

TABLES

Table 1

Author (Year)	Description of Study	Classification Process / Data Class	Conclusions
Andersen et al (2001) ³⁶	Prospective observational study of 10 patients with NFPAs. Patients were analyzed with in vivo secretory capacity testing. They were then given the combination of a somatostatin analog, octreotide, and a D2 agonist for 6 months of therapy.	Therapeutic / III	Three of 10 patients (30%) demonstrated no change in tumor size, 1 of 10 (10%) demonstrated increased size, and 6 of 10 (60%) demonstrated reduced size. A reduction in tumor volume (mean 30%) was recorded only in patients with in vivo secretory potential.
Arita et al (2006) ¹⁰	A prospective observational trial at a single institution of 42 patients with asymptomatic NFPAs that were observed without any other intervention.	Therapeutic / III	Over 4 years of follow-up, incidentally found tumors increased in size in 40% of patients. Symptoms were noted in 10 patients (20%) during follow-up, 4 (9.5%) of whom developed pituitary apoplexy. Twelve patients underwent surgical intervention either due to symptoms or increasing tumor size.
Berkmann et al (2012) ¹²	A retrospective observational study at a single institution in Switzerland. A total of 182 patients who underwent surgical intervention for pituitary lesions were included. One hundred fourteen of 182 patients (63%) had NFPAs. Postoperative recovery of pituitary function and vision were assessed.	Therapeutic / III	Of 114 patients with NFPAs, 83 presented with preoperative hypopituitarism. Forty-two of these 83 patients (50.6%) recovered significant pituitary function postoperatively. Additionally, 88 patients presented with preoperative visual field deficits. Of these 88 patients, 78 (89%) demonstrated significant recovery of vision postoperatively.

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Chakera et al (1985) ³⁰	Prospective observational study of 11 patients with macroadenomas. Five of these patients had NFPAs. All patients were given a course of bromocriptine therapy.	Therapeutic / III	Zero of 5 patients with NFPAs treated with bromocriptine showed any change in tumor size on follow-up CT scans.
Chen et al (2011) ¹¹	A prospective observational study of 385 patients with NFPAs who underwent surgical intervention for resection of tumor. Resolution of visual complaints and symptoms of hypopituitarism were analyzed.	Therapeutic / III	Of 385 patients who underwent endoscope-assisted transsphenoidal resection of tumor, 242 had complained of visual symptoms preoperatively. Of these patients, 215 (87.6%) noted improvement in visual symptoms postoperatively. Eight patients (2.1%) required lifetime hormone replacement therapy postoperatively. Residual tumors were found in 79 patients (20.8%) on 4-month postoperative MRI.
Comtois et al (1991) ¹³	Retrospective analysis of 126 patients with NFPAs who underwent transsphenoidal resection at a single institution.	Therapeutic / III	After surgery, vision was normalized or improved in 71 of 94 patients (75%) who had presented with visual field deficits. Permanent diabetes insipidus occurred in 5% (7 of 126). The recurrence rate (mean follow up time of 6.4 +/- 4.2 years) was 21%.

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Dallapiazza, Grober et al (2014) ¹⁴	Retrospective analysis of 80 patients who underwent endoscopic resection of NFPA's who had more than 5 years of follow-up.	Therapeutic / III	Gross total resection was achieved in 71% of patients. There were 7 (12%) recurrences within the group, occurring at a mean time of 53 months postoperatively. Rates of endoscopic resection were comparable compared to published rates via microsurgical techniques.
de Herder et al (2006) ³³	Prospective cohort study of patients with NFPA's and response to dopamine. Pituitary uptake of 123I-epidepride was classified on scale of 0 to 3 (high uptake). Patients were then given DA agonist therapy and response classified according to follow-up imaging.	Therapeutic / III	NFPA stabilization or shrinkage with DA agonist therapy showed no significant difference between grade 0, 1, and 2 tumors. There is limited clinical utility of dopamine D2 receptor imaging for predicting efficacy of DA agonist therapy. Eleven of 18 patients (61%) showed shrinkage of tumor >20%.
Dekkers et al (2006) ¹⁵	Retrospective study of 109 consecutive patients with NFPA's who underwent transsphenoidal surgery between 1992 and 2004. Ninety-seven patients received surgery as the only therapeutic intervention. Mean follow-up period of 6.0 ± 3.7 years.	Therapeutic / III	Of 97 patients who underwent transsphenoidal resection without subsequent therapeutic interventions, 9 patients had evidence of tumor regrowth, and recurrence was noted in 1 patient. Mean follow-up time was 6.0 ± 3.7 years. The mean time to tumor regrowth/recurrence was 6.9 years. Authors concluded that transsphenoidal surgery without subsequent radiation therapy controlled tumor in 90% of all patients.

