Perioperative Management of Patients Undergoing Transsphenoidal Pituitary Surgery

Edward C. Nemergut, MD*, Aaron S. Dumont, MD†, Usha T. Barry, MD*, and Edward R. Laws, MD†

Departments of *Anesthesiology and †Neurosurgery, University of Virginia Health System, Charlottesville, Virginia

Pituitary adenomas often present with the symptoms of hormonal hypersecretion, and although medical therapy is available for most hyperfunctioning states, it is not curative. As a result, transsphenoidal pituitary surgery has become a commonly performed neurosurgical procedure with unique challenges for the anesthesiologist due to the distinct medical comorbidities associated with various adenomas. Any type of pituitary tumor may also produce hypopituitarism and local mass effects secondary to the expanding intrasellar mass. Here we review the perioperative concerns surrounding surgery to remove adenomas and decompress the sellar space. Special attention is given to Cushing’s disease (hypercortisolism secondary to an adrenocorticotrophic hormone-secreting adenoma), acromegaly (secondary to a growth hormone-secreting adenoma), and hyperthyroidism in the setting of thyrotropic adenomas. Operative risks, including bleeding, diabetes insipidus, the syndrome of inappropriate antidiuretic hormone secretion, and hypopituitarism, are addressed in detail. Understanding preoperative assessment, intraoperative management, potential complications, their management, and strategies for avoidance are fundamental to successful perioperative patient care and avoidance of morbidity and mortality.


Tumors of the pituitary gland are often encountered and represent approximately 10% of diagnosed brain neoplasms. Indeed, the transsphenoidal resection of pituitary brain tumors may account for as much as 20% of all intracranial operations performed for primary brain tumors at academic medical centers (1). Patients with pituitary disease present unique challenges to the anesthesiologist secondary to the prominent role of the pituitary gland in the endocrine system. These challenges begin during preoperative assessment and continue through surgery and into the postoperative period. Successful surgical management of patients harboring pituitary tumors requires a multidisciplinary approach and is critically dependent on the quality of perioperative care.

Preoperative Assessment and Related Perioperative Concerns

Pituitary adenomas are normally found in adults, with a peak incidence during the fourth to the sixth decade of life (2). Adenomas are often classified by their size at the time of discovery. Tumors larger than 1 cm are classified as “macroadenomas” whereas tumors smaller than 1 cm are classified as “microadenomas.” Pituitary adenomas may be further classified as “functioning” or “nonfunctioning.” Functioning tumors are usually composed of a single cell type and produce a single, predominant hormone. Patients with functioning adenomas typically present with the symptoms of anterior pituitary hormone excess. As nonfunctioning tumors are not associated with symptoms of hormone excess, they tend to present later and are more likely to be macroadenomas.

Local mass effect on adjacent structures by the expanding intrasellar mass may be encountered in any type of pituitary tumor. The most common presenting complaints of patients with a sellar mass are headache and, in patients with a macroadenoma, visual loss (classically temporal or bitemporal hemianopsia) from compression of the optic chiasm (3). Intrassellar growth...
can cause anterior pituitary compression and dysfunction, resulting in hypopituitarism. Finally, patients with any tumor may become hyperprolactinemic secondary to a loss of tonic inhibition of prolactin secretion.

As in the case of any expanding intracranial mass, patients can experience increased intracranial pressure (ICP). Although such presentation is rare, patients presenting with headache accompanied by papilledema, nausea, and vomiting may have increased ICP. A pituitary tumor may increase ICP either directly from the tumor itself or indirectly from its obstruction of the third ventricle. If intracranial hypertension is suspected, it is critical to avoid any maneuver that might further increase ICP. The preoperative use of mannitol to decrease ICP should be considered. If the operative plan includes the placement of a lumbar intrathecal drain, the possibility of herniation should always be considered.

All patients require thorough preoperative laboratory evaluation before surgery. Evaluation should include a complete blood count to assess the presence of anemia or other hematologic abnormalities. Men presenting with pituitary tumors and low testosterone have an increased incidence of preoperative anemia (4). Although otherwise asymptomatic patients with pituitary disease are rarely anemic, surgery can occasionally be associated with blood loss, and a baseline hemoglobin is appropriate. If the patient has no history of or risk factors for bleeding, coagulation studies (prothrombin time or partial thromboplastin time) are not mandatory. A metabolic panel to evaluate possible hyponatremia, hypercalcemia, hyperglycemia, and other metabolic abnormalities is also indicated. Hyponatremia may indicate posterior pituitary dysfunction and the presence of diabetes insipidus (DI). This will be discussed in detail below. Patients with hypercalcemia are evaluated for the possible diagnosis of multiple endocrine neoplasia, type I. The endocrine evaluation of each patient should include a thyroid panel [thyroxine, thyroid-stimulating hormone (TSH)], and serum levels of cortisol, adrenocorticotropic hormone, insulin-like growth factor-1, testosterone, luteinizing hormone, follicle-stimulating hormone, α subunit, and prolactin. Women presenting with secondary amenorrhea should always have a pregnancy test before an elective surgical procedure.

