Doi.org/10.36721/PJPS.2025.38.1.REG.165-173.1

# Relationship between serum CEACAM1 levels and prognosis and temozolomide chemotherapy sensitivity in patients undergoing neuroendoscopic transsphenoidal pituitary tumor resection

**Chong Chen Ma, Er Ping He, Yue Qing Zhang, Yong Jing Wang, Chun Ming Zhu and Xuan Yu***

Department of Neurosurgery, Huai'an Hospital of Huai'an City, Huai 'an City, Jiangsu Province, China

**Abstract**: Pituitary tumors are common intracranial neoplasms with complex pathogenesis. Temozolomide (TMZ) has shown potential in treatment, but its efficacy and related biomarkers require further investigation. This study explores the relationship between serum CEACAM1 levels, prognosis after neuroendoscopic transsphenoidal pituitary tumor resection, and TMZ sensitivity. A retrospective analysis of 70 patients who underwent surgery from 2020 to 2022 was conducted. Patients were classified into high- and low-CEACAM1 groups. Baseline characteristics showed no significant differences ($P>0.05$). After six months, patients with poor prognosis had significantly higher preoperative CEACAM1 levels ($P<0.05$). TMZ-resistant patients also had elevated levels ($P<0.05$). The AUC of preoperative CEACAM1 for predicting prognosis was 0.716 (cutoff: 5857.5 pg/mL), and for TMZ resistance was 0.742 (cutoff: 6431 pg/mL). High preoperative CEACAM1 levels are associated with poor prognosis and TMZ resistance, serving as a potential biomarker to guide clinical evaluation and treatment.

**Keywords**: CEACAM1, neuroendoscopic transsphenoidal pituitary tumor resection, prognosis, temozolomide, chemosensitivity.

*Submitted on 26-07-2024 – Revised on 09-12-2024 – Accepted on 30-12-2024*

## INTRODUCTION

Pituitary tumors commonly occur in adenohypophyseal cells and account for 8% - 15% of all intracranial tumors (Tritos and Miller, 2023). They are classified into functional tumors, such as prolactinomas, growth hormone-secreting tumors, adrenocorticotropic hormone-secreting tumors, gonadotropinomas, thyroid-stimulating hormone-secreting tumors and non-functional tumors. Most pituitary tumors are benign and exhibit non-invasive growth (Araujo-Castro, Berrocal and Pascual-Corrales, 2020; Marrero-Rodríguez *et al*., 2023). According to the European Society of Endocrinology guidelines for the diagnosis and treatment of aggressive pituitary tumors and carcinomas, among radiologically aggressive tumors, those that grow abnormally rapidly or have clinically relevant tumor activity despite treatment should be considered as aggressive pituitary tumors (Bonneville *et al*., 2020). Aggressive pituitary tumors account for 25%-55% of pituitary tumors, and the main treatment method is surgery. However, due to their rapid growth and high recurrence rate after surgery, patient management is difficult (Wang *et al*., 2020). Traditional craniotomy has been used in clinical practice for a relatively long time, and the technology is relatively mature. However, craniotomy has a high risk and is prone to cause a series of complications such as brain injury or intracranial hemorrhage, which is not conducive to postoperative recovery of patients (Spada *et al*., 2022). With the continuous development of contemporary endoscopic equipment and the gradual improvement of medical support facilities, neuroendoscopic transnasal transsphenoidal pituitary tumor resection has the characteristics of quick recovery, less trauma and fewer complications, and has been gradually widely used in clinical practice (Toader *et al*., 2023). However, the prognosis of postoperative patients has always been a research hotspot.

Temozolomide (TMZ) can induce cytotoxicity by alkylating adenine at the N3 position and guanine at the O6 and N7 positions of the deoxyribonucleic acid molecule, causing double-stranded DNA breaks in the genome, inducing tumor cell apoptosis and cell cycle arrest (He *et al*., 2024). At the same time, TMZ can easily cross the blood - brain barrier and can be completely and rapidly absorbed. Long - term large - sample clinical studies have shown that TMZ can prolong the progression - free survival period of patients, improve the survival rate, improve the quality of life, and reduce the pain of illness. Currently, TMZ has become the first - choice chemotherapy drug for the clinical treatment of pituitary tumors. However, in clinical practice, there are still a considerable number of patients whose chemotherapy effect is not satisfactory after using TMZ, showing acquired resistance (Rao *et al*., 2023). Therefore, it is of great clinical significance to find biomarkers that can predict the postoperative prognosis and temozolomide chemotherapy sensitivity of pituitary tumor patients.

