

A Comparative Study on Clinical Features, Surgical Outcomes, and Postoperative Complications in Pituitary Apoplexy vs. Non-Apoplexy Patients

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Xiaoxu Li¹, Xialin Zheng¹, Zhiquan Jiang¹, Dongqi Shao¹, Yu Li¹

¹Department of Neurosurgery, The First Affiliated Hospital of Bengbu Medical University, 233004 Bengbu, Anhui, China

AIM: To explore the differences in clinical features between patients with pituitary apoplexy and those without, analyze the risk factors for pituitary apoplexy, evaluate the incidence of postoperative complications between patients with pituitary apoplexy and those without, and investigate the risk factors for postoperative complications to provide clinical guidance for diagnosis and treatment.

METHODS: In this retrospective analysis, clinical data of 108 pituitary tumor patients admitted between January 2020 and July 2024 were collected. The patients were divided into two groups: the pituitary apoplexy group ($n = 50$) and the pituitary non-apoplexy group ($n = 58$). Baseline data, surgical outcomes, and postoperative complications were compared between the two groups. Multivariate logistic regression analysis was performed to identify the risk factors for pituitary apoplexy and postoperative complications.

RESULTS: Multivariate logistic regression analysis revealed that tumor size (odds ratio [OR] = 1.064, 95% confidence interval [CI]: 1.010–1.120, $p < 0.05$) and hypertension (OR = 5.552, 95% CI: 1.660–18.572, $p < 0.05$) were independent risk factors for pituitary apoplexy. The incidence of postoperative pituitary dysfunction and the average length of hospital stay were higher in the apoplexy group than in the non-apoplexy group ($p < 0.05$). Multivariate logistic regression analysis showed that tumor size (OR = 1.142, 95% CI: 1.061–1.229, $p < 0.05$) and preoperative hypothyroidism (OR = 12.002, 95% CI: 1.129–127.648, $p < 0.05$) were identified as independent risk factors for postoperative complications in pituitary tumor patients.

CONCLUSIONS: The occurrence of pituitary apoplexy is closely related to tumor size and hypertension. Patients with apoplexy face a higher risk of postoperative pituitary dysfunction and experience a longer hospital stay compared to the non-apoplexy patients. Postoperative complications are associated with tumor size and preoperative hypothyroidism.

Keywords: pituitary tumor; pituitary apoplexy; clinical features; surgical efficacy; complications; risk factors

Introduction

Pituitary tumors are among the most common endocrine tumors in the intracranial region [1,2]. Owing to the advancements in imaging techniques and improvements in endocrine diagnostic methods, the detection rate of pituitary tumors has surged in recent years. Pituitary apoplexy is one of the most severe complications of pituitary tumors [3], while its pathogenesis remains largely unclear [4,5]. It is generally believed that hemorrhage or infarction within the pituitary tumor is the primary pathological driver, which is possibly related to factors such as insufficient blood supply due to rapid tumor growth, microvascular lesions, and various triggering factors [6].

Clinically, pituitary apoplexy exhibits significant heterogeneity. In typical cases, patients may present with sudden severe headaches, visual disturbances, and ocular movement disorders, while some patients exhibit more insidious

symptoms [7,8]. The variability in clinical manifestations not only hampers early diagnosis but also complicates the selection of treatment strategies. Identifying risk factors for pituitary apoplexy is crucial for the treatment of pituitary tumor patients and can potentially improve the prognosis of the affected patients. At present, however, systematic study on the risk factors for this pathological condition remain scarce [9].

Perioperative management of pituitary apoplexy patients has always been an important issue. Research has shown that, compared to general pituitary tumor patients, those with pituitary apoplexy have a significantly higher incidence of postoperative complications, such as pituitary dysfunction and electrolyte imbalances [10,11]. However, research on the risk factors and preventive strategies for these complications is relatively limited. Specifically, there is a lack of systematic analysis of the impact of factors such as tumor size and preoperative endocrine function status on postoperative outcomes.

Therefore, this study aims to compare the clinical features of patients with and without pituitary apoplexy, identify the risk factors for pituitary apoplexy, and evaluate the incidence and risk factors of postoperative complications in both groups, thereby providing new insights and guidance for clinical diagnosis and treatment.