Some patients evaluated for transsphenoidal surgery will have preoperative hypopituitarism. These patients should receive hormone replacement therapy with hydrocortisone and/or thyroxine, as guided by laboratory studies. Perioperative care of these patients includes resumption of preoperative hormone replacement regimens and consideration of additional stress doses of steroids in the perioperative period.

**Endocrine Disease**

A discussion of preoperative assessment would be incomplete without considering the clinical disease associated with each tumor. Medical therapy is available to abrogate some of the systemic effects of functional adenomas (Table 1). Special attention will be given to acromegaly and Cushing’s disease because they several unique challenges to the anesthesiologist (Fig. 1).

### Table 1. Functioning Adenomas: Clinical Disease and Medical Therapy

<table>
<thead>
<tr>
<th>Clinical disease</th>
<th>Hormone produced by tumor</th>
<th>Estimated frequency (%)</th>
<th>Medical therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acromegaly</td>
<td>Growth hormone</td>
<td>5–10</td>
<td>Somatostatin analog (octreotide)</td>
</tr>
<tr>
<td>Cushing’s disease</td>
<td>ACTH</td>
<td>10–15</td>
<td>Ketoconazole (blocks cortisol synthesis)</td>
</tr>
<tr>
<td>Gonadotroph</td>
<td>FSH, LH</td>
<td>5</td>
<td>None</td>
</tr>
<tr>
<td>Prolactinoma</td>
<td>Prolactin</td>
<td>20–30</td>
<td>Dopamine agonist (bromocriptine, cabergoline, pergolide)</td>
</tr>
<tr>
<td>Null cell</td>
<td>None</td>
<td>20–25</td>
<td>None</td>
</tr>
<tr>
<td>Thyrotropic</td>
<td>TSH</td>
<td>&lt;3</td>
<td>Somatostatin analog (octreotide)</td>
</tr>
<tr>
<td>Other (including mixed cell adenomas)</td>
<td>None</td>
<td>20</td>
<td>Propylthiouracil</td>
</tr>
</tbody>
</table>

**ACTH** = adrenocorticotropic hormone, **FSH** = follicle-stimulating hormone, **LH** = luteinizing hormone, **TSH** = thyroid-stimulating hormone.

---

**Prolactinoma.** Prolactinomas are the most frequently observed type of hyperfunctioning pituitary adenoma and represent 20%–30% of all clinically recognized tumors. In women, hyperprolactinemia causes amenorrhea, galactorrhea, loss of libido, and infertility (5). Osteopenia may also be noted (6). In men, symptoms of hyperprolactinemia are relatively nonspecific and include decreased libido, impotence, premature ejaculation, erectile dysfunction, and oligospermid. Because of an earlier diagnosis in women, prolactin-secreting microadenomas have 20:1 female predominance whereas macroadenomas are equally common in men and women (7). More than 90% of patients respond to medical therapy with a dopamine agonist such as bromocriptine and thus few patients present for surgery. Unlike other endocrine disease states such as acromegaly and
Cushing’s disease, there are fewer anesthesia-specific ramifications associated with hyperprolactinemia. The anesthetic management in these patients focuses primarily on the mass effect of the prolactinoma.

Acromegaly. Cardiac disease is a major cause of morbidity and mortality in acromegalic patients (8). Indeed, the most frequent cause of death in untreated acromegaly is cardiovascular (9) with 50% of patients dying before the age of 50. Hypertension occurs in approximately 40% of acromegalic patients (10). Left ventricular hypertrophy can occur in the presence of systemic hypertension, but also occurs in at least 50% of normotensive acromegalic patients (10). Left ventricular hypertrophy can occur in the presence of systemic hypertension, but also occurs in at least 50% of normotensive acromegalic patients (10). Echocardiography reveals an increase in left ventricular mass, stroke volume, cardiac output, and isovolumic relaxation time (10). These changes occur independently from systemic hypertension (11). Diastolic dysfunction may be an early sign of acromegalic cardiomyopathy, but systolic function is generally preserved (12). A poorly compliant left ventricle and its accompanying need for high filling pressures may be considered the hallmark of acromegalic cardiomyopathy. Diastolic dysfunction may exist even in the absence of clinically appreciable left ventricular hypertrophy (12). Although hypertrophy of the left ventricle may be prominent, evidence of right ventricular enlargement may also exist (13). Left ventricular size often returns to normal after therapy; however, associated return of normal diastolic function may not occur and may reflect the persistence of interstitial myocardial fibrosis (14–17).

