (≤ 0.87) groups.

The study further stratified SF-1 mRNA expression into quartiles (Q1-Q4). Logistic regression analysis was performed using these quartiles as the independent variable (assigned values: Q1 = 0, Q2 = 1, Q3 = 2, Q4 = 3) and postoperative recurrence as the dependent variable (no recurrence = 0, recurrence = 1). The results indicated that SF-1 mRNA expression at the Q2 and Q3 levels were significant factors influencing postoperative recurrence ($P < 0.05$). Notably, the correlation effect increased as SF-1 mRNA expression levels rose, and the trend test was statistically significant ($P < 0.05$), as shown in .

To evaluate the predictive value of SF-1 mRNA expression for recurrence in PA patients, a Receiver Operating Characteristic (ROC) curve was constructed.

The ROC analysis yielded an Area Under the Curve (AUC) of 0.705 (95% CI = 0.604–0.806, $P < 0.005$). The optimal cut-off value was determined to be 0.87, providing a sensitivity of 0.806 and a specificity of 0.634, as illustrated in [Figure 1: see original paper].

1 - Specificity. [Figure 1: see original paper]: ROC curve for SF-1 mRNA level predicting postoperative recurrence in PA patients.

2.8 限制性立方样条及阈值效应分析

Restricted cubic spline (RCS) analysis revealed a non-linear relationship between SF-1 mRNA expression levels and the risk of recurrence in patients with primary aldosteronism (PA) (P for non-linearity < 0.001). To further investigate this association, a threshold effect analysis was performed on SF-1 mRNA expression levels. The results indicate that the impact of SF-1 mRNA expression on recurrence risk varies significantly across different concentration ranges.

Clinical characteristics of recurrence and non - recurrence groups

2 值

Clinical Feature	n (%)
Pituitary Gland Type	
Type A	25 (39.1)
Type B	39 (60.9)
Tumor Stage	
Early Stage	52 (81.3)
Advanced Stage	12 (18.8)
Histological Differentiation (Grade)	
Well-differentiated	55 (85.9)
Poorly-differentiated	9 (14.1)
Tumor Diameter (mm)	

Clinical Feature	n (%)
< 10 mm	41 (64.1)
≥ 10 mm	23 (35.9)
Depth of Invasion (cm)	
Shallow	31 (48.4)
Deep	33 (51.6)
Additional Metric	
Group 1	33 (51.6)
Group 2	31 (48.4)

2 值

Results

Relationship between SF-1 mRNA Expression and PA Recurrence

The analysis of SF-1 mRNA expression levels (using low expression as the reference) and their association with pituitary adenoma (PA) recurrence is presented in Table 6 . When using the first quartile (Q1) of SF-1 mRNA expression as the reference, the data indicates that the recurrence risk for PA patients increases significantly as SF-1 mRNA expression levels rise.

A threshold effect analysis identified a clinical inflection point for PA recurrence at an SF-1 mRNA expression level of 0.87. Before this inflection point, the Odds Ratio (OR) was 1.006 (95% CI = 1.002-1.011, $P = 0.026$). After the inflection point, the OR was 1.007 (95% CI = 1.005-1.009, $P = 0.017$). These results demonstrate a consistent positive correlation between SF-1 mRNA levels and the risk of recurrence.

The non-linear relationship and the overall trend between SF-1 mRNA expression and the risk of PA recurrence are further illustrated in the restricted cubic spline (RCS) plot [FIGURE:N].

Table 6: Odds Ratios (OR) for PA Recurrence Based on SF-1 mRNA Expression Levels

[FIGURE:N] **Restricted cubic spline showing the relationship between SF-1 mRNA expression and recurrence risk**

2.9 SF-1 mRNA

The relationship between expression levels and recurrence in patients with Pituitary Adenoma (PA) was analyzed using Kaplan-Meier survival curves. The results demonstrated that the group with high SF-1 mRNA expression had a median recurrence-free survival of 15 months (95% CI = 11.16-18.43). In contrast, the group with low SF-1 mRNA expression had a median recurrence-free survival of 28 months (95% CI = 23.54-31.54).

Log-rank test results indicated that the difference between the two groups was statistically significant ($\chi^2 = 7.861$, $P < 0.001$), as shown in [Figure 3: see original paper].