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Correspondence to: Xiaoxu Li, Department of Neurosurgery, The First Affiliated Hospital of Bengbu Medical University, 233004 Bengbu, Anhui, China (e-mail: xiaoxulidocor@hotmail.com).

Table 1. Univariate analysis of pituitary apoplexy.

Characteristic	Apoplexy group (n = 50)	Non-apoplexy group (n = 58)	t/χ^2	p
Gender			0.001	0.997
Male	24	28		
Female	26	30		
Mean age (years)	50.68 ± 14.49	53.07 ± 13.31	0.893	0.374
Hormone type			2.745	0.433
Non-functional	39	41		
Prolactin	8	8		
Growth hormone	3	8		
Adrenocorticotrophic hormone	0	1		
Tumor size (maximum diameter) (mm)	25.87 ± 10.01	20.77 ± 7.53	3.015	0.003*
Diabetes	5	10	1.773	0.278
Hypertension	19	11	4.849	0.028*
Hypothyroidism	4	1	1.185	0.276

* $p < 0.05$.

Materials and Methods

General Information

This study included 108 patients with pituitary tumors who were admitted to the First Affiliated Hospital of Bengbu Medical University between January 2020 and July 2024. All study subjects met the inclusion criteria. Non-apoplexy patients from the same period who fulfilled the exclusion criteria were not included in the study. The patients were classified into two groups based on the diagnostic criteria for pituitary apoplexy [12]: the apoplexy group ($n = 50$) and the non-apoplexy group ($n = 58$).

Inclusion Criteria

Inclusion criteria of this study are as follows: (1) All enrolled patients were diagnosed with pituitary tumor, as confirmed with preoperative magnetic resonance imaging (MRI) and postoperative pathology tests. The diagnostic criteria for pituitary apoplexy include: ① postoperative pathology confirming pituitary apoplexy (high weight); ② intraoperative confirmation of old hemorrhage within the tumor and postoperative pathology confirming pituitary tumor (medium weight); ③ preoperative MRI showing non-uniform signal intensity of the pituitary tumor and postoperative pathology confirming pituitary tumor (low weight). Satisfying any one of these three conditions is sufficient for confirming a diagnosis of pituitary apoplexy. (2) All patients underwent the same surgery—transsphenoidal resection of pituitary tumors—without having been subjected to other surgical methods. (3) Patients were aged ≥ 18 years. (4) Patients had complete preoperative clinical data (hormone levels, imaging reports), intraoperative records, and postoperative follow-up data (symptom improvement, recurrence, complications, hormone recheck).

Exclusion Criteria

Exclusion criteria of this study are as follows: (1) patients with other intracranial tumors (such as meningiomas,

gliomas) or vascular malformations (such as aneurysms); (2) patients with a history of pituitary radiation therapy, multiple pituitary tumor surgeries, or long-term dopamine agonist therapy (for prolactinomas, if the drug withdrawal time was less than 3 months); (3) patients who received only conservative drug treatment or had not underwent complete surgery; (4) pregnant or breastfeeding women; (5) patients with missing clinical data or who had lost to follow-up; and (6) patients with severe coagulation disorders or recent use of anticoagulants (≤ 1 month).

Table 2. Multivariate logistic regression analysis of pituitary apoplexy.

Risk factor	B	S.E.	Wald	p	Exp (B)	95% CI
Tumor size	0.062	0.026	5.552	0.018*	1.064	1.010–1.120
Hypertension	1.714	0.616	7.741	0.005*	5.552	1.660–18.572

* $p < 0.05$. CI, confidence interval.

Data Collection

Patient information was collected from the hospital's information system. Based on the diagnostic criteria for pituitary apoplexy, patients were classified into apoplexy and non-apoplexy groups. The following information was collected from the enrolled patients: (1) baseline information, including gender, age, hormone types, tumor size (maximum tumor diameter), preoperative comorbidities, preoperative clinical symptoms, and preoperative and postoperative hormone status; and (2) postoperative complications (including diabetes insipidus, cerebrospinal fluid rhinorrhea, and pituitary dysfunction) and length of hospital stay. These data were compared between the apoplexy and the non-apoplexy groups.

