Research & Reviews: Journal of Clinical and Medical Case Studies

Predictive Model of Delayed Hyponatremia after Endoscopic Endonasal Transsphenoidal Resection of Pituitary Adenoma

Faan Miao[1]*, YuKang Pei[2]

[1]Department of Neurosurgery, Affiliated Hospital of Xuzhou Medical University, Xuzhou, China

[2]Department of Skull Base Oncology, Affiliated Hospital of Xuzhou Medical University, Xuzhou, China

Research Article

Received: 19-April-2024, Manuscript No. JCMCS-24- 132614; **Editor assigned:** 22-April-2024, PreQC No. JCMCS-24- 132614(PQ); **Reviewed:** 08-May-2024, QC No. JCMCS-24-132614; **Revised:** 15-May-2024, Manuscript No. JCMCS-24-132614(R); **Published:** 22-May-2024, DOI: 10.4172/J Clin Med Case Stud.9.2.005.

***For Correspondence:** Faan Miao, Department of Neurosurgery, Affiliated Hospital of Xuzhou Medical University, Xuzhou, China

E-mail: m_fan1825@xzhmu.edu.cn

Citation: Miao F, et al. Predictive Model of Delayed Hyponatremia after Endoscopic Endonasal Transsphenoidal Resection of Pituitary Adenoma. J Clin Med Case Stud. 2024;9:005.

ABSTRACT

Objective: This study aims to establish the risk factors and predictive model for the occurrence of delayed hyponatremia after endoscopic endonasal transsphenoidal resection of pituitary adenoma.

Methods: Data from 155 patients who underwent endoscopic endonasal transsphenoidal resection of pituitary adenoma at the affiliated hospital of Xuzhou Medical University from January 2018 to May 2023 were analyzed. These patients were randomly divided into a training group (108 cases, 70%) and a validation group (47 cases, 30%). Univariate and multivariate logistic regression analyses were conducted on the training group to identify risk factors for delayed hyponatremia after surgery. A predictive model was established using R software and validated.

Results: After conducting univariate and multivariate logistic regression analysis, factors influencing the occurrence of delayed hyponatremia after endoscopic endonasal transsphenoidal resection of pituitary adenoma were identified as follows: Elevated preoperative prolactin levels, higher preoperative suprasellar cistern height, and hyponatremia in the first 1-2 days after surgery. The area under the Receiver Operating Characteristic (ROC) curve for forecasting Delayed Postoperative Hyponatremia (DPH) in training and validation sets was 0.943 and 0.959 respectively. The DCA curve indicated a higher benefit in clinical application.

Conclusion: The risk prediction model for delayed hyponatremia after endoscopic endonasal transsphenoidal resection of pituitary adenoma, developed in this study, demonstrates favorable predictive performance. The nomogram can be utilized for early identification of high-risk individuals for DPH.

Keywords: Pituitary adenoma; Transsphenoidal surgery; Delayed hyponatremia; Nomograms

INTRODUCTION

Pituitary Adenoma (PA) is a tumor that grows in the sellar region of the anterior pituitary gland. Its incidence ranks only after gliomas and meningiomas [1,2]. Most pituitary adenomas can be removed through Transsphenoidal Surgery (TSS) using an endoscopic endonasal approach. This surgical technique not only avoids traction on brain tissue and cranial nerves but also maximizes tumor removal while reducing postoperative complications, thereby shortening hospital stays [3]. Delayed Postoperative Hyponatremia (DPH) refers to hyponatremia occurring on or after the third day following surgery [4]. The incidence of DPH after transsphenoidal surgery for pituitary adenoma varies between 7.4% and 14.7% [5]. Patients with hyponatremia may present with various clinical symptoms, and severe cases can lead to altered mental status, seizures, coma, and even death [6]. Additionally, research suggests that DPH is a major risk factor for readmission within 30 days postoperatively for pituitary adenoma [7]. The objective of this study is to explore the risk factors for DPH after endoscopic endonasal transsphenoidal resection of pituitary adenoma and to construct a predictive model to identify and screen high-risk patients, thereby assisting clinical decision-making.

MATERIALS AND METHODS

Patient cohort

A retrospective analysis was conducted on clinical data collected from 155 patients who underwent endoscopic endonasal transsphenoidal surgery at the affiliated hospital of Xuzhou Medical University between January 2018 and May 2023. Inclusion criteria were: a) Patients diagnosed with pituitary adenoma based on clinical and pathological confirmation; b) first-time recipients of endoscopic endonasal transsphenoidal resection of pituitary adenoma; c) availability of complete clinical data. Exclusion criteria were: a) History of previous pituitary surgery or radiotherapy; b) preoperative hyponatremia; c) patients with concomitant other pituitary lesions or endocrine disorders. The same surgical team performed all surgeries. Ethical approval was obtained from the Ethics Committee of the affiliated hospital of Xuzhou Medical University, and all patients were exempt from informed consent (XYFY2023-KL[illegible]01).

