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Pituitary Adenoma Surgery: A Single-center Experience of Over 8,500 Operations

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PITUITARY ADENOMA SURGERY: A SINGLE-CENTER EXPERIENCE OF OVER 8,500 OPERATIONS

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Kalinin Pavel and Shkarubo Alexey contributed to the study conception and design. Material preparation and data collection were permored by Chernov Ilia, Konyashin Daniil, Donskoy Artem, Andreev Dmitry, Diana Adueva, Olga Rastvorova. Analysis was performed by Kutin Maxim, Fomichev Dmitry, Oleg Sharipov, Ludmila Astafieva, Julia Sidneva, Irina Voronina, Irina Klochkova. The first draft of the manuscript was written by Chernov Ilia.

All authors read and approved the final manuscript.

Ethics approval

Name of the Approval Committee: *local ethics committee of the The Burdenko neurosurgical center*

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Local Ethics Committee of the The Burdenko neurosurgical center

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Clinical trial number: not applicable

Abstract

Background: Pituitary adenoma surgery has evolved from simple decompression to maximally safe radical resection with preservation of endocrine and neurological function. Treatment requires a multidisciplinary approach and is increasingly centralized in high-volume centers, though long-term outcome data from large series remain limited.

Objective: To present a 21-year single-center experience in the surgical management of pituitary adenomas, focusing on outcomes, complications, and evolving treatment protocols.

Methods: Retrospective analysis of 8,514 patients operated for pituitary adenomas at the Burdenko Neurosurgery Center (2005–2025), including all subtypes and sizes. The primary approach was endoscopic transnasal adenomectomy, with transcranial or staged approaches in selected cases. Outcomes included resection extent, biochemical remission, visual outcomes, complications, and mortality.

Results: Median age was 46.5 years (range 2–86), with female predominance (1:1.5). Endoscopic resection was used in 96.3%. Gross total resection was achieved in 80%, and biochemical remission in 90% of functioning adenomas (best in corticotropinomas and tumors ≤20 mm). Visual improvement occurred in 66%, deterioration in 4%. Overall complication rate was 7%: CSF leakage 0.5–3%, meningitis 1%, ICA injury 0.06%. Mortality was 0.59%, declining to <0.5% in the last decade.

Conclusion: Endoscopic transnasal surgery for pituitary adenomas in experienced high-volume centers achieves excellent outcomes with low morbidity and mortality. Complex and functioning adenomas should be managed in reference centers with multidisciplinary expertise. Our findings support establishing surgical volume and remission rate benchmarks to optimize patient care.

Introduction

Skull base surgery is one of the most complex and dynamically evolving fields of neurosurgery. A significant portion of this discipline is dedicated to the treatment of patients with pituitary adenomas. At the present stage, this is not merely a tumor removal technique, but a comprehensive neurosurgical discipline at the intersection of endocrinology, ophthalmology, neurology, otorhinolaryngology, psychiatry, and radiology. Over the past 50 years, the goal of surgical treatment for patients with pituitary adenomas has evolved from simple decompressive intervention to the maximally possible radical removal of the tumor while preserving and restoring pituitary function, vision, and the patient's neurological status, with a minimal complication rate. Key factors determining the success of surgical treatment, in addition to the surgeon's skill, include multidisciplinary team collaboration, institutional experience, and the technical and material resources of the medical facility.

In this article, we present a 21-year experience in pituitary adenoma surgery, based on the treatment of over 8,500 patients, demonstrating how the introduction of advanced technologies, surgical techniques, and a systematic approach have allowed us to develop new quality standards in the management of these patients.

Materials and Methods

From 2005 to 2025, a total of 8,514 patients with pituitary adenomas were treated at the Burdenko neurosurgical clinic (male-to-female ratio 1:1.5), with a median age of 46.5 years (range 2–86 years). The introduction of the endoscopic transnasal technique for pituitary adenoma removal has revolutionized the ratio of transcranial to transnasal procedures, shifting the preference decisively toward the latter (Figure 1). According to the B. Kadashev classification of pituitary adenomas by size, the majority of patients (65%) underwent surgical treatment for medium-sized (26–35

mm) and large (36–59 mm) tumors of endosuprasellar localization. Giant tumors (>60 mm) were observed in 6% of patients.

