



## Pituitary

## Pituitary function after endonasal surgery for nonadenomatous parasellar tumors: Rathke's cleft cysts, craniopharyngiomas, and meningiomas

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**Abstract**

**Background:** Transsphenoidal surgery for parasellar nonadenomatous lesions has the possibility to either improve or worsen pituitary hormonal function. Herein we present the rates and risk factors of new hormonal failure and recovery in patients undergoing surgery for either an RCC, craniopharyngioma, or tuberculum sella meningioma.

**Methods:** All consecutive patients treated over an 8-year period by endonasal surgery for an RCC, craniopharyngioma, or tuberculum sella meningioma were analyzed. Patients treated with prior sellar radiotherapy were excluded. Preoperative and postoperative pituitary hormonal status was determined. Patient characteristics, tumor size, intraoperative and postoperative events, and extent of tumor resection were correlated with new or resolved hypopituitarism.

**Results:** In total, 50 patients with an RCC, 18 with a craniopharyngioma and 13 with tuberculum sellae meningioma, were analyzed. New anterior pituitary failure and permanent DI occurred as follows: in RCCs, 6% and 2%; in craniopharyngiomas, 31% and 39%; and in meningiomas, 9% and 0%. Overall, improved hormonal function occurred in 57% of patients with an RCC including recovery of one or more anterior axes in 9 (41%) of 22 patients and resolution of hyperprolactinemia in 12 (67%) of 18 patients; no patients with a craniopharyngioma or meningioma had resolution of hypopituitarism. Younger age was predictive of hormonal recovery in patients with an RCC ( $P = .026$ ).

**Conclusions:** New hypopituitarism after transsphenoidal surgery occurs in approximately one third of patients with a craniopharyngioma and in less than 10% of patients with an RCC or suprasellar meningioma. Hormonal function improves in the majority of patients undergoing drainage of an RCC but is unlikely to occur after removal of a craniopharyngioma or suprasellar meningioma.

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**Keywords:**

Transsphenoidal surgery; Pituitary failure; Meningioma; Craniopharyngioma; Rathke's cleft cyst

*Abbreviations:* DI, diabetes insipidus; FSH, follicle stimulating hormone; GH, growth hormone; IGF-1, insulin-like growth factor 1; LH, leuteinizing hormone; MRI, magnetic resonance imaging; RCC, Rathke's cleft cyst; TSH, thyroid stimulating hormone; UCLA, University of California at Los Angeles.

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## 1. Introduction

Postoperative hypopituitarism is a well-known complication of transsphenoidal surgery for nonadenomatous tumors. Although most reports on outcomes after transsphenoidal tumor removal document rates of new hypopituitarism, to our knowledge, there have been few analyses of hormonal loss and recovery across different tumor types of parasellar tumors [35]. As the use of transsphenoidal surgery for parasellar tumors has expanded, it is important to document the impact of such procedures on pituitary function.

In this report, we analyze 81 consecutive patients treated over an 8-year period with transsphenoidal removal of an RCC, craniopharyngioma, or tuberculoma sellae meningioma. These 3 diagnoses comprise more than 75% of all nonadenomatous tumors treated by the transsphenoidal approach and are the 3 pathologies most likely to impact pituitary function or have pituitary function impacted by their surgical treatment [1,6,7,12,14,15,28,36,40]. Patients with other parasellar tumors that are typically more distant from the pituitary such as cavernous sinus schwannomas, clival chordomas, or sphenoid sinus carcinomas were excluded, as were sellar arachnoid cysts which are uncommon [36]. Individuals treated with prior radiation were also excluded given the known impact of radiotherapy on pituitary function [31,35,39]. We also sought to determine whether specific factors were predictive of postoperative hormonal status such as tumor pathology and size, prior surgery, intraoperative events, surgical complications, extent of tumor removal, and preoperative diabetes mellitus, hypertension, and smoking, all 3 of which are risk factors for cerebrovascular disease and stroke [19,34].

## 2. Methods

### 2.1. Patient population

From July 1998 to December 2006, all patients in the UCLA Pituitary Tumor database who underwent endonasal transsphenoidal removal of an RCC, craniopharyngioma, or tuberculoma sellae meningioma at UCLA or Harbor-UCLA Medical Centers were included in this retrospective analysis. All surgeries were performed by the senior author (DFK). Patients' medical records were reviewed to document pre- and postoperative hormonal status, pathology reports, MRI for tumor size and location, operative notes, postoperative events, and clinical follow-up notes. Patients were excluded if they had received preoperative cranial or sellar radiotherapy or if they did not have at least a 3-month postoperative hormonal evaluation. Patients were also excluded if they did not have adequate pre- and postoperative hormonal studies to determine pituitary axes recovery and losses. Selection criteria for operating on craniopharyngioma and tuberculoma sellae meningioma by the transsphenoidal route, rather than the transcranial route, have been previously described [14]. In general, only tumors

smaller than 35 to 40 mm that were predominantly midline without significant lateral extension were selected. This retrospective analysis was approved by the UCLA Institutional Review Board.

