

RESEARCH

Predictive factors for delayed hyponatremia after transsphenoidal surgery in patients with pituitary adenomas

Kunzhe Lin^{1,2,*}, Lingling Lu^{2,*}, Zhijie Pei², Shuwen Mu², Shaokuan Huang³ and Shousen Wang^{2,4}¹Department of Neurosurgery, Affiliated Fuzhou First Hospital of Fujian Medical University, Fuzhou, China²Fuzong Clinical Medical College of Fujian Medical University, Fuzhou, China³Department of Neurosurgery, Guiqian International General Hospital, Guiyang, China⁴Department of Neurosurgery, 900th Hospital, Fuzhou, ChinaCorrespondence should be addressed to S Huang or S Wang: 1123228680@qq.com or wshsen1965@126.com

*(K Lin and L Lu contributed equally to this work)

Abstract

Objective: The aim of this study was to evaluate the incidence and duration of delayed hyponatremia and to assess the factors influencing the development of delayed hyponatremia after transsphenoidal surgery (TSS) in pituitary adenomas.

Methods: We retrospectively analyzed the clinical data of patients with pituitary adenoma who underwent TSS. Univariable and multivariable statistics were carried out to identify factors independently associated with the occurrence of delayed hyponatremia.

Results: Of the 285 patients with pituitary adenoma who underwent microscopic TSS, 44 (15.4%) developed postoperative-delayed hyponatremia and 241 (84.6%) did not. The onset of delayed hyponatremia occurred an average of 5.84 days post-surgery and persisted for an average of 5.36 days. Logistic regression analysis showed the highest risk of delayed hyponatremia in patients with significant change in tumor cavity height (odds ratio (OR), 1.158; 95% CI, 1.062, 1.262; $P = 0.001$), preoperative hypothalamus-pituitary-thyroid axis hypofunction (OR, 3.112; 95% CI, 1.481, 6.539; $P = 0.003$), and significant difference in blood sodium levels before and 2 days after TSS (OR, 1.101; 95% CI, 1.005, 1.206; $P = 0.039$).

Conclusions: Preoperative hypothyroidism, difference in blood sodium levels before and 2 days after TSS, and the change in tumor cavity height after TSS played important roles in predicting postoperative-delayed hyponatremia onset in patients with pituitary adenomas.

Key Words

- ▶ hyponatremia
- ▶ hypothyroidism
- ▶ pituitary adenoma
- ▶ transsphenoidal surgery

Endocrine Connections
(2022) **11**, e210497

Introduction

Delayed hyponatremia refers to hyponatremia that occurs ≥ 3 days after transsphenoidal surgery (TSS) (1). Patients with hyponatremia may have various clinical manifestations, ranging from asymptomatic to mild (headache, nausea, and vomiting) or severe symptoms. Severe hyponatremia can cause altered levels of consciousness, cerebral edema, seizures, and even death (2, 3). Delayed hyponatremia is often ignored by clinicians,

but it is the main cause of readmission (4, 5). The most common cause of delayed hyponatremia is the syndrome of inappropriate antidiuretic hormone secretion (SIADH), while cerebral salt wasting syndrome is a rare cause (6).

Following TSS for pituitary tumors, patients are at high risk of developing water balance disorders, including diabetes insipidus and delayed hyponatremia. The management of delayed hyponatremia is challenging, as there is limited understanding of the predictive factors of its occurrence. Moreover, its clinical treatment is

complex, and most treatments require close observation and frequent laboratory testing in the intensive care unit, resulting in high hospital costs (7). Therefore, screening and identifying patients at high risk for delayed hyponatremia after surgery, in addition to close monitoring and timely treatment, are crucial. Previous studies reported old age, low sodium concentration on postoperative days 1–2, long operation duration, low BMI, younger age, and lower preoperative serum sodium as predictors of delayed hyponatremia (3, 6, 8). However, delayed hyponatremia is generally believed to be caused by mechanical damage to the hypothalamus–neurohypophyseal system caused by TSS. Unfortunately, clinicians cannot modify the above factors to reduce the degree of injury and the incidence of postoperative–delayed hyponatremia.

