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Surgical management of growth hormone-secreting pituitary adenomas

A retrospective analysis of 33 patients

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Abstract

The endoscopic endonasal transsphenoidal approach (EETA) is the primary treatment for growth hormone (GH) adenoma. This study aimed to investigate the outcomes of EETA in 33 patients with GH-secreting pituitary adenoma (PA).

Thirty-three patients who underwent EETA in Eighth People's Hospital of Shenzhen between January 2013 and December 2017 were included in the comprehensive analysis. Factors affecting the extent of resection and postoperative remission rates were also reviewed.

The total cut rate was 63.6% (21), and the total remission rate was 66.7% (22) in all patients after surgery. The cure rate was 60.6% (20) for 33 patients. The total removal rate and remission rate were significantly different ($P = .01$, $P = .007$) for microadenomas, macroadenomas, and giant adenomas. In addition, the total removal rate and remission rate were significantly different ($P = .004$, $P = .007$) for patients with noninvasive and invasive GH-secreting PAs. Furthermore, there were significant differences ($P = .003$, $P = .005$) in the total removal rate and remission rate of patients with different preoperative GH levels. All patients with hypertension and diabetes mellitus were normalized. Three patients exhibited recurrence after surgery. Several patients suffered from postoperative complications, including transient diabetes insipidus in 3 (9.1%) patients and postoperative transient cerebrospinal fluid leakage in 2 (6.1%) patients.

EETA is an effective therapeutic approach for treating patients with GH-secreting PA with high remission and low complication rates. Therefore, EETA should be considered a primary treatment for patients with GH-secreting PA.

Abbreviations: CSF = cerebrospinal fluid, EETA = endoscopic endonasal transsphenoidal approach, GH = growth hormone, IGF-1 = insulin-like growth factor 1, MRI = magnetic resonance imaging, PA = pituitary adenoma.

Keywords: endoscopic endonasal transsphenoidal approach, neuro-endoscopy, secreting pituitary adenoma, surgical effect

1. Introduction

Pituitary adenomas (PAs), one of the most common intracranial tumors, are generally benign monoclonal tumors arising from adenohypophyseal cells.[1,2] PA is clinically classified into functional adenomas and nonfunctional adenomas. Growth hormone (GH)-secreting PA is a common functional PA, the classical clinical symptom of which is acromegaly. The clinical characteristics of acromegaly include facial changes, such as thickening of lips and a widened nose, and thickening of hands and feet because of the over secretion of GH and insulin-like growth factor 1 (IGF-1). Furthermore, some patients exhibit unilateral or bilateral vision loss with or without visual defects, headaches, hypertension, and diabetes mellitus. In addition, the biological behavior and clinical outcome of GH-secreting PA is different in women and men.[3,4] The serum GH levels in such patients are significantly increased compared with healthy patients, and magnetic resonance imaging (MRI) can be used to illustrate the size and extent of the GH-secreting adenoma.

In recent years, neurosurgical techniques regarding advances in the treatment of PAs have rapidly developed. Currently, almost all patients with PAs undergo endoscopic endonasal transsphenoidal surgery, which has been suggested to be a highly effective therapeutic strategy, with a high remission rate and limited complications.[5] The endoscopic endonasal transsphenoidal approach (EETA) is considered the primary treatment for GH-secreting PA.[6–9] However, some, including tumor size, invasion, preoperative GH level, preoperative IGF-1 level, and experience of the surgeon, factors affect postoperative remission.[6,10–16]

This research presents the outcome of 33 patients with GH-secreting PAs who underwent EETA in Eighth People's Hospital of Shenzhen from January 2013 to December 2017. We analyzed the postoperative outcomes and factors affecting the extent of resection and postoperative remission rates.

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The datasets generated during and/or analyzed during the current study are publicly available.

The authors have no conflicts of interest to disclose.