### 2.2. Preoperative and postoperative pituitary hormonal status assessment

Because many patients who were referred to UCLA or Harbor-UCLA Medical Centers came with complete hormonal testing from outside laboratories, a standard reference range for hormone values was not used and instead the patients' results were interpreted as normal or abnormal based on the available reference range from the outside laboratory. Although not all patients had identical evaluations, the following preoperative and postoperative tests (at least 3 months after surgery) were used for assessing the different hormonal axes.

The *corticotroph axis* evaluation included morning plasma adrenocorticotropic hormone (normal range, 9-52 pg/mL [2-11.4 pmol/L]) and serum cortisol (normal range, 8-25 µg/dL [221-690 pmol/L]). Dynamic testing of the hypothalamic-pituitary-adrenal axis (either via cortrosyn or metyrapone) was done in a subset of patients who had subnormal serum cortisol levels and/or those with clinical features suspicious for adrenal insufficiency.

The *thyrotroph axis* evaluation included serum levels of TSH (normal range, 0.3-4.7 mIU/L), total T4 (normal range, 4.9-11.4 ng/dL [63-147 pmol/L]) and/or free T4 by dialysis (normal range, 0.7-2.2 ng/dL [9-28.3 pmol/L]).

The *gonadotroph axis* evaluation in women included serum levels of LH (normal premenopausal range, 2-15 IU/L), FSH (normal premenopausal range, 2-23 IU/L), and estradiol levels. In premenopausal women, hypogonadism was diagnosed if amenorrhea and/or infertility was present and if gonadotropins were low or low normal in the setting of low estradiol levels (<21 pg/mL [ $<77.1$  pmol/L]). Hypogonadism was diagnosed in postmenopausal women when serum LH (normal postmenopausal range, 16-63 IU/L) and/or FSH (normal postmenopausal range, 21-106 IU/L) was low. In men, LH (normal range, 2-12 IU/L) and FSH (normal range, 1.6-9 IU/L) were assessed; total testosterone (normal, 250-1100 ng/dL [8.7-38.2 nmol/L]) and/or free testosterone (normal range, 35-155 pg/mL [1213-5374 pmol/L]) was also assessed. Secondary hypogonadism was diagnosed in men if total or free testosterone was low in the setting of a normal or low LH and FSH.

The *lactotroph axis* was assessed with serum prolactin levels (normal range, 5-20 ng/mL [5-20 µg/L] for men and 5-25 ng/mL [5-25 µg/L] for women). Because no patients with prolactinoma were included in this study, all patients with elevated prolactin were assumed to have "stalk compression" hyperprolactinemia.

The *somatotroph axis* evaluation included random serum GH (normal range, 0-6 ng/mL [0-6 µg/L]) and age- and sex-adjusted IGF-1 levels (normal ranges for age/sex not shown);

stimulation tests with GH-releasing hormone–arginine or the insulin tolerance test was performed on some patients postoperatively in whom the IGF-1 levels were near or below the lower limit of normal or when other anterior pituitary axes were deficient. In the absence of stimulation testing for GH deficiency, any patient who had 3 other anterior hormonal axis deficiencies (corticotroph, thyrotroph, and gonadotroph) was categorized as being GH deficient, whether in the preoperative or postoperative state [2-4,11]. When values were available, the change in IGF-1 level from the preoperative to the postoperative period was used as an additional means of assessing somatotroph function [2-4,11].

*Posterior pituitary function* was assessed based upon urine-specific gravity, serum sodium, and urine output. Patients were diagnosed as having DI if urine specific gravity was 1.005 or less and urine volume was greater than 200 mL/h for at least 3 consecutive hours.

### 2.3. Characterization of hormonal dysfunction

Patients were categorized preoperatively as to which pituitary hormonal abnormalities were present including hypoadrenalism, hypothyroidism, hypogonadism, “stalk compression” hyperprolactinemia [26,29,38], and DI. New pituitary dysfunction was defined as any abnormality occurring at least 3 months after surgery based on hormonal testing or new hormone replacement for a new deficiency. Recovery of preoperative pituitary dysfunction was categorized by hormonal axis. In patients with preoperative hyperprolactinemia, the change in serum prolactin from the preoperative to the postoperative period was assessed [26,29,38]. Recovery of low prolactin or new postoperative low prolactin was not investigated in this analysis.