The present study evaluated delayed hyponatremia incidence and duration after pituitary adenoma resection via microscopic TSS and identified the predictive factors affecting its occurrence.

Methods

Patient cohort

This study retrospectively analyzed clinical data of patients with pituitary adenoma who underwent TSS in our Neurosurgery Department between January 2017 and December 2020. This study was approved by the 900th hospital Institutional Review Board (2019-017). The patients gave consent to use their clinical data for research purposes, and all data were anonymized.

We included (i) patients who underwent microscopic TSS for pituitary adenomas; (ii) patients who were operated

on by the same surgeon; and (iii) cases in which the tumor grew upward and through the tuberculum sellae–dorsum sellae plane. We excluded (i) patients with pathologically confirmed non-pituitary adenoma or pituitary adenoma with other concomitant sellar lesions and (ii) cases in which the tumor growth did not reach the tuberculum sellae–dorsum sellae plane.

MRI evaluation

The pituitary gland was scanned using a 3.0-T MRI scanner (Tim Trio; Siemens Medical Solutions). Images were evaluated to identify potential factors for postoperative–delayed hyponatremia, including tumor cavity height (preoperative and postoperative), tumor volume, tumor volume of the superior part, invasiveness, intratumoral cysts or hematoma, location of the posterior pituitary bright spot (PPBS), and extent of tumor resection. The tumor was divided into superior and inferior parts using the tuberculum sellae–dorsum sellae plane as the boundary (9). The tumor cavity height was measured pre- and postoperatively at the same coronal position on contrast-enhanced images, and the difference between the two was taken as the change in tumor cavity height after TSS (Fig. 1). Patients with Knosp grades 3 and 4 were identified as having cavernous sinus invasion (10). All patients underwent routine postoperative MRI at 1–3 days and 4–6 months to evaluate the extent of tumor resection. The extent of tumor resection was classified as: gross total resection, without any evidence of residual adenoma; subtotal resection, residual adenoma < 20%; and partial resection, residual adenoma < 50% (11). Tumor volume was calculated using the platform-like volume calculation formula (12). The magnetic resonance images were independently evaluated and measured by

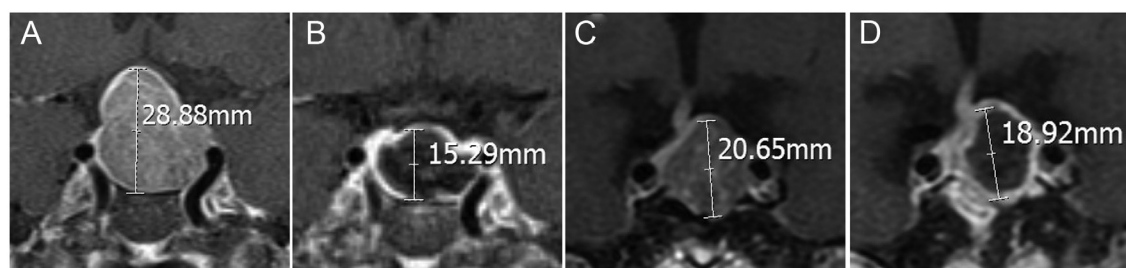


Figure 1

Coronal contrast-enhanced images of the change in tumor cavity height after transsphenoidal surgery in two cases. Panels A and B and panels C and D are from the same patient, respectively. (A) Before surgery, the tumor cavity height is 28.88 mm. (B) After surgery, the tumor cavity height is 15.29 mm, and the change in tumor cavity height after transsphenoidal surgery of this patient is 28.88–15.29 mm. (C) Before surgery, the tumor cavity height is 20.65 mm. (D) After surgery, the tumor cavity height is 18.92 mm, and the change in tumor cavity height after transsphenoidal surgery of this patient is 20.65–18.92 mm.

two neurosurgeons. In cases in which the measurement differed by >20% among the reviewers, a consensus was reached through a discussion and the mean of the measurements was used for the statistical analysis.