Research data

Collected and compiled clinical data, including demographic information, surgical procedures, and postoperative outcomes. Laboratory data encompassed hormone levels before and after surgery: Adrenocorticotropic Hormone (ACTH), cortisol, Prolactin (PRL), Growth Hormone (GH), Thyroid-Stimulating Hormone (TSH), and insulin-like growth factor, as well as serum sodium levels (preoperatively and postoperatively for the first 1 to 3 days; in case of hyponatremia, daily monitoring until normalization, otherwise every three days). Imaging data included pre- and postoperative pituitary MRI scans (plain and enhanced scans) for evaluating tumor size, Knosp grading, pre- and postoperative angle of pituitary stalk deviation, height increase of the diaphragma sellae before and after surgery, and extent of tumor resection.

Diagnostic criteria and definitions

Considering potential variations in reference values across different laboratories [8], low serum sodium concentration is defined as below 137 mmol/L based on the laboratory settings of our institution. Upon admission, all patients undergo radiological examination to observe tumor location and its relationship with surrounding tissues, classified into Knosp grades 0-4 [9]. The angle of deviation of the pituitary stalk is recorded on T1+C scans, defined as the angle at which the pituitary stalk deviates from the midline at its point of origin [10] (Figure 1). On T2W1 scans, the height of the diaphragma sellae elevation (the distance between the plane where the elevation of the diaphragma sellae begins and the plane of the highest point of the sellae) is calculated (Figure 2). Tumor volume is calculated using the simplified ellipsoid volume formula V=ABC/2.

Figure 1. The difference in pituitary stalk deviation angle before and after transsphenoidal surgery. (a) Before surgery, the pituitary stalk deviates 20.893° to the right; (b) After surgery, the tumor was totally removed, and the pituitary stalk deviation angle was 9.246°.

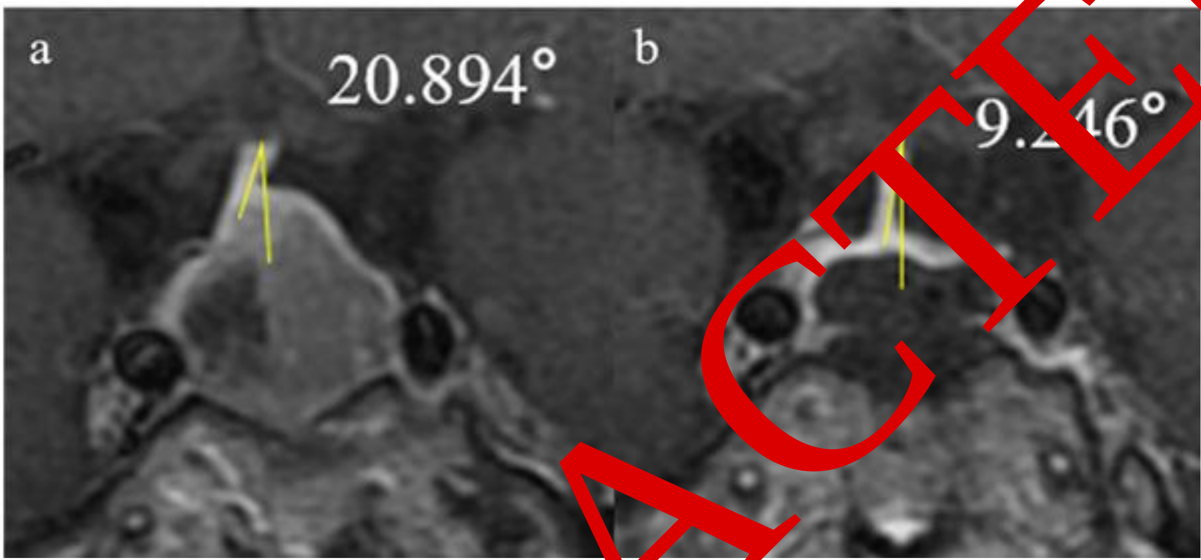
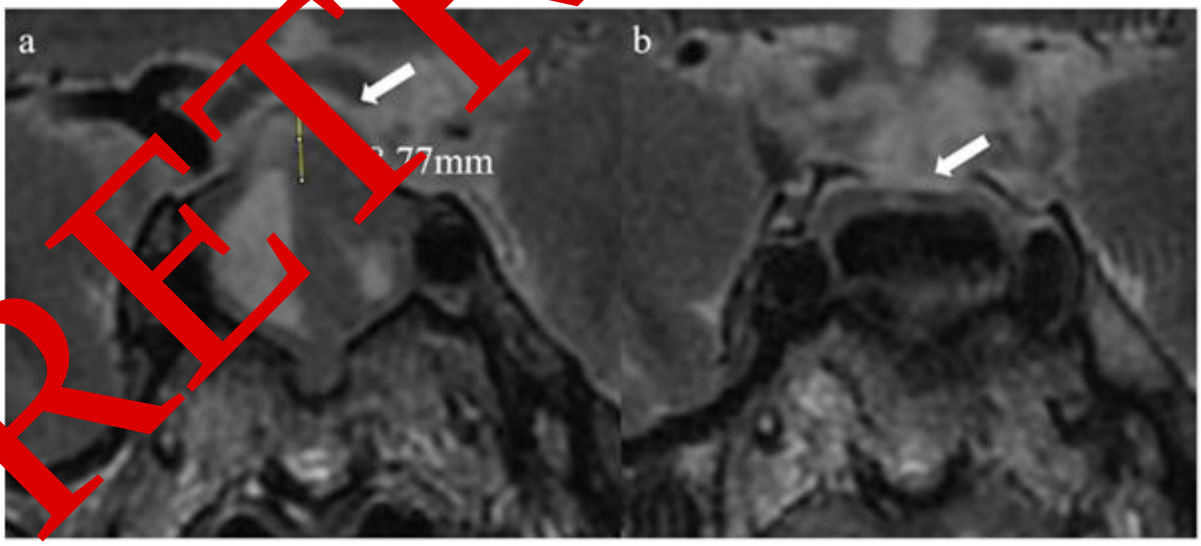


