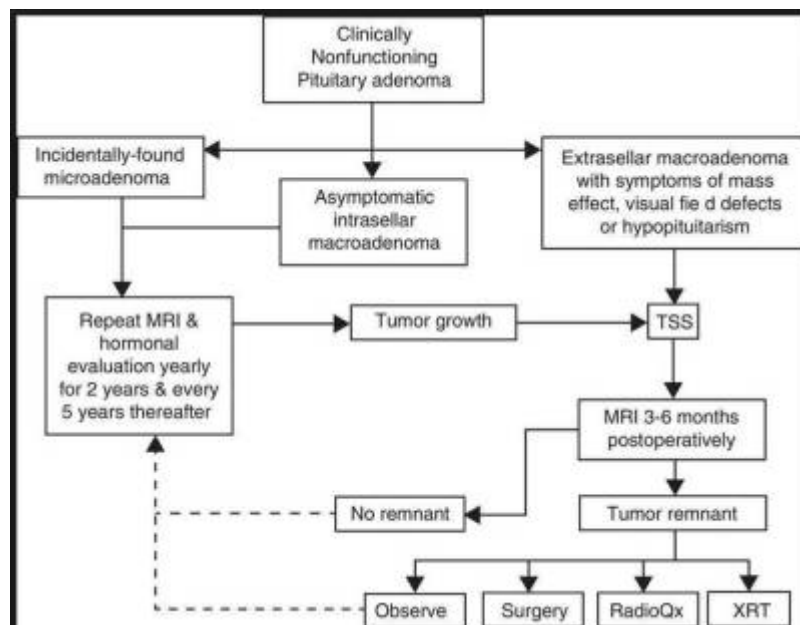


# Clinically Non-Functioning Pituitary Neuroendocrine Tumor outcome after surgery



**Nonfunctioning pituitary neuroendocrine tumors** (NFPAs) present low growth rates; however, some are aggressive and invasive. In 2017 the World Health Organization recognized clinically aggressive adenomas as “high-risk pituitary neuroendocrine tumors”. These include the sparsely granulated somatotroph adenoma, the Crooke’s cell adenoma, the silent corticotroph adenoma and the plurihormonal Pit-1-positive adenoma (subtype 3) <sup>1)</sup>.

**Clinically Non-Functioning Pituitary Neuroendocrine Tumors**, although benign in nature, need individualized treatment and lifelong radiological and endocrinological follow-up <sup>2)</sup>.

There are anecdotal reports of tumor shrinkage during therapy with either **dopamine agonists** or **somatostatin agonists**; however tumor response to medical treatment is not reliable. For most patients, **transsphenoidal** resection of the tumor is the preferable primary treatment. Surgery improves **visual deficits** in the majority of patients and a lesser number will recover pituitary function. In the past, pituitary radiation was commonly administered following **pituitary surgery**; however the need for routine radiation has been reevaluated. Although tumor recurrence at 10 years post surgery may be as high as 50%, few patients with recurrence will have clinical symptoms. Close follow-up with surveillance pituitary scans should be performed after surgery and radiation therapy reserved for patients having significant tumor recurrence <sup>3)</sup>.

**Hypopituitarism** is observed in NFPAs due to tumour- or treatment-related factors and may increase mortality risk.

The main aim of surgical treatment is improvement of visual function, which is achieved in over 80% of cases <sup>4) 5)</sup>.

Studies on the effect of surgery in NFMA on pituitary function show conflicting results. Some studies report, to a variable degree, an improvement in pituitary function <sup>6) 7) 8) 9) 10) 11)</sup>, whereas others could not demonstrate significant improvement in pituitary function, or even showed decreased pituitary function after transsphenoidal surgery <sup>12) 13) 14)</sup>.

The microscopic and endoscopic techniques provide similar outcomes in the surgical treatment of [Knosp Grades 0-2 nonfunctioning pituitary macroadenomas](#) <sup>15)</sup>

The surgical removal of a nonfunctioning [pituitary macroadenoma](#) (NFP-Mac) is often incomplete.

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## Quality of Life

The QOL of NFMA patients is affected both physically and mentally by surgical treatment and symptoms. This QOL assessment is important for planning treatment strategies <sup>16)</sup>.

## Cognition

Patients with NFA score significantly worse on cognition compared to reference populations. Radiotherapy does not appear to have a major influence on cognition. <sup>17)</sup>.

## Sleeping

Daytime sleepiness is increased despite normal sleep patterns in patients treated for NFMA <sup>18)</sup>.

Patients treated for nonfunctioning pituitary macroadenoma (NFMA) with suprasellar extension show disturbed sleep characteristics, possibly related to hypothalamic dysfunction. In addition to hypopituitarism, both structural hypothalamic damage and sleep restriction per se are associated with the [metabolic syndrome](#), mainly due to decreased HDL-cholesterol and increased triglycerides. Risk factors included hypopituitarism and preoperative visual field defects. Hypothalamic dysfunction may explain the metabolic abnormalities, in addition to intrinsic imperfections of hormone replacement therapy. Additional research is required to explore the relation between derangements in circadian rhythmicity and metabolic syndrome in these patients <sup>19)</sup>.

## Recurrence/Residual tumor

The outcome of surgical treatment of NFPAs was improved by the use of intraoperative MRI owing to more radical resection. The remission rate seems to depend on tumor characteristics. Recurrent disease might be reduced by the use of intraoperative MRI leading to more complete surgical resection of NFPAs <sup>20)</sup>.

Tumour progression rates are high in patients with postoperative remnants. Therefore, long-term monitoring is necessary to detect tumour growth, which may be asymptomatic or manifest with visual

field defects and/or pituitary dysfunction. In view of the generally slow-growing nature of these tumours, yearly magnetic resonance imaging, neuro-ophthalmologic and pituitary function evaluation are appropriate during the first 3-5 years after surgery. If there is no evidence for tumour progression during this period, testing intervals may be extended thereafter <sup>21)</sup>.

see [Recurrent Nonfunctioning pituitary macroadenoma](#)

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Early and effective surgical treatment is essential for rapid recovery of visual and/or hormonal deficits, particularly in symptomatic cases <sup>22)</sup>.

[Tumor size](#) and [cavernous sinus](#) extension are the main predictors for [subtotal resection](#) STR. Notably, recovery of the gonadal axis in a large proportion of patients supports the surgical resection of NFPAM in patients suffering from gonadal deficiency, even in the absence of [visual field defect](#) (VFD) <sup>23)</sup>.

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Of 18 grossly complete resection was achieved in 71% of patients. [Knosp grade](#) 0-2 tumors and [tumor volumes](#) <10 cm were significantly more likely to have received a grossly complete resection. There were 7 (12%) recurrences in patients who had received grossly complete resections, with a mean time to recurrence of 53 months. Among the 23 patients who had subtotal resections, 11 (61%) progressed radiographically and 3 (17%) had symptomatic progression. Knosp score, surgical and radiographic evidence of invasion, and preoperative visual deficits were predictive of recurrence in a univariate analysis, but Knosp grade was the only independent predictor in a multivariate analysis. Kaplan Meier analysis projected a 10-year progression-free survival rate of 80% and 21% for patients with grossly total resections and subtotal resections, respectively <sup>24)</sup>.

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