Although the larger, more proximal coronary arteries are rarely stenotic in acromegaly, coronary artery disease of the smaller vessels has been described (18). As such, the presence of angina should alert the physician to the possibility of myocardial ischemia, regardless of the patient’s age. Although acromegaly does not increase the incidence of cardiac rhythm disturbances at rest, there is evidence that the incidence of both supraventricular and ventricular ectopy significantly increases with stress and physical exercise (19). Disorders of conduction, such as bundle branch blocks, can also occur (19,20). Electrocardiography (ECG) changes such as ST segment depression,
T-wave abnormalities, and conduction defects are noted in >50% of patients.

In addition to the enlarged hands and feet characteristic of acromegaly, patients also display hypertrophy of the facial bones, especially the mandible. Soft tissues of the nose, mouth, tongue, and lips become thicker. Thickening of the laryngeal and pharyngeal soft tissues (21) leading to a reduction in the size of the glottic opening, hypertrophy of the periepiglottic folds, calcinosis of the larynx (22), and recurrent laryngeal nerve injury can all contribute to airway obstruction and respiratory disease. Indeed, after cardiovascular disease, respiratory disease is the most common cause of death in untreated acromegaly. Hoarseness should alert the physician to the possibility of laryngeal stenosis (23) or recurrent laryngeal nerve injury.

An obstructive respiratory syndrome is observed in 25% of female and 70% of male patients (24). Obstructive sleep apnea (OSA) secondary to upper airway obstruction (25) can affect up to 70% of acromegalic patients (24); however, central respiratory depression of unknown etiology may also occur (24,26). There is evidence that the disordered nocturnal breathing characteristic of acromegaly may continue even after adrenalectomy (27), but vocal cord function may return to normal within 10 days of surgery (28). Given the large percentage of patients with OSA, any history of excessive daytime somnolence, snoring, or frank sleep apnea (often noted by the patient’s spouse) should alert the physician to the possibility of OSA. In acromegaly complicated by OSA, a documented high risk of perioperative airway compromise has been well described (29). In these patients, narcotics and benzodiazepines should be used with extreme caution and always in the presence of continuous monitoring by qualified personnel.

**Cushing’s Disease** As many as 80% of patients with Cushing’s disease have systemic hypertension and 50% of untreated patients have a diastolic blood pressure >100 mmHg (30). Increased endogenous corticosteroids have been shown to cause systemic hypertension by a variety of mechanisms. Hydrocortisone has been shown to increase cardiac output (31) as well as the hepatic production of angiotensinogen (32). The increase in angiotensinogen activates the renin-angiotensin system (32), which leads to an increase in plasma volume. In addition, glucocorticoids markedly increase the influx of Na⁺ in vascular smooth muscle cells (33) and glucocorticoid inhibition of phospholipase A₂ leads to a reduction in the synthesis of vasodilatory prostaglandins. Patients with Cushing’s disease have an increased expression of the angiotensinogen II (type I) receptor (34) and enhancement of inositol triphosphate production in vascular smooth muscle cells (35). This leads to increased sensitivity to endogenous vasoconstrictors such as angiotensin II, epinephrine, and norepinephrine. Sensitivity to exogenous catecholamines may also be increased (36).

As might be expected in the setting of systemic hypertension, ECG abnormalities are common in patients with Cushing’s disease. High-voltage QRS complexes and inverted T waves suggesting left ventricular hypertrophy and left ventricular strain have been described (37). It is interesting to note that, after successful resection of the adenoma, these changes usually revert to normal in <1 yr (38). Echocardiography can reveal disproportionate hypertrophy of the intraventricular septum (37,38) and reduced midwall systolic performance and with diastolic dysfunction in at least 40% of patients (39). Similar to ECG changes, echocardiographic abnormalities usually regress after curative resection. As the left ventricular hypertrophy is more severe and the frequency of asymmetric hypertrophy much greater in Cushing’s disease than in those with essential hypertension or high aortic pressure, it seems likely that excess plasma cortisol may be, at least, a second etiologic factor (38).

OSA is also common among patients with Cushing’s disease. Polysomnographic studies indicate that as many as 33% of patients with Cushing’s disease have mild sleep apnea and 18% of patients have severe sleep apnea (40). Patients with Cushing’s disease also have decreased δ-sleep time and decreased δ-sleep-inducing peptide (41). Complaints of daytime sleepiness are therefore common.