### 2.4. Predictors of postoperative hypopituitarism or recovery of hormonal axis

Univariate analysis of predictors of postoperative hypopituitarism or recovery of pituitary function was performed using multiple factors. Patient age and sex as well as preoperative comorbidities of treated hypertension, treated diabetes mellitus, and cigarette smoking history (at least 5 cigarettes per day) were noted [19,34]. Patients with previous operations (either transsphenoidal or trans-cranial procedures for tumor removal) were identified. Preoperative pituitary hormonal status including hyperprolactinemia, preexisting hypopituitarism, and number of axes affected was identified. Several types of data related to the tumor itself were collected from MRI reports, clinical notes, and intraoperative findings: tumor pathology, tumor size (maximal tumor diameter), and cavernous sinus invasion. Intraoperative events were noted, including the presence of an intraoperative cerebrospinal fluid leak and the use of full-strength hydrogen peroxide in the resection site. Postoperative complications including intrasellar hematoma, cerebrospinal fluid leak, and bacterial meningitis were also

noted. Other postoperative factors including transient and permanent DI and delayed hyponatremia were noted [23].

### 2.5. Transsphenoidal surgical technique

The direct endonasal approach, as described previously, was used in all cases with the operating microscope and endoscopic assistance in select cases [14,42].

For intrasellar RCCs, as such cysts are typically located behind the anterior lobe, their removal involves an approach through the anterior gland via a low midline vertical glandular incision [12]. Through this small corridor, the cyst contents are removed with suction, curettes, and irrigation. At the completion of cyst removal, the resection cavity is inspected for residual cyst lining. Given that the resection cavity is generally formed by the anterior and posterior pituitary lobes, no attempt was made to vigorously strip the cyst wall off of the normal gland. For purely suprasellar RCCs, which were all attached to the pituitary stalk and often embedded within the superior aspect of the pituitary gland, the surgical trajectory was to reach the superior gland surface. In some cases of supraglandular RCCs, craniopharyngiomas, and suprasellar meningiomas, an anterior superior incision was made in the pituitary gland to facilitate exposure directly above the gland and to minimize traction on the gland and infundibulum. When tumor or cyst lining remained densely adherent to the stalk, optic apparatus, or vasculature despite attempts to remove them, a subtotal removal was accepted to minimize the chances of new hypopituitarism or neurologic deficits.

For craniopharyngiomas, if pituitary gland function was largely intact preoperatively, an attempt was made to identify the pituitary stalk and its site of insertion to the pituitary gland early in the dissection and to avoid traction on the stalk during tumor removal. However, when preoperative DI or multiple anterior gland deficiencies were present and/or the pituitary stalk was engulfed by tumor on the preoperative MRI, persevering gland function was less of a priority although an effort was made in every case to identify the pituitary stalk.

For tuberculoma sellae meningiomas, in all cases the tumors sat atop the diaphragma sella often compressing the normal gland from above and stretching the infundibulum posteriorly. In these cases, the infundibulum and its insertion site to the gland are identified with preservation of these structures and the overlying arachnoid plane as a major goal of the surgery.

Over the last 6 years, full-strength hydrogen peroxide has been placed in the tumor or cyst bed for up to 5 minutes for its hemostatic effects but also for its potential tumoricidal effects [32]. In this series, peroxide was used in patients with an RCC but not in those with a meningioma of craniopharyngioma in which there was a large surgical defect in the diaphragma sella.

*Surgical outcome* for RCCs, craniopharyngiomas, and meningiomas was defined as a complete tumor removal,

near-complete (>90%), or subtotal (<90%) removal as seen on the early or 3-month postoperative MRI [14].

### 2.6. Statistical analysis

Predictors of outcome (loss or recovery of pituitary function) were analyzed if sufficient numbers of patients were available by univariate statistics using a 2-tailed Fisher exact test for dichotomous variables and a Student *t* test for normally distributed continuous variables. The *P* value for significance was set at .05. Because of the relatively small number of cases of hormonal loss and recovery across the 3 tumor types, a multivariate model could not be applied to the data. All statistical analyses were performed using the R programming language (R Development Core Team, 2007. R: *A language and environment for statistical computing*. R Foundation for Statistical Computing. Vienna, Austria. Version 2.5.1).

## 3. Results

### 3.1. Study cohort

Over an 8-year period, 81 patients (median age, 36; range, 7-78 years; 60 females, 21 males) underwent 88 procedures for tumor removal. As shown in Table 1, tumor pathologies were 50 RCCs, 18 craniopharyngiomas, and 13 tuberculom sellae meningiomas. There were 9 (11%) patients with prior transsphenoidal or transcranial tumor surgery performed at outside institutions, including 4%, 22%, and 23% of RCC, craniopharyngiomas, and meningiomas. In total, 8 other patients were excluded: 6 who had prior radiotherapy and 2 who had insufficient pre- and/or postoperative hormonal data.