Perioperative evaluations

All patients have serum sodium levels checked every day and received sodium chloride solution (0.9%) as maintenance fluid postoperatively. Preoperative routine examination of the hypothalamus–pituitary–adrenal (HPA) axis and hypothalamus–pituitary–thyroid (HPT) axis functions was performed to determine the low function and the need for oral glucocorticoid and thyroxine replacement therapy. Intraoperative stress doses of glucocorticoids were administered intravenously to all patients (except to those with Cushing’s disease) to prevent the rapid surgery-related decline in HPA axis functions. Patients with HPA axis and HPT axis dysfunction were given glucocorticoid and thyroxine replacement therapy. On the first postoperative day, patients fasted and were given i.v. fluids of 2000–2500 mL. The patients were allowed to start on a liquid diet the day after surgery, with a gradual transition to a semi-liquid diet depending on the patient’s condition. Patients with comorbidities (e.g. cardiac insufficiency, diabetes) should be treated with individualized fluid rehydration to maintain energy needs. Patients with diabetes insipidus should drink water to relieve thirst, and oral desmopressin was given if necessary. For patients with delayed hyponatremia, the cause needs to be determined carefully. If delayed hyponatremia is caused by SIADH, fluid intake should be restricted. If the cause is cerebral salt wasting syndrome, treatment is administered to correct the low blood volume and to provide sodium supplementation.

The patient’s age, sex, MRI features, intraoperative cerebrospinal fluid leakage, pathological tumor type, HPT axis function, HPA axis function, and electrolyte levels were recorded. The criteria for HPT and HPA hypofunction were based on Bordo *et al.* (2).

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp.). The clinical data were expressed as mean and s.d.; median, interquartile range; and frequency and percentage. Independent samples *t*-test, Wilcoxon rank-sum test, Fisher’s exact test, chi-squared test, and logistic regression analysis were applied as appropriate.

Table 1 Demographic characteristics of 285 patients who underwent transsphenoidal surgery for pituitary adenomas.

Variable	No.
Age, mean ± s.d., years	49.2 ± 12.9
Sex	
Male	146
Female	139
Tumor size, cm ³	6.6 ± 6.4
Tumor height, mm	25.7 ± 8.5
Pathological tumor type	
Gonadotropinoma	93
Null cell adenoma	78
PRL cell adenoma	41
GH cell adenoma	19
ACTH cell adenoma	24
Plurihormonal	28
TSH cell adenoma	2
Intratumoral cysts or hematoma	
Yes	115
No	170
Location of the PPBS	
Superior parts	146
Inferior parts	97
Superior and inferior parts	13
None	29
Invasiveness	
Yes	44
No	241

ACTH, adrenocorticotropic hormone; GH, growth hormone; TSH, thyroid-stimulating hormone; PPBS, posterior pituitary bright spot; PRL, prolactin.

Results

Participant characteristics

This study included a total of 285 eligible patients with pituitary adenomas (Table 1). Our cohort included 146 men and 139 women, with a mean age of 49.2 ± 12.9 years. Forty-four cases (15.4%) developed postoperative-delayed hyponatremia, while 241 cases (84.6%) did not. The onset of hyponatremia occurred at an average of 5.84 days post-surgery and persisted for an average of 5.36 days. The lowest average blood sodium level was 123.6 mEq/L, which occurred 7.88 days after surgery.

Factors influencing postoperative-delayed hyponatremia

Table 2 summarizes the results of comparisons between the delayed hyponatremia and normonatremia groups. The change in tumor cavity height was significantly larger in patients with delayed hyponatremia compared to those without delayed hyponatremia (*P* < 0.001). The postoperative tumor cavity height of the delayed

Table 2 Univariate analysis of postoperative-delayed hyponatremia.