Glucose intolerance occurs in at least 60% (42) of patients with Cushing’s disease, with overt diabetes mellitus present in up to one-third of all patients. It has been clearly established that hyperglycemia can aggravate ischemic injury in the brain and spinal cord (43–46). Although there are no randomized studies that demonstrate a “safe” level of hyperglycemia, current practice suggests that any blood glucose >180 mg/dL (10.1 mmol/L) should be treated with IV insulin.

Exophthalmos, secondary to increased retro-orbital fat deposition may be present in up to one-third of patients with Cushing’s disease (47). The anesthesiologist and neurosurgeon should be cognizant of the presence of exophthalmos, as a corneal abrasion can be a painful complication to an otherwise successful surgery. Hypercortisolism results in skin thinning (48). Cannulation of superficial veins for IV access can be extremely difficult and minimal trauma may result in bruising.

Although myopathy of the proximal muscles of the lower limb and the shoulder girdle are common complaints among patients with Cushing’s disease (49), there are no data to suggest a change in the susceptibility to succinylcholine or nondepolarizing neuromuscular blockers. Infections are more common in
patients with Cushing’s disease (50); however, an empiric change in usual perioperative antibiotics is unnecessary. Detectable osteoporosis may occur in up to 50% of patients presenting with Cushing’s disease and almost 20% of patients may have pathologic fractures (49). Therefore, particular care should be taken when positioning patients during surgery.

Thyrotropic (TSH-Producing) Adenomas  Thyrotropic adenomas are rare and represent no more than 2.8% of all pituitary tumors (51). Thyrotropic adenomas can cause pituitary hyperthyroidism. Signs and symptoms of hyperthyroidism include palpitations, tremor, weight loss, difficulty sleeping, and sweating. A goiter is often observed. A case of periodic paralysis has been reported (52). Because a pituitary adenoma is a rare cause of hyperthyroidism, most patients are initially treated for other causes of hyperthyroidism such as Graves’ disease. Thus, these tumors are often allowed to grow and can be quite large upon diagnosis. Patients often have symptoms related to the local mass effect of the tumor. In addition, >60% of thyrotropic adenomas are locally invasive at the time of surgery (53). Given the large, potentially invasive characteristics of this tumor, the theoretical risk for blood loss should be considered. Hyperthyroidism should be controlled before a patient undergoes surgical resection. Antithyroid medication such as propylthiouracil may reduce thyroid hormone production and somatostatin analogs such as octreotide can suppress TSH production and may reduce tumor size (54). The implications of hyperthyroidism on anesthesia have been discussed elsewhere (55).

Nonfunctioning Tumors: Nonfunctioning Adenomas, Rathke Cleft Cyst, Craniopharyngioma

Nonfunctioning (null cell) adenomas are the second most common type of pituitary tumors accounting for 20%–25% of pituitary adenomas. Craniopharyngiomas and Rathke cleft cysts are very rare. Because each of these tumors is not associated with the hypersecretion of a hormone, they almost always present with symptoms related to local mass effect (see above). Therefore, patients must be screened for hypopituitarism with associated hypothyroidism and adrenal insufficiency evaluated prior to surgery. Posterior pituitary dysfunction and DI can also occur, but are much less common.

Perioperative Corticosteroid Administration

Historically, patients undergoing transsphenoidal surgery are given “stress doses” of 50–100 mg of hydrocortisone every 6–8 h for several days before being gradually weaned. This is often not necessary, and postoperative corticosteroid supplementation is rarely required beyond the first 24 postoperative hours (56) (see below). Nevertheless, patients with hypopituitarism may not effectively absorb orally administered corticosteroids in the perioperative period, and parenteral administration is preferred (56).

Patients with Cushing’s disease are typically given dexamethasone, because it does not interfere with postoperative serum cortisol assays. A more modern approach to the care of patients with Cushing’s disease avoids the administration of all perioperative corticosteroids. With this approach, serum cortisol is assayed every 6 h after surgery to document laboratory evidence of a disease remission (56,57). Hydrocortisone is withheld until patients have symptoms of adrenal insufficiency with a serum cortisol level of <2 µg/dL. This approach is only possible if the hospital laboratory is able to rapidly (<1 h) report serum cortisol levels (3,57).

Intraoperative Considerations

Surgical Approach

Sellar tumors are usually approached transnasally (Fig. 2). The older sublabial transseptal approach is only necessary in patients with extremely large tumors and in young children in whom endonasal exposure may prove inadequate (58). Traditionally, resection has been guided by the use of intraoperative fluoroscopy; however, computer-guided frameless stereotaxy may also be used (59). The endonasal approach can also be performed or assisted by an endoscope (60–62). The endoscopic endonasal approach has become more common and may be associated with fewer cosmetic, dental, and nasal complications as well as a shorter recovery. In addition, there is some evidence that the incidence of postoperative DI may be less frequent if the procedure is performed endoscopically (63).