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2. Materials and methods

Written informed consent was obtained from all patients, and the study was approved by the Medical Ethics Committee of Eighth People's Hospital of Shenzhen. All the methods were performed in accordance with the relevant guidelines and regulations. Thirty-three patients with GH-secreting PA who underwent endoscopic endonasal transsphenoidal surgery were included in this study. These patients comprised 18 (54.5%) women and 15 (45.5%) men, with a mean age of 43.24 years. The patients were categorized according to tumor size: 7 (21.2%) patients with microadenoma ($\leq$ 1 cm), 18 (54.6%) patients with macroadenoma (1–4 cm), and 8 (24.2%) patients with giant adenoma ($\geq$ 4 cm) (Table 1). In general, tumors are classified into 5 grades on the basis of the Knosp classification[17]: grades 0, I, and II are defined as noninvasive tumors, and grades III and IV are defined as invasive tumors (Fig. 1 and Table 2). There were 23 (69.7%) patients with invasive tumors and 10 (30.3%) with noninvasive tumors. Of the 33 patients, 15 (45.5%) had preoperative GH level of $\leq$ 20 ng/mL, 13 (39.4%) with preoperative GH level of $>$ 20 ng/mL but $<$ 40 ng/mL, and 5 (15.1%) with preoperative GH level of $\geq$ 40 ng/mL (Table 1).

The preoperative clinical manifestations of the 33 patients are shown in Table 3. These groups included 20 patients (60.6%) with acromegaly. Two women (6.1%) had amenorrhea with infertility, and 1 man (3.03%) had impotence and decreased libido. Four patients (12.1%) had different degrees of vision loss, 13 patients (39.4%) had different degrees of headache, 3 patients (9.1%) had hypertension, and 3 patients (9.1%) had diabetes mellitus.

The serum endocrine levels and MRI examination of the 33 patients were tested to investigate the tumor before surgery during hospitalization. GH levels and IGF-1 levels were elevated in all patients. Acromegaly was diagnosed on the basis of relevant clinical features: a mean GH level $>$ 5 ug/L, plasma IGF-1 level greater than normal age- and sex-matched levels, or nadir GH after OGTT $>$ 1 μg/L.[18] The tumor of GH-secreting PAs was obvious as shown on MR images (Fig. 2). All 33 patients underwent an EETA from the same surgeon. The tumor can be clearly seen in the neuroendoscope (Fig. 3).

Table 1

Patients and tumor characteristics.

Variables	Total(n = 52)
Age (mean, range)	43.24 ± 11 (56, 21–68)
Male	15 (45.5%)
Female	18 (54.5%)
Tumor diameter	
Diameter $\leq$1 cm	7 (21.2%)
1 cm $<$ diameter $<$ 4 cm	18 (54.6%)
Diameter $\geq$4 cm	8 (24.2%)
Invasion	23 (69.7%)
No invasion	10 (30.3%)
Pre-GH levels	
GH$\leq$20 ng/mL	15 (45.5%)
20 ng/mL$<$GH$<$40 ng/mL	13 (39.4%)
GH$\geq$40 ng/mL	5 (15.1%)
Long-term follow-up results	
Remission	22 (66.7%)
Persistence	8 (24.2%)
Recurrence	3 (9.1%)

GH = growth hormone.

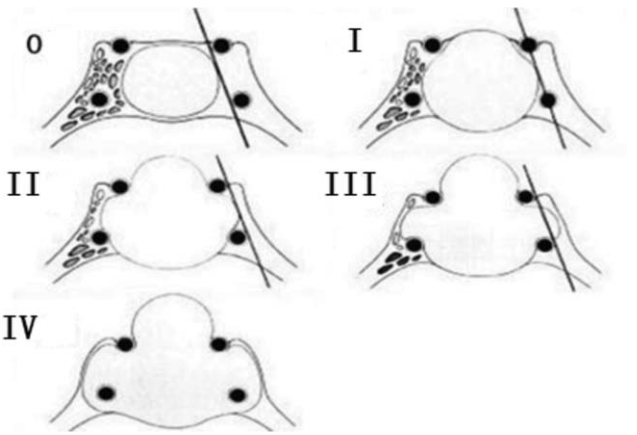

Figure 1. The Knosp–Steiner classification.