Factors	Delayed hyponatremia	Normonatremia	P value
Age	41 (49, 58.7)	50 (40.5, 58.5)	0.901
Sex			0.92
Male	23	124	
Female	21	117	
Tumor volume, cm ³	5.4 (3.5, 11.1)	4.3 (2.5, 7.6)	0.126
Tumor volume of superior part, cm ³	1.5 (0.5, 2.7)	1.1 (0.4, 2.1)	0.155
Tumor cavity height (preoperative), mm	22.8 (18.9, 26.5)	21.2 (18.6, 25.5)	0.195
Tumor cavity height (postoperative), mm	15.3 (12, 18.4)	17.9 (13.8, 21.3)	0.01
Pathological tumor type			0.333
Gonadotropinoma	18	75	
Null cell adenoma	10	68	
PRL cell adenoma	8	33	
GH cell adenoma	1	18	
ACTH cell adenoma	2	22	
Plurihormona	3	25	
TSH cell adenoma	1	1	
Intratumoral cysts or hematoma			0.801
Yes	17	98	
No	27	143	
Location of the PPBS			0.063
Superior parts	22	124	
Inferior parts	13	84	
Superior and inferior parts	5	8	
None	4	25	
Invasiveness			0.584
Yes	8	36	
No	36	205	
Preoperative HPT axis function			<0.001
Hypofunction	24	67	
Normofunction	20	174	
Preoperative HPA axis function			0.533
Hypofunction	9	40	
Normofunction	35	201	
Extent of tumor resection			0.245
Total resection	38	195	
Subtotal resection	4	15	
Partial resection	2	31	
Intraoperative cerebrospinal fluid leaks			0.964
Yes	7	39	
No	37	202	
Change in tumor cavity height, mm	7.1 (1.8, 10.8)	2.76 (0.38, 5.92)	<0.001
Postoperative HPT axis function			<0.001
Hypofunction	32	86	
Normofunction	12	155	
Postoperative HPA axis function			0.523
Hypofunction	6	25	
Normofunction	38	216	

ACTH, adrenocorticotrophic hormone; GH, growth hormone; HPA, hypothalamus–pituitary–adrenal; HPT, hypothalamus–pituitary–thyroid; PPBS, posterior pituitary bright spot; PRL, prolactin; TSH, thyroid-stimulating hormone.

hyponatremia group was significantly lower than that of the normonatremia group ($P=0.01$). We also observed a significant difference in the number of patients with preoperative and postoperative HPT axis hypofunction between the two groups ($P < 0.001$ for both). We observed no significant differences between the delayed hyponatremia and normonatremia groups in terms of

age, sex, immunohistochemical types, PPBS location, tumor cystic degeneration or hemorrhage, and pre- and postoperative HPA function.

Patients with and without postoperative-delayed hyponatremia showed no significant differences in blood sodium levels preoperatively and at 1 and 2 days post-TSS. However, the delayed hyponatremia group showed

Table 3 Analysis of the difference of blood sodium before and after TSS.

Factors	Delayed hyponatremia	Normonatremia	P value
Preoperative serum sodium, mEq/L	140.9 (139.2, 143)	141 (139, 142.4)	0.545
Blood sodium on the first day after surgery, mEq/L	140.7 (137.5, 142.3)	140.2 (138.6, 142.5)	0.484
Serum sodium on the second day after surgery, mEq/L	139.7 (137.4, 142.7)	141 (139.2, 143)	0.326
The difference in blood sodium levels before and 1 days after TSS, mEq/L	0.85 (−1.17, 3.0)	0.4 (−2.0, 2.6)	0.119
The difference in blood sodium levels before and 2-day after TSS, mEq/L	1.4 (−2.4, 3.35)	0 (−3, 2)	0.026

TSS, transsphenoidal Surgery.

greater differences from the preoperative levels than the normonatremia group ($P=0.026$), in which patients with postoperative-delayed hyponatremia group experienced substantial declines in blood sodium levels at 2 days post-TSS (Table 3).