Figure 2. Changes in the Diaphragma Sellae (DS) before and after transsphenoidal surgery. (a) Preoperative elevation of DS was 8.77 mm; (b) After resection of the tumor, the elevation of DS was 0 mm.



Statistical analysis

The data analysis was performed using SPSS 25.0 software. Patients were randomly divided into two groups: A training group (108 cases, 70%) and a validation group (47 cases, 30%). Continuous variables were expressed as mean ± standard deviation ($\bar{x} \pm s$), and differences between the two groups were compared using the t-test. Categorical variables were presented as case numbers, and intergroup comparisons were made using the chisquare test (χ^2 test). Non-parametric tests were used for comparing ordinal data. Logistic regression analysis was conducted to determine independent risk factors in the training group. Differences were considered statistically significant when p-values were less than 0.05. The identified independent risk factors were then imported into R software (version 4.3.3) for analysis. Based on this, a nomogram predictive model was constructed for the training group. The predictive performance of this model was evaluated in the validation group by calculating the Area Under Curve (AUC), the Receiver Operating Characteristic (ROC) curve, calibration curve, and Decision Curve Analysis (DCA). These assessments were used to evaluate the predictive ability of the nomogram generated from the training group.

RESULTS

The basic characteristics of the cases

The study retrospectively analyzed 155 patients who underwent endoscopic endonasal transsphenoidal resection of pituitary adenoma at the affiliated hospital of Xuzhou Medical University from January 2018 to May 2023. Among them, 50 patients (32%) developed delayed hyponatremia. These patients were randomly divided into a training group (108 cases) and a validation group (47 cases) at a ratio of 7:3. In the training group, 39 patients developed delayed hyponatremia, while in the validation group, there were 11 cases. A comparison of clinical data between the training and validation groups showed no significant differences (Table 1).

Table 1. Comparison of the characteristics between the training and validation cohorts.

Factors	Training group (n=108)	Validation group (n=47)	t /c²/Z	*P*
Age, yrs	47.9 ± 12.5	50.9 ± 15.6	1.617	0.106
Sex			1.166	0.243
Male	51（47.2）	27（57.4）		
Female	57（52.8）	20（42.6）		
Dizziness and Headache	64（59.3）	26（55.3）	0.455	0.649
Visual damage and optic filed defect	51（47.2）	23（48.9）	0.196	0.845
Altered menstrual period	9（8.3）	6（12.8）	0.855	0.392
Galactorrhea	1（0.9）	1（2.1）	0.607	0.544
Changes in sexual function	0（0.0）	1（2.1）	1.516	0.13
Acromegalia	4（3.7）	3（6.4）	0.736	0.462
Preoperative ACTH (pg/ml)	25.6（19.8， 34.8）	29.1（19.2， 35.6）	1.094	0.274
Preoperative cortisol (ug/dl)	9.9（7.5， 13.1）	11.2（7.2， 15.4）	0.938	0.348
Preoperative PRL (ng/ml)	24.6（15.7， 256.8）	22.9（12.5， 40.1）	1.308	0.108
Preoperative GH (ng/ml)	0.6（0.2， 1.6）	0.3（0.1， 0.9）	1.829	0.067
Postoperative ACTH（pg/ml）	22.4（15.6， 35.9）	28.3（16.3， 35.9）	1.633	0.102
Postoperative cortisol (ug/dl)	14.8（7.9， 18.7）	18.6（8.9， 25.1）	2.423	0.015

