



# Management of non-functioning pituitary adenomas: surgery

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Published online: 26 December 2017  
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## Abstract

Non-functional pituitary adenomas (NFPAs) are benign tumors of the pituitary gland that do not over-secrete hormonal products, therefore, they are generally detected through symptoms of mass effect, including headache, vision loss, or hypopituitarism. There are multiple pathological subtypes of NFPAs, such as null cell adenomas, silent gonadotrophs, silent somatotrophs, silent corticotrophs, and silent subtype 3, all of which can be classified based on immunohistochemical studies and electron microscopy. Despite these numerous pathological subtypes, surgical resection remains the first-line treatment for NFPAs. Diagnosis is best made using high resolution MRI brain with and without gadolinium contrast, which is also helpful in determining the extent of invasion of the tumor and recognizing necessary sinonasal anatomy prior to surgery. Additional pre-operative work-up should include full laboratory endocrine evaluation with replacement of hormone deficiencies, and ideally, full neuro-ophthalmologic exam. Although transcranial surgical approaches to the pituitary gland can be performed, the most common approach used is the transnasal transsphenoidal approach with endoscopic or microscopic visualization. This approach avoids retraction of the brain and cranial nerves during tumor removal. Surgery for symptoms caused by mass effect, including headaches and visual loss, are successfully treated with surgical resection, resulting in improvement in pre-operative symptoms as high as 90% in some reports. Although the risk of complications is low, major and minor events, such as permanent hypopituitarism, persistent CSF leak, and carotid artery injury can occur at rates ranging from zero to about 9%.

**Keywords** Non-functioning pituitary adenomas · Transsphenoidal surgery · Perioperative management · Postoperative outcomes

## Introduction

Pituitary tumors are common lesions accounting for 10–15% of all primary brain tumors, representing the third most common pathology [1, 2]. Of the different types of pituitary tumors, pituitary adenomas manifest in many different ways based on their functional status. Before advanced imaging techniques, non-functioning pituitary adenomas presented with visual decline, classically bitemporal hemianopsia, and were diagnosed with careful visual field testing. Early radiographic signs were enlargement of the sella on plain X-ray or distortion of the normal vasculature on angiography [3].

With increased use of magnetic resonance imaging (MRI), non-functioning pituitary adenomas (NFPA) are being detected for a plethora of symptoms, including headaches, endocrinopathies, and even as incidental lesions [4].

Non-functional pituitary adenomas are typically not associated with clinical or biochemical signs of hormonal hypersecretion and represent about one-third of all pituitary adenomas [5, 6]. Most NFPAs are detected during or after middle age and occur with slight male predominance. There exist multiple subtypes of NFPAs, including null cell adenomas and silent hormone staining adenomas [7]. Unlike hypersecretory adenoma types, NFPAs tend to present after sufficient growth produces mass effect on surrounding brain structures, particularly the optic nerves and chiasm causing visual defects, the normal pituitary gland resulting in varying degrees of hypopituitarism, and stretching of dural pain fibers resulting in headaches.

On a basic level, NFPAs can be divided into two overarching pathological subgroups: null cell adenomas and physiologically silent hormone staining adenomas. In

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contrast to hypersecretory adenomas, null cell adenomas are believed to be pathologically derived from precursor stem cells, as opposed to differentiated adenohypophyseal cells. They lack expression of both pituitary hormones and the necessary transcription factors causing secretory differentiation. Histologically, these NFPA demonstrate no histological, immunohistochemical, or ultra-structural components of differentiated secretory cells of the anterior pituitary gland [8]. Silent adenomas are morphologically, histologically, and ultra-structurally similar to functioning adenomas and demonstrate immunoreactivity for specific pituitary hormones and/or cell specific transcription factors; however, this category of NFPA does not present clinically with symptoms of hormonal hypersecretion [9, 10]. Despite the subtype of NFPA, surgical resection remains the first-line therapy.

As with the majority of other pituitary tumors, NFPAs are benign tumors. They do have the capability to grow and invade nearby structures. They can enter the suprasellar cistern superiorly or the cavernous sinuses laterally through natural openings in the dura or by creating their own openings through chronic dural thinning and stretching. Additionally, these tumors can invade and erode portions of the sphenoid bone anteriorly through the sella or postero-inferiorly into the clivus.