### 3.2. Preoperative hormonal status

#### 3.2.1. Rathke's cleft cysts

Of 50 patients with RCC (mean age,  $33.5 \pm 15$  years), 28 (56%) had preoperative hormonal dysfunction. Of these, 22 (44%) had hypopituitarism of one or more axis and 20 (40%) had hyperprolactinemia (with or without coincident hypopituitarism). Of the patients with hypopituitarism, 14 had loss of 1 axis, 3 had loss of 2 axes, 1 had loss of 3 axes, and 4 had loss of 4 axes; the adrenal, thyroid, gonadal, and growth

Table 1  
Pathology type, size, and patient age

Pathology	No. of procedures	Age (y)	Max tumor diameter (mm)
Rathke's cleft cyst (n = 50)	52	$34 \pm 15$	$14.5 \pm 7$
Craniopharyngioma (n = 18)	23	$39 \pm 23$	$26 \pm 16$
Meningioma (n = 13)	13	$52 \pm 15$	$23 \pm 4$

\*Age and tumor diameter are presented as means  $\pm$  SD.

Table 2

Pre- and postoperative hormonal dysfunction by tumor type (including "stalk compression" hyperprolactinemia)

	Preoperative	Postoperative		
	Any dysfunction	Anterior loss	Posterior loss	Any loss
Rathke's cleft cyst	56%	6.4%	2%	8%
Craniopharyngioma	83%*	31%	39%	33%#
Meningioma	39%	9%	0%	8%

\* *P* = .03 compared to other pathologies; *P* = .07 for hypopituitarism (not including hyperprolactinemia).

# *P* = .02 compared to other pathologies.

hormone axes were affected in 6%, 14%, 38%, and 16%, respectively. Two patients (4%) had DI. No patients had panhypopituitarism with DI. The median follow-up was  $12 \pm 17$  months (range, 3-94 months). Total, near total (>90%), and subtotal (<90%) cyst removal was achieved in 47 (94%), 2 (4%), and 1 (2%) patient; 2 (4%) patients after total cyst removal had cyst reaccumulation requiring a second endonasal cyst drainage.

#### 3.2.2. Craniopharyngiomas

Of 18 patients with craniopharyngioma (mean age,  $39 \pm 23$  years), 15 (83%) had preoperative hormonal dysfunction including 9 (50%) with hyperprolactinemia and 12 (67%) with hypopituitarism of one or more axes. Of these 12 patients, the number of hormonal axes deficits was 1 axis in 1 patient, 2 axes in 5 patients, 3 axes in 1 patient, 4 axes in 2 patients, and all axes with DI (panhypopituitarism) in 3 patients. The corticotroph, thyrotroph, gonadotroph, somatotroph, and posterior pituitary (DI) axes were affected in 39%, 33%, 50%, 56%, and 28% of patients, respectively. All patients with DI also had anterior pituitary loss. Patients with craniopharyngioma had the highest rate of preoperative hormonal dysfunction (hypopituitarism and hyperprolactinemia combined) (83%) compared to the other 2 pathologies (52%; *P* = .03) and had the highest rate of hypopituitarism (67%) compared to the other 2 pathologies (41%; *P* = .07). Median follow-up was  $21.5 \pm 17$  months (range, 3-60 months). Total, near total (>90%), and subtotal (<90%) tumor removal was 5 (28%), 8 (44%), and 4 (22%), and 1 patient had only cyst drainage. Twelve patients completed stereotactic radiotherapy and/or radiosurgery 3 to 53 months after operation (median,  $3 \pm 14$  months). Of these patients, one with multiple recurrences received additional stereotactic radiosurgery 28 months after initial subtotal tumor removal. One patient with initial total tumor removal had a recurrence 47 months after operation and was treated with stereotactic radiosurgery.

#### 3.2.3. Meningiomas

Of 13 patients with meningioma (mean age,  $52 \pm 15$  years), 5 (39%) had preoperative hormonal dysfunction including 2 (15%) with hyperprolactinemia and 4 (31%) with

Table 3  
Recovery of hypopituitarism and hyperprolactinemia by pathology

	Recovery of hypopituitarism	Resolution of hyperprolactinemia
Rathke's cleft cyst	41% (9/22)*	67% (12/18)
Craniopharyngioma	0% (0/12)	43% (3/7) <sup>#</sup>
Meningioma	0% (0/4)	0% (0/1)

\*  $P = .005$  compared to other pathologies.

<sup>#</sup> Resolution of hyperprolactinemia may be related to new loss of lactotroph function.

hypopituitarism of 1 or more axis; of 10 patients without prior surgery only 1 (10%) had preoperative dysfunction. Of the patients with hypopituitarism, 1 patient each had losses of 1, 2, 4, and 5 axes (panhypopituitarism with DI); the corticotroph, thyrotroph, gonadotroph, and somatotroph axes were affected in 15%, 23%, 31%, and 15% of patients, respectively. Only 1 patient (8%) had posterior gland dysfunction with DI. The 2 patients with 4 or 5 axes deficits both had prior attempted tumor removal at an outside institution. Follow-up range was 4 to 51 months (median,  $24 \pm 15$  months). Total, near total (>90%), and subtotal (<90%) tumor removal was achieved in 7 (54%), 3 (23%), and 3 (23%) patients. Four patients 5 to 28 months after operation (median,  $11 \pm 11$  months) received stereotactic radiation or radiosurgery.