Risk of postoperative hyponatremia onset

Based on the above results of univariate analyses, we selected the following variables with $P < 0.05$ for logistic regression analysis: the difference in blood sodium levels before and 2 days after TSS, change in tumor cavity height, postoperative tumor cavity height, and preoperative and postoperative HPT axis function. This analysis showed a higher risk of delayed hyponatremia in patients with a significant change in tumor cavity height (odds ratio (OR), 1.158; 95% CI, 1.062, 1.262; $P=0.001$), preoperative HPT axis hypofunction (OR, 3.112; 95% CI, 1.481, 6.539; $P=0.003$), and a difference in blood sodium levels before and 2 days after TSS (OR, 1.101; 95% CI, 1.005, 1.206; $P=0.039$) (Table 4).

Discussion

This clinical study investigated the incidence and predictors of delayed hyponatremia after TSS. Our results demonstrated that the incidence of delayed hyponatremia was 15.4%. Furthermore, the independent predictors of postoperative-delayed hyponatremia onset were changes

in tumor cavity height after TSS, preoperative HPT axis function, and the difference in blood sodium levels before and 2 days after TSS.

Previous studies reported that the incidence rate of delayed hyponatremia after TSS for pituitary adenomas is between 4 and 23% (6). The main clinical manifestation of SIADH is delayed hyponatremia due to the uncontrolled release of antidiuretic hormone secretion (ADH) following damage to the hypothalamus-neurohypophyseal system, leading to water retention. We identified predictors of delayed hyponatremia that are different from those reported previously. Age (young and old) has been identified as a predictor of postoperative-delayed hyponatremia (3, 6, 13). Moreover, owing to the sex-specific difference in the response to antidiuretic hormone, women are more likely than men to develop postoperative-delayed hyponatremia (14). Another study reported that the larger the tumor, the more the disruption of the pituitary stalk during surgery and the more likely the development of delayed hyponatremia after surgery (13). Our study found that age, sex, and tumor size did not predict the occurrence of delayed hyponatremia after surgery.

Pituitary adenomas can extend into the cavernous sinus, suprasellar space, sphenoid sinus, or clivus (15). When a pituitary adenoma grows, it may compress the pituitary stalk, resulting in its chronic distortion and may lead to changes in the position of the posterior pituitary gland (i.e. an ectopic posterior pituitary). The display rate and location of the PPBS of patients with pituitary adenoma can be clearly visualized via MRI (16, 17). The presence of

Table 4 Logistic regression analysis of the risk of postoperative-delayed hyponatremia onset.

Factors	Odds ratio	95% CI	P value
Change in tumor cavity height after TSS	1.158	1.062, 1.262	0.001
Postoperative tumor cavity height	0.984	0.908, 1.066	0.688
Preoperative HPT axis function	3.112	1.481, 6.539	0.003
Postoperative HPT axis function	0.883	0.392, 1.989	0.764
The difference in blood sodium levels before and 2-day after TSS	1.101	1.005, 1.206	0.039

OR, odds ratio; HPT, hypothalamus-pituitary-thyroid; TSS, transsphenoidal surgery.

PPBS reflects the accumulation of ADH, which is a sign of the functional integrity of the neurohypophysis; however, its absence does not necessarily imply impaired function of the neurohypophysis (18). Therefore, in patients with pituitary adenomas, diabetes insipidus or SIADH is rarely seen before surgery. In other words, for pituitary adenomas with different growth directions, there is no abnormal ADH secretion before surgery. However, after the tumor resection, observing the changes in the PPBS and pituitary stalk may be helpful to determine whether there is a change in ADH secretion; this requires further research.

Jahangiri reported that preoperative hypopituitarism was a sign of the mechanical manipulation of the pituitary stalk and posterior lobe of the pituitary gland during surgery and was, therefore, a potential risk factor for the occurrence of postoperative hyponatremia (19). The results of the multivariate analysis in the present study suggested that preoperative hypothyroidism was an independent predictor of postoperative-delayed hyponatremia. Hypothyroidism can cause hyponatremia by increasing ADH levels and intrarenal mechanisms (2). Low thyroxine levels cause decreased cardiac output, stimulate baroreceptors in the carotid sinus, and release ADH. Moreover, low thyroxine levels can also reduce the glomerular filtration rate and the excretion of free water by reducing the original urine volume delivered to the distal tubules and collecting ducts (20). Therefore, for patients with hypothyroidism before surgery, appropriate thyroxine supplementation may be used to reduce the occurrence of postoperative hyponatremia.