Although advances have been made in the use of medical therapy for many tumor types, surgery remains the primary treatment choice for NFPAs [11]. Because they are largely benign tumors, the primary goal of surgery is decompression and preservation of the important surrounding neural structures, in particular, the cranial nerves and pituitary gland. Although gross total resection of the tumor is ideal, this should be balanced with the fact that these tumors are benign, and the safety of the patient needs to be considered. Currently, radiotherapy is reserved as adjuvant treatment for tumors that are demonstrated to be more aggressive and demonstrate a high propensity for regrowth [12–14].

The history of pituitary surgery has been extensive, with a number of different approaches attempted to remove these precarious tumors. The first account of an operation performed for a pituitary tumor was in 1892 when a British surgeon attempted to remove a tangerine-sized tumor from a 34-year-old woman with acromegaly, presenting with headaches and visual loss, using a transcranial subtemporal approach [15]. The tumor proved inaccessible, and although this approach did alleviate some of her symptoms from elevated intracranial pressure, the patient died a few months later. Numerous other transcranial approaches were attempted over the years, with high levels of morbidity and mortality. The first transsphenoidal approach was attempted in 1907 by an Austrian, Hermann Schloffer [16]. This radical surgery was performed over three stages via an incision along the nose, and while the pre-operative symptoms improved, the patient ultimately died several months later

from obstructive hydrocephalus caused by intraventricular extension of the tumor. Over the past century, numerous surgeons—Harvey Cushing, Gerard Guiot, and Jules Hardy—helped advance and refine surgery of pituitary tumors to the less invasive and significantly less morbid transnasal transsphenoidal techniques commonly used today. Improvements ranging from development of the transnasal speculum to introduction of the operating microscope, and eventually the endoscope have made surgery for NFPAs both safe and effective [16–19].

## Clinical presentation

Non-functional pituitary adenomas tend to present with symptoms caused by growth and the exertion of mass effect on nearby structures, as opposed to symptoms and signs of hormonal hypersecretion. With increased use of MRI for numerous different symptoms, incidental NFPAs are also frequently discovered on the work up of symptoms clearly unrelated to the discovery of the tumor [4]. One of the common presenting symptoms is headaches with an incidence ranging from 16 to 62.1% [20–22]. As the tumor enlarges, this causes stretching of the diaphragma sellae causing activation of pain fibers within the dura. Commonly, these headaches are referred to the frontal regions and the occiput [23]. In today's medical practice, patients with many types of headaches are undergoing advanced imaging studies that demonstrate pituitary lesions that may or may not be incidental, making it more difficult to decipher exactly what type of headaches can be attributed to pituitary lesions.

In addition to headaches, one other common presentation of patients with NFPAs is visual loss, classically described as a bitemporal hemianopsia caused by midchiasmal compression. When tumors grow asymmetrically, however, many patterns of visual loss can occur, including junctional scotoma from compression of the anterior chiasm and asymmetric homonymous hemianopsia from compression of posterior chiasm and optic tracts. In addition to visual field loss, NFPAs can also cause decreased visual acuity and color vision, typically loss of red and green distinction, caused by optic nerve compression. A number of series demonstrate that patients present with visual deficits with an incidence ranging from 13 to 60.8% [20–22]. Diplopia can also be a presenting symptom as the tumor grows into the cavernous sinus, most commonly a third cranial nerve palsy, as the tumor grows superiorlaterally between the loops of the carotid siphon.

Non-functional pituitary adenomas can also present with symptoms from hypopituitarism caused by compression of the normal pituitary gland with an incidence ranging from approximately 30–40% [20–22]. In general, gonadotrophic function is the first to be lost, manifesting as decreased

sexual function or libido. Thyrotrophic, somatotrophic, and corticotrophic function can be lost, as well, again usually after loss of gonadotrophic function. Virtually never does compression of the posterior pituitary result in loss of function and diabetes insipidus (DI). One exception worthy of noting is that mass effect from the enlarging pituitary tumor can cause hyperprolactinemia from interruption of inhibitory input down the pituitary stalk from the hypothalamus to the anterior pituitary gland.