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Dekkers, de Keizer et al (2007) ¹⁶	Retrospective follow-up study of 43 consecutive patients treated with transsphenoidal resection of NFPAs. Analysis was primarily to assess for continuing improvement in visual acuity following surgical intervention.	Therapeutic / III	Visual acuity improved significantly within 3 months after transsphenoidal surgery, from 0.65 ± 0.37 to 0.75 ± 0.36 ($P < .01$) (right eye), and from 0.60 ± 0.32 to 0.82 ± 0.30 ($P < .01$) (left eye). Further improvement was seen at 1 year following surgical intervention, as the mean visual acuity increased from 0.75 ± 0.36 to 0.82 ± 0.34 ($P < 0.05$) (right eye) and from 0.82 ± 0.30 to 0.88 ± 0.27 ($P < 0.05$) (left eye).
Dekkers, Hammer et al (2007) ⁹	Retrospective analysis of 28 patients diagnosed with NFPAs who had no treatment following diagnosis. Mean duration of follow-up was 118 months.	Therapeutic / III	Radiologic evidence of tumor growth was observed in 14 of 28 patients (50%). Six patients (21%) required operation due to onset of visual field deficits. Spontaneous reduction in tumor volume was observed in 8 patients (29%).
Fleseriu et al (2009) ¹⁷	Retrospective analysis of 41 patients who underwent surgical intervention for pituitary adenoma. All patients presented with complaint of headache. Analysis was focused on effects of surgical intervention on resolution of headache.	Therapeutic / III	Of 41 patients with pituitary adenoma in this study, 15 (36.6%) had documented NFPAs. No patient was on hormone replacement. Eight of 15 patients (53.3%) reported complete resolution of headaches postoperatively, 4 of 15 (26.6%) reported improvement in headaches, and 3 of 15 (20%) reported no change in headaches.
Gasperi et al (1993) ³⁴	Prospective observational study of 8 patients with NFPAs treated for 6 months with octreotide therapy. Tumor size assessed at follow-up with CT scan.	Therapeutic / III	No significant change in visual field or tumor size occurred after octreotide therapy in 7 of 8 patients (88%), whereas 1 patient (12%) demonstrated improvement in visual fields and decreased tumor size.

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Halvorsen et al (2014) ²⁵	Retrospective study of all (506) transsphenoidal procedures performed on 446 patients in a defined population, analyzing complication rates specifically.	Therapeutic / III	The overall complication rate was 7.1%, with the most common complications being CSF leak (4.7%), meningitis (2%), and visual deterioration (2%). No difference was observed between endoscopic and microsurgical resection.
Kurosaki et al (2000) ¹⁸	Retrospective analysis of 32 cases of NFPAs in patients greater than 70 years of age identified in a review of 982 patients with pituitary adenomas treated at a single institution.	Therapeutic / III	All 32 patients underwent transsphenoidal resection of the tumor. Complete microscopic resection was achieved in 24 patients, and subtotal resection in 8 cases. No severe complications were encountered. Hormonal deficiencies persisted in all patients with preoperative insufficiencies. Visual disturbances were improved for 19 of 23 patients (82.6%).
Lee et al (2014) ²⁸	Retrospective analysis of 41 patients in which NFPAs were initially treated with gamma knife radiosurgery because of high surgical risk.	Therapeutic / III	Forty-one patients underwent gamma knife radiosurgery as primary treatment for their NFPA. The tumor control rates were 94% and 85% at 5 and 10 years after treatment, respectively. Three patients underwent surgical resection post-procedurally. New onset cranial nerve palsy was noted in 1 patient.

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Mingione et al (2006) ²⁶	Retrospective analysis of 100 consecutive patients who underwent gamma knife radiosurgery for NFPAs. Eight patients were treated with GKS as primary treatment. Mean follow-up time of 49 months.	Therapeutic / III	Of 8 patients with NFPAs treated with gamma knife radiosurgery as primary treatment, 3 (38%) demonstrated decrease in size of tumor on follow-up imaging, while 5 (62%) showed stable tumor size.
Mortini et al (2005) ¹⁹	Retrospective analysis of 1140 patients undergoing transphenoidal resection of pituitary adenoma at a single institution.	Therapeutic / III	NFPAs accounted for 378 patients (33.2% of total patients). No residual adenoma was present in 234 patients (64.8%). Normalization of visual defects occurred in 117 (40.5%) of the 289 patients with visual disturbances and improved in another 148 patients (51.2%).
Nobels et al (2000) ²⁹	Prospective observational study of 10 patients with NFPAs treated with quinagolide. Median treatment duration was 57 months. Imaging was done at regular intervals of follow-up.	Therapeutic / III	Of 8 patients with follow-up greater than 48 months, tumor shrinkage was seen in 2 (25%). Six of 8 patients (75%) showed an increase in tumor size of >10%.