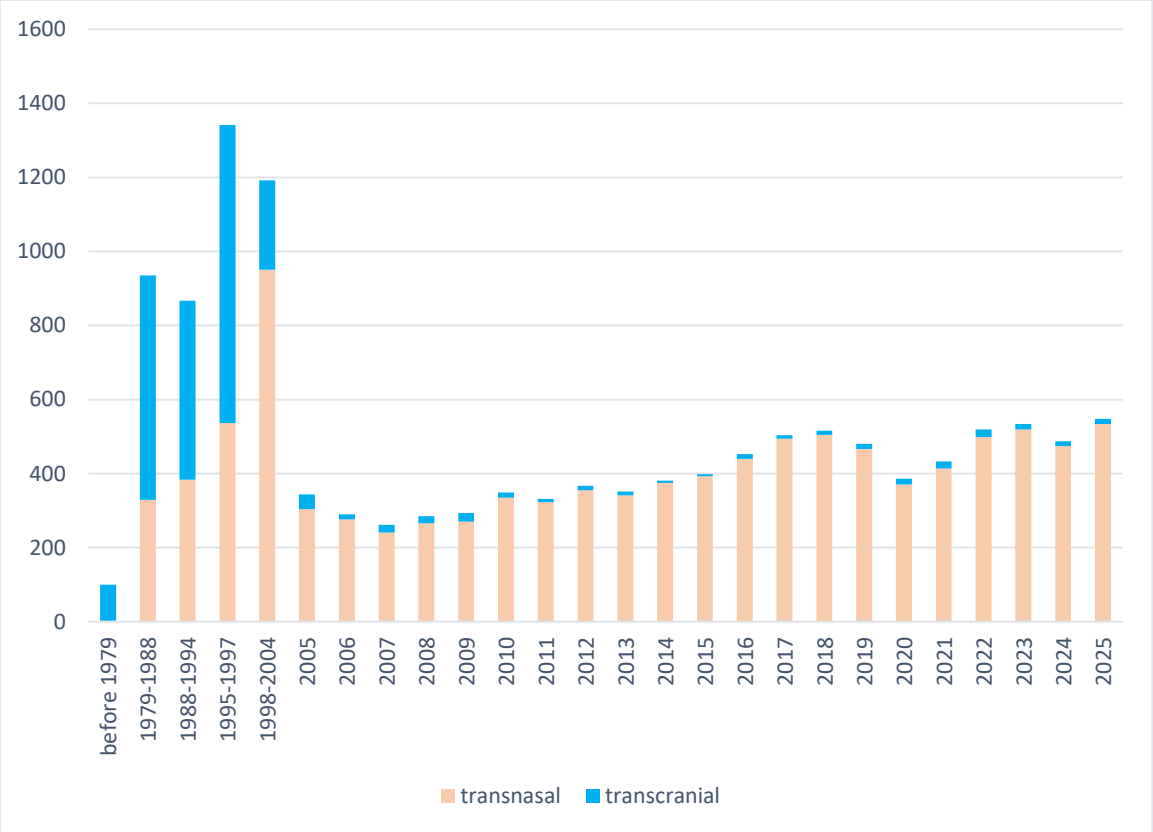


Figure 1. *Annual number of surgical procedures*

Figure 2 shows the distribution of adenomas by type.

