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The Most Common Complications Associated with Endoscopic Endonasal Transsphenoidal Surgery for Pituitary Tumors: A Review

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ABSTRACT

Endoscopic endonasal transsphenoidal surgery (EETS) is currently the preferred surgical technique for the treatment of most pituitary tumours. Its advantages include wide, panoramic access to the sella turcica and perisellar structures. It simultaneously reduces the need for brain tissue retraction. When performed at experienced multidisciplinary centres, EETS is associated with a favourable safety profile. However, EETS can lead to complications affecting the endocrine system, fluid and electrolyte balance, the skull base, the nasal cavity, the optic chiasm, other cranial nerves and the great vessels. The most observed complications include transient vasopressin deficiency, delayed hyponatremia, the development of new anterior pituitary dysfunction, and postoperative cerebrospinal fluid leakage. Less common complications, such as internal carotid artery injury, postoperative hematoma, decreased visual acuity or visual field deficits, meningitis, or cerebral vasospasm, can lead to significant mortality and morbidity. The incidence of specific complications varies between studies. Risk reduction requires individualised patient assessment, precise surgical management, and standardised postoperative monitoring. Prompt detection of polyuria, sodium abnormalities, adrenal insufficiency, nasal cerebrospinal fluid leakage, visual disturbances, neurological deterioration, and epistaxis is particularly important. This review presents the mechanisms of development, clinical manifestations, preventive methods, and treatment options for complications associated with EETS.

Keywords: pituitary tumor; endoscopic endonasal surgery; transsphenoidal surgery; complications

1. INTRODUCTION

In recent years, there has been an increase in the incidence of pituitary tumours (Daly and Beckers, 2020). They may account for 5% to 20% of intracranial tumours (Graffeo et al., 2022). The type of tumour determines the choice of appropriate treatment options (whether the tumour secretes excess hormones - functioning or non-functioning). For functioning tumours, the first-line treatment is surgery (Tritos and Miller, 2023). The exception is tumours secreting prolactin – in these cases, the treatment is primarily pharmacological - patients receive dopamine agonists such as cabergoline (Oki, 2014).

The aims of surgery are gross total resection/debulking and, in the case of functioning tumours, endocrine remission. Currently, the most common type of surgical approach is endoscopic endonasal transsphenoidal surgery (EETS). EETS has largely replaced the previously known microscopic technique (Tanioka et al., 2026). Its advantages include a wider, panoramic and clearer operative view of the sellar region. It enables assessment of the structures being operated from a short distance and from a lateral perspective. It is a significant advantage compared with the classic microscopic approach (Tanioka et al., 2026). The endoscopic approach has shortened the duration of the transsphenoidal surgery and reduced the incidence of complications. In cases of non-functioning pituitary macroadenomas, the endoscopic technique was also associated with a higher rate of gross total resection than the microscopic method (Møller et al., 2020). However, the risk of complications must be considered during EETS due to the proximity of important anatomical structures such as the optic chiasm, the internal carotid arteries, or the pituitary stalk. Therefore, safety depends not only on tumour removal but also on maintaining normal endocrine, visual, neurological, and sinonasal function. Regardless of the type - microscopic or endoscopic approach – reported complication rates range from 22.1% to 41.72% (Paja et al., 2025; Zhang et al., 2020). Reoperation is associated with a higher risk of complications, with remission achieved in approximately 50% of patients with secretory tumours undergoing repeat surgery (Jahangiri et al., 2014; Heringer et al., 2016).