### 3.3. Rates and predictors of new hypopituitarism and recovery of hormonal function

#### 3.3.1. Rathke's cleft cysts

As shown in Tables 2 and 3 and Fig. 1, 4 patients (8%) had new hypopituitarism, each of whom lost 1 axis. Three (6.4%) of 47 patients with functioning anterior axes preoperatively became GH deficient, and 1 patient (2%) developed new permanent DI. There was no loss of thyrotroph, corticotroph, or gonadotroph axes.

No risk factors were found to be significantly predictive of postoperative loss of hormonal function although 2 showed trends. Patients with diabetes mellitus (50% vs 4.3% for others;  $P = .1$ ) and patients with cysts that were entirely supraglandular and adherent to the infundibulum (33% vs 4.5%;  $P = .07$ ) were more likely to lose an axis.

Of 28 patients (56% of cohort) with preoperative hormonal dysfunction (including hyperprolactinemia and/or hypopituitarism), 16 (57%) had improved function after surgery including 12 (43%) who had resolution of hyperprolactinemia and 9 (41%) who had recovery of 1 or more anterior axes; 7 recovered 1 axis, 1 recovered 2 axes, and 1 recovered 4 axes. Axes recovered included thyrotroph (3 patients), corticotroph (1 patient), gonadotroph (8 patients), and somatotroph (1 patient). No patients had resolution of DI. Patients who recovered axes were on average younger than those who did not recover axes (32 vs 49 years;  $P = .03$ ). No other factors were found to predict hormonal recovery.

Of 25 patients who had pre- and postoperative IGF-1 levels available, overall there was no significant change in these values:  $197 \pm 102$  vs  $187 \pm 126$  ng/mL, respectively ( $P = .76$ ). Of 41 patients with pre- and postoperative prolactin levels, average values were significantly lower postoperatively:  $46 \pm 58$  ng/mL preoperatively vs  $17 \pm 13$  ng/mL postoperatively ( $P = .003$ ). Of 18 patients with preoperative hyperprolactinemia, 67% resolved, 22% improved, 5.6% did not change (<5 ng/mL increase or decrease), and 4.8% worsened.

#### 3.3.2. Craniopharyngiomas

As shown in Tables 2 and 3 and Fig. 2, 5 patients (33%) had new hypopituitarism, including 1 patient who lost 1 axis, 1 who lost 2 axes, 2 who lost 3 axes, and 1 who lost 4 axes. Loss of anterior pituitary function occurred in

### Rathke's Cleft Cysts: Loss and Recovery of Pituitary Function

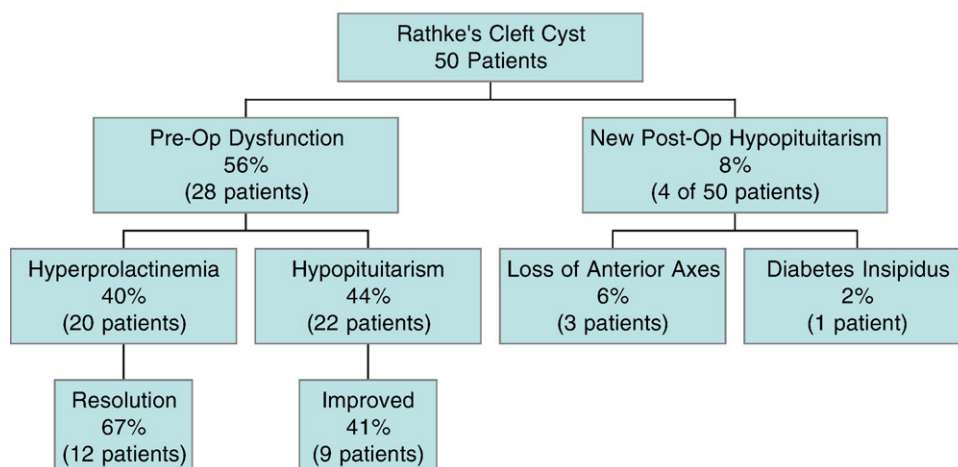


Fig. 1. Rathke's cleft cysts: loss and recovery of pituitary function. See Results section and tables for explanation of calculated percentages.