Postoperative PRL (ng/ml)	21.3（9.5，139.5）	19.1（7.0，66.4）	1.03	0.303
Postoperative GH (ng/ml)	0.9（0.6，1.6）	0.8（0.5，1.6）	0.152	[illegible].879
Preoperative sodium levels（mmol/L）	141.5（139.0，142.3）	141.5（140.5，142.5）	1.7[illegible]2	0.087
Sodium levels 1-2 days after surgery（mmol/L）	139.7（136.5，141.9）	141.6（139.3，142.8）	1.[illegible]37	0.[illegible]
Sodium levels 3 days after surgery（mmol/L）	139.5（134.7，141.9）	141.1（139.4，14[illegible]）	2.9[illegible]	0.003
Maximum tumor diameter（mm）	25（16，34）	20（16，25）	[illegible]548	0.011
Tumor volume（cm³）	4.7（2.2，10.0）	3.2（2.0，[illegible]）	2.06[illegible]	0.039
Preoperative pituitary stalk deviation angle（°）	37.0（20.0，45.7）	[illegible]（20.1，38.9）	1.681	0.093
Postoperative pituitary stalk deviation angle（°）	20.0（2.1，29.1）	12.3（0.0，22.0）	1.681	0.12
Preoperative elevation of the diaphragma sellae（mm）	13.5（5.0，20.0）	8.0（5.0，1[illegible].0）	1.719	0.097
Postoperative elevation of the diaphragma sellae（mm）	4.5（0.0，[illegible]）	3.0（0.0，8.0）	1.824	0.068
Knosp grade			1.659	0.097
Grade 0~2	[illegible]（57.5）	36（76.6）		
Grade 3~4	4[illegible]（42.5）	11（23.4）		
Extent of tumor resection			1.486	0.137
Total resection	9[illegible]（85.2）	44（93.6）		
Subtotal resection	14（13.0）	3（6.4）		
Partial resection	2（1.9）	0（0.0）		
Intraoperative CSF leakage	14（13.0）	7（14.9）	0.322	0.748
Postoperative diabetes insipidus	49（45.4）	12（25.5）	2.316	0.021
Hyponatremia 1-2 days after surgery	32（29.6）	7（14.9）	1.937	0.053
Hyponatremia 3 days after surgery	39（36.1）	11（23.4）	2.934	0.121
Note: Adrenocorticotropic Hormone (ACTH); Prolactin (PRL); Growth Hormone (GH); Cerebral Spinal Fluid (CSF).				

Univariate and multivariate logistic regression analysis of delayed hyponatremia

Comparison of univariate analysis between the delayed hyponatremia group (39 cases) and the normal sodium group (69 cases) in the training group revealed significant differences in pre- and postoperative prolactin levels, maximum tumor diameter, tumor volume, pre- and postoperative pituitary stalk deviation angle, pre- and postoperative elevation of the diaphragma sellae, tumor invasiveness, preoperative serum sodium levels, hyponatremia on the first 1-2 days postoperatively, and postoperative diabetes insipidus (P<0.05). Further logistic regression analysis identified preoperative hyperprolactinemia, higher preoperative elevation of the diaphragm sellae, and occurrence of hyponatremia on the first 1-2 days postoperatively as independent risk factors for delayed hyponatremia following transsphenoidal surgery in patients with pituitary adenoma (P<0.05) (Table 2)

Table 2. Univariate and multivariate Logistic regression analysis of delayed hyponatremia after transsphenoidal surgery for pituitary adenomas [n(%)].