During the postoperative follow-up, the serum GH was tested at 2 days, 1 month, 3 months, 6 months, and 1 year after surgery. The criteria for endocrinological remission or cure were a nadir serum GH level of $<$ 0.4 ng/mL after an oral glucose load, and subsequent normal sex- and age-adjusted IGF-1 levels.[19] Long-term recurrences were generally rare after postoperative biochemical remission was clearly determined.[20–22] In this study, the postoperative complications included transient diabetes insipidus (3, 9.1%) and transient cerebrospinal fluid (CSF) leakage (2, 6.1%).

Statistical analysis was performed using SPSS software (v. 24.0; IBM SPSS, Armonk, NY). Categorical variables were analyzed using Fisher exact test or χ^2 test. $P < .05$ was considered statistically significant.

3. Results

The outcomes of tumor removal in all patients are presented in Table 4. The total tumor resection rate was 63.6% (21) and the subtotal resection rate was 36.4% (12). Tumor size, tumor

Table 2

The Knosp–Steiner classification for 52 patients.

Knosp–Steiner classification	Number of patients (%)
0	2 (6.1%)
I	3 (9.1%)
II	5 (15.2%)
III	13 (39.4%)
IV	10 (30.3%)

Table 3

The clinical symptoms for 52 patients.

Symptom and sign	Number of patients (%)
Acromegaly	20 (60.6%)
Amenorrhea, infertility (female)	2 (6.1%)
Impotence, decreased libido (male)	1 (3.03%)
Visual field defect	4 (12.1%)
Headache	13 (39.4%)
Hypertension	3 (9.1%)
Diabetes mellitus	3 (9.1%)