**Corresponding author:* e-mail: muron898@163.com

Carcinoembryonic antigen-related cell adhesion molecule 1 is a member of the immunoglobulin subfamily. Some studies have shown that it has complex functions and can promote cell apoptosis in various disease models (Matsumoto *et al*., 2024). As an adhesion molecule, CEACAM1 was first discovered in the mouse liver, central nervous system, and vascular lumen and can participate in various physiological and pathological responses such as cell growth, differentiation, apoptosis, intercellular adhesion, immune response, and inflammatory response (Yi *et al*., 2024). CEACAM1 has many similarities with CTLA - 4 and PD - 1 in terms of co - inhibitory receptors or immunomodulation, such as expression patterns and ITIM patterns and can bind to SHP - 1 to inhibit T lymphocyte activation or attenuate the immune response. In melanoma, the anti - CEACAM1 antibody (MRG1) binding to its N - domain can help T cells attack melanoma cells; in colorectal cancer, antibody blockade of CEACAM1 binding to Tim - 3, WL5 antibody binding to CEACAM1 and CC4 antibody blocking the interaction between CEA and CEACAM1 all have anti - tumor effects. Therefore, specific antibodies against CEACAM1 are expected to restore the body's anti - tumor immune function to inhibit tumor development. Previous studies have confirmed that CEACAM1 has shown the potential of a tumor marker in the risk prediction of lung cancer and glioma (Liu, 2022; JKonieva *et al*., 2024).

This study aims to investigate the relationship between serum CEACAM1 levels and the prognosis of patients undergoing neuroendoscopic transsphenoidal pituitary tumor resection and the sensitivity to temozolomide chemotherapy. By detecting the preoperative and postoperative serum CEACAM1 levels of patients, the predictive value for patient prognosis and its correlation with temozolomide chemotherapy sensitivity were analyzed, hoping to provide new ideas and a basis for the individualized treatment of pituitary tumors and improve the treatment effect and quality of life of patients.

## MATERIALS AND METHODS

***Sample size calculation***

The TMZ resistance rate of pituitary tumor patients previously admitted to our hospital was approximately 30%; the allowable error rate was 5% and the total number of the finite population in the study was 93 cases. According to formula (1), it was calculated that the sample size included in the sample study should be 70 cases.

$$n = \frac{(\frac{Z_\alpha}{\delta})^2 * \rho * (1-\rho)}{1+[(\frac{Z_\alpha}{\delta})^2 * \rho * (1-\rho)]/N} \quad (1)$$

Note: n: sample size; $Z_\alpha$: the Z value corresponding to the significance level α, when α = 0.05, for a two - sided test, $Z_\alpha$ = 1.96; ρ: the previous detection rate; δ: the allowable error; N: the total number of the finite population.

***General information***

Seventy patients with pituitary tumors who underwent neuroendoscopic transsphenoidal pituitary tumor resection from January 2020 to January 2022 in Huai'an Hospital of Huai'an City were retrospectively selected. Inclusion criteria: (1) patients with pituitary tumors diagnosed by MRI and pathology according to the World Health Organization Endocrine Organ Tumor Classification Criteria (Veleno *et al*., 2024); (2) between the ages of 18 and 60 years old; (3) all of them were first-time brain surgery; postoperative chemotherapy with temozolomide and completion of more than two courses of chemotherapy. Exclusion criteria: (1) patients with missing clinical data; (2) patients with severe liver and kidney insufficiency or other tumor diseases; (3) patients in pregnancy and lactation. This study was approved by the Medical Ethics Committee of our hospital.

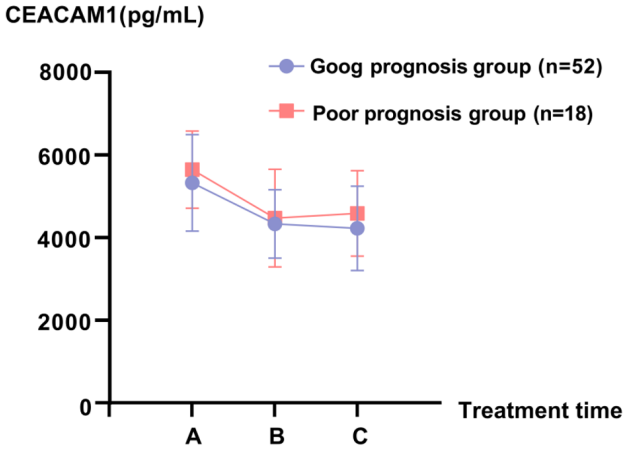
***Temozolomide chemotherapy program***

The starting dose of temozolomide was 150 mg/m$^2$ once/d for 5 days and the dose was adjusted according to the hematological examination. Temozolomide chemotherapy was administered for 28 d in one cycle, with a total of 4 courses of treatment and the CT examination was repeated at the end of the second and final courses of treatment for evaluation of the therapeutic efficacy.