## Craniopharyngiomas: Loss and Recovery of Pituitary Function

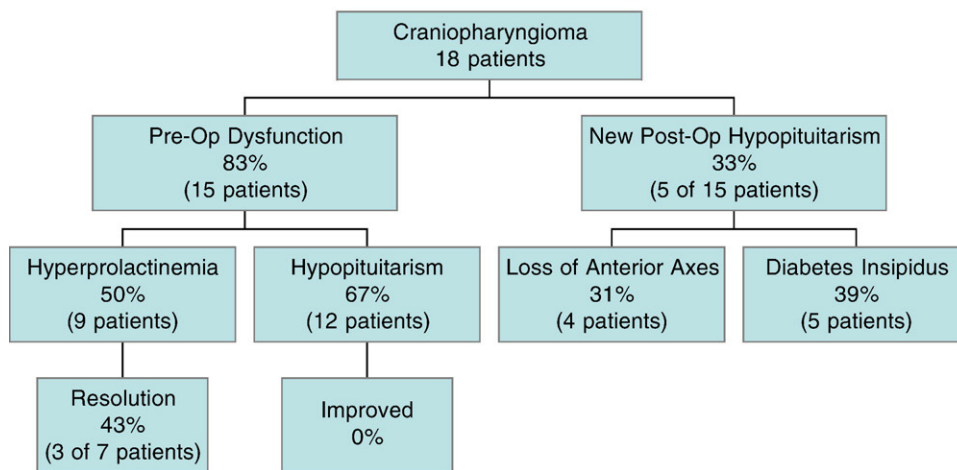


Fig. 2. Craniopharyngiomas: loss and recovery of pituitary function. See Results section and tables for explanation of calculated percentages.

4 (31%) of 13 patients with functioning anterior axes preoperatively. Three patients (25%) lost thyrotroph function, 4 (36.4%) lost corticotroph function, and 1 (12.5%) became GH deficient. No patients lost gonadotroph function. Loss of posterior pituitary function (new DI) occurred in 5 (38.5%) of 13 patients who did not have DI preoperatively. Patients with craniopharyngioma had the highest rate of new hypopituitarism compared to patients with RCC and meningioma (33% vs 8%;  $P = .02$ ). No factors were found to predict postoperative hormonal loss. Hyperprolactinemia resolved in 3 patients but no patients recovered from hypopituitarism.

Of 12 patients who had pre- and postoperative IGF-1 levels available, overall there was no change in these values:  $134 \pm 65$  vs  $135 \pm 74$  ng/mL, respectively ( $P = .98$ ). Of 15 patients with pre- and postoperative prolactin levels

available, the average prolactin overall decreased modestly after surgery from  $34 \pm 30$  to  $20 \pm 19$  ng/mL ( $P = .1$ ). Of patients with preoperative hyperprolactinemia, 43% resolved, 43% improved, and 14% did not change (<5 ng/mL increase or decrease).

### 3.3.3. Meningiomas

As shown in Tables 2 and 3 and Fig. 3, of 11 patients with meningioma with any functioning anterior axes, 1 (9%) had new hypopituitarism affecting the corticotroph axis. This 59-year-old man with a 21-mm tumor treated by previous craniotomy at an outside hospital had preexisting hypothyroidism and hypogonadism. No patients undergoing first-time surgery for a meningioma had new hypopituitarism. However, no patients recovered from preexisting hormonal dysfunction. Of 6 patients who had pre- and postoperative

## Meningiomas: Loss and Recovery of Pituitary Function

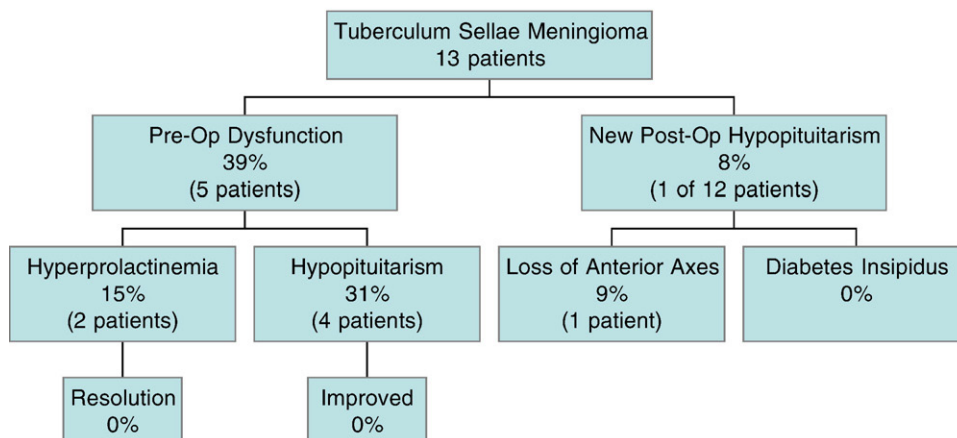


Fig. 3. Tuberculum sellae meningiomas: loss and recovery of pituitary function. See Results section and tables for explanation of calculated percentages.

IGF-1 levels available, the values overall were unchanged:  $138 \pm 79$  vs  $131 \pm 84$  ng/mL ( $P = .89$ ), respectively. Of 6 patients with pre- and postoperative prolactin levels available, the average prolactin decreased minimally after surgery from  $16 \pm 21$  to  $9 \pm 8$  ng/mL, ( $P = .4$ ). Of 2 patients with preoperative hyperprolactinemia, both had partial improvement but neither completely resolved.