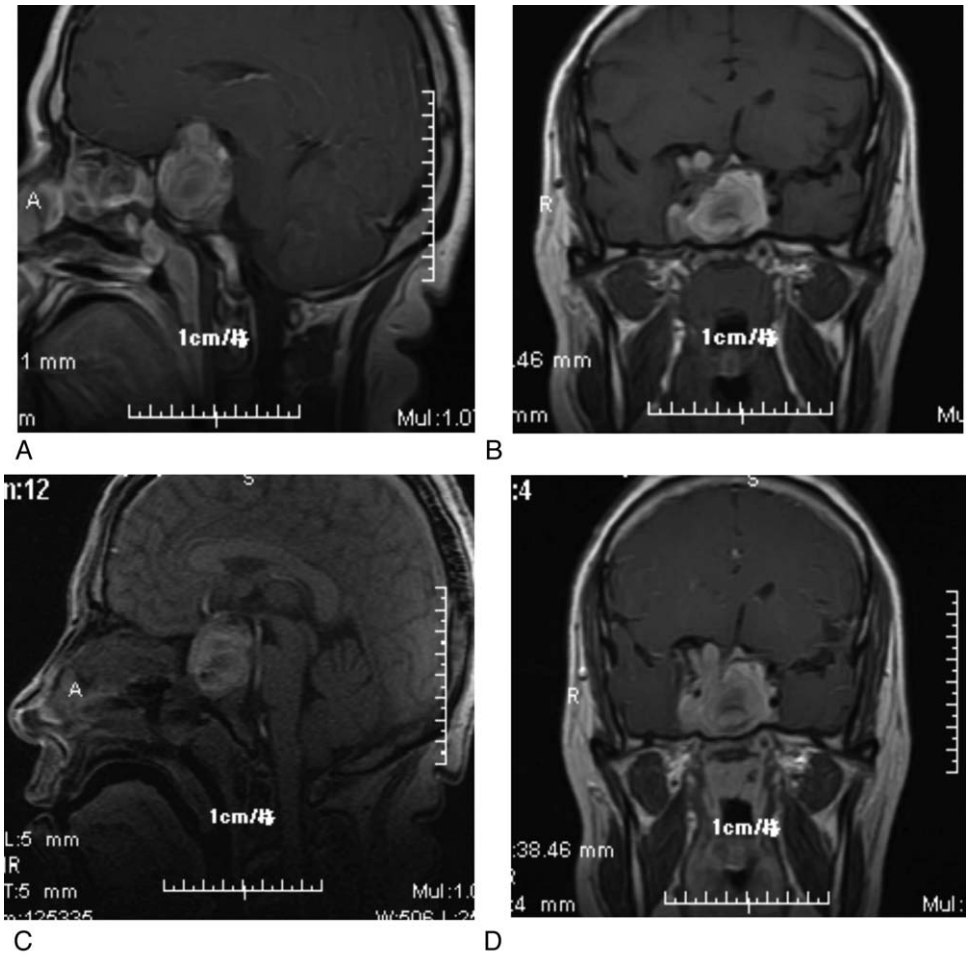

Figure 2. Preoperative MR.

invasion, and preoperative GH were significantly related to total tumor removal ($P < .05$). Sex was not significantly correlated with total tumor removal ($P > .05$). Preoperative GH levels were significantly associated with total tumor resection ($P < .05$).

The outcomes of postoperative remission are presented in Table 5. The overall remission rate was 66.7% (22 of 33) for all patients. Tumor size, tumor invasion, and preoperative GH level were significantly related to the remission rate ($P < .05$). Sex was not significantly correlated with the remission rate ($P > .05$). Preoperative GH levels were significantly associated with the remission rate ($P < .05$). The remission rate was 100% (21 of 21) for the group with total resection and 8.3% (1 of 12) for the group with subtotal resection. Total resection was significantly correlated with remission ($P < .001$) (Table 6).

All patients displayed improvement in the postoperative clinical characteristics during the follow-up period. The postoperative condition was slightly improved in patients with acromegaly. Amenorrhea was normalized in the 2 female patients and sexual function was normalized in the single affected male patient. Vision was improved in 4 patients and headache improved in 12 patients. Hypertension and diabetes mellitus in 6 patients were controlled. Three patients exhibited a recurrence following surgery. Several patients suffered from postoperative complications, including transient diabetes insipidus in 3 (9.1%) patients and postoperative transient cerebrospinal fluid leakage in 2 (6.1%) patients.

Postoperative GH levels in 21 patients and postoperative IGF-1 levels in 20 patients were significantly decreased on the second day after surgery, and 20 (60.6%) and 18 patients (54.5%) exhibited normal levels during the follow-up period. However, postoperative GH and IGF-1 levels did not change and even increased in 6 patients (18.2%). Postoperative MRI examination showed that the tumor had vanished in 20 patients (60.6%), and the tumor had recurred in 3 patients (9.1%).

4. Discussion

Transsphenoidal approaches are the most common options for most of pituitary adenomas. Numerous pituitary adenomas, especially smaller enclosed ones, including GH-secreting PAs, can be removed completely, and selective pituitary adenomectomy is usually attempted.[23] Most patients with GH-secreting PAs benefit from EETA, which can improve impaired visual function, influence regression of acromegalic features, reduce the risk of cardiovascular disease, and decrease long-term mortality by realizing rapid liberation from GH excess. Currently, EETA is the primary treatment for GH-secreting PAs .[6–9] In this study, the results revealed that EETA presented high rates of remission