Statistical Methods

Data were analyzed using SPSS 22.0 statistical software (IBM, Armonk, NY, USA). Continuous variables were first

Table 3. Comparison of postoperative complications and length of hospital stay between apoplexy and non-apoplexy groups.

Group	n	Diabetes insipidus	Cerebrospinal fluid rhinorrhea	Hypopituitarism	Mean length of hospital stay (days)
Apoplexy group	50	9	3	14	16.36 ± 5.65
Non-apoplexy group	58	4	1	2	14.50 ± 3.82
t/χ^2	-	3.127	0.439	12.826	2.027
p	-	0.077	0.508	<0.001*	0.045*

* $p < 0.05$.**Table 4. Risk factor analysis for postoperative complications in pituitary apoplexy and non-apoplexy patients.**

Characteristic	Complication group (n = 27)	Non-complication group (n = 81)	t/χ^2	p
Gender			0.791	0.324
Male	11	41		
Female	16	40		
Average age (years)	50.41 ± 12.12	52.48 ± 14.42	0.671	0.504
Hormone type			4.818	0.186
Non-functional	20	60		
Prolactin	5	11		
Growth hormone	1	10		
Adrenocorticotrophic hormone	1	0		
Tumor size (maximum diameter) (mm)	31.24 ± 13.42	21.89 ± 5.49	5.143	<0.001*
Surgical duration (min)	117.59 ± 30.07	115.43 ± 22.12	0.400	0.690
Hypothyroidism	4	1	5.662	0.017*
Abnormal preoperative prolactin levels	16	32	3.200	0.074
Abnormal preoperative growth hormone levels	1	10	0.843	0.358
Abnormal preoperative cortisol levels	14	23	4.947	0.026*
Abnormal preoperative thyroid hormone levels	4	10	0.000	1.000

* $p < 0.05$.

tested for normality using the Shapiro–Wilk test. Normally distributed variables are expressed as mean ± standard deviation (SD), and independent samples t -test was used for data comparison. Expressed as rates or proportions, categorical variables were compared using the chi-square test or Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to identify independent risk factors associated with pituitary apoplexy. A p -value of <0.05 was considered statistically significant.

Results

Baseline Characteristics and Univariate Analysis of Pituitary Apoplexy

Preoperative baseline data, including gender, age, hormone types, tumor size, and preoperative comorbidities (hypertension, diabetes, hypothyroidism), were collected from both apoplexy and non-apoplexy groups. Group comparison showed significant differences in tumor size and hypertension between the apoplexy and non-apoplexy groups ($p < 0.05$), as shown in Table 1.

Multivariate Logistic Regression Analysis of Pituitary Apoplexy

Statistically significant indicators from the univariate analysis, such as tumor size and hypertension, were integrated in multivariate logistic regression analysis, with the occur-

rence of apoplexy as the dependent variable. The results indicated that tumor size and hypertension are independent risk factors for pituitary apoplexy ($p < 0.05$), as shown in Table 2.

Comparison of Postoperative Complications and Length of Hospital Stay Between Pituitary Apoplexy and Non-Apoplexy Groups

There were no significant differences in the incidence of diabetes insipidus and cerebrospinal fluid rhinorrhea between the apoplexy and the non-apoplexy patients ($p > 0.05$). However, apoplexy patients had a higher incidence of postoperative pituitary dysfunction and experienced a longer average hospital stay compared to non-apoplexy patients ($p < 0.05$), as shown in Table 3.

Analysis of Risk Factors for Postoperative Complications in Pituitary Apoplexy and Non-Apoplexy Patients

Multivariate logistic regression analysis was performed on postoperative complications (including diabetes insipidus, cerebrospinal fluid rhinorrhea, and pituitary dysfunction) in apoplexy and non-apoplexy patients. Preoperative baseline data were used as independent variables. Variables with $p < 0.05$ in the univariate analysis were integrated into the multivariate analysis. The results indicated that tumor size, preoperative hypothyroidism and abnormal preoperative cortisol levels were associated with postoperative complications

Table 5. Multivariate logistic regression analysis of postoperative complications for patients with pituitary tumors.