Patients with NFPAs can present with acute onset of headaches, visual loss, or hypopituitarism from intratumoral hemorrhage or infarction, known as pituitary apoplexy [24, 25]. Pituitary apoplexy is defined as a clinical syndrome consisting of headache, nausea, diminished visual acuity/fields, ophthalmoparesis, and decreased mental status. Although the pathophysiology of this syndrome is unclear, it is hypothesized these events occur as the tumor outstrips its vascular supply and becomes ischemic and necrotic [26, 27].

## Clinical work-up

### Imaging and staging

Although CT scan can be useful for initial detection of pituitary lesions, because of artifact from nearby bone, detailed evaluation can be limited. The best imaging study for anatomic diagnosis of NFPAs is MRI with and without gadolinium contrast. Because of the highly efficient portal blood supply to the pituitary gland, it avidly enhances with contrast. NFPAs, like all pituitary adenomas, are hypovascular and exhibit delayed enhancement causing them to appear hypointense relative to the pituitary parenchyma. Although high resolution MRI sequences through the pituitary gland make localization of very small microadenomas possible, other subtle signs, such as stalk deviation, asymmetry of the gland, and upward bowing of the diaphragm, can indicate presence of a lesion.

In addition, high-resolution contrast enhanced MRI can also be useful for staging and surgical planning. These images can demonstrate the relation of the mass to the optic apparatus, the degree of invasion into the cavernous sinuses, the relationship of the mass to the carotid arteries, anatomical configurations of the sella that can pose challenges, and location of the normal pituitary gland (Fig. 1) [28, 29]. On the most basic level, NFPAs are described based on size with microadenomas being less than 1 cm, macroadenomas being larger than 1 cm, and giant adenomas measuring greater than 4 cm. Hardy developed one of the more popular classification systems that was later modified by Wilson [30, 31]. In this system, graded as I–V, the pituitary tumor is defined by its relation within the sella and its violation of the floor and suprasellar space. The Knosp classification of invasive

tumors describes the relationship of the tumor to the cavernous carotid arteries in the coronal plane with Grade 0 being confined medially to the artery and Grade 4 encasing it completely [32].

### Pre-operative planning

Patients undergoing transsphenoidal surgery for a pituitary mass have a full endocrine work-up checking all pituitary hormonal levels. Any subclinical deficiencies discovered on lab work are replaced prior to surgery, in particular, thyroid and cortisol replacement, with the help of our endocrinologists. Hypothyroid patients will receive levothyroxine and adrenal insufficient patients are started on stress dose hydrocortisone peri-operatively, which is tapered over the post-operative period to physiologic doses.