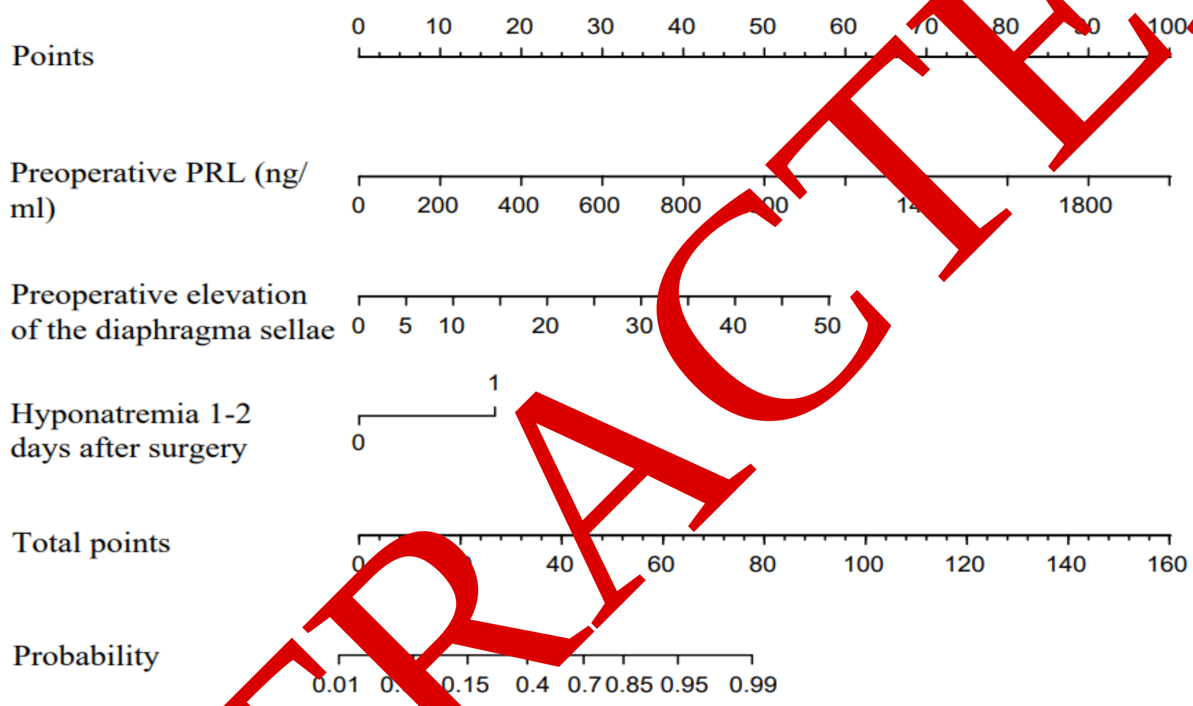
Univariate annalysis					Logistic regression analysis		
Factors	Delayed hyponatremia group（n=39）	Normal sodium group（n=69）	t /c²/Z	*P*	Odds ratio	95%CI	*P*
Preoperative PRL (ng/ml)	506.7（24.3, 1897.5）	21.1（13.9, 35.9）	5.28	0	[illegible]	[illegible]03~1.018	0.005
Postoperative PRL (ng/ml)	111.9（10.6, 323.3）	18.6（9.2, 27.6）	3.682	0			
Maximum tumor diameter（mm）	34（26， 41）	20（14， 27）	5.5[illegible]	0			
Tumor volume（cm³）	10.0（5.4, 16.5）	3.8（1.3， 6.2）	[illegible].149	0			
Preoperative pituitary stalk deviation angle（°）	45.6（40.1, 56.4）	28.7（11.4, 39.[illegible]）	5.66[illegible]	[illegible]			
Postoperative pituitary stalk deviation angle（°）	24.1（17.6, 32.8）	12.7（0.0, 24.6）	3.[illegible]91	0			
Preoperative elevation of the diaphragma sellae（mm）	20（1[illegible], 25）	8（5, [illegible]）	6.062	0	1.651	1.190~2.290	0.003
Postoperative elevation of the diaphragma sellae（mm）	7（3, [illegible]）	3.0（0.0， 8.0）	3.697	0			
Knosp grade Grade 0~2 Grade 3~4	12（30.7） 27（[illegible]9.3）	50（72.5） 19（27.5）	4.799	0			
Postoperative diabetes insipidus	[illegible]9（45.4）	12（25.5）	4.929	0			
Preoperative sodium levels（mmol/L）	140.2（138.0, 141.7）	141.3（139.7, 142.3）	2.329	0.02			
Hyponatremia 1-2 days after surgery	32（29.6）	7（14.9）	5.434	0	32.65	2.188~487.280	0.011

Note: Adrenocorticotropic Hormone (ACTH); Prolactin (PRL); Growth Hormone (GH); Cerebral Spinal Fluid (CSF).

Development of prediction model in the training cohort

Using R software (version 4.3.3), a predictive model was constructed based on the three variables selected from the logistic regression analysis conducted on the training set. This model is represented by a nomogram, which is used to estimate the likelihood of delayed hyponatremia occurrence after endoscopic transsphenoidal surgery for pituitary adenoma. The nomogram assigns a composite score based on the parameter values in the nomogram, which is then mapped to corresponding risk levels to estimate the risk of developing hyponatremia postoperatively (Figure 3).

Figure 3. Nomogram of delayed hyponatremia after transsphenoidal adenoma surgery. The predictor points can be found on the uppermost point scale that correspond to each patient variable and can be added up. The total points projected to the bottom scale indicate the risk of delayed hyponatremia. (For Hyponatremia 1-2 days after surgery, 0 means "No", 1 means "Yes").



Validation of the nomogram for delayed hyponatremia

External validation of the model was performed using data from the validation group comprising 47 patients. The area under the Receiver Operating Characteristic (ROC) curve for the nomogram model in the training set was 0.943 (95% CI 0.[illegible]98-0.98[illegible]), while in the validation set, it was 0.959 (95% CI 0.910-0.979) (Figure 4). These results indicate that the model has good discriminative ability on both internal and external data. In the calibration curve analysis, the predicted results of the model closely matched the observed outcomes in both groups, demonstrating a high level of fit (Figure 5). Additionally, DCA revealed that the application of this model within the threshold range of 0.01 to 0.93 (training group) and 0.01 to 0.87 (validation group) could lead to improved clinical utility, indicating its practical value in the clinical setting (Figure 6).