SIADH-related hyponatremia after TSS usually occurs approximately 5–7 days after surgery, appearing on average on the sixth day (1, 8, 21). Patients with serum sodium concentrations <138 mEq/L after 1–2 days are more likely to develop delayed hyponatremia (3). Krogh *et al.* (5) also reported an increased risk of hyponatremia in patients with decreased blood sodium concentrations on the first day after surgery. Our results suggest that compared to preoperative serum sodium, a large decrease in serum sodium concentration 2 days post-TSS is an independent predictor of delayed hyponatremia. We speculate that the abnormal secretion of ADH may occur from the second day after TSS, despite blood sodium concentrations being within the normal range.

Owing to the limited field of vision during the operation, none of the previous predictors of delayed hyponatremia involved damage assessment. Recently, some researchers have proposed that diaphragma sellae descent could be a cause of hypothalamus-neurohypophysis tract injury, which

further leads to SIADH after pituitary surgery (22). However, patients with thin or no diaphragma sellae showed no descent of the diaphragma sellae. We measured the height of the tumor cavity before and after TSS and found that the difference in tumor cavity height predicted the occurrence of delayed hyponatremia after surgery. One advantage of this study was that it was easier to observe and measure the height of the tumor cavity than the height of the diaphragma sellae. The difference in tumor cavity height before and after TSS reflected the sinking depth of the saddle diaphragm, tumor capsule, arachnoid, or flat pituitary tissue above the pituitary tumor owing to tumor removal. This sinking pulls, changes the position and shape, and damages the pituitary stalk, further leading to SIADH. Reducing the tumor cavity's height change may help lessen damage to the pituitary stalk. Therefore, with the gradual removal of the tumor during surgery, the tumor cavity should be filled with a certain volume of gelatin sponge to prevent lowering of the saddle diaphragm to reduce the change in height of the tumor cavity.

The diaphragma sellae can be elevated up to or beyond the level of the corpus callosum by the growing tumor (23, 24). The surgical removal of the tumor makes the diaphragma sellae sink, indicating that the operation can be terminated. For tumors with cystic changes, the outflow of cystic fluid causes the intrasellar pressure to decrease sharply, the sellar diaphragm descends, and the height of the tumor cavity decreases rapidly. However, after we pack the gelatin sponge into the tumor cavity, the sellar diaphragm can be elevated to reduce the change in the tumor cavity height after TSS, thereby reducing the degree of traction of the pituitary stalk. This study found no difference in the incidence of postoperatively delayed hyponatremia between cystic and non-cystic patients. If there is little or no intrasellar packing, the height of the tumor cavity changes greatly after the operation, and the pituitary stalk exhibits a process of continuous pulling that leads to abnormal ADH secretion and delayed hyponatremia.

Conclusion

The results of this study provide evidence of the important role of changes in tumor cavity height before and after TSS in predicting the onset of postoperative-delayed hyponatremia in patients with pituitary adenomas. We also showed that patients with preoperative hypothyroidism had a risk of delayed hyponatremia. The difference in blood sodium levels before and 2 days after

TSS was an independent predictor of postoperative-delayed hyponatremia onset.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This work was supported by the Natural Science Foundation of Fujian Province (2021J011306), the Department of Science and Technology of Fuzhou City (2021-S-180), and Startup Fund for scientific research of Fujian Medical University (2018QH1244).