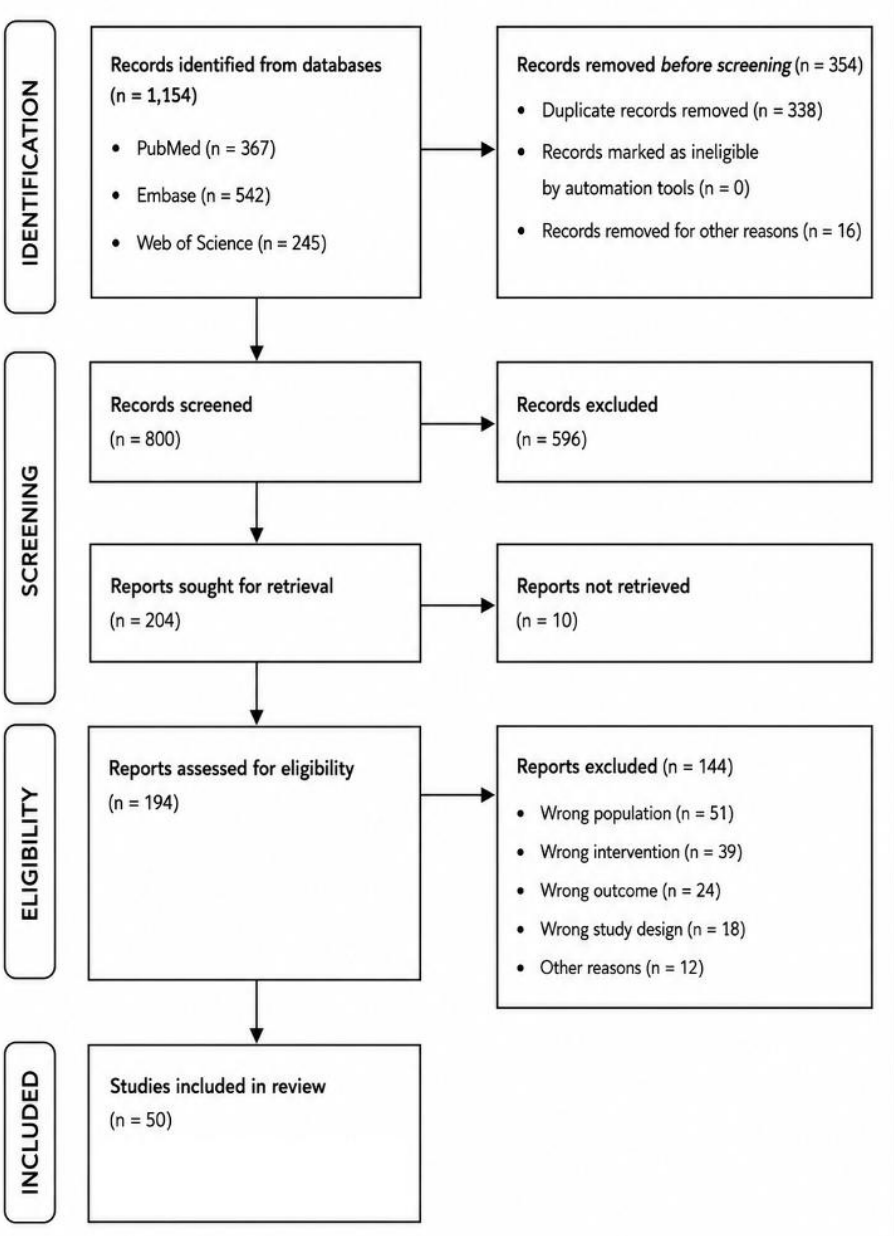

Figure 1. PRISMA 2020 flow diagram of the literature search and study selection process.

Previous studies indicate that endoscopic and microscopic transsphenoidal surgery have generally comparable safety profiles. The incidence of specific complications differs between studies depending on the population analyzed and the methodological approach (Goudakos et al., 2011; Stefanidis et al., 2022; Yu et al., 2018). Their retrospective nature complicates interpretation of the studies, heterogeneity in definitions of complications, variable operator experience, and a lack of homogeneity across the patient populations compared. Patients with large, invasive macroadenomas, tumours with suprasellar or intraventricular extension, cases requiring reoperation, tumours with a hard consistency, and patients undergoing extended surgical approaches are at higher risk of complications compared to patients with small adenomas confined to the sella turcica (Lobatto et al., 2018; Stefanidis et al., 2022). A greater number of complications were associated with tumour diameter >30 mm, suprasellar extension, parasellar involvement, diaphragm sella violation, non-functional adenoma, and intraoperative arachnoid tearing (Namvar et al., 2023). Complication rates should be considered in relation to procedural complexity, tumour characteristics and operator experience rather than as a universal measure of procedural safety.

Endoscopic access can facilitate multidisciplinary collaboration between otolaryngology and neurosurgery specialists, reducing the risk of complications. Postoperative complications substantially affect patients' quality of life, underscoring the importance of effective preventive measures and timely, appropriate interventions when complications arise (Zhang et al., 2020).

2. REVIEW METHODS

A structured literature search was conducted using PubMed, Embase, and Web of Science. Search terms combined pituitary tumours and endoscopic endonasal transsphenoidal surgery (EETS) with terms related to postoperative endocrine, neurological, vascular, infectious, and sinonasal complications. These included "pituitary tumor", "pituitary adenoma", "pituitary neuroendocrine tumor", "endoscopic nasal treatment", "transsphenoidal surgery", "complications", "cerebrospinal fluid leak/leakage", "diabetes insipidus", "vasopressin deficiency", "hyponatremia", "hypopituitarism", "carotid artery injury", "visual acuity deterioration", "meningitis", "epistaxis" and "quality of life related to paranasal sinus function". The study selection process is presented in the PRISMA 2020 flow diagram (Figure 1).