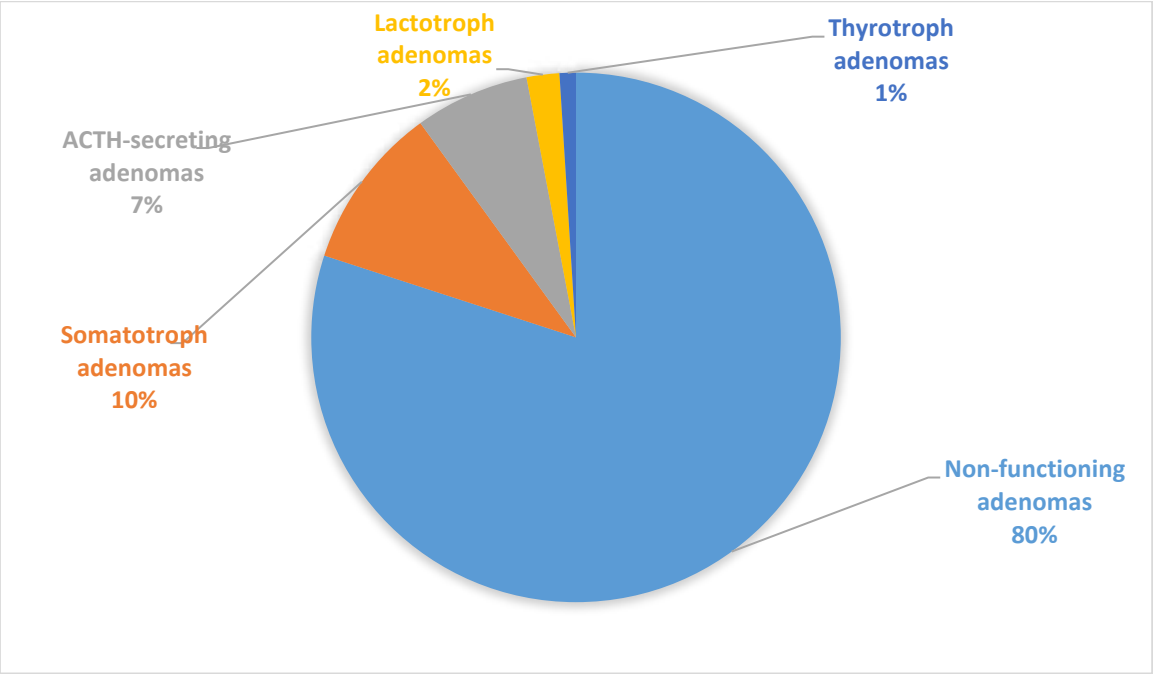


Figure 2. *Distribution of patients based on the hormonal activity of the tumor.*

Tumor hypersecretion (GH, TSH, ACTH) was an indication for resection. Indications for non-functioning adenomas included growth, neurological symptoms (headache, visual/oculomotor/endocrine deficits), and giant tumor-associated hydrocephalus. For prolactinomas, indications for surgery included pharmacoresistance, intolerance to dopamine agonists, patient preference against medical therapy, as well as complications of conservative treatment (hemorrhage into the tumor stroma, nasal CSF leakage).

In the majority of cases (n = 8,196, 96.3%), we employed the endoscopic transnasal technique for pituitary tumor removal [1,2]. Over the years of its use, the technique has undergone a number of refinements. In our institution, we routinely use a monomanual technique (without an endoscope holder), in which the operating surgeon holds the endoscope in the left hand and a surgical instrument in the right hand. The assistant manipulates a surgical instrument with the left hand and also ensures continuous irrigation of the endoscope lens. In some cases, the surgeon simultaneously holds both the endoscope and an instrument (e.g., an aspirator, curette, or rongeur) in the left hand, manipulating them together, which allows two

or three instruments to be present in the surgical field at the same time, or enables the surgeon to work more autonomously without an assistant. In some cases, the assistant manipulates two instruments, and irrigation is then performed by the operating room nurse.

Over time, the steps of the surgical approach, tumor removal, and skull base repair have been continuously improved. We consider that the current standardized algorithm represents the most reliable and safe protocol.

The approach to the sphenoid sinus is performed with preservation of the arteries supplying the mucosa of the nasal septum and the nasal floor (the sphenopalatine artery and its branches – Figure 3). This is achieved either by a vertical mucosal incision at the level of the ostium or by a horizontal incision of the nasal septal mucosa, also at the level of the natural ostium, which allows for the formation of a mucoperiosteal flap if needed during skull base defect reconstruction.