## 4. Discussion

### 4.1. Summary of findings

In 81 patients who underwent transsphenoidal surgery for a parasellar tumor, new postoperative pituitary dysfunction was highest in those with a craniopharyngioma (33%) and less for those with an RCC (8%) or meningioma (8%). Hypopituitarism and hyperprolactinemia resolved in 41% and 67% of patients with an RCC, respectively. No patients with a craniopharyngioma or meningioma had resolution of hypopituitarism. Risk factor analysis revealed that new hypopituitarism for patients with RCC was somewhat increased in patients whose cysts were entirely supraglandular and adherent to the infundibulum. Hormonal recovery in patients with RCC was associated with younger age.

### 4.2. Rathke's cleft cysts

Preoperative hypopituitarism is a common finding in patients with RCC, ranging from 38% to 81% [1,17,22,24,35,39]. Studies that detailed losses of individual axes vary widely. Preoperative loss of corticotroph function has ranged from 6% to 46%, GH deficiency from 4% to 66%, and DI from 0% to 25% [1,22,36]. Shin et al [35] reported 39% of patients had preoperative hypothyroidism. Hyperprolactinemia has ranged from 18% to 39% [1,17,22,24,36,40]. In the present series, similar rates of preoperative hypopituitarism (44%) and hyperprolactinemia (40%) were observed.

Relatively few studies have detailed rates of new loss of axes after transsphenoidal surgery for RCCs. In 22 patients with an RCC, Shin et al [35] reported new hypogonadism, hypothyroidism, and new DI in 17%, 22%, and 30% of patients, respectively. Aho et al [1], in 118 patients with RCC, reported new hypogonadism and new DI in 4% and 18% of patients, respectively. Others, including our present series, have reported lower rates of new DI ranging from 5% to 7% [7,17,22,24]. A high likelihood of permanent DI and anterior gland dysfunction may be related to attempts to resect the cyst capsule, which can be quite adherent to the anterior and posterior lobes. Capsule removal is not a practice we advocate nor do Aho et al or Benveniste et al [7] after their experience. As shown in this series, simple cyst drainage through a vertical gland incision appears to be quite safe for gland function in the great majority of patients with a typical RCC in which the cyst is located between the anterior and posterior pituitary lobes. Not surprisingly, there appears to a higher risk of new hormonal loss in patients undergoing removal of an RCC adherent to the pituitary stalk.

Regarding postoperative hormonal recovery after surgery for an RCC, Aho et al [1], Kim et al [24], and Shin et al [36] performed detailed analyses showing that many preoperative hormonal deficits are potentially reversible. Kim et al [24] found 29% of preoperative DI improved, whereas Aho et al [1] and Shin et al [36] found no recovery of DI. Shin et al reported recovery by axes varying from 37% for hypothyroidism to 63% for resolution of GH deficiency. In the present series, 41% of patients with preoperative anterior gland hypopituitarism improved and 67% had resolution of hyperprolactinemia, similar to that seen in other series [1,7,17,24,40]. Interestingly, in this series, younger age was predictive of hormonal recovery.

### 4.3. Craniopharyngioma

As demonstrated in prior studies, given the tendency for craniopharyngiomas to engulf the pituitary stalk, preoperative hormonal loss and postoperative hormonal worsening are common [5,8,10,13,20,21,33,36,37,43]. In prior reports, preoperative hormonal dysfunction has ranged from 56% to 95% [8,10,20,21,33,36,37]. Diabetes insipidus is a relatively frequent finding being observed in 6% to 57% of patients [8,10,13,20,21,33,36,37,43]. Our findings are similar with 83% of patients demonstrating some degree of preoperative dysfunction including 28% with DI.

Relatively few studies of patients undergoing surgery for craniopharyngioma distinguish new postoperative hormonal loss by axis. These studies tend to show overall postoperative hypopituitarism rates ranging from 50% to 90% of patients [5,20,21,27,33,36,41]. The highest rates of postoperative hypopituitarism ranging from 79% to 95% are reported in a series in which total tumor removal was the goal [41,43]. Lower rates were reported by Honegger et al [20], Chakrabarti et al [10], and Shin et al [36] who documented new anterior hormonal loss in 3% to 39% of patients and new DI in 44% to 67% of patients. A transsphenoidal route was used in the majority of the patients in the Chakrabarti et al [10] study, whereas the Honegger et al [20] and Shin et al [36] series had more patients operated on by craniotomy. The subset of patients in the Honegger et al series who had transsphenoidal surgery had higher rates of preoperative pituitary dysfunction, but similar rates of new hypopituitarism compared to the transcranial approach. Our study found new anterior dysfunction overall in 31% and new DI in 39%.