3. RESULTS AND DISCUSSION

Endocrine and water-balance complications

Arginine vasopressin deficiency (AVP-D)

AVP-D (previously known as diabetes insipidus) is the most prevalent water-balance disorder after EETS. It is one of the most common causes of rehospitalisation of patients after EETS (Almalki et al., 2021). Transient AVP-D typically appears abruptly within the first 12–24 hours. It manifests as hypotonic polyuria, polydipsia, rising serum sodium, increasing serum osmolality and low urine osmolality. Permanent AVP-D after surgery for pituitary adenoma is uncommon (approximately 2%) however the risk of permanent AVP-D is higher after surgery for craniopharyngioma or Rathke cleft cyst (Almalki et al., 2021; Fountas et al., 2024). Contributing factors are: manipulation or injury of the stalk or posterior pituitary, larger or suprasellar lesions, intraoperative CSF leakage and certain non-adenomatous pathologies (Fountas et al., 2024; Sorba et al., 2021). It is crucial to determine whether AVP-D is transient or permanent. Excessive treatment should be avoided because, in cases of transient AVP-D, endogenous vasopressin secretion may rapidly return, leading to water retention and hyponatremia. Management involves: careful assessment of fluid balance, serum sodium levels, urine output, and serum and urine osmolality. Desmopressin should be administered when clinically indicated.

The main challenges in AVP-D management include: determining the appropriate timing and dosage of desmopressin therapy, its duration and the optimal follow-up schedule for patients with persistent AVP-D (Almalki et al., 2021). The risk of AVP-D may be minimized by atraumatic dissection and preservation of the anatomical and functional integrity of the hypothalamic–pituitary structures, with limited manipulation of the surrounding neurovascular tissues. Injury to the infundibulum or hypothalamus may disrupt vasopressin transport and secretion, resulting in postoperative AVP-D. (Schreckinger et al., 2013).

Delayed hyponatremia, syndrome of inappropriate antidiuretic hormone secretion (SIADH)

SIADH is characterized by excessive secretion of antidiuretic hormone, leading to increased water retention and secondary development of hyponatremia. The incidence ranges from 1.7% to 28% (Brooks and Inder, 2023). Delayed hyponatremia most often emerges between postoperative days 4 and 10, commonly near day 7. As many patients have already been discharged, symptom onset may necessitate hospital readmission (Hong et al., 2021; Lee et al., 2021; Perez-Vega et al., 2021; Zada et al., 2007). Symptoms may

present as nausea, headache, fatigue, confusion, seizures or coma. Adrenal insufficiency and hypothyroidism should be taken into account in the differential diagnosis. Female sex, younger or older age (>60 years), early postoperative AVP-D, Cushing disease, low body mass index and larger perioperative sodium changes have been reported as risk factors but are inconsistent between studies (Brooks and Inder, 2023; Lee et al., 2021; Perez-Vega et al., 2021; Zada et al., 2007). Routine measurement of serum sodium concentration approximately 6–8 days after surgery may help prevent the development of SIADH. Postoperative fluid restriction reduces hyponatremia and the number of rehospitalizations, but it cannot be routinely used in patients with AVP-D or other contraindications (Perez-Vega et al., 2021). Patients' clinical condition, serum sodium level and volume status determine the treatment of SIADH. If hyponatremia is severe, the patient presents clinical symptoms - SIADH should be managed with hypertonic saline, frequent serum sodium monitoring and carefully controlled correction. Rapid changes in sodium concentration should be avoided. In stable SIADH, therapeutic management typically involves fluid restriction (1000-1500 ml/day) and regular monitoring of biochemical parameters (Castle-Kirszbaum et al., 2022).

Hypopituitarism

New-onset hypopituitarism after EETS has been reported in up to approximately 30% of patients. It is most often multiaxial. If it is uniaxial, adrenal insufficiency is most common (Sampedro-Nuñez et al., 2016). Several factors, including the degree of preoperative compression of normal pituitary tissue, tumour size, and the extent of surgical resection, influence the incidence of hormonal dysfunction. In the immediate postoperative period, assessment of the hypothalamic-pituitary-adrenal axis is important. Untreated acute adrenal insufficiency can lead to hypotension, nausea, vomiting, abdominal discomfort, weakness, hypoglycemia, fever, and hyponatremia. Perioperative glucocorticoid supplementation is not standardized and varies across centers. Management strategies include either routine perioperative glucocorticoid supplementation or selective replacement guided by morning serum cortisol levels and the patient's clinical condition (Ausiello et al., 2008; Prete et al., 2017).