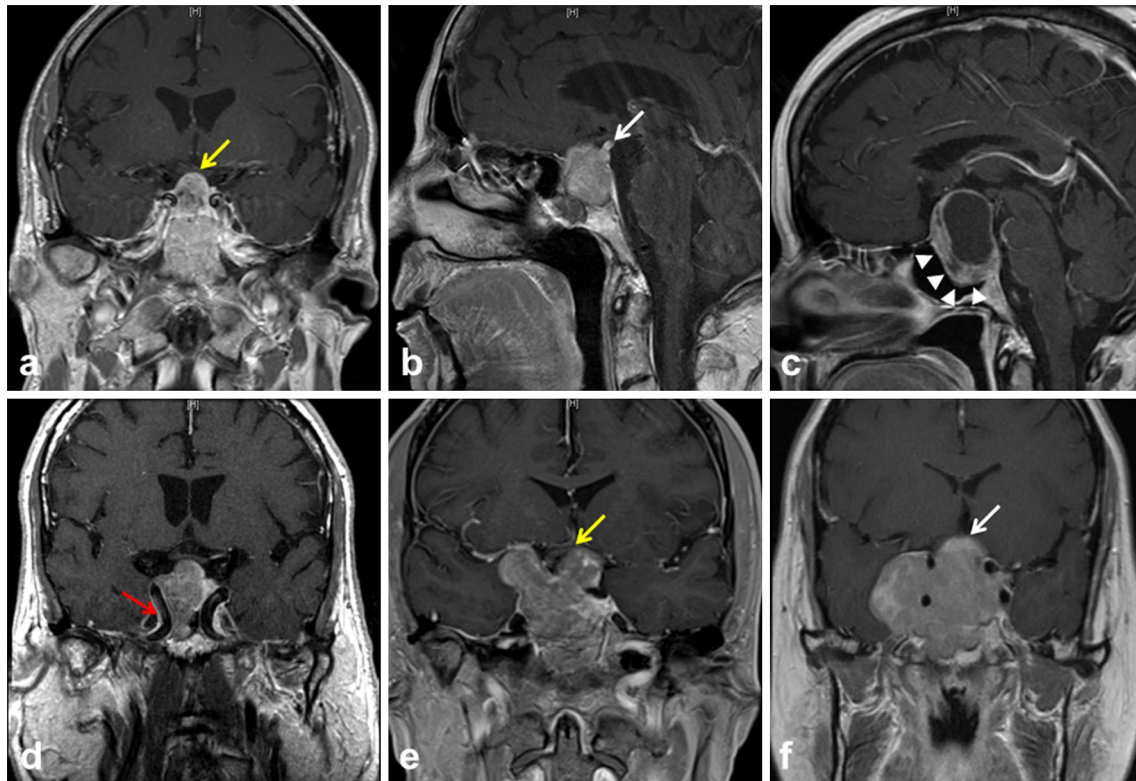
Non-urgent patients with visual field deficits will generally undergo full neuro-ophthalmologic evaluation to establish a pre-operative baseline. This evaluation includes assessment of visual acuity and color vision, Humphery Automated Perimetric Assessment of Visual Fields, evaluation for pupillary response and ophthalmoparesis, and Optical Coherence Tomography to assess structural changes in the retinal nerve fiber layer.

Additional imaging studies beyond high resolution MRI are often unnecessary. In patients with tortuous vasculature or small inter-carotid artery distances, thin cut CT Angiography can be helpful to more reliably define the relationships among these structures and the bony anatomy of the sphenoid sinus. High resolution sequences (MRI or CT) can be used in conjunction with many neuro-navigation systems, allowing surgeons to know the location of instruments in relation to important anatomy in real-time, throughout the operation.

## Surgery

Indications for surgical resection of NFPAs include the following: (1) mass effect with visual loss, ophthalmoparesis, neurological deficit, or obstructive hydrocephalus (2) asymptomatic tumors with anatomic signs of impending visual loss, (3) signs of hypopituitarism, in particular, adrenal insufficiency, (4) acute pituitary apoplexy resulting in the previously listed indications.

The principal surgical approach to NFPAs is the transnasal transsphenoidal approach performed under endoscopic or microscopic visualization. This approach involves entering the sphenoid sinus, and subsequently the sella through the nasal cavity. NFPAs are generally soft in consistency and can be readily removed from the sella, as well as supra- and parasellar regions, with a number of ring curettes through this conduit. Because NFPAs are generally benign and slow



**Fig. 1** MRI obtained from multiple patients for pre-operative work up of NFPAs. **a** Incidental 1.8 cm sellar mass, abutting the optic chiasm (yellow arrow). **b** 3.3 cm recurrent NFWA in a patient with near total visual loss in the left eye, temporal field deficit in the right, and hyponatremia. Kinking of the pituitary stalk is noted (white arrowhead). **c** 3.8 cm cystic NFWA compressing the optic chiasm and expanding the sella turcica (arrowheads). **d** Incidental NFWA causing right inferior temporal quadrantopsia, invading through the sella into the sphenoid bone along the carotid artery (arrow). **e** 4.2 cm enhancing

giant pituitary adenoma with extensive suprasellar extension, compression of the left side of the optic chiasm (arrow), and invasion into the clivus (not depicted). There is extension towards the right sylvian fissure displacing the middle cerebral artery. **f** 5.4 cm giant NFWA invading the cavernous sinuses bilaterally with complete encasement of the carotid artery on the right (Knosp Grade 4) and 270 degrees on the left (Knosp Grade 3). The normal pituitary gland is displaced superiorly (white arrow)