Figure 4. The ROC curves of the nomogram model (Left: Training set, Right: Validation set).

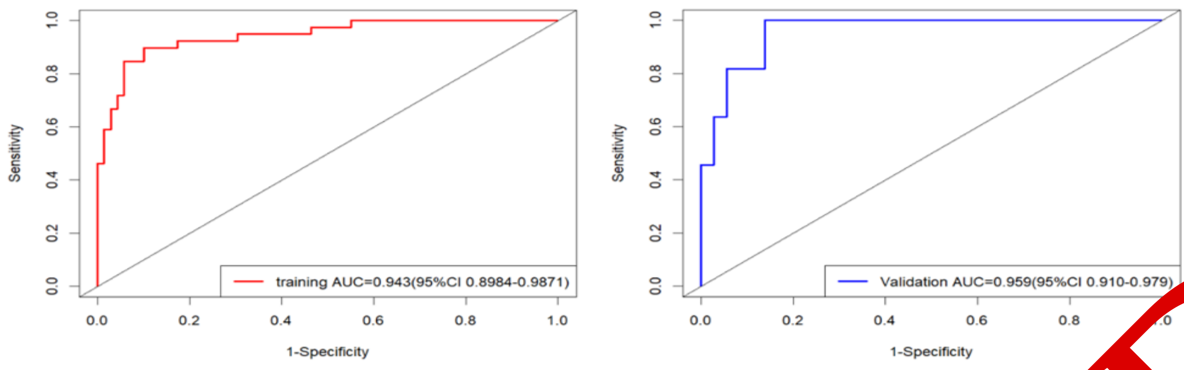


Figure 5. The calibration curves of the nomogram model (Left: Training set, Right: Validation set).

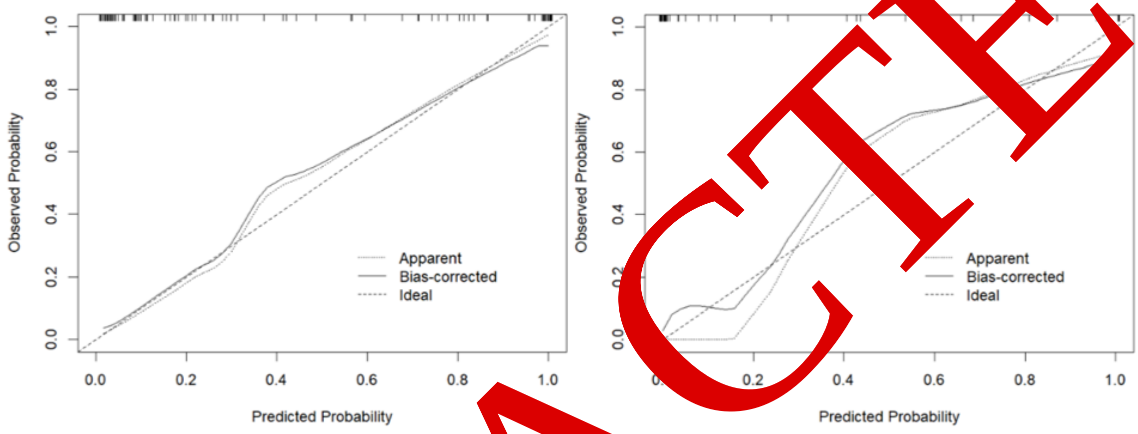
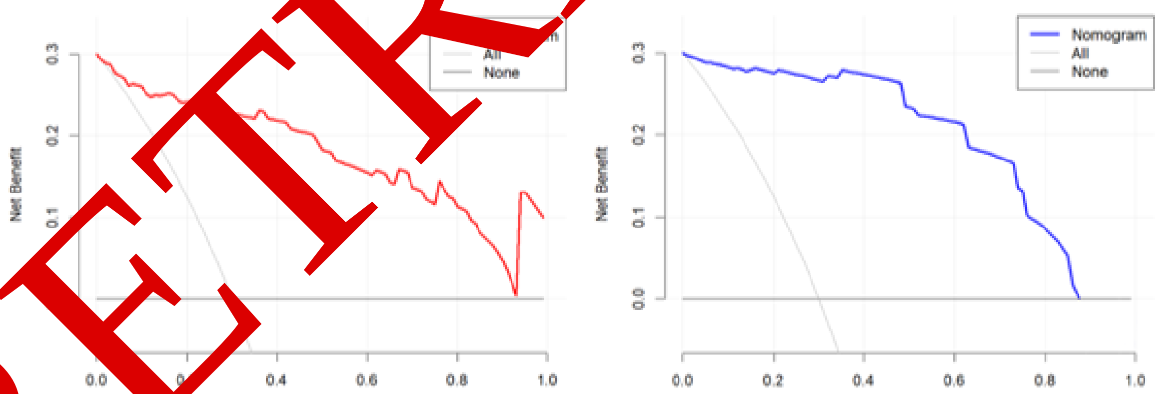


Figure 6. The DCA (Decision Curve Analysis) curves (Left: Training set, Right: Validation set).