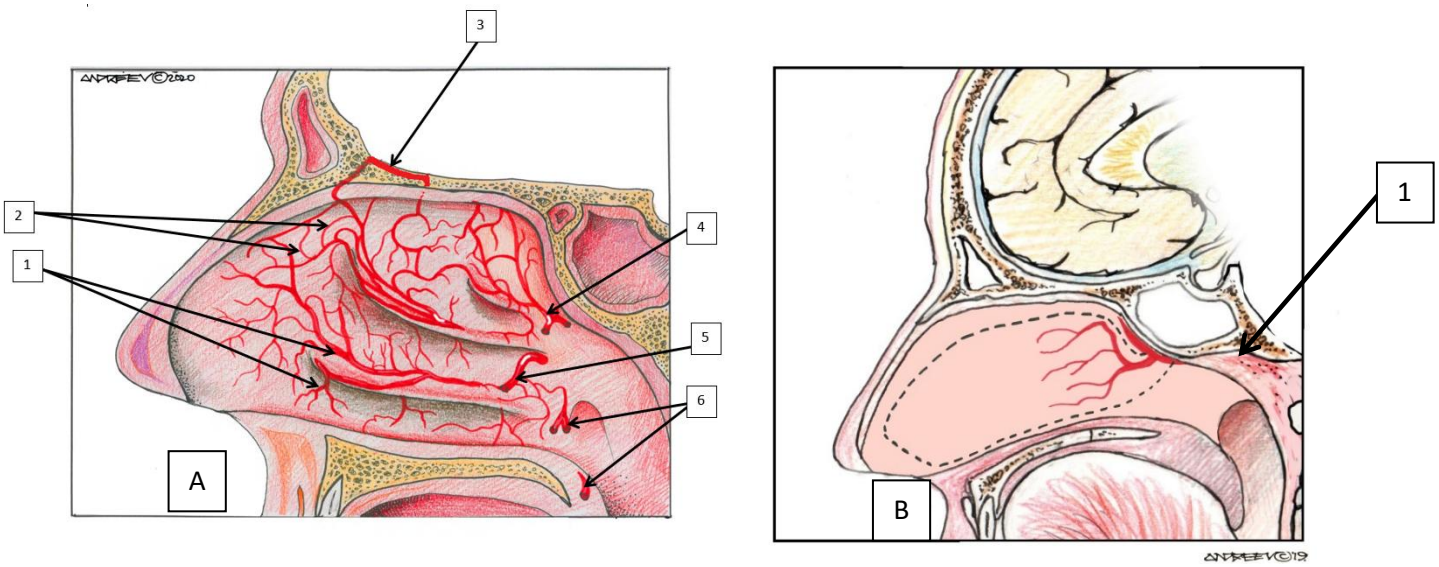


***Figure 3. A** – Arterial network of the nasal cavity mucosa. 1 – lateral nasal branches of the facial artery; 2 – lateral nasal branches of the anterior ethmoidal artery; 3 – anterior ethmoidal artery; 4 – sphenopalatine artery; 5 – posterior lateral nasal arteries (branches of the sphenopalatine artery); 6 – ascending palatine artery.*

***B** – Schematic diagram of the boundaries of the nasal septal mucoperiosteal flap (dashed line). 1 – sphenopalatine artery*

After resection of the anterior wall of the sphenoid bone (the rostrum), removal of the intersinus septa, and the mucosa, the anatomical bony landmarks become visible in most cases (the bony canals of the optic nerves, the internal carotid arteries, the optico-carotid recess, the sellar floor, the clivus, and the planum sphenoidale). The sellar floor is drilled with a diamond burr within the carotid canals, planum, and clivus. The dura is vertically incised and coagulated as needed for intrasellar visualization.

Tumor removal is performed using 0°, 30°, 45°, and 70° optics with various aspirators, including those with extended tips. The resection algorithm involves sequential tumor removal, starting with the endo- and infrasellar (when present) components, followed by the suprasellar component and secondary nodules (if present), and finally the laterosellar fragments within the cavernous sinuses along with their secondary extensions. This sequence is dictated by the risk of uncontrolled bleeding from the laterosellar nodules, which would impede further removal of the suprasellar component. In cases of fibrous tumors, resection is performed by gradual dissection from the capsule using various curettes, followed by fragmentation.

Previously, in cases with a pronounced suprasellar component of the tumor, we used external lumbar drainage to reduce intracranial pressure (ICP) and facilitate collapse of the tumor capsule. However, due to the comparable efficacy of hypertonic iso-oncotic sodium chloride solution in lowering ICP, as well as the increased risk of infectious complications associated with lumbar drainage, we have completely abandoned its use over the last 7–8 years, reserving this option only for isolated cases of recurrent postoperative CSF leakage [3].

Skull base defect closure includes the use of autologous nasal septal bone, Tachocomb, and fibrin glue in the absence of CSF leakage, or a 'sandwich' technique using autologous fascia, fat, bone, and a mucoperiosteal flap when defects in the tumor capsule are present [4,5].

The accumulation of experience has allowed us to expand the indications for endoscopic transnasal removal of pituitary adenomas. It has become possible to resect tumors of complex configuration (giant size, lateralized nodules, growth into subcortical regions) via the endonasal route, as well as to operate in challenging anatomical conditions (small sella turcica, close proximity of the cavernous segments of the internal carotid arteries, conchal-type sphenoid sinus), including the use of adjunctive techniques such as Doppler localization of the cavernous segment of the internal carotid artery, neurophysiological mapping of the cranial nerves, and intraoperative MRI/CT [6].

In 318 patients (3.7%) with giant tumors showing significant growth into the posterior cranial fossa or the lateral ventricles, we used transcranial approaches (subfrontal, transcortical) or divided the surgical treatment into two stages (transcranial removal followed by transnasal removal).