***Observation indicators***

Collect patients' baseline data and clinical indicators; conduct follow-up at one month and six months after the operation to evaluate the postoperative prognosis and chemotherapy sensitivity of the patients, and record the postoperative complications. Collect the serum CEACAM1 levels of the patients before the operation, one month after the operation, and six months after the operation; CEACAM1 detection method: collect 3 ml of venous blood from the elbow of the patient in a fasting state, centrifuge it at a speed of 3000 r/min for 10 minutes (centrifugal radius of 8 cm), obtain the upper serum, store it in a refrigerator at - 80°C and complete the test within 72 hours. The serum CEACAM1 level was detected by enzyme-linked immunosorbent assay (ELISA). According to the median preoperative CEACAM1 level of the patient (CEACAM1 = 5189pg/ml), the patients were divided into a low-level group (n = 34) with CEACAM1 ≤ 5189 pg/ml and a high-level group (n = 36) with CEACAM1 >5189 pg/ml. The levels of adrenocorticotropic hormone (ACTH), growth hormone (GH), prolactin (PRL), and thyrotropin (TSH) of the patients were measured by ELISA before the operation and one month and six months after the operation. The mean visual field defect (MD), visual field pattern standard deviation (PSD) and visual field index (VFI) were examined by a perimeter. Postoperative

complications include diabetes insipidus, electrolyte disorders, cerebrospinal fluid leakage and infections. Intracranial infection: (1) High fever occurs, with the highest body temperature exceeding 38.5°C, accompanied by manifestations of intracranial hypertension such as headache, nausea and vomiting, and optic papilla edema, and a positive meningeal irritation sign can be found during physical examination. (2) The color of the cerebrospinal fluid is yellow and turbid, the white blood cell count of the cerebrospinal fluid is higher than $10\times10^6$/L, the glucose content of the cerebrospinal fluid is lower than 3.9mmol/L and the lactate content is higher than 2.4mmol/L.




Note: A: preoperative serum CEACAM1 level; B: one-month postoperative serum CEACAM1 level; C: six-month postoperative serum CEACAM1 level; F time = 38.567, F interaction =0.726, F within group = 2605.326; P time <0.001, P interaction = 0.397, P within group <0.001

**Fig. 1**: Changes in serum CEACAM1 levels in patients with different prognoses.

***Prognosis and TMZ sensitivity grouping***

Prognostic grouping: Cure results in the disappearance of symptoms, endocrine symptoms back to normal and total resection by magnetic resonance imaging; efficacy results in the disappearance of most of the symptoms, endocrine symptoms tend to be normalized and subtotal or partial resection by magnetic resonance imaging; effective results in the disappearance of some of the symptoms, partial recovery of endocrine symptoms, and partial resection by magnetic resonance imaging; ineffective results in the absence of symptomatic improvements, endocrine symptoms The result of invalid result was no improvement of symptoms, endocrine symptoms and partial resection shown by magnetic resonance imaging; good prognosis = the number of cured cases + the number of effective cases + the number of effective cases and invalid was bad prognosis.

TMZ sensitivity grouping: the radiotherapy effect was evaluated with reference to the solid tumor efficacy evaluation standard (Schwartz *et al*., 2016) and was divided into four grades: complete remission (disappearance of the target lesion, no new lesion), partial remission (≥50% reduction of the target lesion), stable condition (<50% reduction of the target lesion) and disease progression (no reduction of the target lesion or new lesion), of which complete remission and partial remission were defined as radiotherapy sensitivity and stable and progressive disease were defined as chemotherapy sensitivity. Complete remission and partial remission were defined as sensitive to radiotherapy, while stable disease and disease progression were defined as chemotherapy-resistant.