Many neurosurgeons place a lumbar intrathecal catheter to assist in visualization of the tumor. The catheter can be used to manipulate cerebrospinal fluid (CSF) pressure by the injection of saline or removal of CSF. In addition, in patients with large macroadenomas with suprasellar extension, some pituitary surgeons will inject intrathecal air. The air serves to increase CSF pressure and may “push” the tumor down into the surgical field. The injected air may also serve to outline a tumor, allowing for fluoroscopic visualization. If intrathecal air is injected, nitrous oxide should be discontinued to avoid expansion of the intracranial airspace and unnecessary increases in ICP.

Airway Management

Intubation with a standard endotracheal tube is acceptable and should allow the surgeon adequate space
to complete the procedure; however, some surgeons prefer intubation with an oral RAE tube. Obviously, nasal intubation is contraindicated (64).

As noted above, acromegaly induces significant changes in airway anatomy. Successful endotracheal intubation of acromegalic patients is potentially difficult (21,65,66). Enlargement and overgrowth of the upper airway can make airway management difficult. Indeed, routine tracheostomy (67) had been historically advocated for management of the acromegalic airway; however, this is rarely necessary (68,69). Nevertheless, the greatest challenge in dealing with the acromegalic airway is the unpredictable nature of difficult tracheal intubation. In a prospective study of 128 acromegalic patients, Schmitt et al. (66) found that 20% of acromegalic patients assessed as Mallampati class 1 and 2 were difficult to intubate. As such, the prudent anesthesiologist should have a variety of alternative airway management tools readily available. Insertion of an intubating laryngeal mask airway (Fast-Trach LMA™) may prove difficult given the large tongue and hypertrophied upper airway. It should be noted that use of the intubating laryngeal mask airway (ILMA) has been associated with a small (52.6%) first-attempt success rate in unparalyzed patients (70). Again, preoperative airway assessment failed to predict difficulty when using the ILMA. Flexible fiberoptic laryngoscopy can also be more difficult (71). Awake techniques always offer the greatest margin of safety.

At present, there are no data to suggest that Cushing’s disease represents an independent risk factor for a difficult intubation; however, Cushing’s disease is clearly associated with characteristics known to be associated with more difficult intubations [e.g., OSA (72), obesity (73)]. Therefore, the airway should always be approached with caution. The presence of diabetes should also suggest the possible presence of gastroesophageal reflux disease (74) and slowed gastric emptying and the possible need for a rapid sequence induction.

**Positioning and Preparation for Surgery**

After the induction of anesthesia, the patient is positioned for surgery (Fig. 2). Transsphenoidal pituitary resections are generally performed with the patient in some degree of head-up position to reduce venous engorgement. Such positioning makes venous air embolism (VAE) a theoretical risk. Precordial Doppler, end-tidal CO2, and end-tidal N2 monitoring may be considered. Although a 10% risk of VAE in the semi-seated position has been reported (75), a clinically significant VAE associated with significant morbidity or mortality has not been reported.

During surgical preparation, the mucosal surfaces of the nose are infiltrated with local anesthetic and epinephrine solution to reduce bleeding and facilitate dissection. The addition of lidocaine to epinephrine increases the arrhythmogenic threshold dose of epinephrine when compared with epinephrine in saline (76). Injection may be associated with dysrhythmias and hypertension (36,77). Hypertension can be significant and myocardial ischemia with cardiac troponin
increase has been reported in patients without coronary artery disease (78). Patients taking β-adrenergic blockers may develop dangerously high arterial blood pressure secondary to the unopposed α effects of epinephrine. IV therapy with phenolamine or direct vasodilator therapy may be necessary; however, increasing the patient’s depth of anesthesia may prove adequate. At least one case report describes a total spinal anesthetic after the inadvertent local anesthetic injection through the cribiform plate (79). If an endoscopic approach is planned, infiltration of mucosal surfaces may be unnecessary and the administration of topical vasoconstrictor may prove adequate.

**Monitoring**

An arterial catheter should be considered for patients with poor exercise tolerance, in patients with signs and symptoms of congestive heart failure, in patients with poorly controlled hypertension, or in patients with documented cardiomyopathy. Given the potential for sudden hypertensive episodes during transsphenoidal surgery, some anesthesiologists will place an arterial catheter to facilitate early diagnosis and treatment. It should be noted that blood flow through the ulnar artery may be compromised in up to 50% of acromegalic patients (80). This is made more likely by the presence or history of carpal tunnel syndrome. In these patients, blood flow to the hand may be completely dependent on radial artery flow. Catheterization of the radial artery could potentially result in hand ischemia. The catheterization of alternative sites (e.g., femoral) for intraarterial monitoring should be considered.