Assessment of thyroid, gonadal, and growth hormone secretion axis function should typically be deferred until the acute postoperative phase has resolved. Early postoperative hormonal testing may not reflect the true, long-term pituitary function. Following surgical decompression of the pituitary gland, partial or complete improvement in its function is possible. Therefore, the decision to implement long-term hormone replacement therapy should not be based solely on early postoperative results and should be preceded by a reassessment of hormonal function. However, normal pituitary function observed in the early postoperative period does not exclude the possibility of later development of hormonal deficiencies, which justifies long-term endocrine follow-up – often 6-12 weeks after EETS (Ausiello et al., 2008; Giraldi and Ioachimescu, 2025; Prete et al., 2017).

Cerebrospinal fluid leakage and meningitis

Cerebrospinal fluid (CSF) leakage results from an unintended opening of the arachnoid. CSF leakage after EETS occurs in 0.5% to approximately 15% of cases. Reported risk factors for postoperative CSF leakage include intraoperative CSF leakage, increased intracranial pressure, reoperation, high Body Mass Index (BMI) and tumour-related features such as size, invasiveness, and consistency. Management of CSF leakage may include lumbar drainage or reoperation with skull base reconstruction (using materials such as a collagen sponge, fat, muscle, fascia lata, or a nasal septal flap). CSF leakage may predispose to headache, meningitis, and intracranial infections (Slot et al., 2022; Zhao et al., 2024).

The reported incidence of postoperative meningitis ranges from 0.67% to 8.7%. Risk factors may include the duration of surgery, the size of the tumour and the occurrence of CSF leakage (Saleh et al., 2022; Zhou et al., 2025). When meningitis is suspected, monitoring of inflammatory parameters, blood and cerebrospinal fluid cultures and appropriate antibiotic therapy are necessary (Jin et al., 2018).

Vascular and hemorrhagic complications

Internal carotid artery injury

Internal carotid artery injury is an uncommon but life-threatening complication that can occur during endoscopic transsphenoidal surgery. The incidence is estimated at approximately 0.1% to 1%. If this complication occurs, two surgeons are required, using an additional suction device to maintain visibility in the surgical field. Endovascular treatment should be available in pituitary surgery centers (Mishra et al., 2025). Before operation, it is recommended to analyze MRI and CT images carefully to reduce the risk of vascular injury. Particular attention should be paid to the anatomy of the internal carotid artery and its variants, such as the "kissing carotid arteries." Intraoperative Doppler ultrasonography may further assist in identifying and localizing the internal carotid arteries (Meyer et

al., 2020). Various strategies have been described for the management of internal carotid artery bleeding, including local packing with muscle, fat or other hemostatic materials, bipolar coagulation, surgical clipping and endovascular treatment (De Souza Júnior et al., 2022).

Sellar hematoma, epistaxis, and thromboembolism

If a patient experiences sudden visual impairment, ophthalmoplegia, severe headache, altered consciousness, or new endocrine disorders after EETS, this may suggest the development of a hematoma in the tumour resection bed. Blood can cause mass effect, compressing the optic chiasm, so urgent computed tomography and prompt reoperation offer a chance to restore normal vision (El-Asmar et al., 2016).

Delayed epistaxis can occur on average about 20 days after surgery. The incidence ranges from approximately 1% to 5% (Liu et al., 2023; Mu et al., 2024; Zimmer and Andaluz, 2018). The posterior nasal septal artery is the most common source of bleeding. Treatment includes: endoscopic transnasal electrocauterisation, nasal packing, and embolisation. Hypertension, nasal septum deviation, chronic sinusitis and growth hormone pituitary tumour are independent risk factors for delayed epistaxis (Mu et al., 2024).

Cushing's disease, obesity, immobilisation, cancer or a previous history of venous thromboembolism could predispose to thromboembolism. Prophylaxis should balance the risk of bleeding with the risk of disease-specific thrombosis (Cheng et al., 2023).

Visual deterioration, cranial nerve palsies and other neurological complications

Visual deterioration is rare (approximately 2%). If the cause is identified promptly and correctly, it can be effectively treated. Potential causes include: postoperative sellar hematoma, direct injury to the optic apparatus and ischemic damage. Early reoperation could reverse visual deficit when the cause is compressive (Carnevale et al., 2022).

New oculomotor nerve (cranial nerve III - CNIII) weakness is the most common cranial nerve deficit in pituitary tumours, but abducens (CN VI) and trochlear (CN IV) nerve palsies may also be observed. When the tumour invades the cavernous sinus, there is a higher risk of cranial nerve palsies. Deficits develop within 12–72 hours after surgery in most cases and commonly, these complications resolve completely within several weeks (Florea et al., 2020; Gupta and Bi, 2025).