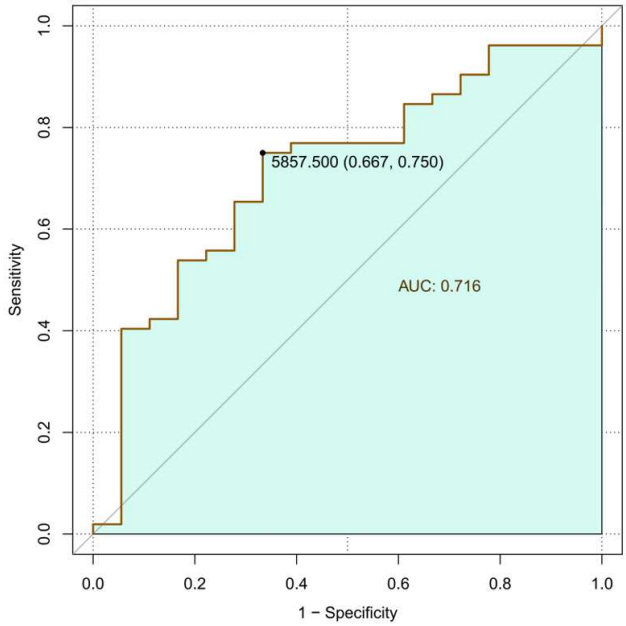



**Fig. 2**: Diagnostic value of preoperative serum CEACAM1 levels on the prognosis of postoperative patients ROC

## STATISTICAL ANALYSIS

Statistical analysis was performed using the statistical software SPSS26.0. The measurement data with a normal distribution were expressed as the mean ± standard deviation ( $\bar{x} \pm s$). The independent sample t - test was used to compare the general information of the patients (age, BMI, disease course, tumor diameter, operation duration, intraoperative blood loss, hospitalization duration) and the preoperative and postoperative pituitary hormones (preoperative and postoperative ACTH, PRL, GH, TSH, MD, PSD, VFI). Gender, pathological type, age subgroup, and BMI subgroup were expressed as the sample size (percentage) [n(%)], and the chi - square test was used for comparison between groups. The one - way ANOVA test was used for the comparison of CEACAM1 level subgroups. The repeated - measures analysis of variance was used for the comparison of different time points between the patients with good prognosis and those with poor prognosis. A P value less than 0.05 was considered statistically significant.

**Table 1**: Comparison of patients' general information

| Group | CEACAM1 high level group (n=36) | CEACAM1 low level group (n=34) | $\chi^2/t$ | *P* |
|---|---|---|---|---|
| Gender [n(%)] | | | | |
| Male | 17(47.22) | 14(41.18) | 2.780 | 0.095 |
| Female | 19(52.78) | 20(58.82) | | |
| Age (years, $\bar{x} \pm s$ ) | 49.13±8.32 | 48.29±8.59 | 0.132 | 0.303 |
| BMI(kg/m², $\bar{x} \pm s$ ) | 23.54±3.49 | 23.79±3.25 | 0.104 | 0.918 |
| Course of disease (years, $\bar{x} \pm s$ ) | 3.19±0.87 | 2.92±0.79 | 1.911 | 0.060 |
| Pathological type [n(%)] | | | | |
| Growth hormone type (GH) | 15(41.67) | 12 (35.29) | | |
| Prolactin type (PRL) | 11(30.56) | 13 (38.24) | 4.324 | 0.229 |
| Adrenocorticotropic hormone | 3(8.33) | 5(14.71) | | |
| Type (ACTH) | 7(19.44) | 4(11.76) | | |
| Thyroid stimulating hormone (TSH) | 22±6.6 | 23±6.4 | 1.553 | 0.125 |
| Tumor diameter [mm, $\bar{x} \pm s$ ] | 90.23±17.3 | 90.62±14.53 | 0.637 | 0.526 |
| Operation duration (min, $\bar{x} \pm s$ ) | 79.36 ±5.78 | 78.47±6.03 | 1.430 | 0.157 |
| Intraoperative blood loss (ml, $\bar{x} \pm s$ ) | 7.96 ±1.77 | 8.03±1.86 | 1.040 | 0.302 |

**Table 2**: Subgroup Analysis of CEACAM1 Levels, TMZ Resistance, and Poor Prognosis[ $\bar{x}$±s,n(%)]

| | Subgroup | CEACAM1 | *F/t* | *p* |
|---|---|---|---|---|
| Age | < 45 years old (n=18) | 5358.72±1123.69 | 0.021 | 0.980 |
| | ≥45 years and < 60 years (n=46) | 5422.30±1115.41 | | |
| | ≥60 years old (n=6) | 5411.67±1276.87 | | |
| Sex | Male (n=31) | 5569.16±1046.22 | 1.100 | 0.275 |
| | Female (n=39) | 5274.59±1162.13 | | |
| BMI(kg/m$^2$) | <18.5 (n=4) | 5794.50±1252.88 | 0.265 | 0.850 |
| | 18.5~24.9 (n=39) | 5444.26±1085.06 | | |
| | 25~29.9 (n=25) | 5288.64±1100.75 | | |
| | ≥30 (n=2) | 5316.50±2471.34 | | |
| Pathological type | ACTH (n=8) | 5221.75±1295.48 | 0.357 | 0.784 |
| | PRL (n=24) | 5321.08±1042.00 | | |
| | GH (n=27) | 5415.67±1203.07 | | |
| | PRL (n=11) | 5695.04±1114.18 | | |