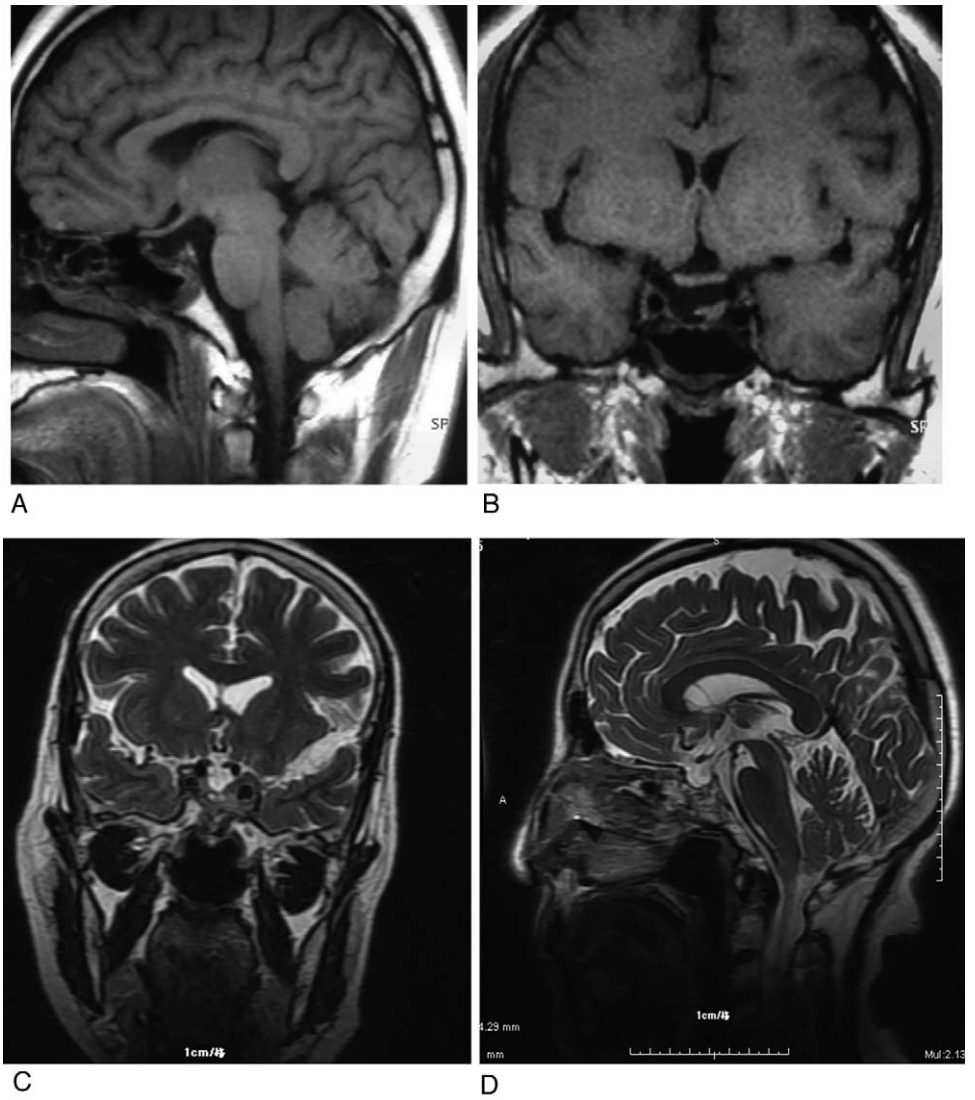

Figure 3. Postoperative MR.

and low rates of complication in 33 patients with GH-secreting PAs.

Acromegaly is the most common and typical clinical characteristic of GH adenomas. The principal aim of treatment for acromegaly is to normalize both GH and IGF-1 levels after surgery. Currently, the remission criteria for acromegaly are continuously improving with developments in medicine. However, the current criteria are definite and concise. The overall remission rates, which range from 60% to 85%, are reported in most surgical series on the basis of current criteria.[24–27] The remission rate in this study was 66.7% (22 of 33), which is similar to those reported. Some reports suggest that tumor invasion and preoperative serum GH levels are the most significant preoperative predictors of remission.[22,24–26] In this study, the remission rate was significantly different between patients with noninvasive and invasive GH adenomas, and there were significant differences in the total removal rate and remission rate of patients with different preoperative GH levels. The remission rate of noninvasive tumors and patients with low preoperative GH levels were higher than those of invasive tumors and patients with high preoperative GH levels ($P < .05$). The results reveal that tumor invasion and preoperative serum GH levels are significantly associated with preoperative predictors of remission. In addition, the remission rates were significantly different ($P = .01$, $P = .007$) for microadenomas, macroadenomas, and giant adenomas. The remission rate of microadenomas was higher than that of macroadenomas and giant adenomas ($P < .05$) (Table 5). Tumor size could also be a significant preoperative predictor of remission.