Placement of a central venous catheter is rarely required, unless necessitated by the patient’s cardiovascular disease. In acromegaly, there may be a poor correlation between central venous pressure (CVP), left ventricular end diastolic pressure (LVEDP), and left ventricular end diastolic volume (LVEDV) or preload. Indeed, a poor correlation may also exist between pulmonary artery occlusion pressure (PAoP), LVEDP, and preload. In the setting of a less-compliant ventricle, a fluid challenge may increase CVP, PAoP, and LVEDP, but this might not reflect a concurrent increase in LVEDV or preload (81). Problems using CVP and PAoP monitoring to predict LVEDV may extend to normal patients as well (82).

In the past, some investigators have found intraoperative visual evoked potential (VEP) monitoring useful in procedures near the visual pathway. Unfortunately, these polysynaptic cortical waveforms are extremely sensitive to the effects of anesthetics. Indeed, even narcotic-induced papillary constriction can interfere with appropriate stimulation of the retina (83). Despite these difficulties, it has been suggested that patients who have intraoperative VEP monitoring have greater postoperative visual field improvements, although no benefit in visual acuity (84). Given the lack of strong evidence to support routine use and the frequent “false positive rate” secondary to exquisite anesthetic sensitivity, the authors do not advocate the use of VEP monitoring during transsphenoidal surgery.

**Intraoperative Management**

There is a broad range of acceptable anesthetics for pituitary surgery. The choice of anesthetic depends on the patient’s medical comorbidities and anesthetic history. The desire for rapid emergence to allow for immediate neurological assessment makes techniques using rapidly cleared drugs, such as propofol and remifentanil, or inhaled anesthetics with low blood solubility such as sevoflurane, reasonable choices. Inhaled anesthesia supplemented with remifentanil may provide for greater hemodynamic stability and an earlier neurological examination (85). Remifentanil has not been shown to result in an earlier tracheal extubation. If remifentanil is used, it is important to provide transitional analgesia with a longer-acting opioid, otherwise emergence may be complicated by patient pain. Muscle relaxation is maintained throughout the procedure because any patient movement during surgery could lead to a CSF leak, visual tract injury, or vascular damage.

Transsphenoidal pituitary surgery is normally associated with minimal blood loss; however, there is a potential for significant hemorrhage given the proximity of the pituitary to the internal carotid arteries (Fig. 3). Indeed, intraoperative carotid artery injury is an infrequent, but potentially fatal, complication of transsphenoidal surgery (86). In the case of inadvertent carotid artery injury, deliberate hypotension may improve visualization and help to facilitate repair. The injury should ideally be sutured; however, in practicality, it is often addressed by compression with hemostatic agents and autologous muscle. A balloon catheter can be inflated and placed in the region for additional tamponade (87).

Moderate venous “oozing” from the cavernous sinus is a more common problem in clinical practice. In one study, moderate bleeding was not related to CVP and cavernous sinus pressure; however, bleeding tended to be more severe in patients with large tumors and suprasellar extension (88). Regardless, the anesthesiologist should have access to an extremity in which additional IV access could be obtained if necessary.

After successful resection of the tumor, a Valsalva maneuver may be used to test for a CSF leak. If a CSF leak is readily observed, most neurosurgeons will pack the sella with autologous fat before it is reconstructed. At the completion of surgery, the oropharynx should also be suctioned meticulously. Patients
with a history of OSA may benefit from an oral airway to facilitate mouth breathing, because nasal packing will make nose breathing impossible. A nasopharyngeal airway can also be placed under direct visualization by the surgeons before the nose is packed. The nasopharyngeal airway can be left in place until the nasal packing is removed and may serve to prevent airway obstruction beyond the immediate postoperative period. Patients prone to upper airway obstruction may benefit from tracheal extubation in a seated position.

Postoperative Considerations

A dynamic state of the hypothalamic-pituitary end-organ axis is often encountered after pituitary surgery. Hence, a significant focus of postoperative care is the vigilant screening and observation for neuroendocrine abnormalities including disorders of water balance, DI, and the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Additionally, one must be cognizant of other potential complications inherent to resection of pituitary tumors, such as visual loss, CSF leakage, and meningitis (Table 2).

Cranial Nerve Dysfunction and CSF Leakage

In the immediate postoperative period, patients undergo a thorough physical examination. Particular attention is given to cranial nerve function, including assessment of visual acuity, visual fields, and extraocular motility. The proximity of cranial nerves II–VI to the pituitary gland makes a postoperative cranial nerve palsy a feared complication (Fig. 3). Any new neurological finding after surgery is addressed with either immediate postoperative computed tomography or magnetic resonance imaging or reexploration in the operating room in the case of visual field deficit.