**Table 3**: Comparison of visual and pituitary hormones before and after surgery in patients with different CEACAM1 levels ( $\bar{x}$±s)

| | Group | CEACAM1 high level group (n=36) | CEACAM1 low level group (n=34) | t | P |
|---|---|---|---|---|---|
| ACTH(pmol/L) | Before operation | 70.31±4.66 | 62.18±5.43 | 2.258 | 0.027 |
| | One month after surgery | 23.76±4.34 | 17.54±3.88 | 2.193 | 0.032 |
| PRL(μg/L) | Before operation | 63.75±5.63 | 58.78±6.45 | 0.409 | 0.684 |
| | One month after surgery | 27.89±4.83 | 22.56±5.76 | 2.284 | 0.025 |
| GH(μg/L) | Before operation | 22.56±2.14 | 20.94±1.78 | 1.309 | 0.195 |
| | One month after surgery | 9.45±1.66 | 7.62±2.01 | 1.298 | 0.199 |
| TSH(mU/L) | Before operation | 22.46±3.62 | 20.11±2.71 | 1.473 | 0.145 |
| | One month after surgery | 11.32±1.67 | 8.38±2.04 | 2.389 | 0.020 |
| MD(dB) | Before operation | 10.53±1.94 | 10.62±2.15 | 1.251 | 0.215 |
| | One month after surgery | 5.42±0.87 | 3.63±0.75 | 0.916 | 0.363 |
| PSD(dB) | Before operation | 8.22±1.63 | 8.43±1.86 | 1.153 | 0.253 |
| | One month after surgery | 4.78±0.93 | 4.24±0.51 | 1.318 | 0.192 |
| VFI(%) | Before operation | 63.25±5.25 | 63.59±5.31 | 0.485 | 0.629 |
| | One month after surgery | 90.32±7.71 | 94.66±8.36 | 0.737 | 0.464 |

**Table 4**: Incidence of adverse reactions [n (%)]

| Group | Hypopituitarism | Electrolyte disorders | Medullary fluid leakage | Intracranial infection | Uremia | Total Adverse Reaction Occurrence |
|---|---|---|---|---|---|---|
| CEACAM1 low level group (n=34) | 1(2.94) | 1(2.94) | 1(2.94) | 2(5.88) | 2(5.88) | 7(20.59) |
| CEACAM1 high level group (n=36) | 4(11.11) | 3(8.33) | 3(8.33) | 5(13.89) | 1(2.78) | 16(44.44) |
| $\chi^2$/t | | | | | | 4.511 |
| P | | | | | | 0.032 |

**Table 5**: Comparison of baseline data between TMZ-sensitive and resistant patients

| Group | Sensitive group (n=47) | Drug-resistant group (n=23) | $\chi^2$/t | P |
|---|---|---|---|---|
| Gender [n(%)] | | | | |
| Male | 22(46.81) | 9(39.13) | 0.369 | 0.544 |
| Female | 25(53.19) | 14(60.87) | | |
| Age (years, $\overline{x} \pm s$ ) | 48.45±8.58 | 498.78±7.98 | 0.626 | 0.534 |
| BMI (kg/m², $\overline{x} \pm s$ ) | 23.59±3.20 | 23.77±3.71 | 0.207 | 0.836 |
| Course of disease (years, $\overline{x} \pm s$ ) | 3.04±0.96 | 3.04±0.56 | 0.004 | 0.997 |
| Tumor diameter [mm, $\overline{x} \pm s$ ] | 22.57±6.46 | 22.96±6.07 | 0.237 | 0.813 |
| Pathological type [n(%)] | | | | |
| Growth hormone type (GH) | 20(42.55) | 7(30.43) | | |
| Prolactin type (PRL) | 17(36.17) | 7(30.43) | 3.984 | 0.263 |
| Adrenocorticotropic hormone | 3(6.38) | 5(21.74) | | |
| Type (ACTH) | 7(14.89) | 4(17.39) | | |
| Preoperative serum CEACAM1 level | 5075.45±901.54 | 6078.57±1219.72 | 3.882 | <0.001 |
| Preoperative ACTH (pmol/L) | 67.16±5.83 | 66.06±6.42 | 0.690 | 0.492 |
| Preoperative PRL (μg/L) | 60.43±6.35 | 62.54±6.74 | 1.285 | 0.203 |
| Preoperative GH (μg/L) | 21.62±2.04 | 22.34±2.17 | 1.368 | 0.176 |
| Preoperative TSH (mU/L) | 15.60±5.17 | 13.94±5.60 | 1.230 | 0.223 |
| Preoperative MD (dB) | 10.43±2.04 | 10.85±2.04 | 0.821 | 0.415 |
| Preoperative PSD (dB) | 8.24±1.73 | 8.45±1.78 | 0.476 | 0.635 |
| Preoperative VFI (%) | 62.60±3.69 | 65.90±5.63 | 2.552 | 0.013 |