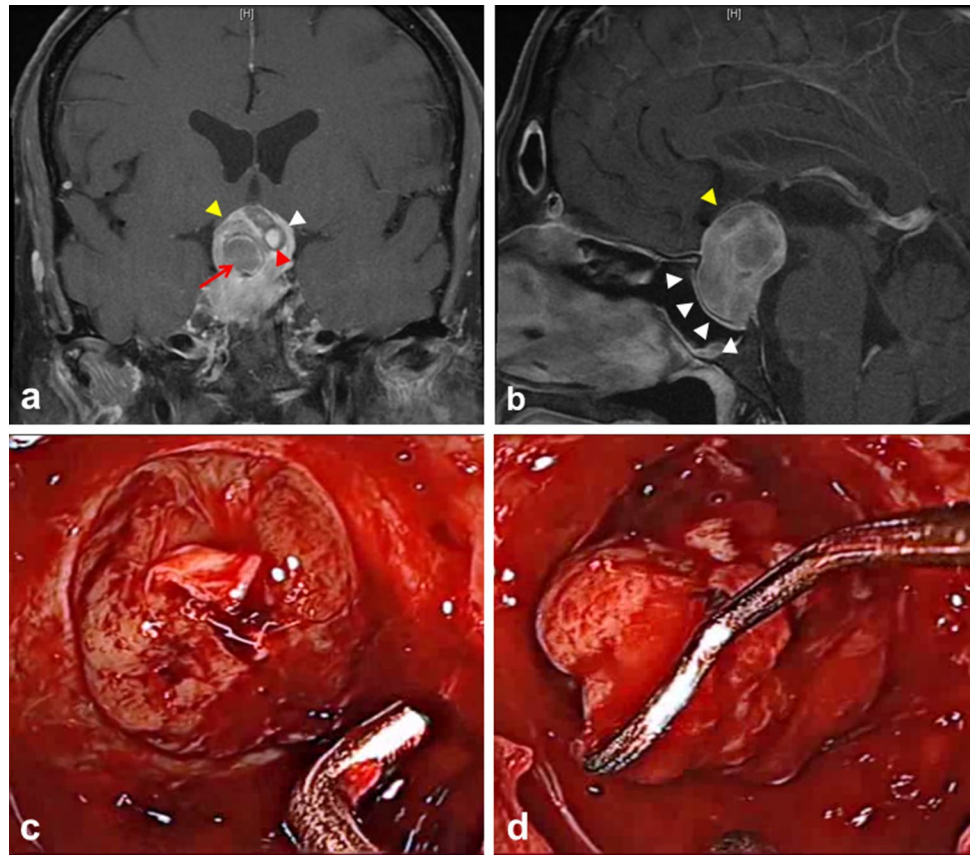
growing, the primary goal of surgery is decompression of neural structures, including the optic nerves and chiasm and cranial nerves within the cavernous sinus, while preserving the normal pituitary gland. In addition, the benefits of gross total resection of the mass must be balanced with the risks of aggressive tumor removal. While softer tumors can be safely resected from the suprasellar cistern and lateral portions of the cavernous sinus, this must be performed with care and with respect for the vital structures surrounding the sella (Fig. 2). For a tumor type where residual mass is unlikely to cause symptoms for the patient and to grow minimally within their lifetime, aggressive tumor removal at the risk of damage to vision or the carotid arteries is not always appropriate.

Another major goal and consideration during surgical resection of NFPAs is preservation of the normal pituitary gland. As with major neurovascular structures, care dissecting the tumor from the gland is necessary to preserve its function. Extra-capsular dissection of the tumor from the

surrounding gland and dura allows disconnection of adhesions and prevention of unnecessary manipulation that can damage the cells in the adenohypophysis and the nerves and vessels running in the pituitary stalk. Inability to adequately separate adhesions from the surrounding normal structures results in surgeons needing to more forcefully pull on the tumor to remove it which can cause injury to highly delicate nerves, blood vessels and the displaced pituitary gland which can be attached to the tumor. This can prevent both temporary and permanent post-operative hypopituitarism, in particular, DI and hypocortisolemia.