Other rare neurological events following EETS include: ischemic or hemorrhagic stroke, tension pneumocephalus, seizures, hypothalamic damage, and delayed cerebral vasospasm. Vasospasm has been reported particularly after subarachnoid haemorrhage. It may present around 7 days later as focal deficits or decreased consciousness (Doat-Sarfati et al., 2025).

Sinonasal complications

EETS utilises the nasal cavity and paranasal sinuses as a route of access to the skull base and may be associated with postoperative complications in patients with pituitary tumours. Following surgery, the most frequently reported sinonasal symptoms include nasal congestion, an urge to blow the nose, impaired smell and taste, and thick nasal discharge (Novák et al., 2021). Regular nasal rinsing with saline is closely associated with fewer nasal complications, while non-selective nasal packing may increase morbidity (Abaza et al., 2026). The first two weeks of nasal symptoms are the most bothersome for patients. Approximately 3-6 months after surgery, the quality of life is the same as before surgery (Abaza et al., 2026; Little et al., 2015; Schreiber et al., 2019). Table 1 summarizes the most common complications following EETS, their incidence, main clinical features and management.

Table 1. The Most Common Complications Associated with Endoscopic Endonasal Transsphenoidal Surgery for Pituitary Tumors.

Complication	Incidence	Main clinical features	Management
AVP deficiency (AVP-D)	Permanent: ~2%	Polyuria, polydipsia, hypernatremia	Fluid replacement, desmopressin when indicated, monitoring of Na^+ and fluid balance
Delayed hyponatremia / SIADH	1.7–28%	Nausea, headache, confusion, seizures	Fluid restriction; hypertonic saline in severe symptomatic cases
New-onset hypopituitarism	Up to ~30%	Deficiency of one or more pituitary hormone axes	Hormone replacement and endocrine reassessment
CSF leakage	0.5–15%	Clear nasal drainage, headache; risk of	Skull-base reconstruction, lumbar drainage

		meningitis	
Meningitis	0.67–8.7%	Headache, fever, meningeal signs, altered consciousness	CSF/blood cultures and antibiotic therapy
Internal carotid artery injury	0.1–1%	Severe hemorrhage, cerebral ischemia	Hemostasis, packing, endovascular treatment
Sellar hematoma	Rare	Acute visual deterioration, headache, ophthalmoplegia	Urgent imaging and surgical evacuation when indicated
Delayed epistaxis	1–5%	Delayed nasal bleeding	Endoscopic cauterization, packing or embolization
Visual deterioration	~2%	Reduced visual acuity or visual field deficits	Urgent assessment; early reoperation if compressive
Cranial nerve palsy	Variable	Diplopia, ophthalmoplegia	Usually observation; often resolves spontaneously
Stroke / cerebral vasospasm	Rare	Focal neurological deficits, reduced consciousness	Urgent neurological management
Sinonasal dysfunction	Common, usually transient	Nasal congestion, discharge, impaired smell/taste	Saline irrigation and symptomatic treatment; usually improves within 3–6 months

Postoperative care and monitoring

Following EETS, neurological and visual status, fluid balance, and biochemical parameters (such as serum sodium, osmolality, and cortisol) should be closely monitored. Before discharge, patients should be informed about warning symptoms that, if they occur, may require medical re-evaluation. Serum sodium should be checked again approximately one week after surgery, followed by appropriate endocrine assessment (Ausiello et al., 2008; Lee et al., 2021; Perez-Vega et al., 2021; Prete et al., 2017; Zada et al., 2007).

4. CONCLUSION

Endoscopic endonasal transsphenoidal surgery of pituitary tumours is generally safe when performed by an experienced multidisciplinary team. Nevertheless, postoperative complications may affect multiple systems, including endocrine, skull-base, vascular, neurological, visual, and sinonasal structures, and may also include infectious complications. AVP-D, delayed hyponatremia, anterior pituitary dysfunction, and CSF leakage are among the complications most frequently encountered after surgery. Although ICA injury, sellar hematoma, meningitis, and visual impairment occur less often, they may have serious consequences and therefore require early recognition and appropriate treatment. Key strategies to improve patient safety and reduce the incidence of postoperative complications include standardizing the definitions and reporting of complications, conducting prospective studies, implementing appropriate postoperative monitoring, educating patients about potential complications and their symptoms, and concentrating surgical care in high-volume centers with extensive neurosurgical expertise.

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Author has read and agreed to the published version of the manuscript.

Informed consent

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Ethical approval

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Conflict of interest

The author declare that he has no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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