All patients had immediate postoperative head CT to rule out intracranial complications. Hormone replacement (hydrocortisone, levothyroxine, desmopressin if needed) was given based on tumor activity and patient status. Patients were examined by an ENT specialist for nasal cavity sanitation and to detect occult CSF leakage, including via endoscopic examination. Uncomplicated patients were discharged on POD 3–5. Follow-up contrast MRI was done at 3–4 months.

Results

In our practice, we use a classification of the extent of pituitary adenoma resection that includes gross total removal (100%), subtotal removal (80–99% of the tumor resected), and partial removal (up to 80% of the tumor resected). [7].

Gross total resection was achieved in 80% of patients. The best results were obtained in tumors without laterosellar or secondary nodules and without infiltrative growth into the bony structures of the skull base (nearly 100% of tumors in this cohort were radically removed). In some cases, resection was limited by tumor consistency, the

presence of dense fibrous bridges between nodules, or tumor geometry that prevented visualization of certain parts even with angled optics. In other cases, radical resection was not advisable from the standpoint of the patient's condition (age, somatic status, including obesity, diabetes mellitus, etc.), where the risks of complications outweighed the potential benefit of complete tumor removal.

In hormone-active tumors, remission was most frequently achieved in corticotropinomas and in tumors not exceeding 20 mm in size (Figure 4).

We adhere to the generally accepted criteria for remission in hormone-hypersecreting diseases. For somatotropinomas, remission is defined as a decrease in IGF-1 to normal levels within 3 months after surgery, as well as a GH level below 1 ng/mL at any time point during the oral glucose tolerance test (OGTT). For ACTH-producing tumors, remission is confirmed by normal salivary cortisol at bedtime, normal 24-hour urinary cortisol, and cortisol suppression during the low-dose dexamethasone suppression test. For prolactinomas, remission is defined as normalization of prolactin levels.

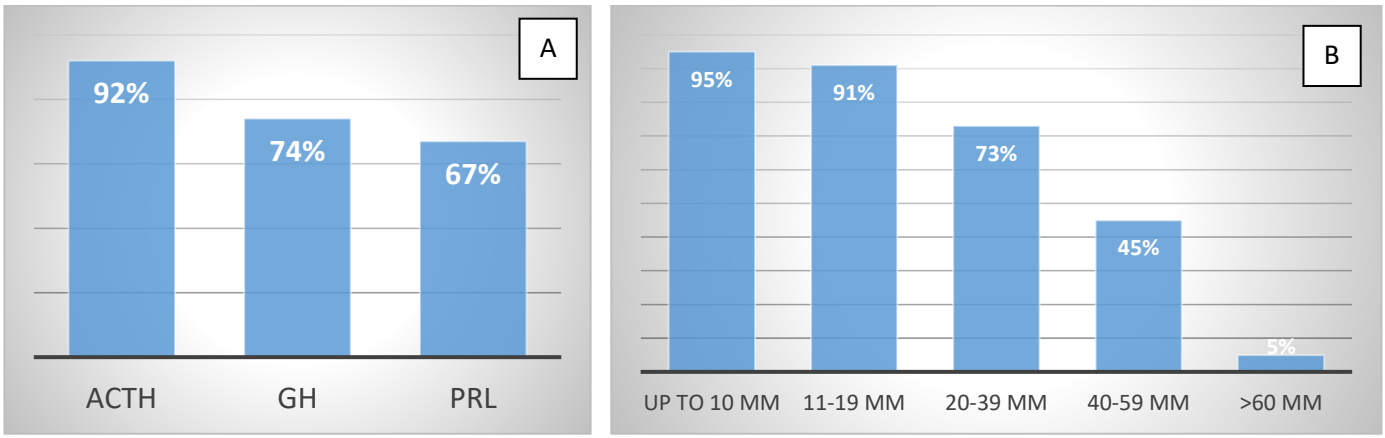


***Figure 4. A** – Frequency of hormone normalization in functioning pituitary adenomas. **B** – Frequency of hormone normalization in functioning pituitary adenomas depending on tumor size.*

In the majority of cases, removal of pituitary adenomas led to regression of clinical symptoms. By the time of discharge, improvement in visual function (visual field and visual acuity) was observed in 66% of patients, while deterioration occurred in 4%. Regression of oculomotor disturbances was noted in 55% of patients and was often dependent on the duration of symptoms before surgery. The rate of newly developed oculomotor disturbances (most commonly involving the abducens nerve) was 3%, and occurred only in patients with laterosellar tumor extension, even when tumor resection from the cavernous sinus was not radical. In most cases, these disturbances resolved within three months after surgery.