Threshold effect analysis results for SF 1 mRNA expression and PA recurrence

Standard linear effect: 1.008 (1.005–1.012), $P < 0.001$

SF-1 mRNA expression level ≤ 0.87: 1.006 (1.002–1.011), $P < 0.001$

SF-1 mRNA expression level > 0.87: 1.007 (1.004–1.009), $P < 0.001$

Difference in effect: 0.013, $P < 0.001$

Log-likelihood ratio test (LRT): $P < 0.001$

Low SF-1 mRNA expression group; High SF-1 mRNA expression group; Cumulative recurrence rate (%); Relationship between relative SF-1 mRNA expression and postoperative recurrence

3 讨论

Pituitary adenomas (PAs) are benign tumors originating from the anterior pituitary gland, typically formed by the abnormal proliferation of adenohypophyseal cells. They represent one of the most common types of benign intracranial tumors. In this study, low expression of SF-1 mRNA was defined as ≤ 0.87, while high expression was defined as > 0.87. Participants were further stratified into quartiles (Q1–Q4) based on SF-1 mRNA expression levels: Q1 (≤ 0.900), Q2 (0.901–1.000), Q3 (1.001–1.099), and Q4 (≥ 1.100). To evaluate the associations, several multivariable models were employed: Model 1 remained unadjusted; Model 2 adjusted for sex, age, BMI, disease duration, hypertension, and diabetes; Model 3 further incorporated pituitary gland type, tumor stage, and histological differentiation; Model 4 added tumor diameter, invasion depth, and vascular space invasion; and Model 5 included GH, AGR2, PRL, TSH, and ACTH levels.

According to the *Chinese Journal of General Practice*, pituitary adenomas are classified into functional adenomas (those with secretory function) and non-functional adenomas (those without secretory function) based on their hormone secretion status. Excessive hormone secretion by these adenomas can lead to significant endocrine abnormalities, manifesting as menstrual irregularities, visual impairment, headaches, and pituitary dysfunction. If left untreated, these tumors may invade adjacent organs and can even become life-threatening, accounting for 10% to 15% of all intracranial tumors. Steroidogenic factor-1 (SF-1) is a member of the nuclear receptor superfamily that regulates steroidogenesis. It is primarily expressed in the adrenal glands, gonads, brain, and other tissues, playing a crucial role in various physiological processes, particularly hormone synthesis and sexual differentiation [**?**]. Its expression is essential for maintaining the normal development and function of the adrenal glands and steroid-producing gonads. Research has indicated that SF-1 plays a role in the onset and progression of various cancers, with extensive studies currently focusing on ovarian, adrenal, and breast cancers. Regarding adrenal tumors, some studies suggest that abnormal SF-1 protein expression promotes malignant progression, making it an important biomarker for prognostic assessment. This study found that SF-1 mRNA expression levels in PA tissues were significantly higher than those in paracancerous tissues, suggesting that SF-1 expression is closely associated with the pathogenesis of PA.

Growth hormone (GH) is a polypeptide hormone secreted by the anterior pituitary; its abnormal secretion leads to PA and adversely affects patient prognosis. Anterior Gradient 2 (AGR2) is a molecular chaperone involved in protein folding and stability regulation, and it has been linked to the development of cancer, immune responses, and certain metabolic diseases. Studies have shown that AGR2 expression promotes tumor cell proliferation and migration. In research on nasopharyngeal carcinoma, tumor staging and recurrence were found to be correlated with serum AGR2 expression. Similarly, in colorectal cancer studies, AGR2 in cancer cells can bind to receptors to activate signaling pathways that promote metastasis and increase the risk of recurrence. Research has also demonstrated that patients with PA exhibit abnormally elevated levels of PRL, GH, and ACTH. Specifically, functional PAs cause excessive secretion of PRL and ACTH, leading to endocrine disorders. Furthermore, abnormal ACTH secretion in PA can result in Cushing’ s disease, characterized by symptoms such as diabetes, hypertension, and psychiatric disorders. Some studies have found that serum GH and AGR2 levels change in patients with functional PA who experience postoperative recurrence, suggesting their potential as biomarkers for predicting recurrence. This study demonstrates that patients with high SF-1 mRNA expression have higher levels of GH, AGR2, PRL, TSH, and ACTH compared to the low-expression group. Statistically significant differences were observed in postoperative recurrence rates concerning SF-1 mRNA expression levels, tumor stage, histological differentiation, and levels of GH, AGR2, PRL, and ACTH. Notably, AGR2 expression was significantly higher in pituitary tumor tissues than in normal pituitary tissues. Stratified regression analysis further revealed that AGR2 has a significant positive influence on SF-1 mRNA expression, suggesting that AGR2 may act synergistically with SF-1 in the pathological process of PA.