DISCUSSION

Delayed Postoperative Hyponatremia (DPH) is a common complication following endoscopic endonasal Transsphenoidal Surgery (TSS) for pituitary adenoma and is a leading cause of unplanned readmission within 30 days postoperatively [11]. Studies suggest that the primary cause may be Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) [12], with Cerebral Salt-Wasting Syndrome (CSWS) being a rare cause in some cases [13].

Manipulation of the pituitary stalk and posterior pituitary during surgery may lead to uncontrolled release of Antidiuretic Hormone (ADH) [14]. This study investigated the risk factors for DPH after pituitary adenoma surgery and identified preoperative hyperprolactinemia, higher preoperative elevation of the diaphragma sellae, and occurrence of hyponatremia on the first 1-2 days postoperatively as independent risk factors for DPH following TSS in patients with pituitary adenoma. The establishment and validation of a risk prediction model based on these findings hold significant clinical relevance for the prevention of DPH. Huang et al. [15] demonstrated that preoperative hyperprolactinemia is an independent risk factor for delayed hyponatremia following endoscopic transsphenoidal surgery for non-functioning pituitary adenomas. Our study shares a similar viewpoint. Although the hypothalamus can secrete PRL inhibitory and releasing factors, it primarily suppresses PRL secretion through the release of inhibitory factors such as dopamine and gamma-aminobutyric acid [16]. Mechanical compression of the pituitary stalk by pituitary adenomas can lead to a so-called "stalk effect" or "pituitary stalk compression syndrome" resulting in decreased dopamine release and corresponding increase in PRL [17]. During tumor resection, the close proximity of the tumor to the pituitary stalk makes it more susceptible to interference or damage, leading to uncontrolled release of ADH. In Lin's study [10, 18], the descent of the diaphragma sellae is of significant importance in predicting the occurrence of DPH. In our study, preoperative elevation of the diaphragma sellae was found to be associated with DPH after TSS. High preoperative elevation of the diaphragma sellae during surgery leads to a rapid decrease in intrasellar pressure and a rapid reduction in tumor cavity height after tumor resection, resulting in passive traction of the pituitary stalk during surgery and mechanical injury, which may trigger the occurrence of SIADH. Similarly, changes in the pituitary stalk deviation angle can also predict the occurrence of DPH after TSS [19-21]. The more pronounced the changes in the pituitary stalk, the greater the likelihood of pituitary stalk injury. However, in our study, the pituitary stalk deviation angle was not identified as an independent risk factor for DPH. This may be due to the use of gelatin sponge packing in the tumor cavity and artificial dura reconstruction at the sellar floor during surgery, which takes approximately 4-6 weeks to be completely absorbed by the body [22]. As a result, changes in the pituitary stalk may not be significant when pituitary MRI was performed approximately 3 days postoperatively. In our study, patients who developed hyponatremia on the first 1-2 days postoperatively had an approximately 32.6-fold increased risk of DPH[23] found that patients with serum sodium concentration <138 mmol/L within 1-2 days after TSS had approximately 2.8 times higher risk of developing delayed hyponatremia, and similar results[24] were reported. Therefore, close monitoring of early postoperative serum sodium levels in TSS patients is crucial to identify the etiology of hyponatremia, implement preventive measures promptly, and reduce the risk of delayed hyponatremia.

In statistics, an AUC value of 0.70 to 0.79 was considered acceptable for predictive models, while a value of 0.80 to 0.89 indicates excellent predictive performance [25]. The predictive model constructed in our study achieved AUC values of 0.943 and 0.959 in the two groups, respectively, demonstrating excellent discriminative ability for predicting delayed hyponatremia after surgery. The calibration curves showed high consistency between the predicted and observed outcomes within a certain range, with a slope close to 1. Additionally, the DCA curves in both groups indicated that adopting relevant preventive measures for high-risk patients could lead to better clinical benefits within a larger threshold range, demonstrating good clinical utility. Although this study has incorporated relatively comprehensive and thorough clinical information, it is limited by being a single-center study with a limited sample size, and the model has not been validated in other centers. Therefore, our next step will be to conduct a broader, multicenter study to further refine the fitted model and validate it using data from external institutions, thereby expanding the applicability of the model.

CONCLUSION

This study utilized three key indicators: Preoperative prolactin levels, preoperative elevation of the diaphragma sellae, and postoperative hyponatremia on the first 1-2 days to construct a nomogram predictive model for predicting delayed hyponatremia after endoscopic transsphenoidal surgery for pituitary adenoma. This model has good reference value for early identification of high-risk patients, and it can help reduce the incidence of postoperative delayed hyponatremia and improve patient outcomes.

