

# Long-term Surgical Outcomes in Patients with Cushing's Disease: A Single-center Study



Yury Shulev, MD, PhD, Ovanes Akobyan, MD, Dmitry Pechiborsch, MD

North-Western State Medical University Named after I.I. Mechnikov, City Multiprofile Hospital #2

## Introduction

Cushing's disease (CD) is rare, with an estimated annual incidence of 1.2-1.7 per million. CD is the result of chronic hypercortisolism caused by an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma. The main goal of treatment is to produce disease remission and provide long-term control. The selective removal of an adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma by transsphenoidal surgery (TSS) has recognized as the first line treatment for CD. Reported remission and recurrence rates after TSS for CD vary widely according to the remission criteria. A number of factors may influence outcomes: size and localization of the tumor, intraoperative tumor visualization, pre-operative ACTH level, urinary free cortisol level, and histological confirmation of corticotroph adenomas. Hypocortisolism after TSS has been shown to be a reliable prognostic factor for indicating remission and a lower risk of recurrence.

This study was performed to analyze the results of patients who underwent the endoscopic endonasal surgery (EES) for CD in our department and to determine the surgical outcomes, recurrence and complication rates.

## Methods and Materials

Data were analyzed from 28 consecutive patients with CD who underwent EES between 2013 and 2024. The mean follow-up period was 39 (18-94) month.

**CD diagnostic criteria:** 1. elevated 24-h urinary-free cortisol at > 250 mkg; 2. failure to suppress serum cortisol to undetectable levels with low-dose dexamethasone; 3. loss of circadian rhythm of cortisol production. When at least two of these screening tests were positive, further testing with a high-dose (8 mg) dexamethasone suppression test was conducted. If basal cortisol levels were suppressed to less than 50% of their initial value, this points towards CD.

**Imaging:** MRI performed to visualize the pituitary gland, identify any adenomas and the invasion to the cavernous sinus (CS). Inferior petrosal sinus sampling (IPSS) conducted if a microadenoma was suspected on MRI to confirm the source of ACTH.

**Surgical Strategy:** An EES was performed for pituitary exploration and resection of the adenoma. The goal was to achieve gross total resection, either en bloc or piecemeal resection depending on the situation. Always we did wide exposure of the sellar dura to control the medial wall of cavernous sinus. In case of tumor invasion, the medial wall could be resected. In cases of negative pre-operative MRI, exploration of the pituitary gland was performed. To confirm the diagnosis of ACTH-secreting adenoma, all removed specimens underwent histopathological and immunohistochemical staining for pituitary hormones.

**Postoperative Care:** No perioperative steroids was given in order to assess remission early. Blood samples for cortisol were taken 6 hours after surgery and then twice daily for the first week. Patients with cortisol levels below 50 nmol/l received intravenous hydrocortisone, transitioning to oral prednisolone once stable. MRI was performed in all cases to confirm postoperative status. Transient cranial diabetes insipidus (DI) was defined as the development of hypotonic polyuria postoperatively requiring at least one dose of desmopressin, which resolved prior to discharge.

**Remission Criteria:** Remission was defined by the presence of hypocortisolemia (basal cortisol < 50 nmol/l) or eucortisolemia (basal cortisol > 50 nmol/l but with suppression to < 138 nmol/l).

## Results

Median age was 37 years (23-62), 15 were female. Median duration of symptoms was 26 months (9-122) and the major symptoms included general fatigue, obesity, hyperpigmentation, proximal myopathy, and menstrual irregularities with hirsutism in women. In preoperative MRI, tumor was verified in 24 (85.7%) cases; 20 microadenoma and 4 macroadenoma. Seven patients had tumors with cavernous sinus invasion. No adenoma was identified in 4 patients (17%) (Table 1). IPSS was performed in 20 (71.4%) patients.

The rate of biochemical remission was 82.1% (23/28) (Table 2). There were 5 cases of recurrence of CD during the follow-up period. Three patients underwent a second EES and two patients received radiosurgery.

Postoperatively, there were no cases of CSF leakage, meningitis, vascular injury or visual deterioration. Transient diabetes insipidus occurred in 7 (25%) patients.

**Table 1.** MRI findings and grade of tumor resection

MRI findings			Grade of tumor resection		
		Tumor size	CS invasion	Total	Subtotal
MRI positive	24 (85.7%)	Macro(>10 mm) - 4 (17%)	3	3	1
		Micro (<10 mm) - 20 (83%)	4	20	-
MRI negative	4 (14.3%)		-		
				2	-

**Table 2.** Endocrinological evaluation and remission rate after the surgery

Morning serum cortisol < 50 nmol/l	17 (60.7%)
Morning serum cortisol < 138 nmol/l	6 (21.4%)
Hypopituitarism	21 (75%)
Transient DI	7 (25%)
Remission rate	23 (82.1%)
Recurrence	5 (17.8%)
Re-operation	3 (10.7%/0)
Radiotherapy	2 (7.1%)

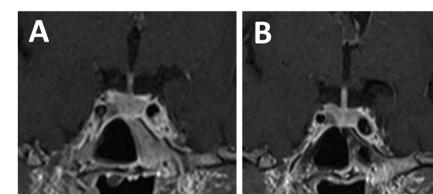
**Table 3.** Complications

CSF	-
Epistaxis	2
Hemorrhage	-
ICA injury	-
Meningitis	-
Sinusitis	2

## Case presentation

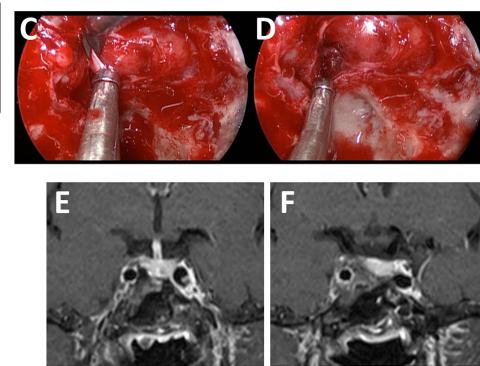
**Figure 1.**

A 27-year-old female who developed symptoms of CD. An adenoma is detected on gadolinium-enhanced T1-weighted MRI imaging (A, B). IPSS confirmed the right side location of the tumor.



Test	ACTH	Prolactin
Peripheral blood	32,2 pg/ml	279 mIU/l
Right IPS	143,3 pg/ml	2212 mIU/l
Left IPS	39,1 pg/ml	264 mIU/l

Medial wall of CS was resected (C). Final stage of surgery (D). Total resection of the adenoma is confirmed on postoperative gadolinium-enhanced T1-weighted imaging (E, F). On postoperative day #1, cortisol was 21 nmol/l and she was replaced with hydrocortisone. Patient achieved remission from her CD.



## Conclusions

EES is a safe and effective treatment method for Cushing's disease with satisfactory remission rates. It provides access to the cavernous sinus. Selective resection of the medial wall of the cavernous sinus in case of invading of tumor, is critical for increasing remission rate.

## Contact

Yury Shulev, MD, PhD,

City Multiprofile Hospital #2

194354, Russian Federation, Saint-Petersburg, Uchebny per, 5

yuryshulev@yahoo.com

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