After removal of giant pituitary adenomas (>60 mm) causing obstructive hydrocephalus and associated general cerebral and psychiatric symptoms, regression of these symptoms occurred in more than half of the patients (56%) within several months after surgery. The need for CSF diversion procedures after tumor removal in cases of preexisting hydrocephalus arose in 20% of cases. In tumors occluding both foramina of Monro, a biventricular drainage technique was employed.

The rate of surgical complications after endoscopic transnasal adenomectomy was 7%. Early complications included nasal CSF leakage, meningitis, hemorrhage into the tumor resection bed (more common) or extracapsular hemorrhage (less common) with consequent visual impairment, vasospasm of intracranial arteries, and cranial nerve dysfunction. Late complications included nasal CSF leakage, meningitis, and epistaxis.

Among endocrine complications, water–electrolyte disturbances (hyponatremia/hypernatremia) occurred with a frequency of 7%, resulting from adrenal insufficiency, diabetes insipidus, or syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Postoperative nasal CSF leakage was noted in 0.5% of cases with an intact tumor capsule, and in 3% of cases with intraoperative CSF leakage.

When analyzing the incidence of CSF leakage by year (Figure 5), we observed a gradual decrease over time, confirming the effectiveness of the developed skull base defect repair technique.



Figure 5 – Incidence of postoperative nasal CSF leakage by year.

The incidence of meningitis was 1%. The most severe intraoperative complication — injury to the internal carotid artery — occurred in 5 patients (0.06%). Hemorrhagic complications with visual disturbances, manifesting as blood accumulation in the tumor resection bed on postoperative CT, were identified in 0.2% of patients. In half of these cases, this complication was accompanied by worsening or new-onset chiasmal compression symptoms, requiring surgical revision. Extracapsular blood accumulation was detected in 0.1% of cases.

Hemorrhagic infiltration of hemostatic agents, occurring at a rate of 0.08%, resulted in visual and/or oculomotor dysfunction. In all such instances, postoperative CT demonstrated blood accumulation within the resection cavity. After surgical revision and removal of the hemostatic materials, clinical improvement was observed in nearly all cases.

Delayed complications occurring after discharge included CSF leakage, meningitis, epistaxis, and water–electrolyte disturbances, including those resulting from patient non-compliance with hormone replacement therapy. Hospitalization at our center was recommended in all cases for complication management; however, due to geographic accessibility issues, this was not always feasible.

The mortality rate was 0.59%. The majority of cases were patients with giant pituitary adenomas. Over time, a trend toward decreasing mortality was observed, and over the past 10 years, it did not exceed 0.5% (Figure 6). The most common causes of death were postoperative hemorrhage into the tumor remnants or its bed with rupture into the basal cisterns/ventricular system (52%), ischemic events in the territories of the anterior and middle cerebral arteries due to vasospasm or infectious complications (22%), and infectious complications directly (18%).