Lastly, significant consideration must be taken when dealing with intraoperative CSF leak. In many cases, this is unavoidable, e.g., when tumor has invaded through the diaphragm sella and the arachnoid or even when progressive stretching of these structures has created thin, delicate layers with adhesions. Surgeons must plan for intraoperative CSF leak and have multiple techniques at their disposal for prevention of persistent post-operative leak. Our preference

**Fig. 2** Preoperative MRI and intraoperative images from endoscopic transsphenoidal surgery for resection. **a, b** Preoperative coronal and sagittal MRI, respectively, demonstrating a 3.4 cm heterogeneous mass indicating multiple apoplectic events (chronic hemorrhage, red arrow and acute hemorrhage, red arrowhead). There is expansion of the bony sella (arrowheads) from growth of the mass and thinning of the optic chiasm (yellow arrowheads) from compression. **c, d** Intraoperative photos demonstrating the classic tan, gray and soft appearance of NFPAs resected with blunt instruments and ringed curettes, preventing damage to vital surrounding neurovascular and pituitary structures



is to use autologous abdominal fat held in place with an absorbable Porex plate (Porex, MedPor, Stryker, Portage, MI, USA). Additional techniques, include autologous fascia lata harvested from the right thigh, allograft dural substitutes, and fibrin glues. Lastly, when performing extended endoscopic approaches, a vascularized nasal septal flap can be used in conjunction with many of the previously listed techniques which has been demonstrated to significantly reduce post-operative leak rates [33]. Although some surgeons use this technique routinely, we believe that for most NFPAs; the benefits do not outweigh the risks and morbidity.

### Post-operative management

Post-operatively, patients are routinely cared for in our post-anesthesia unit and then transferred to the floor. Patients undergo regular neurological checks, every 4 h, including monitoring of visual fields and acuity. Adrenal insufficiency is treated at the time of surgery and patients are maintained on steroid replacement, generally with hydrocortisone, which is tapered over 2 days to physiological levels. The total length of replacement is determined in conjunction with our endocrine colleagues based on severity of pre-operative symptoms and laboratory findings. For example, patients with clinical manifestations of hypoadrenalism

or fasting serum cortisol levels severely below normal are generally maintained on hydrocortisone replacement for a minimum of 6 weeks, under our assumption that since this has manifested symptomatically there has been greater damage to the normal pituitary gland which will take longer to recover. Conversely, patients with only subclinical laboratory evidence of hypoadrenalism can be weaned from replacement, sometimes as early as 1 week post-operatively. Patients not requiring adrenal replacement peri-operatively are monitored with daily fasting morning serum cortisol checks as a laboratory marker to assess appropriate function of the remaining pituitary gland. Full post-operative endocrine laboratory evaluation is routinely performed at 6 and 12 weeks after the operation. Further endocrine testing is performed as needed.

While hospitalized, serum sodium and urine output and specific gravity are closely monitored for signs of DI and the syndrome of inappropriate anti-diuretic hormone (SIADH). Serum sodium and urine specific gravity are checked every 6 h. Patients experiencing DI following pituitary surgery will experience increased urinary output, often defined as greater than 250 mL/h over three consecutive hours, urine specific gravity less than 1.005, and serum sodium greater than 145 mEq/dL. Usually this is transient and we try to manage this by allowing the patient to drink to thirst. In

cases where patients exhibit clinical signs of dehydration or increasing urinary frequency is bothersome to the patient or preventing sleep and recovery, administration of intravenous or oral ddAVP is used. Patients experiencing SIADH can exhibit hyponatremia with serum sodium concentrations less than 135 mEq/dL often with minimal changes in urine output and sometimes an increased urine specific gravity. At our center, given the consequences of severe hyponatremia, we aggressively treat patients with fluid restriction when sodium levels are below normal limits or trending downward quickly. Since patients who have undergone pituitary surgery can be at risk for SIADH as long as 10 days after their operation, patients are discharged on a 1 L daily fluid restriction until their sodium is rechecked at their 1-week post-operative visit [34–36]. Patients with severe damage to the posterior pituitary gland or pituitary stalk from surgical manipulation can exhibit triple phasing—a period of DI, followed by SIADH, and then return to permanent DI. Routine post-operative MRI is obtained 3 months following the operation and then annually and biannually once stability is confirmed.