References

- Patel KS, Shu Chen J, Yuan F, Attiah M, Wilson B, Wang MB, Bergsneider M & Kim W. Prediction of post-operative delayed hyponatremia after endoscopic transsphenoidal surgery. *Clinical Neurology and Neurosurgery* 2019 **182** 87–91. (<https://doi.org/10.1016/j.clineuro.2019.05.007>)
- Bordo G, Kelly K, McLaughlin N, Miyamoto S, Duong HT, Eisenberg A, Chaloner C, Cohan P, Barkhoudarian G & Kelly DF. Sellar masses that present with severe hyponatremia. *Endocrine Practice* 2014 **20** 1178–1186. (<https://doi.org/10.4158/EP13370.OR>)
- Yoon HK, Lee HC, Kim YH, Lim YJ & Park HP. Predictive factors for delayed hyponatremia after endoscopic transsphenoidal surgery in patients with nonfunctioning pituitary tumors: a retrospective observational study. *World Neurosurgery* 2019 **122** e1457–e1464. (<https://doi.org/10.1016/j.wneu.2018.11.085>)
- Bohl MA, Ahmad S, Jahnke H, Shepherd D, Knecht L, White WL & Little AS. Delayed hyponatremia is the most common cause of 30-day unplanned readmission after transsphenoidal surgery for pituitary tumors. *Neurosurgery* 2016 **78** 84–90. (<https://doi.org/10.1227/NEU.0000000000001003>)
- Krogh J, Kistorp CN, Jafar-Mohammadi B, Pal A, Cudlip S & Grossman A. Transsphenoidal surgery for pituitary tumours: frequency and predictors of delayed hyponatraemia and their relationship to early readmission. *European Journal of Endocrinology* 2018 **178** 247–253. (<https://doi.org/10.1530/EJE-17-0879>)
- Sorba EL, Staartjes VE, Voglis S, Tosic L, Brandi G, Tschopp O, Serra C & Regli L. Diabetes insipidus and syndrome of inappropriate antidiuresis (SIADH) after pituitary surgery: incidence and risk factors. *Neurosurgical Review* 2021 **44** 1503–1511. (<https://doi.org/10.1007/s10143-020-01340-0>)
- Winograd D, Stagers KA, Sebastian S, Takashima M, Yoshor D & Samson SL. An effective and practical fluid restriction protocol to decrease the risk of hyponatremia and readmissions after transsphenoidal surgery. *Neurosurgery* 2020 **87** 761–769. (<https://doi.org/10.1093/neuros/nyz555>)
- Matsuyama J, Ikeda H, Sato S, Yamamoto K, Ohashi G & Watanabe K. Early water intake restriction to prevent inappropriate antidiuretic hormone secretion following transsphenoidal surgery: low BMI predicts postoperative SIADH. *European Journal of Endocrinology* 2014 **171** 711–716. (<https://doi.org/10.1530/EJE-14-0530>)
- Lin K, Li J, Lu L, Zhang S, Mu S, Pei Z, Wang C, Lin J, Xue L, Wei L, *et al.* Diaphragma sellae sinking can predict the onset of hyponatremia after transsphenoidal surgery for pituitary adenomas. *Journal of Endocrinological Investigation* 2021 **44** 2511–2520. (<https://doi.org/10.1007/s40618-021-01611-7>)
- Knosp E, Steiner E, Kitz K & Matula C. Pituitary adenomas with invasion of the cavernous sinus space: a magnetic resonance imaging classification compared with surgical findings. *Neurosurgery* 1993 **33** 610–617; discussion 617–618. (<https://doi.org/10.1227/00006123-199310000-00008>)
- Karki M, Sun J, Yadav CP & Zhao B. Large and giant pituitary adenoma resection by microscopic trans-sphenoidal surgery: surgical outcomes and complications in 123 consecutive patients. *Journal of Clinical Neuroscience* 2017 **44** 310–314. (<https://doi.org/10.1016/j.jocn.2017.07.015>)
- Wang S, Lin S, Wei L, Zhao L & Huang Y. Analysis of operative efficacy for giant pituitary adenoma. *BMC Surgery* 2014 **14** 59. (<https://doi.org/10.1186/1471-2482-14-59>)