Improvements in hormonal function after craniopharyngioma removal appear to be relatively uncommon. The series by Shin et al [36], however, reported an 86% rate of resolved GH deficiency and 22% rate of resolved hypoadrenalism [10,20]. Notable in this series of 21 patients is that only 14% of patients had a gross total tumor removal and 62% had tumor recurrence, suggesting that the surgical goals were for a limited tumor removal. König et al [25], in a series of 31 patients, found a 19% improvement in hormonal function overall. In the larger series of 143 patients by Honegger et al [20],

hormonal improvement ranged from 1% to 6.7% of patients, varying by axis; resolution of hypoadrenalism, hypothyroidism, and DI was observed in 6.7%, 5.7%, and 4%, respectively. However, Karavitaki, in 121 patients, reported no gains in any axes [21]. Our experience is similar as none of the patients in our series gained any hormonal function except for resolution of hyperprolactinemia which occurred in 43% of patients. Honegger et al [20] found hyperprolactinemia resolved in 51% of patients. However, it is likely that, in many patients, this resolution of hyperprolactinemia reflects a loss of lactotroph function and not elimination of “stalk compression” hyperprolactinemia.

#### 4.4. *Tuberculum sellae meningiomas*

Prior studies addressing hormonal outcomes after surgery for suprasellar meningiomas are few and have been limited predominantly to tumors approached by the transcranial route [6,9,16,18]. However, these studies and our previous report indicate that rates of preexisting hypopituitarism are lower than for craniopharyngioma or RCC [6,9,14,16,18]. This finding is likely related to the fact that these tumors are situated above the gland and anterior to the pituitary stalk; although they may compress these structures, they typically become symptomatic because of chiasmal compression and visual loss before the onset of hormonal dysfunction. Overall rates range from 7% to 14.5% with primarily anterior pituitary hypopituitarism [6,9,16,18] and 7% to 20% with hyperprolactinemia [6,16,30]. Similarly, our study found that only 10% of patients without prior surgery had preoperative hypopituitarism.

From the sparse transcranial literature, it appears that new postoperative pituitary dysfunction is relatively uncommon. Bassiouni et al [6] reported rates of loss for individual axes, ranging from 2% for GH, gonadal, thyroid, and posterior pituitary function, to 13.7% for corticotroph function. In their series, 9 of 62 patients had preoperative endocrinopathy; hypoadrenalism and hyperprolactinemia resolved in 29% and 86% of patients, respectively, but no other axes recovered. Fahlbusch and Schott [15] reported a 66% (2/3 patients) improvement in gonadal dysfunction and no permanent worsening of function. Hyperprolactinemia resolved in 1 patient (50%) in our series, but we did not observe any improvement of hypopituitarism, nor did we observe any new hypopituitarism in patients undergoing first-time surgery. Similar to the transcranial approach, our results indicate that the transsphenoidal route is an effective means for removing relatively small midline suprasellar meningiomas while preserving normal pituitary function in the great majority of cases [14].

#### 4.5. *Study limitations*

This study was limited by its retrospective nature and small sample size, especially for patients with craniopharyngioma and meningioma, which precluded an assessment of predictors of postoperative hormonal status. Also because of

the retrospective nature, the hormonal testing was not uniform and most patients did not undergo stimulation testing for assessment of GH deficiency. Prior studies have also varied in their definition of deficiencies and hormonal testing protocols, therefore making direct comparisons to the prior reports problematic. Extent of resection of these tumors can clearly affect postoperative pituitary function. We have generally tended to err on the side of caution, leaving residual tumor that was very adherent to neurovascular structures or to the infundibulum in patients with relatively normal preoperative hormonal function. Aggressive attempts at total removal, particularly for craniopharyngiomas, have been shown to lead to higher rates of postoperative pituitary failure [41,43].

## 5. Conclusion

Endonasal transsphenoidal surgery is being increasingly used to remove nonadenomatous parasellar tumors. New hormonal deficits after transsphenoidal surgery for craniopharyngioma occur in approximately one third of patients, whereas they occur in less than 10% of patients undergoing removal of a suprasellar meningioma or RCC. In contrast, improvement of pituitary hormonal function occurs in more than 50% of patients undergoing RCC drainage but is unlikely to occur in patient with a suprasellar meningioma or craniopharyngioma.

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## Commentary

Although the results arrived at from the analysis are somewhat intuitive, it is necessary and important that the factual and scientific underpinnings of such assumptions be available. The authors deliver a clear statement of what to expect in the endocrine outcome after surgical treatment of

these lesions. It is very important to provide patients with reasonable and realistic surgical expectations—these authors have done just that.

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The authors have reviewed a fair-sized group of patients who underwent transsphenoidal surgery for 3 lesions other than adenoma. The paper has limitations as one would expect from a retrospective study, but the data are interesting and worthwhile. Particular attention ought to be given to the group with RCCs. I agree entirely with the authors' comments

that the cyst wall should not be aggressively removed as that will lead to a significant incidence of hypopituitarism. We have published that in our series as well. More importantly, the data here show the very significant opportunity for improvement of pituitary deficiencies. In some patients presenting with only partial hypopituitarism, but no neurologic deficit, surgery with drainage of the cyst ought to be discussed and considered for the opportunity of improving pituitary function, negating the need for replacement therapy. This paper gives some valuable data enabling some statistics on the likelihood of improvement.

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