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Park et al (2011) ²⁷	Retrospective study of 125 patients with NFPAs treated with GKS over 22 years at a single institution. Fifteen of 125 patients had GKS as the primary treatment. Radiologic progression-free survival was used as primary analysis. Patients must have had >2 years of follow-up.	Therapeutic / III	Of 15 patients treated with primary GKS, 9 (60%) showed size reduction on follow-up imaging and 4 (26.7%) showed no change. Two patients demonstrated tumor progression, 1 at 14 months and 1 at 30 months postoperatively. Tumor control rate in this group was therefore 86.7%. Total tumor control rate for all patients combined (primary treatment, residual, and recurrent) was 89.6%.
Petruson et al (1995) ²⁰	Retrospective analysis of 48 patients with NFPAs treated with transsphenoidal resection at a single institution. Follow-up was done at the 5-year postoperative interval.	Therapeutic / III	CT scans were performed in 44 patients after an average of 4 years and revealed no signs of recurrent tumor in any patient. New pituitary hormonal insufficiencies developed in 6 of 48 (12%). Improvement in vision was seen in 38 patients (79%).
Van Schaardenburg et al (1989) ³¹	Prospective cohort study of 43 patients with NFPAs. Twenty-five patients were treated with bromocriptine therapy, while 18 patients were treated with surgery alone. The medically treated group was analyzed retrospectively. Fifteen of the 25 patients treated with bromocriptine had no history of surgery or radiation.	Therapeutic / III	In the 15 patients treated primarily with bromocriptine, 3 (20%) showed tumor growth while 12 (80%) showed no changes on follow-up CT scan. Visual fields worsened in one of these patients, who demonstrated no change on CT.

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Verde et al (1985) ³²	Prospective observational analysis of 20 patients with NFPAAs treated with bromocriptine. Patients were followed with CT scans and ophthalmologic evaluations.	Therapeutic / III	One patient of 20 (5%) demonstrated a marked reduction in tumor size and improvement in visual fields. The remaining 19 patients (95%) showed no changes on imaging during treatment. Four of these patients had worsening visual fields and were referred for neurosurgery.
Warnet et al (1997) ³⁵	Twenty-four patients with visual changes caused by histologically confirmed NFPAAs were given octreotide. Visual symptoms were assessed at 4 days, 1 month, and 2 months. Patients who did not experience changes in visual symptoms were able to discontinue use of octreotide. Tumor size was also assessed at 2 months in individuals who did not discontinue octreotide due to inefficacy.	Therapeutic / III	Visual improvement was noted in 9 of 22 patients (40.9%) at 2 months. Octreotide was stopped in 13 of 22 patients (59.1%) due to inefficacy. Of those who continued taking octreotide, 3 patients demonstrated reduction in tumor size, 3 showed stable tumor size, and 1 had tumor growth.

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Webb et al (1999) ²¹	Retrospective analysis of 234 patients with pituitary adenomas treated with transsphenoidal resection. Preoperative and postoperative (within 6 months) anterior pituitary function was evaluated for recovery or development of new deficits.	Therapeutic / III	Of 56 patients with NFPAs, 24 had complete hormonal axis function preoperatively. Three of 56 patients (5%) developed new postoperative pituitary axis dysfunction. Twenty-four of 56 patients (43%) had normal function preoperatively, and 30 of 56 (54%) had completely normal function postoperatively. Twenty-nine patients had some element of dysfunction preoperatively. Nineteen of 29 (65%) had no change in function postoperatively, whereas 10 of 29 (35%) gained some function.
Wichers-Rother et al (2004) ²²	Retrospective analysis of 155 patients with NFPA to evaluate improvement of anterior pituitary function after transsphenoidal and/or transcranial surgery. Patients were evaluated preoperatively and 3 months, 1 year, and 2 years postoperatively.	Therapeutic / III	Anterior pituitary function in patients with NFPAs did not improve significantly postoperatively. Most clinical symptoms, including visual deficits, headache, and fatigue did show improvement.