As a molecular chaperone, AGR2 contains a typical cleavable N-terminal signal peptide and can promote tumor metastasis by regulating receptor adhesion and interactions with the extracellular matrix. It may participate in the folding and maturation of hormone synthesis-related proteins in pituitary tumor cells, thereby indirectly promoting the abnormal secretion of hormones such as GH, PRL, and ACTH. Consequently, AGR2 serves as a potential biomarker for the diagnosis of PA. SF-1 mRNA expression level is an independent factor for predicting hormone secretory function. Compared with low expression, high SF-1 mRNA expression is independently associated with recurrence in PA patients. ROC curve analysis showed that the sensitivity and specificity of SF-1 mRNA expression levels in predicting PA recurrence were 0.806 and 0.634, respectively. The odds ratio (OR) for PA recurrence increased with higher SF-1 mRNA expression levels. This indicates that elevated SF-1 mRNA can further promote hormone secretion and exacerbate secretory abnormalities, thereby affecting postoperative prognosis and increasing the risk of recurrence. Therefore, SF-1 mRNA expression levels may serve as a novel biomarker for predicting the recurrence of pituitary adenomas.

4 小结

The expression levels of GH, AGR2, PRL, TSH, and ACTH vary among pituitary adenoma (PA) patients with different SF-1 mRNA expression levels. Specifically, patients with high SF-1 mRNA expression exhibit higher hormone levels, which is associated with a poorer postoperative prognosis. Consequently, GH, AGR2, and PRL may serve as biomarkers for predicting postoperative recurrence in PA patients. This study has certain limitations: it is a single-center, prospective observational study with a relatively limited sample size, and it did not account for the potential impact of different surgical approaches on patients' hormone levels.

Author Contributions: Wei Dong was responsible for the study conception and design, implementation of the research, and data collection and organization. Li Zhang and Huan Zhang were responsible for statistical analysis and the creation and presentation of figures and tables. Yu Zhang performed the revision of the manuscript. Xiaoliu Dong was responsible for quality control and critical review of the article.

The authors declare no conflicts of interest.

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Research Progress of MRI Radiomics in Pituitary Neuroendocrine Tumors

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Abstract

Pituitary neuroendocrine tumors (PitNETs) are common tumors of the central nervous system. While most are benign, some exhibit aggressive behavior, such as invading the cavernous sinus or surrounding bone tissues, and are prone to recurrence after surgery. MRI is the primary imaging modality for diagnosing PitNETs; however, conventional MRI has limitations in predicting the biological behavior, subtypes, and treatment response of these tumors. Radiomics, as an emerging image analysis method, can extract high-throughput features from MRI images to quantitatively describe tumor heterogeneity. In recent years, MRI-based radiomics has demonstrated significant potential in the differential diagnosis, subtype identification, aggressiveness prediction, and therapeutic response assessment of PitNETs. This article reviews the basic workflow of MRI radiomics and its research progress in PitNETs, aiming to provide a reference for clinical decision-making and personalized treatment.

Introduction

Pituitary neuroendocrine tumors (PitNETs), formerly known as pituitary adenomas, are the second most common primary intracranial tumors, accounting for approximately 10% to 15% of all primary central nervous system tumors. According to the 2022 World Health Organization (WHO) classification of endocrine and neuroendocrine tumors, "pituitary adenoma" has been renamed "pituitary neuroendocrine tumor" to better reflect its biological characteristics and clinical behavior. Although most PitNETs are benign, approximately 30% to 45% exhibit aggressive growth, invading surrounding structures such as the cavernous sinus, sphenoid sinus, and internal carotid artery. This aggressiveness often leads to incomplete surgical resection and a high rate of postoperative recurrence.

Magnetic Resonance Imaging (MRI) is the gold standard for the clinical diagnosis and postoperative follow-up of PitNETs due to its excellent soft-tissue contrast and multi-planar imaging capabilities. However, traditional MRI evaluation relies primarily on the radiologist' s visual inspection of morphological features, which is subjective and lacks quantitative data to reflect the internal heterogeneity of the tumor. Radiomics, by transforming medical images into exploitable

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Progress in the Diagnosis and Treatment of Pediatric Pituitary Adenomas

Pediatric pituitary adenomas (PPAs) are rare clinical entities, accounting for approximately 1% to 3.5% of all pediatric brain tumors and less than 3% of all pituitary adenomas. Despite their rarity, these tumors present unique challenges due to their impact on growth, development, and endocrine function during critical developmental windows. Recent advancements in neuroimaging, molecular biology, and surgical techniques have significantly altered the diagnostic and therapeutic landscape for these patients.