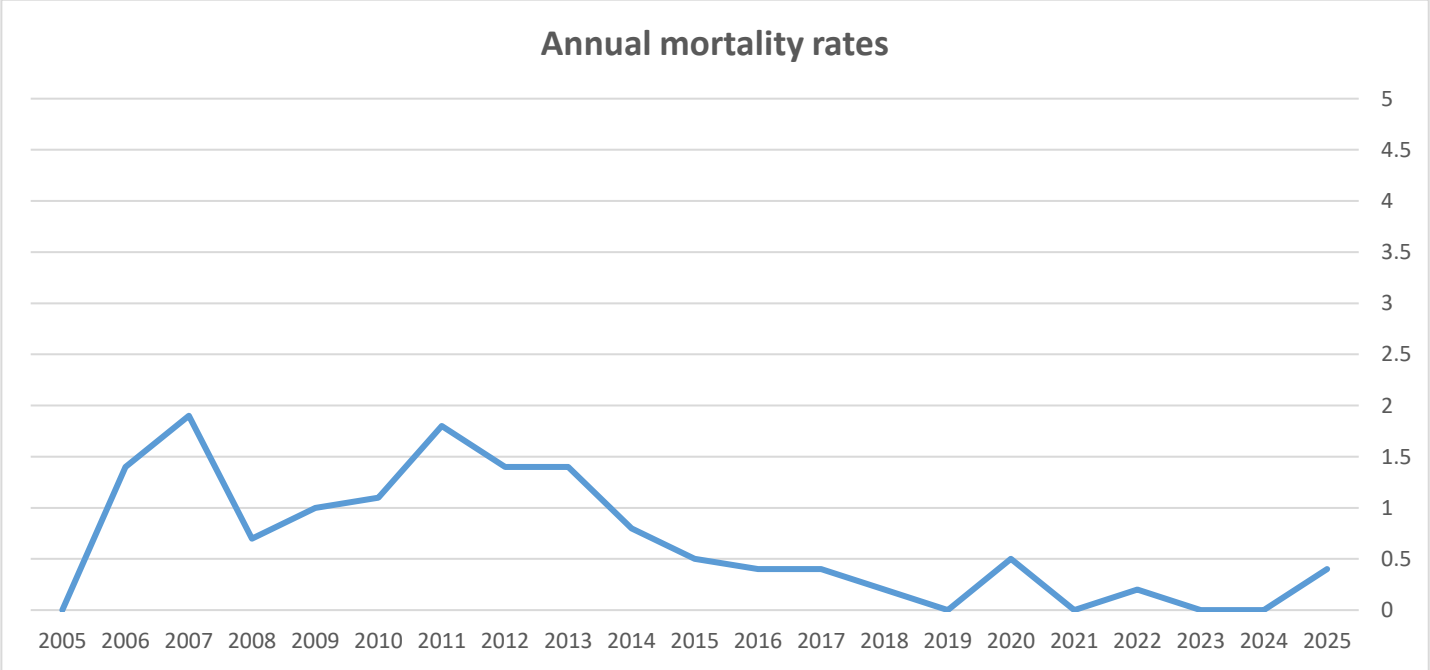


Figure 6 – Postoperative mortality rate in patients with pituitary adenomas by year.

Discussion

Over the past 20 years, pituitary adenoma surgery has evolved significantly and, in the hands of experienced surgeons at major neurosurgical centers, has become a routine procedure. At the Burdenko Neurosurgery Center, approximately 500 operations for pituitary adenomas are performed annually, with the vast majority using the endoscopic transnasal approach. Over the years, a well-established treatment algorithm for patients with these tumors has been developed, encompassing the entire pathway from preoperative workup and preparation to discharge criteria and outpatient follow-up. The key issues in pituitary adenoma surgery include the selection of an appropriate surgical approach, the safe extent of tumor resection considering its topographic and anatomical relationship with surrounding critical structures, complication prevention, and skull base defect repair techniques.

According to our data, endoscopic transnasal removal is feasible in 95% of patients, even in cases with a small sella turcica, lateralized or anteriorly displaced tumor nodules, tumor growth into the third ventricle, and a narrow intercarotid distance. In some cases (such as tumor growth into the lateral ventricles, the presence of giant secondary nodules, or compromised somatic status), a combination of approaches may be more appropriate, starting with a transcranial approach followed by transnasal removal of any residual endo-infrasellar tumor components — either during the same hospitalization or with a gap of several months [8].

Given that the majority of pituitary adenomas have no secondary nodules and are of soft consistency, gross total resection is achievable in nearly all cases. Firm tumors can also often be completely removed by dissecting the tumor from the capsule and fragmenting it; however, this is associated with a higher risk of intraoperative CSF leakage [9]. According to current understanding, the tumor capsule does not always contain tumor cells and is represented by a stretched, thinned dura mater and flattened pituitary gland [10–12]; therefore, we adhere to a strategy of preserving it, which allows us to maintain the integrity of the intradural space. This is reflected in

the rates of postoperative CSF leakage and meningitis, which do not exceed 1%, demonstrating the effectiveness and safety of our developed tumor resection techniques, skull base defect repair methods, and antibiotic prophylaxis protocols. Current literature data report postoperative CSF leak rates of up to 7%, with tumor consistency, large size, invasive growth, and surgical experience identified as the most significant contributing factors [13–16].

In cases of intraoperative CSF leakage grade 2 or 3 according to F. Esposito [17], the use of a vascularized nasoseptal flap has become the standard [18]. However, a review of the literature indicates that the initial enthusiasm following its introduction has been tempered by some skepticism, owing to accumulated data on nasal complications associated with mucosal flap elevation and exposed septal bone and cartilage [19]. Some authors advocate against the use of the nasoseptal flap altogether due to these associated complications, preferring non-vascularized tissues (fat, fascia) instead [20]. Nevertheless, the majority — including ourselves — remain proponents of vascularized tissue reconstruction [18,21,22].