***Ethical Approval***

This study was approved by Huai'an Hospital of Huai'an City (HJ2023113).

## RESULTS

***Comparison of different serum CEACAM1 levels***

*Comparison of patients' general information*

The difference between patients with high and low expression of serum CEACAM1 levels was not statistically significant (P>0.05) when comparing the baseline data with the perioperative situation (table 1).

***Subgroup Analysis of CEACAM1 Levels***

Subgroup analyses of age and pathological type were performed on the CEACAM1 levels of the patients. The results indicated that there was no statistically significant difference in the preoperative CEACAM1 levels among pituitary tumor patients of different ages, genders, BMIs, and pathological types (P>0.05) (table 2).

***Comparison of visual and pituitary hormones***

Before operation, the pituitary hormone ACTH levels were significantly higher in patients with high serum CEACAM1 levels compared to those with low levels (P<0.05). One month after surgery, the pituitary hormones ACTH, PRL, and TSH levels were significantly higher in patients with high serum CEACAM1 levels than in those with low levels (P<0.05). The expression level of serum CEACAM1 had no statistically significant effect on visual recovery before operation and one month after surgery (P>0.05), as shown in table 3.

***Comparison of the occurrence of adverse reactions***

The incidence of adverse reactions in patients with high CEACAM1 level and low CEACAM1 level was recorded in the six-month follow-up of the patients after the operation and the rate of adverse reactions was 20.59% in the patients in the low level group and 44.44% in the patients in the high level group (table 4).

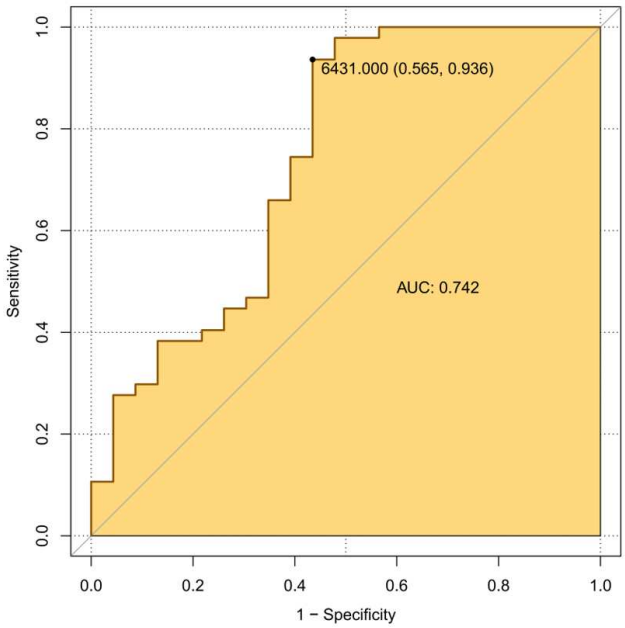



**Fig. 3**: Diagnostic value of preoperative serum CEACAM1 levels for TMX chemosensitivity ROC

***Serum CEACAM1 levels and prognosis***

*Before and after neuroendoscopic resection of transsphenoidal pituitary tumor*

According to the grouping criteria for efficacy assessment, 52 patients were included in the good prognosis group and 18 patients were included in the poor prognosis group. The preoperative serum CEACAM1 levels of the patients with good prognosis were significantly lower than those of the patients in the poor prognosis group (P<0.05), and one month and six months after the operation, the serum CEACAM1 levels of the patients in the two groups were significantly reduced compared with those of the preoperative group (P<0.05) (fig. 1).