FUNDING

This project was supported by the National Natural Science Foundation of China (Grant No.8[illegible]2632).

CONFLICT OF INTEREST

The authors have no conflict of interest.

INFORMED CONSENT

With the consent of the Ethics Committee of the affiliated Hospital of Xuzhou Medical University, all patients were exempted from informed consent (XYFY2023-KL250-01).

REFERENCES

1. Monica Livia Gheorghiu, et al. Updates in the medical treatment of pituitary adenomas. Horm Metab Res. 2020;1:8-24.
2. Jiajia Zhang, et al. Postoperative complications and quality of life in patients with pituitary adenoma. Gland Surg. 2020;5:1521-1529.
3. Carlos Takahiro Chone, et al. Endoscopic endonasal transsphenoidal resection of pituitary adenomas: preliminary evaluation of consecutive cases. Braz. J. Otorhinolaryngol.2014;2:146-151.
4. Kunal S Patel, et al. Prediction of postoperative delayed hyponatremia after endoscopic transsphenoidal surgery. Clin Neurol Neurosur. 2019;87-91.
5. Cheng-Chi Lee, et al. Incidence and factors associated with postoperative delayed hyponatremia after transsphenoidal pituitary surgery: A meta-analysis and systematic review. Int J Endocrinol. 2021;1-13.
6. Horacio J Adrogué, et al. Hyponatremia. N Engl J Med. 2000;21:1581-1589.
7. Kelly A Shaftel et al. National trends in hospital readmission following transsphenoidal surgery for pituitary lesions. Pituitary. 2020;2:79-91.
8. Helbert Rondon, et al. Hyponatremia. 2023.
9. E Knosp, et al. Pituitary adenomas with invasion of the cavernous sinus space: A magnetic resonance imaging classification compared with surgical findings. Neurosurgery. 1993;4:610-617.
10. Kunzhe Lin, et al. Novel nomograms to predict delayed hyponatremia after transsphenoidal surgery for pituitary adenoma. Front Endocrinol. 2022.
11. Michael A Bohl, et al. Delayed hyponatremia is the most common cause of 30-day unplanned readmission after transsphenoidal surgery for pituitary tumors. Neurosurgery. 2016;1:84-90.
12. Sean M Barber, et al. Incidence, etiology and outcomes of hyponatremia after transsphenoidal surgery: experience with 344 consecutive patients at a single tertiary center. J Clin Med. 2014;4:1199-1219.
13. M Cerda-steve, et al. Cerebral salt wasting syndrome: Review. Eur J Intern Med. 2008;4:249-54.
14. Evan T Blair, et al. Physiologic mechanisms of water and electrolyte disturbances after transsphenoidal pituitary surgery. World Neurosurg. 2017;429-436.

15. Yinxing Huang, et al. Risk factors for delayed postoperative hyponatremia in patients with non-functioning pituitary adenomas undergoing transsphenoidal surgery: A single-institution study. Front Neurol. 2022;13.
16. Cao ZS, et al. The molecular structure and secretion regulation mechanism of prolactin. Practical Obstetrics and Gynecology Journal. 2007;2:65-67.
17. Donal C Skinner. Rethinking the stalk effect: a new hypothesis explaining suprasellar tumor-induced hyperprolactinemia. Med Hypotheses. 2009;3:309-310.
18. Kunzhe Lin, et al. Predictive factors for delayed hyponatremia after transsphenoidal surgery in patients with pituitary adenomas. Endocr Connect. 2022;1.
19. Lin k, et al. Diaphragma sellae sinking can predict the onset of hyponatremia after transsphenoidal surgery for pituitary adenomas. J Endocrinol Invest. 2021;11:2511-2520.
20. Kunzhe Lin, et al. The difference between preoperative and postoperative pituitary stalk deviation angles can predict delayed hyponatremia after transsphenoidal surgery. World Neurosurg. 2021.
21. John W Rutland, et al. Tumor T2 signal intensity and stalk angulation correlates with endocrine status in pituitary adenoma patients: A quantitative 7 tesla MRI study. Neuroradiology. 2020;4:473-482
22. Chinese Medical Association Neurosurgery Branch. Expert consensus on prevention and treatment of perioperative bleeding in neurosurgery. Chinese Medical Journal. 2018;7:483-495.
23. Hyun-Kyu Yoon, et al. Predictive factors for delayed hyponatremia after endoscopic transsphenoidal surgery in patients with nonfunctioning pituitary tumors: a retrospective observational study. World Neurosurg. 2019.
24. Jesper Krogh, et al. Transsphenoidal surgery for pituitary tumours: Frequency and predictors of delayed hyponatremia and their relationship to early readmission. Eur J Endocrinol. 2018;3:247-253.
25. R Wang, et al. Risk factors of hemorrhagic transformation after intravenous thrombolysis with rt-PA in acute cerebral infarction.Int J Med. 2019;5:323-326.