## Outcomes

Although Harvey Cushing was able to achieve an acceptable mortality rate of 5.6% prior to abandoning the surgical approach, advances in technique and technology have improved our ability to perform this operation safely and effectively [37]. Recent Guidelines by the Congress of Neurological Surgeons recommend resection of symptomatic NFPAs as first-line treatment [11, 20, 38–41]. Surgical management of NFPAs provides successful symptom relief with acceptable morbidity and mortality. Relief of symptoms caused by mass effect, such as headaches and visual loss, is where surgical intervention is most effective [42–45]. In patients presenting with visual field and acuity deficits, 56.4–90.0% reported improvement in vision [20, 21, 39, 43, 44, 46]. In our most recent series of 281 patients with NFPAs, undergoing 292 transsphenoidal procedures between 2008 and 2017, 89.7% of patients with pre-operative headaches reported improvement with 5.6% reporting stable headaches and 70.1% patients presenting with visual disturbances achieved improvement while 5.1% had stable vision. No patient in either the headache or vision group experienced worsening of pre-operative symptoms on long-term follow up (Table 1).

Surgical intervention can also be effective in reversing hypopituitarism. Retrospective analysis in a large series of 822 patients with NFPAs that underwent primary surgery—transcranial or transsphenoidal approaches—showed acceptable rates of return of pituitary function [47]. In this series, it was found that 85% of patients that underwent

**Table 1** Symptom improvement in patients undergoing transsphenoidal resection for NFPAs

Study	Headache (%)	Vision (%)	Hypopituitarism (%)
Current series	89.7	70.1	–
Chen et al. [20]	–	87.6	2.1
Fleseriu et al. [45]	80.0	–	–
Dekkers et al. [46]	–	90.0	–
Nomikos et al. [47]	–	–	49.7
Petruson et al. [41]	–	69.3	73.9
Comtois et al. [39]	90	56.4–82.2	11.0–41.0
Ebersold et al. [42]	100	73.6	16.4

transsphenoidal operations had laboratory evidence of hypopituitarism compared to 86.8% of patients that underwent transcranial procedures. Analysis showed superiority of the transsphenoidal approach over the transcranial approach for improvement and preservation of pituitary function with 19.6% of transsphenoidal patients achieving normalized pituitary function and 30.1% improving, while 1.4% had worsened function. In contrast, zero patients normalized and 11.6% of patients in the transcranial group had improved function with 15% of patients having worsened pituitary function. Although the number of studies specific to NFPAs is limited, recovery of pituitary function for all adenomas has been reported to range from 16 to 48% [38, 42, 48].

Transsphenoidal pituitary surgery can be performed using either the operative microscope or the endoscope. While both techniques get the surgeon to the face of the sella through the same corridor, there are subtle differences in the procedure and degree of visualization. Use of the operating microscope involves use of the nasal speculum which is placed on the perichondrial surface of the mucosa of the nasal septum. The speculum is then opened and the nasal septum removed to get the surgeon into sphenoid sinus and to the face of the sella. The microscope provides a lighted corridor through the speculum into the operative field. Technical disadvantages include smaller field of vision, limited illumination of the field, and collision of instruments with the microscope [49]. The endoscopic approach involves placement of the endoscope through the nasal cavity with removal of the nasal septum in a posterior to anterior fashion. The sphenoid sinus is then opened and the sella can be accessed. While this approach decreases three-dimensional perspective by operating through a two-dimensional image, illumination is improved with the light source at the tip of the endoscope and visualization is improved with a panoramic view from the tip of the camera being placed directly in the operative field.

Both approaches are safe and effective and the use of each has become largely surgeon preference. While data

specific to NFPAs is limited, there have been a number of studies examining outcomes and extent of resection of pituitary adenomas using microscopic or endoscopic techniques [49–52]. One study examined outcomes in NFPA resection using the microscopic compared to the endoscopic technique and demonstrated no statistically significant differences in endocrine outcomes, visual improvement, post-operative CSF leak, and extent of tumor resection [51]. Other studies, not specific to NFPAs have demonstrated similar outcomes and despite the demonstrated non-superiority of these techniques there has been a shift towards increasing use of the endoscope likely based on the perceived minimal invasiveness of the procedure, decreased post-operative pain and hospitalization length, and improved quality of life as reported by patients [53–56]. Ultimately, the ability of surgeons to achieve optimal results in both routine and complex cases is experience with pituitary surgery [57, 58]. Expertise and excellence in pituitary surgery is achieved by participation in both a residency and fellowship at centers with high volume and maintaining a practice with a heavy workload of pituitary tumors [59].