Risk factor	B	S.E.	Wald	<i>p</i>	Exp (B)	95% CI
Tumor size	0.132	0.038	12.465	<0.001*	1.142	1.061–1.229
Hypothyroidism	2.485	1.205	4.255	0.039*	12.002	1.129–127.648
Abnormal preoperative cortisol levels	0.847	0.596	2.022	0.155	2.333	0.724–7.514

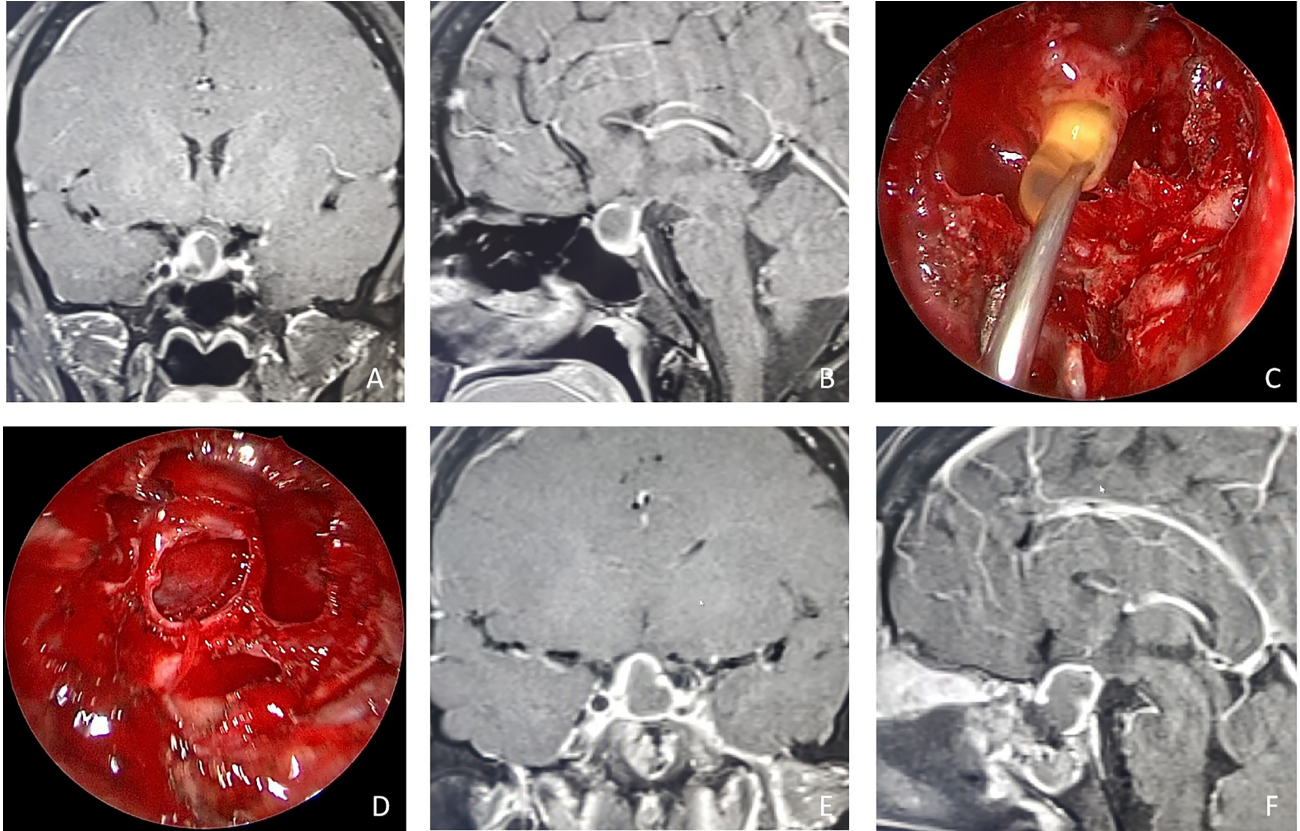
* $p < 0.05$.

Fig. 1. Magnetic resonance imaging (MRI) images of a representative case of pituitary apoplexy before and after transsphenoidal endoscopic surgery. (A,B) Preoperative MRI (coronal and sagittal views) showing pituitary apoplexy. The images highlight an irregular signal within the tumor, consistent with hemorrhagic or ischemic changes typical of pituitary apoplexy. (C) After dural opening, brownish fluid was observed, confirming the presence of hemorrhage within the tumor. (D) Following total resection of the tumor, the diaphragm sellae was found to have descended, an indication of successful removal and relief of pressure. (E,F) Postoperative MRI (coronal and sagittal views) at 72 hours post-surgery confirming total tumor resection, with no residual mass observed in the sella turcica.