Furthermore, the total removal rate was significantly different for microadenomas, macroadenomas, and giant adenomas. The total removal rate was significantly different for patients with noninvasive and invasive GH-secreting PAs. There were significant differences in the total removal rate for patients with different preoperative GH levels. The results showed that the total resection rate of microadenomas, noninvasive tumors, and in patients with low preoperative GH levels were higher than those of macroadenomas, giant adenomas, invasive tumors, and

Table 4

The relationship between surgical resection and sex, tumor size, tumor invasion, and preoperative GH.

	Number of total resection (n)	Number of subtotal resection (n)	Total (n)	Total removal rate (%)	χ^2	*P*
Sex					0.109	.741
Male	10	5	15	66.7%		
Female	11	7	18	61.1%		
Tumor size (cm)					9.232	.010
Microadenoma	7	0	7	100%		
Macroadenoma	12	6	18	66.7%		
Giant adenoma	2	6	8	25%		
Tumor invasion					8.199	.004
Invasive adenoma	11	12	23	47.8%		
Noninvasive adenoma	10	0	10	100%		
Preoperative GH (ng/mL)					11.548	.003
GH≤20	14	1	15	93.3%		
20<GH<40	6	7	13	46.2%		
GH≥40	1	4	5	20.0%		

The total resection rate of sex was statistically analyzed by using the method of the χ^2 test, and the difference was not statistically significant ($P > .05$). The total resection rate of tumor size, tumor invasion, and preoperative GH was statistically analyzed by using the method of the χ^2 test, and the difference was statistically significant ($P < .05$).

Table 5

The relationship between postoperative relief and sex, tumor size, tumor invasion, and preoperative GH.

	Total (n)	Effective number of cases (n)	Postoperative remission rate (%)	χ^2	*P*
Sex				0.550	.458
Male	15	11	73.3%		
Female	18	11	61.1%		
Tumor size				10.000	.007
Microadenoma	7	7	100%		
Macroadenoma	18	13	72.2%		
Giant adenoma	8	2	25.0%		
Tumor invasion				7.174	.007
Invasive adenoma	23	12	52.2%		
Noninvasive adenoma	10	10	100%		
Preoperative GH (ng/mL)				10.662	.005
GH≤20	15	14	93.3%		
20<GH<40	13	7	53.8%		
GH≥40	5	1	20.0%		

The postoperative remission rate of sex was statistically analyzed by using the method of the χ^2 test, and the difference was not statistically significant ($P > .05$). The postoperative remission rate of tumor size, tumor invasion, and preoperative GH was statistically analyzed by using the method of the χ^2 test, and the difference was statistically significant ($P < .05$).

patients with high preoperative GH levels (Table 4). Tumor size, tumor invasion, and preoperative GH levels could be considered significant preoperative predictors of total resection.

The tumor was completely removed, and GH levels were normalized in 10 patients with noninvasive tumors. However, the total removal and remission rates were only 47.8% and 52.2%, respectively, in 23 patients with invasive tumors. The invasive GH adenomas, cavernous sinus invasion of Knosp grade III and IV, could not be completely resected because of the involvement of structures of the cavernous sinus. Residual tumors can secrete GH, so the postoperative GH levels are not normalized and the remission rate is low. For patients with invasive GH adenomas, the incidence of postoperative complications and recurrence is also high.

Other clinical manifestations, such as headaches, visual loss, hypertension, diabetes mellitus, amenorrhea, and decreased libido, improved or normalized after surgery. Even if the tumor was not completely removed, these clinical characteristics would likely be improved. However, the results were also influenced by tumor size, tumor invasion, and preoperative GH levels.

Table 6

The relationship between postoperative relief and resection degree.