The extent of resection affects the likelihood of tumor recurrence [21]. Dallapiazza et al. examined a group of 80 patients with NFPAs that had been followed for at least 5 years post-operatively. Seventy-one percent of these patients had obtained a gross total resection of the tumor. In patients who had received a gross total resection, 12% had recurrence of tumor with a mean of 53 months to recurrence. Of the patients where only a subtotal resection was achieved, 61% (n = 11) had radiographic progression and 17% (n = 3) had symptomatic progression. Current guidelines from the Congress of Neurological Surgeons regarding the management of recurrent NFPAs recommend treatment for symptomatic with either repeat surgical resection or radiation therapy [60]. While Level II evidence demonstrates that radiosurgery lowers the risk of tumor progression, it is also recommended that small post-operative residual tumor should be followed with serial neuroimaging [61]. Repeat surgical resection for recurrent or residual NFPAs is recommended based on Level III evidence unless the risk of resection is high. In our practice, patients with no residual or small, asymptomatic residual tumors are followed with MRI 3 months post-operatively and then annually and biannually after demonstration of stability. We recommend that patients with recurrent disease that is either symptomatic or with impending neurologic deficits undergo repeat resection. Radiation can be used as an adjunctive therapy if there is high risk of continued recurrence.

## Complications

There are a number of complications associated with transnasal transsphenoidal operations ranging from minor to

severe. Severe complications include injuries to the major surrounding vasculature including the internal carotid arteries and the anterior cerebral artery complex. Visual loss can also occur through a number of different mechanisms, including direct injury to the optic apparatus, hemorrhage, over-packing with sellar closure material, and devascularization of the minute vessels that supply the optic chiasm. Temporary or permanent anterior and/or permanent hypopituitarism can occur. Persistent post-operative CSF leak, which in some instances can be benign, can significantly increase the risk of infection and meningitis, pneumocephalus, and intracranial hemorrhage, and therefore, must be treated urgently. Additionally, sinonasal complications can occur, such as crusting, septal perforation, or epistaxis. Complication data, specific to NFPAs are limited; however, one large single center analysis demonstrates that transsphenoidal surgery for pituitary adenomas can be performed safely with an overall complication rate of 9.1% [62]. The most common complications in this series were CSF leak (4.7%), meningitis (2.0%), and visual deterioration (2.0%), with severe complications like carotid injury and mortality occurring at a rate of 0.4 and 0.6%, respectively. In our recent series of 292 procedures for NFPAs, our common complications include epistaxis (3.4%, n = 10), permanent DI (3.1%, n = 9), CSF leak (1.7%, n = 5), visual loss (1.7%, n = 5), and meningitis (1.0%, n = 3). There were zero carotid injuries or mortalities in our series (Table 2).

## Conclusions

Non-functional pituitary adenomas are benign tumors of the pituitary gland that commonly present with symptoms of mass effect—headaches, visual loss, and hypopituitarism—as opposed to symptoms of hormonal hypersecretion. Although multiple pathologic subtypes of NFPAs exist, first line treatment for symptomatic lesions remains surgical resection, most commonly through a transnasal transsphenoidal approach, with adjunctive radiotherapy being reserved for more aggressive and recurrent tumor types. Pre-operative work-up should include thorough endocrinologic,

**Table 2** Complication rates in a series of 292 transsphenoidal operations for NFPAs

Complication	Incidence (%)
Epistaxis	10 (3.4)
Permanent diabetes insipidus	9 (3.1)
CSF leak	5 (1.7)
Immediate post-operative visual loss	5 (1.7)
Carotid artery injury	0 (0.0)
Mortality	0 (0.)

ophthalmologic, and radiographic studies and post-operative care requires close attention to neurologic exam and monitoring for signs of DI and SIADH. Although complications can be severe, in trained hands, surgery for NFPAs can be performed safely with low morbidity and mortality.

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