In addition to frequent screening for abnormalities of cranial nerve function, patients are questioned regarding rhinorrhea or fluid leakage down the back of the throat. Some nasal drainage is expected in the postoperative period; however, suspicious drainage (for example, continuous fluid leakage exacerbated by leaning forward, associated with headache) should be further investigated. Drainage may be collected and sent to the laboratory for examination for \( \text{IgG} \)-transferrin. If the fluid tests positive for \( \text{IgG} \)-transferrin, the diagnosis of CSF leak is strongly supported. Operative re-packing of the defect with autologous fat best treats postoperative CSF leakage.

Nausea and Vomiting

Nausea and vomiting are very common postoperative complications in patients undergoing neurosurgical procedures, with nearly 40% of patients reporting some such complaint (89). Given the high risk for vomiting in patients undergoing this procedure and the detrimental effect of vomiting on ICP, routine pharmacologic prophylaxis seems reasonable. There are no randomized controlled studies in this specific patient population to guide therapy toward any specific drug or drug class. Thus, drugs should be selected after taking patient-specific risk factors into due consideration (90).

Pain

The most common patient complaint after transsphenoidal surgery is headache. Pain may be treated with
narcotics, nonsteroidal drugs such as ketorolac, or acetaminophen. As noted above, narcotics should be used with care in any patient with a history of OSA.

**Disorders of Water Balance**

Disorders of water balance resulting from perturbations in secretion of antidiuretic hormone (ADH) are one of the most frequently encountered acute perioperative complications of transsphenoidal surgery (58,91–96). Abnormalities in ADH secretion resulting in postoperative DI and SIADH have been reported in 0.5%–25% (58,92,94,95) of cases and 9%–25% (58,93,95,97) of cases, respectively. Table 3 summarizes the differences between DI and SIADH.

**DI** DI is a relatively common complication of transsphenoidal surgery but is most often transient. For instance, although 31% of 1571 patients undergoing transsphenoidal surgery experienced early postoperative DI, only 6% still had persistent DI 1 wk after surgery (91). Postoperative DI typically manifests in the first 24–48 h after pituitary surgery. Its onset is heralded by the abrupt onset of polyuria along with accompanying thirst and polydipsia. The urine is diuretic (specific gravity <1.005) and voluminous (4–18 L/d). Because most patients in the postoperative period after transsphenoidal surgery are awake, alert, with intact thirst mechanisms, and have adequate access to fluid intake, the development of significant volume contraction and hyperosmolarity with severe hyponatremia is relatively uncommon.

Treatment should be considered if there is a significant discrepancy in fluid intake and output, an increasing serum sodium (above 145 mEq/L), and when excessive urine output significantly interferes with sleep. Specific treatment of DI may be undertaken with a synthetic analog of ADH, desmopressin (DDAVP). It works quickly and effectively without undesirable increases in arterial blood pressure. The oral formulation is effective and should be considered first-line treatment. An initial dose of 0.1 mg of DDAVP can be administered orally and usually is effective in controlling postoperative DI. Alternatively, if the patient is unable to take oral medications, 1 µg of DDAVP can be administered subcutaneously. The IV administration of DDAVP is rarely necessary. Because DI is transient >95% of the time, a single dose may be sufficient. When DDAVP is administered, close monitoring of urine output and serum electrolytes is mandatory to avoid “overshoot” hyponatremia.

It is important to distinguish DI from some frequently encountered processes seen in the postoperative pituitary patient (Table 4). Note that patients with acromegaly demonstrate a robust physiological diuresis after successful tumor resection and early treatment with DDAVP should be avoided (58).

**Syndrome of Inappropriate ADH Secretion** Hyponatremia after pituitary surgery is a common and important complication of pituitary surgery that manifests in a delayed manner (58,93,94,97). In SIADH, free water intake exceeds free water excretion. Consequently, increased urinary excretion of sodium is observed in the context of inappropriately concentrated urine.

The diagnosis of hyponatremia after pituitary surgery is often biochemical; however, symptoms can arise if the onset is particularly rapid. The basis for laboratory diagnosis of SIADH resulting in hyponatremia is contingent upon demonstration of low serum sodium in the context of a hyposmolar serum, hyperosmolar urine, and a euvolemic state. The serum sodium concentration is <135 mEq/L, serum uric acid levels are low (reflecting underlying renal loss of uric acid), and excess sodium excretion in the urine (>40 mEq/L) is observed. SIADH is characterized by a general euvolemic (or mildly hypervolemic) state and should be distinguished from cases of hyponatremia associated with volume contraction such as cerebral salt wasting (98). As noted above, it is important to eliminate overzealous treatment with DDAVP as a cause of hyponatremia.