***Preoperative serum CEACAM1 level predicts patient prognosis ROC***

The area under the curve (AUC) of the ROC curve of preoperative serum CEACAM1 level for predicting the prognosis of neuroendoscopic transsphenoidal pituitary tumor resection was 0.716>0.500 (P<0.05), suggesting that the preoperative serum CEACAM1 level has a certain predictive value for the prognosis of pituitary tumor resection. The optimal cutoff point was 5857.5pg/mL, suggesting that patients with preoperative serum CEACAM1 levels higher than 5857.5pg/mL had a significantly increased risk of poor postoperative prognosis (fig. 2).

***Comparative chemosensitivity of temozolomide***

*General information of patients*

Patients were grouped according to their sensitivity after chemotherapy with TMZ, including 47 patients in the sensitive group and 23 patients in the resistant group, and there was no statistically significant comparison of baseline data, preoperative visual acuity and preoperative pituitary hormone status between the two groups (P> 0.05) and the preoperative serum CEACAM1 level of patients in the sensitive group was significantly lower than that of patients in the resistant group (P<0.05) (table 5).

***Serum CEACAM1 level predicts patients' sensitivity to chemotherapy***

The area under the curve (AUC) of the ROC curve of preoperative serum CEACAM1 level for predicting TMZ chemotherapy resistance was 0.742>0.500 (P<0.05), suggesting that the preoperative serum CEACAM1 level has a certain predictive value for TMZ chemotherapy sensitivity in patients with pituitary tumors. The optimal cutoff point was 6431 pg/mL, suggesting that patients with preoperative serum CEACAM1 levels higher than 6431 pg/mL had a significantly increased risk of postoperative TMZ chemotherapy resistance (fig. 3).

## DISCUSSION

The treatment of clinical pituitary tumors generally includes surgical treatment, radiotherapy and medical treatment. However, the high recurrence rate after surgery remains a non-negligible issue. To effectively prevent the postoperative recurrence of pituitary tumors, drug treatment is usually supplemented during the treatment process. Bromocriptine, a dopamine receptor agonist, mainly functions by inhibiting the abnormal secretion of pituitary tumor hormones and reducing the tumor volume (Iglesias *et al*., 2020). TMZ, an imidazotetrazine antineoplastic drug, is a commonly used first-line chemotherapy drug in clinical practice. TMZ has shown good efficacy in related clinical studies on the adjuvant treatment of gliomas. However, some pituitary tumor patients have congenital or acquired resistance to TMZ, limiting the clinical benefits for patients. For these patients, increasing the TMZ dose will not improve the prognosis of pituitary tumor patients and is prone to lead to the recurrence of pituitary tumors (Markel *et al*., 2009). Therefore, reversing the resistance of pituitary tumors to TMZ is considered one of the keys to improving the quality of life and survival status of pituitary tumor patients.

***CEACAM1 and postoperative prognosis of pituitary tumor patients***

Markel *et al*. found in their research (Muturi *et al*., 2024) that CEACAM1 can inhibit the specific killing ability of NK cells and tumor-infiltrating T cells in melanoma patients. In lung cancer and gastric cancer, the high expression of CEACAM1 makes cancer cells more prone to metastasis (Matsumoto *et al*., 2024; Southekal *et al*., 2023). Götz L reported in a study (Götz *et al*., 2024) that CEACAM1 participates in the interaction of various immune cells, affects the function of immune cells and

the immune escape of tumor cells, and regulates the body's immune killing ability against tumors. In T lymphocytes, the CEACAM1 - L subtype inhibits T cell function by suppressing the TCR signaling pathway and reducing cytokine secretion, while the CEACAM1 - S subtype regulates cytokine production and the ratio of the two affects the immune response. In natural killer cells, the high expression of CEACAM1 inhibits their proliferation, cytokine secretion and cytolytic properties, helping tumor cells escape. For B lymphocytes, CEACAM1 can negatively regulate their immune function. In myeloid-derived cells, CEACAM1 regulates granulocyte generation and apoptosis, affects DC cell maturation and activation, and interferes with the anti-tumor immune response.