Resection degree	Total (n)	Effective number of cases (n)	Postoperative remission rate (%)	χ^2	*P*
Total resection	21	21	100%		
Subtotal resection	12	1	8.30%		
Sum	33	22		28.875	<.001

The postoperative remission rate of resection degree was statistically analyzed by using the method of the χ^2 test, and the difference was statistically significant ($P < .05$).

In 21 patients who underwent total tumor resection, postoperative GH levels and IGF-1 levels normalized, and clinical characteristics improved in all patients (100%, 21 of 21). However, for 12 patients who underwent subtotal resection, postoperative GH and IGF-1 levels were not normalized, and only part of the clinical symptoms had improved. Therefore, we should try to completely cut the tumor, which can enhance the cure rate and increase the patient's quality of life.

Complications included transient diabetes insipidus in 3 (9.1%) patients and postoperative transient CSF leakage in 2 (6.1%) patients. Some authors have reported the incidence of postoperative CSF leaks in 0 to 7% of cases.[16,28–31] The results are similar to those reported in this study. Moreover, 3 patients with transient diabetes insipidus and 2 patients with CSF leaks had normalized after treatment.

5. Conclusions

The results of this study demonstrated that tumor size, preoperative GH levels, and tumor invasion are independent factors that affect the therapeutic outcomes of patients postsurgery. In addition, the results suggested that tumors should be resected to the greatest degree possible and that serum GH levels of patients required monitoring for extended durations of time postsurgery to improve the remission rate and quality of life of patients. Finally, EETA may represent a primary treatment for patients with GH-secreting PAs who do not respond to medical or radiation therapy.