1. Clinical Presentation and Diagnosis

The clinical manifestations of PPAs differ significantly from those in adults, often presenting with symptoms related to hormonal hypersecretion or mass effect. Prolactinomas are the most common subtype in children and adolescents, frequently leading to delayed puberty, primary or secondary amenorrhea in females, and growth retardation. Somatotroph adenomas, while less common, typically manifest as gigantism due to the lack of epiphyseal closure in younger patients.

Diagnostic evaluation requires a multidisciplinary approach combining clinical assessment, biochemical testing, and advanced neuroimaging. Magnetic resonance imaging (MRI) remains the gold standard for localizing the tumor and assessing its relationship with surrounding structures such as the optic chiasm and cavernous sinuses. Recent studies have highlighted the potential of radiomics in predicting tumor behavior. For instance, Zhang et al. [**?**] demonstrated that a radiomics approach could effectively predict the recurrence of non-functioning pituitary macroadenomas, offering a personalized tool for clinical decision-making.

2. Therapeutic Strategies

The primary goals of treating PPAs are to normalize hormone levels, reduce tumor volume, and preserve normal pituitary function to ensure proper growth and development.

2.1 Medical Management Medical therapy is often the first-line treatment for specific subtypes, particularly prolactinomas. Dopamine agonists, such as cabergoline and bromocriptine, are highly effective in normalizing prolactin levels and inducing tumor shrinkage. For somatotroph adenomas, somatostatin analogs may be utilized, although surgical intervention is more frequently required.

2.2 Surgical Intervention Surgery is indicated for most non-prolactinoma secreting adenomas and cases where medical therapy fails or is poorly tolerated. The endoscopic endonasal approach (EEA) has become the preferred surgical modality due to its minimal invasiveness and superior visualization of the sellar region. However, the smaller anatomical dimensions

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Pathogens and Influencing Factors of Intracranial Infection After Transsphenoidal Resection of Pituitary Adenoma

Authors: HUANG Wei-li, REN Ming-jun, PENG Gen-ying, et al. **Journal:** *Chinese Journal of Nosocomiology*, 2021

Abstract

Objective: To investigate the distribution of pathogenic bacteria and the factors influencing intracranial infection in patients undergoing transsphenoidal resection of pituitary adenomas.

Methods: A retrospective analysis was conducted on 352 patients who underwent transsphenoidal resection of pituitary adenomas at our hospital between January 2017 and December 2019. Patients were divided into an infection group (n=24) and a non-infection group (n=328) based on the occurrence of postoperative intracranial infection. The distribution of pathogenic bacteria in the infection group was analyzed. Univariate and multivariate logistic regression analyses were performed to identify the factors influencing postoperative intracranial infection.

Results: Among the 352 patients, 24 developed intracranial infections, representing an infection rate of 6.82%. A total of 28 pathogenic strains were isolated from these 24 patients, including 18 strains of Gram-positive bacteria (64.29%), 9 strains of Gram-negative bacteria (32.14%), and 1 strain of fungus (3.57%). Univariate analysis indicated that age $\geq$ 60 years, diabetes mellitus, preoperative hospital stay $\geq$ 7 days, operation duration $\geq$ 3 hours, intraoperative cerebrospinal fluid (CSF) leakage, and postoperative CSF leakage were significantly associated with postoperative intracranial infection ($P < 0.05$). Multivariate logistic regression analysis revealed that age $\geq$ 60 years (OR=2.314), diabetes mellitus (OR=2.532), operation duration $\geq$ 3 hours (OR=2.145), and postoperative CSF leakage (OR=2.841) were independent risk factors for intracranial infection after transsphenoidal resection of pituitary adenomas ($P < 0.05$).

Conclusion: Gram-positive bacteria are the primary pathogens causing intracranial infection after transsphenoidal resection of pituitary adenomas. Clinical interventions should target identified risk factors—such as advanced age, comorbid diabetes, prolonged operative time, and postoperative CSF leakage—to reduce the

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(Received: 2025-04-10; Revised: 2025-12-20) (Editor: Zhao Yuecui)