Current studies believe that CEACAM1 can not only be an effective diagnostic marker for various malignant tumors such as breast cancer, lung cancer, melanoma, colorectal cancer, and pancreatic cancer (Zhang *et al*., 2024; Zhao *et al*., 2024; Yu *et al*., 2024; Gheorghe *et al*., 2024), but currently, there are relatively few studies on the relationship between CEACAM1 expression and pituitary tumors. In this study, the incidence of adverse reactions was higher in patients with high serum CEACAM1 levels, and the preoperative serum CEACAM1 level of patients with good prognosis was significantly lower than that of patients with poor prognosis, which is somewhat similar to the relationship between CEACAM1 biomarkers and prognosis in other tumor studies (Yi *et al*., 2024). It is suggested that serum CEACAM1 may become a potential indicator for evaluating the prognosis of pituitary tumors. The possible reasons for the analysis are as follows: The Wnt signal is a secreted protein between cells, which is extremely conserved in evolution and participates in processes such as cell proliferation, apoptosis, and development. Its abnormal activation can cause abnormal cell proliferation and differentiation, leading to tumorigenesis. CEACAM1 expressed on human micro vascular endothelial cells can stimulate the activity of vasculogenesis dependent on vascular endothelial growth factor (VEGF) and fibroblast growth factor through the Wnt signaling pathway, thereby promoting tumor growth and metastasis (Tang *et al*., 2023).

***CEACAM1 Level and Patient's TMZ Resistance***

In this study, patients with lower preoperative serum CEACAM1 levels were more sensitive to TMZ chemotherapy. The possible reasons for the analysis are as follows: (1) Fiori V's research shows that CEACAM1 can prevent T lymphocyte activation and proliferation, inhibit the activity of tumor-infiltrating lymphocytes, promote tumor cell invasion, promote angiogenesis, and regulate vascular remodeling (Fiori *et al.*, 2012). (2) CEACAM1 is also one of the immune checkpoint molecules and participates in the activation and inhibition of T cells through inhibitory signaling pathways (Sauer *et al*., 2023). It may be that CEACAM1 inhibits the activation of T cells, which may lead to the aggravation of the local immunosuppressive state of pituitary tumors. (3) After oral administration, TMZ can be metabolized into 5-(3-methyltriazin-1)-imidazole-4-carboxamide, thereby protecting tumor cells from TMZ damage (Jeon *et al*., 2023; Modestov *et al*., 2024; Huang *et al*., 2024). (4) Under normal circumstances, MGMT can restore the normal structure of DNA and counteract the alkylation effect of TMZ, leading to the resistance of tumor cells to TMZ. Huang YH indicated in the study that the high expression of CEACAM1 level can weaken the sensitivity of NK cells to lyse tumor cells, thereby weakening the body's anti-tumor immune ability, which may be the key to the patient's resistance to TMZ. Tumor cells can use this pathway to evade the immune attack of the body. Therefore, a high level of CEACAM1 is not conducive to the effectiveness of TMZ chemotherapy drugs and may be related to affecting DNA repair, apoptotic signal transduction, and the tumor microenvironment. It makes patients with high levels of CEACAM1 more likely to develop resistance and is expected to become a biomarker for predicting resistance and a target for developing new treatment strategies. Future research can further study the specific molecular mechanisms by which serum CEACAM1 affects the prognosis and chemotherapy sensitivity of pituitary tumors to further verify the results of this study.

***Limitations of this study***

The sample size of this study is relatively small, which may lead to insufficient statistical power of the results and the inability to detect some subtle but important differences. Secondly, the study only focused on the CEACAM1 level in the serum and the expression of CEACAM1 in tumor tissues and its relationship have not been involved. In addition, this study is a single-center observational study, and there may be a certain selection bias. Future research can expand the sample size and conduct a multicenter prospective study; moreover, the postoperative prognosis of pituitary tumor patients is usually jointly determined by multiple factors, and serum CEACAM1 is only one of them. The interaction and comprehensive influence between it and other factors need to be further explored. Explore the value of the combined use of serum CEACAM1 and other biomarkers in predicting prognosis and chemotherapy sensitivity to more comprehensively understand the role of CEACAM1 in pituitary tumors.

## CONCLUSION

In summary, this study explored the relationship between serum CEACAM1 level and the prognosis of neuroendoscopic transsphenoidal pituitary tumor resection and the sensitivity to temozolomide chemotherapy. The preoperative serum CEACAM1 level

can predict the prognosis of pituitary tumor resection and TMZ chemotherapy resistance to a certain extent. When the preoperative serum CEACAM1 level is higher than 5857.5pg/mL, the risk of poor postoperative prognosis is significantly increased; when the preoperative serum CEACAM1 level is higher than 6431pg/mL, the risk of postoperative TMZ chemotherapy resistance is significantly increased. However, this study has limitations such as a small sample size and single-center observation. Future research needs to expand the sample size and conduct multicenter studies to deeply explore the related molecular mechanisms.

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