If hyponatremia develops and SIADH is diagnosed, fluid restriction remains an important part of therapy (93,97). In recalcitrant cases, or in patients with severe, symptomatic hyponatremia (usually sodium <120 mEq/L with headache and nausea/vomiting as well as in patients with altered mental status or seizures), hypertonic saline (3% or 1.8% saline) can be added to fluid restriction to help (partially) restore serum sodium. Excessively rapid correction must be avoided to prevent the relatively rare, but potentially serious, complication of central pontine myelinolysis. IV urea is also an effective adjunct in patients with severe hyponatremia (97,99).

---

**Table 2. Complications of Transsphenoidal Surgery**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Major complications (cerebrospinal fluid leak, meningitis, ischemic stroke,</td>
<td>1.5</td>
</tr>
<tr>
<td>intracranial hemorrhage, new cranial nerve palsy, and visual loss)</td>
<td>1.5</td>
</tr>
<tr>
<td>Minor complications (sinus disease, septal perforation, epistaxis, wound</td>
<td>6.5</td>
</tr>
<tr>
<td>infections, and hematomas)</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Adapted from Jane and Laws (58).
Table 3. Syndrome of Inappropriate Antidiuretic Hormone (SIADH) Versus Diabetes Insipidus (DI)

<table>
<thead>
<tr>
<th></th>
<th>SIADH</th>
<th>DI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presentation</strong></td>
<td>Hyponatremia</td>
<td>Polyuria</td>
</tr>
<tr>
<td><strong>Plasma volume</strong> (awake patients)</td>
<td>Euvolemic (or slightly hypervolemic)</td>
<td>Euvolemic</td>
</tr>
<tr>
<td><strong>Serum</strong></td>
<td>Hypotonic (&lt;275 mOsm/L)</td>
<td>Hypertonic (&gt;310 mOsm/L)</td>
</tr>
<tr>
<td><strong>Serum sodium</strong></td>
<td>Decreasing (&lt;135 mEq/L)</td>
<td>Increasing (&gt;145 mEq/L)</td>
</tr>
<tr>
<td><strong>Urinary sodium</strong></td>
<td>Relatively high (&gt;100 mOsm/L)</td>
<td>Voluminous (4 to 18 L/d)</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Fluid restriction if Na &lt;120 mEq/L, consider hypertonic saline to correct sodium (but no faster than 1 mEq/L/h) Intravenous urea Demeclocycline</td>
<td>Supportive DDAVP (desmopressin)</td>
</tr>
</tbody>
</table>

Table 4. Potential Causes of Postoperative Polyuria

<table>
<thead>
<tr>
<th>Cause</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iatrogenic perioperative fluid administration</td>
<td>Urine specific gravity usually &gt;1.005</td>
</tr>
<tr>
<td>Diabetes insipidus</td>
<td>Urine specific gravity &lt;1.005; increasing serum sodium Elevated serum and urine glucose</td>
</tr>
<tr>
<td>Glycosuria</td>
<td></td>
</tr>
<tr>
<td>Acromegalic diuresis</td>
<td>Urine specific gravity usually &gt;1.005</td>
</tr>
</tbody>
</table>

**Hypopituitarism**

At least 27% of patients with preoperative hypopituitarism will experience ultimate normalization of function after tumor resection (58). The majority of patients (90%–95%) with normal preoperative pituitary function will retain this postoperatively (58); however, all patients should be screened for signs of hypopituitarism.

Some centers continue corticosteroid supplementation after discharge with the intent of evaluating the hypothalamic-pituitary-adrenal axis at a later date. An alternative approach is to rapidly wean patients from corticosteroid supplementation after 24 h and assay morning cortisol on a daily basis. With this approach, patients are only given additional corticosteroid if they have symptoms of adrenal insufficiency. If patients feel well and morning cortisol is >10 μg/dL, additional steroid supplementation is unnecessary and patients may be discharged without additional steroid replacement (3,56,57). With this approach, most patients do not require additional corticosteroid supplementation.

**Conclusion**

Patients with tumors of the pituitary gland represent a heterogeneous yet commonly encountered neurological population. The successful surgical management of patients harboring pituitary tumors requires a multidisciplinary approach and is critically dependent on the quality of perioperative care. All patients with tumors of the pituitary gland require meticulous preoperative evaluation and screening. Knowledge of potential complications, their management, and strategies for avoidance are fundamental to successful perioperative patient care.

The authors thank Marcel E. Durieux, MD, PhD, for his helpful comments regarding the manuscript.

**References**