Blood accumulation in the tumor resection bed was an uncommon event (in our series, the rate was 0.2%, which does not exceed the literature data [15,16]), and even less frequently did this situation require revision surgery. Nevertheless, in cases of giant tumors, hemorrhage into the tumor remnants or the resection bed was the leading cause of mortality.

Modern technologies, including Doppler ultrasonography, and — to an even greater extent — surgical experience, help minimize the risk of intraoperative injury to major vessels. In our practice, such complications occurred in only 5 cases [23], representing 0.06%, which is consistent with the literature [24]. The management strategy for internal carotid artery injury during endoscopic transnasal removal of pituitary adenomas should include rapid hemostasis through tight packing, including with autologous tissues, followed by assessment of the possibility of endovascular closure of any resulting pseudoaneurysm. Particularly dangerous is surgery in the

setting of reoperation with altered anatomy, loss of anatomical landmarks, and destroyed bony structures, where even the use of navigation systems cannot ensure accurate mapping of the internal carotid artery.

Most commonly, the primary goal of adenomectomy is decompression of the optic nerves and chiasm, and according to our data, surgery leads to visual improvement in two-thirds of cases (according to the literature, vision is completely restored in 30–40% of patients [25]). A significant problem remains the time from the onset of visual disturbances to neurosurgical referral, which often exceeds 6 months or more. In cases with established late-stage optic nerve atrophy, the likelihood of visual improvement is low, and the primary goal is preservation of the existing status. Visual deterioration occurred in no more than 4% of cases in our series, which is consistent with published data [25,26]. The main causes of deterioration are spasm or avulsion of vessels shared by the chiasm and the tumor capsule [27]. Visual decline due to excessive packing of the resection bed, which occurred in 0.08% of cases in our series, served as a cautionary event that led us to avoid such practices; over the years, this complication has ceased to occur in our practice [28].

In functioning pituitary adenomas (corticotropinomas, somatotropinomas, pharmacoresistant prolactinomas, and thyrotropinomas), we always aim for radical tumor removal without compromising safety. Our results — hormone normalization in 90% of cases across the entire cohort — are comparable to the literature and reflect the effectiveness of both preoperative diagnosis in terms of tumor localization (even at small sizes) and surgical technique [29]. Nevertheless, current surgical options are insufficient to achieve hormone normalization in all patients; therefore, radiotherapy and conservative medical therapy for patients with functioning adenomas remain an integral component of the treatment strategy [30].

Given the established and well-defined principles of safe surgery with a low complication rate, according to our data, 3–5 days of inpatient care are sufficient to prepare patients for discharge, taking into account the correction of endocrine status.

One important aspect of managing patients with pituitary adenomas is regular outpatient follow-up, monitoring for complications, and their timely treatment. Management of complications remains one of the most challenging components of pituitary adenoma care. The success of surgery can be entirely negated by severe endocrine disturbances; therefore, such surgery should preferably be performed in specialized centers with a multidisciplinary team.

Conclusion

Over the past 21 years, the Burdenko Neurosurgery Center has accumulated a unique experience in the surgical treatment of more than 8,500 patients with pituitary adenomas. Our experience, as well as observations of patients who underwent surgical treatment at other institutions, has shown that many aspects of this pathology remain the domain of expert-level surgeons working in a limited number of medical centers. This applies primarily to the category of 'complex' pituitary adenomas, which should include all microadenomas, as well as macroadenomas larger than 30 mm, tumors extending into the cavernous sinus, and those with secondary nodules. The treatment of patients with complex and functioning pituitary adenomas at a contemporary and safe level is only possible in 'reference' centers. Their removal should be entrusted only to surgeons with extensive experience in endoscopic transnasal skull base surgery. In our opinion, it is debatable whether all functioning pituitary adenomas should be removed by surgeons with fewer than 200 adenomectomies and a remission rate of less than 60–65% for acromegaly, which is the most frequently operated functioning tumor.

Abbreviations

Endoscopic endonasal surgery - EES
cerebrospinal fluid – CSF

Growth hormone - GH
Thyroid-stimulating hormone – TSH
Adrenocorticotropic hormone - ACTH
intracranial pressure - ICP
Ear, Nose, and Throat – ENT
Postoperative day – POD
oral glucose tolerance test - OGTT

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