($p < 0.05$), as shown in Table 4. Further multivariate logistic regression analysis revealed that tumor size and hypothyroidism significantly influence the occurrence of postoperative complications ($p < 0.05$), as shown in Table 5.

Imaging Studies on a Representative Case

A typical case of a patient from the apoplexy group was selected. Preoperative and postoperative endoscopic transsphenoidal surgical images of this case were obtained. The patient was a 31-year-old female admitted with a complaint of amenorrhea for over one year. She was diagnosed with a prolactin-secreting pituitary apoplexy. Despite a history of hypertension, her blood pressure was well-controlled. Preoperative MRI indicated a maximum tumor diameter of 17 mm, and preoperative pituitary prolactin

level was 485.10 ng/mL. A transsphenoidal pituitary adenoma resection was performed, achieving complete tumor removal. One week postoperatively, the pituitary prolactin level dropped to 51.96 ng/mL. The patient did not develop diabetes insipidus, cerebrospinal fluid rhinorrhea, or pituitary insufficiency after surgery.

Complete MRI images of this representative case are shown in Fig. 1.

Discussion

This paper presents a comparative analysis of the clinical data of 108 pituitary tumor patients to systematically explore the risk factors for pituitary apoplexy, evaluate the incidence of postoperative complications and average length of hospital stay between the apoplexy and non-apoplexy

groups, and investigate the associated risk factors for postoperative complications in patients who had undergone pituitary tumor surgery. The main findings of this study include: (1) tumor size and hypertension are independent risk factors for pituitary apoplexy; (2) apoplexy patients have a higher risk for postoperative pituitary dysfunction and experience longer average hospital stays than non-apoplexy patients; (3) tumor size and preoperative hypothyroidism are independent risk factors for postoperative complications in pituitary tumor patients.

Multivariate logistic regression analysis in this study identified tumor size (odds ratio [OR] = 1.064) and hypertension (OR = 5.552) as independent risk factors for pituitary apoplexy. These findings are consistent with those of Li *et al.* [13], who studied 843 pituitary tumor patients and found that 121 patients experienced pituitary apoplexy, with an incidence of 14.4%. In their study, tumors with a diameter >2 cm were 3.952 times more likely to cause apoplexy than tumors ≤2 cm (95% confidence interval [CI]: 2.211–7.053), and hypertensive patients carried a 2.765 times higher risk of pituitary apoplexy compared to non-hypertensive patients (95% CI: 1.411–5.416). Kajal *et al.* [14] also found that tumor size is an independent risk factor for pituitary apoplexy, suggesting that larger pituitary tumors may be inadequately supplied with blood, a condition leading to ischemic necrosis. Additionally, large tumors may compress the surrounding vessels, increasing the risk of ischemic infarction; hypertension can increase the pressure in the blood vessel walls, accelerating atherosclerosis in blood vessel networks surrounding the tumor, leading to vessel rupture and hemorrhage, which in turn causes apoplexy.

This study found that apoplexy patients had a significantly higher incidence of postoperative pituitary dysfunction, which is likely attributed to several factors. On the one hand, acute ischemic/hemorrhagic damage caused by apoplexy may lead to irreversible damage to the pituitary tissue, particularly in the anterior pituitary region. Reperfusion injury may further exacerbate the tissue damage [15]. Additionally, the pituitary tissue has limited tolerance to ischemia, and if the ischemic damage exceeds a critical threshold, irreversible functional loss may occur. Previous studies have indicated that inflammatory factors released during the apoplexy (such as Interleukin [IL]-1 β , Tumor Necrosis Factor [TNF]- α , etc.) may affect the function of residual pituitary tissue, leading to microcirculation dysfunction, exacerbating tissue damage, and potentially affecting the remaining pituitary cells for the long term due to the activation of autoimmune responses [16,17]. Based on these findings, for the perioperative management of pituitary apoplexy patients, it is recommended to assess the endocrine function status preoperatively, develop an individualized surgical strategy, and protect normal pituitary tissue as much as possible. Postoperatively, more frequent monitoring of endocrine function is needed, especially during the first 3–6 months. For high-risk patients, preventive hormone replacement therapy should be considered. Fur-

thermore, a long-term follow-up mechanism should be established to dynamically assess changes in hormone levels. Implementing these measures may help improve patient prognosis and quality of life.