Author contributions

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References

[1] Aflorei ED, Korbonits M. Epidemiology and etiopathogenesis of pituitary adenomas. J Neurooncol 2014;117:379–94.
[2] Mete O, Lopes MB. Overview of the 2017 WHO classification of pituitary tumors. Endocr Pathol 2017;28:228–43.
[3] Arasho BD, Schaller B, Sandu N, et al. Gender-related differences in pituitary adenomas. Exp Clin Endocrinol Diabetes 2009;117:567–72.
[4] Schaller B. Gender-related differences in growth hormone-releasing pituitary adenomas. A clinicopathological study. Pituitary 2002;5:247–53.
[5] Cappabianca P, Cavallo LM, de Divitiis E. Endoscopic endonasal transsphenoidal surgery. Neurosurgery 2004;55:933–40.
[6] Bourdelot A, Coste J, Hazebroucq V, et al. Clinical, hormonal and magnetic resonance imaging (MRI) predictors of transsphenoidal surgery outcome in acromegaly. Eur J Endocrinol 2004;150:763–71.
[7] Hardy J. Transsphenoidal hypophysectomy. J Neurosurg 2007;107: 459–71.
[8] Krieger MD, Couldwell WT, Weiss MH. Assessment of long-term remission of acromegaly following surgery. J Neurosurg 2003;98:719–24.
[9] Melmed S, Jackson I, Kleinberg D, et al. Current treatment guidelines for acromegaly. J Clin Endocrinol Metab 1998;83:2646–52.
[10] Babu H, Ortega A, Nuno M, et al. Long-term endocrine outcomes following endoscopic endonasal transsphenoidal surgery for acromegaly and associated prognostic factors. Neurosurgery 2017;81:357–66.
[11] Hazer DB, Isik S, Berker D, et al. Treatment of acromegaly by endoscopic transsphenoidal surgery: surgical experience in 214 cases and cure rates according to current consensus criteria. J Neurosurg 2013;119:1467–77.
[12] Shimon I, Cohen ZR, Ram Z, et al. Transsphenoidal surgery for acromegaly: endocrinological follow-up of 98 patients. Neurosurgery 2001;48:1239–43.
[13] Kaltsas GA, Isidori AM, Florakis D, et al. Predictors of the outcome of surgical treatment in acromegaly and the value of the mean growth hormone day curve in assessing postoperative disease activity. J Clin Endocrinol Metab 2001;86:1645–52.
[14] Ahmed S, Elsheikh M, Stratton IM, et al. Outcome of transphenoidal surgery for acromegaly and its relationship to surgical experience. Clin Endocrinol (Oxf) 1999;50:561–7.
[15] Lissett CA, Peacey SR, Laing I, et al. The outcome of surgery for acromegaly: the need for a specialist pituitary surgeon for all types of growth hormone (GH) secreting adenoma. Clin Endocrinol (Oxf) 1998;49:653–7.
[16] Kreutzer J, Vance ML, Lopes MB, et al. Surgical management of GH-secreting pituitary adenomas: an outcome study using modern remission criteria. J Clin Endocrinol Metab 2001;86:4072–7.
[17] Knosp E, Steiner E, Kitz K, et al. Pituitary adenomas with invasion of the cavernous sinus space: a magnetic resonance imaging classification compared with surgical findings. Neurosurgery 1993;33:610–7.
[18] Shirvani M, Motiei-Langroudi R. Transsphenoidal surgery for growth hormone-secreting pituitary adenomas in 130 patients. World Neurosurg 2014;81:125–30.
[19] Nishioka H, Fukuhara N, Yamaguchi-Okada M, et al. Pitfalls in early biochemical evaluation after transsphenoidal surgery in patients with acromegaly. Endocr J 2017;64:1073–8.
[20] Leopoldo C, Leopoldo F, Santos A, et al. Long term follow-up of growth hormone-secreting pituitary adenomas submitted to endoscopic endonasal surgery. Arq Neuropsiquiatr 2017;75:301–6.
[21] Kristof RA, Grote A, Redel L, et al. The common consensus criteria have high predictive values for long-term postoperative acromegaly remission. Acta Neurochir (Wien) 2011;153:19–25.
[22] Takahashi JA, Shimatsu A, Nakao K, et al. Early postoperative indicators of late outcome in acromegalic patients. Clin Endocrinol (Oxf) 2004;60:366–74.
[23] Buchfelder M, Schlaffer SM, Zhao Y. The optimal surgical techniques for pituitary tumors. Best practice & research. Clin Endocrinol Metab 2019;33:101299.
[24] Jane JAJr, Starke RM, Elzoghby MA, et al. Endoscopic transsphenoidal surgery for acromegaly: remission using modern criteria, complications, and predictors of outcome. J Clin Endocrinol Metab 2011;96:2732–40.
[25] Nishioka H, Fukuhara N, Horiguchi K, et al. Aggressive transsphenoidal resection of tumors invading the cavernous sinus in patients with acromegaly: predictive factors, strategies, and outcomes. J Neurosurg 2014;121:505–10.
[26] Starke RM, Raper DM, Payne SC, et al. Endoscopic vs microsurgical transsphenoidal surgery for acromegaly: outcomes in a concurrent series of patients using modern criteria for remission. J Clin Endocrinol Metab 2013;98:3190–8.
[27] Hofstetter CP, Mannaa RH, Mubita L, et al. Endoscopic endonasal transsphenoidal surgery for growth hormone-secreting pituitary adenomas. Neurosurg Focus 2010;29:E6.
[28] De P, Rees DA, Davies N, et al. Transsphenoidal surgery for acromegaly in wales: results based on stringent criteria of remission. J Clin Endocrinol Metab 2003;88:3567–72.
[29] Ludecke DK, Abe T. Transsphenoidal microsurgery for newly diagnosed acromegaly: a personal view after more than 1,000 operations. Neuroendocrinology 2006;83:230–9.
[30] Abosch A, Tyrrell JB, Lamborn KR, et al. Transsphenoidal microsurgery for growth hormone-secreting pituitary adenomas: initial outcome and long-term results. J Clin Endocrinol Metab 1998;83:3411–8.
[31] Abbassioun K, Amirjamshidi M, Mehrazin A, et al. A prospective analysis of 151 cases of patients with acromegaly operated by one neurosurgeon: a follow-up of more than 23 years. Surg Neurol 2006;66: 26–31.