- Lee JI, Cho WH, Choi BK, Cha SH, Song GS & Choi CH. Delayed hyponatremia following transsphenoidal surgery for pituitary adenoma. *Neurologia Medico-Chirurgica* 2008 **48** 489–492; discussion 492–494. (<https://doi.org/10.2176/nmc.48.489>)
- Barber SM, Liebelt BD & Baskin DS. Incidence, etiology and outcomes of hyponatremia after transsphenoidal surgery: experience with 344 consecutive patients at a single tertiary center. *Journal of Clinical Medicine* 2014 **3** 1199–1219. (<https://doi.org/10.3390/jcm3041199>)
- Zada G, Lin N & Laws Jr ER. Patterns of extrasellar extension in growth hormone-secreting and nonfunctional pituitary macroadenomas. *Neurosurgical Focus* 2010 **29** E4. (<https://doi.org/10.3171/2010.7.FOCUS10155>)
- Saeki N, Tokunaga H, Wagai N, Sunami K, Murai H, Kubota M, Tatsuno I, Saito Y & Yamaura A. MRI of ectopic posterior pituitary bright spot with large adenomas: appearances and relationship to transient postoperative diabetes insipidus. *Neuroradiology* 2003 **45** 713–716. (<https://doi.org/10.1007/s00234-003-1018-9>)
- Saeki N, Hayasaka M, Murai H, Kubota M, Tatsuno I, Takashi J, Uno T, Iuchi T & Yamaura A. Posterior pituitary bright spot in large adenomas: MR assessment of its disappearance or relocation along the stalk. *Radiology* 2003 **226** 359–365. (<https://doi.org/10.1148/radiol.2262011616>)
- Bonneville F, Narboux Y, Cattin F, Rödier E, Jacquet G & Bonneville JF. Preoperative location of the pituitary bright spot in patients with pituitary macroadenomas. *American Journal of Neuroradiology* 2002 **23** 528–532.
- Jahangiri A, Wagner J, Tran MT, Miller LM, Tom MW, Kunwar S, Blevins Jr L & Aghi MK. Factors predicting postoperative hyponatremia and efficacy of hyponatremia management strategies after more than 1000 pituitary operations. *Journal of Neurosurgery* 2013 **119** 1478–1483. (<https://doi.org/10.3171/2013.7.JNS13273>)
- Katoh CD, Brar KS & Singh B. Evaluation of thyroid and adrenal functions in patients with hyponatremia. *Medical Journal, Armed Forces India* 2013 **69** 237–240. (<https://doi.org/10.1016/j.mjafi.2013.01.003>)
- Kristof RA, Rother M, Neuloh G & Klingmüller D. Incidence, clinical manifestations, and course of water and electrolyte metabolism disturbances following transsphenoidal pituitary adenoma surgery: a prospective observational study. *Journal of Neurosurgery* 2009 **111** 555–562. (<https://doi.org/10.3171/2008.9.JNS08191>)
- Lin K & Wang S. Letter: Focus on syndrome of inappropriate antidiuretic hormone after resection of pituitary lesions via transsphenoidal approach. *Neurosurgery* 2021 **89** E80–E81. (<https://doi.org/10.1093/neuros/nyab110>)
- Goel A, Nadkarni T, Muzumdar D, Desai K, Phalke U & Sharma P. Giant pituitary tumors: a study based on surgical treatment of 118 cases. *Surgical Neurology* 2004 **61** 436–445; discussion 445–446. (<https://doi.org/10.1016/j.surneu.2003.08.036>)
- Goel A. Correspondence: Pituitary tumors and diaphragma sellae. Re: Cabuk B, Anik I, Kokturk S, Ceylan S, Ceylan S: Anatomic and histologic features of diaphragma sellae that effects the suprasellar extension. *Journal of Clinical Neuroscience* 71(2020) 234–244. *Journal of Clinical Neuroscience* 2020 **77** 253. (<https://doi.org/10.1016/j.jocn.2020.04.093>)

Received in final form 12 November 2021

Accepted 3 December 2021

Accepted Manuscript published online 3 December 2021