In the present study, the patients in the apoplexy group were hospitalized longer than those in the non-apoplexy group. The difference in the average length of hospital stay could be attributed to several reasons: (1) apoplexy patients often suffer from varying degrees of pituitary dysfunction prior to surgery [18], requiring preoperative hormone replacement therapy; (2) apoplexy patients tend to have a higher incidence of postoperative complications, and the treatment of these complications extends their hospital stay; (3) the delayed recovery of vision and cranial nerve damage in some apoplexy patients prolongs hospitalization.

This study identified two independent risk factors for postoperative complications (including diabetes insipidus, cerebrospinal fluid rhinorrhea, and pituitary dysfunction): tumor size (OR = 1.142) and preoperative hypothyroidism (OR = 12.002). These findings partially support previous study, such as Zhao *et al.* [19], who reported a correlation between tumor size and postoperative complications. However, this study is the first to highlight a strong association between preoperative hypothyroidism and postoperative complications, which warrants special attention. Regarding tumor size, this study found that patients with larger tumors carry a higher risk of complications. This association may be due to several factors: (1) large tumors often require more extensive surgical manipulation, increasing the risk of injury to surrounding critical structures; (2) resection of larger tumor may require longer surgical duration, increasing the risk of complications; (3) large tumors often cause more significant anatomical changes, further complicating the surgery.

Lastly, this study revealed a significant correlation between preoperative hypothyroidism and postoperative complications (including diabetes insipidus, cerebrospinal fluid rhinorrhea, and pituitary dysfunction). We speculate that this correlation may involve several mechanisms: (1) preoperative thyroid dysfunction can lead to cardiovascular instability [20], affecting the patient's surgical tolerance; (2) thyroid hormone levels may significantly impact the postoperative tissue repair process, and abnormal thyroid hormone levels may interfere with wound healing and tissue regeneration [21]; (3) pre-existing thyroid dysfunction may indicate more complex endocrine regulation disorders, which could increase the risk of postoperative complications; (4) thyroid dysfunction may be related to immune system dysfunction [22], affecting postoperative inflammation and healing.

Based on these findings, we recommend that patients with pituitary tumor should be subjected to comprehensive preoperative evaluation. In the case of a large tumor, a more detailed surgical plan and thorough preoperative preparation are necessary. Finally, an individualized follow-up plan should be established postoperatively, with preventive

measures targeting different risk factors. The implementation of these strategies may help reduce the incidence of postoperative complications.

Conclusions

In conclusion, the occurrence of pituitary apoplexy is closely associated with tumor size and hypertension. Patients in the apoplexy group demonstrated a higher risk of postoperative hypopituitarism and were hospitalized for a longer period, on average, compared to those in the non-apoplexy group. Furthermore, the incidence of postoperative complications was found to be significantly correlated with tumor size and preoperative hypothyroidism. This study is the first to highlight the strong association between preoperative hypothyroidism and postoperative complications. Nevertheless, we noted the relatively wide 95% CI for hypothyroidism in the multivariate logistic regression analysis of postoperative complications, which may be result of the limited number of pituitary tumor cases with preoperative hypothyroidism included in this study. The limitations of this research include the small sample size, retrospective design of the investigation, and the short follow-up period. Additionally, confounding factors such as intraoperative blood loss, anesthesia time and surgeon experience were not included in the analysis. Further studies should address these shortcomings accordingly.

Availability of Data and Materials

The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

XXL and DQS conceived the experiments. XXL designed the experiments. XXL and XLZ collected the patients' cases. ZQJ and YL analyzed the data. XXL drafted the manuscript. All authors have been involved in revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

All patients signed an informed consent form and adhered to the principles outlined in the Declaration of Helsinki by the World Medical Association. The study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Bengbu Medical University (ethics approval number: 2022KY064).

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Conflict of Interest

The authors declare no conflict of interest.

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