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Prognosis of pituitary adenomas in the early 1970s and today—Is there a benefit of modern surgical techniques and treatment modalities?

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ABSTRACT

Objective: Neurosurgical techniques for the treatment of sellar pathologies have been evolving continuously over the last decades. Additionally to the innovation of approaches and surgical techniques, this progress yielded to the application of modern intraoperative surgical tools as well as peri- and intraoperative imaging. Until now, no long-term analysis of the impact of new therapy concepts on the patient's outcome exists. Aim of this study was to analyse the impact of new operative approaches on perioperative mortality and morbidity as well as the long-term outcome after pituitary surgery.
Patients and methods: Three groups of patients were compared in this retrospective analysis of surgically treated pituitary adenomas between the years of 1963 and 2014. Group A contains 93 patients, treated between 1963–1980 with a mean follow-up of 12.1 years (±14.3 years), group B comprises 89 patients treated between 1990 and 2000 with a mean follow-up of 10.1 years (±8.1 years) and group C consists of 95 patients treated between 2011–2014 with a mean follow-up of 3.4 years (±1.9 years).
Results: The surgical treatment was performed significantly earlier today on smaller tumors with less preoperative complaints ($p < 0.01$). Panhypopituitarism was detected only in 9.5% of the cases in group C compared to 50.8% in group A ($p < 0.01$). Also, the incidence of revision surgery (5.6 vs. 2% vs 0%), postoperative hemorrhage (10.8% vs. 3.4% vs. 1%) and diabetes insipidus (34.4% vs. 11.2% vs. 5.2%) was decreased ($p < 0.01$). Moreover, a significant postoperative improvement of ophthalmological complaints was detected ($p < 0.001$).

The long-term follow-up showed 40% of the entire recurrence rate occurring after the ninth postoperative year. The progression-free survival time increased significantly from group A to group B ($p < 0.05$).
Conclusions: The results demonstrate a benefit of the recent developments of pituitary surgery in the short-term results as well as in the long-term outcome. The prognosis of pituitary adenoma patients could be improved by the introduction of new surgical approaches and techniques in the last decades. Also the perioperative morbidity and mortality rate has been reduced clearly since the 1970s. Furthermore our results emphasise the necessity of lifelong follow-up of all patients with successfully treated pituitary adenomas.

1. Introduction

The development of new diagnostic modalities, surgical techniques and treatment strategies has changed the concept of pituitary adenoma therapy over the last 30 years remarkably. The computer tomographic (CT) scanning introduced by Hounsfield in 1973 [2,24–26] and the magnetic resonance (MR) imaging in 1978 as described in detail by Doyle et al. in 1981 [17] represent the 'gold standard' methods for the diagnosis and follow up of intracranial tumors, in general. The use of the operating microscope has become a standard technique in most intracranial procedures since the 1960s [33,56]. The microsurgical transsphenoidal approach was investigated and established over almost a century of research [32]. It used to represent the "gold standard" for surgical treatment of sellar lesions in the neurosurgical field [1,11,19,23,34]. However, further developments of endoscopic techniques and its applications in neurosurgery influenced also transnasal approaches [8,20,39,40,45,50–53,57]. Continuous efforts to improve surgical techniques are still being made [3–7,12,30,31]. Many publications on endonasal endoscopic surgery stress the less invasive nature of this technique, [35,36,38,42,43] providing a wider field of view. Additionally, angled telescopes allow inspection of retrocarotid, intracavernous and suprasellar space [42].

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Although the mortality and morbidity rate in patients with gliomas [9,44], meningiomas [37] and in those with brain abscesses [49] has been reduced in the last decades due to modern neurosurgical interventions, evidence of better prognosis for patients with pituitary adenomas is still lacking.

To evaluate the influence of the new modern diagnostic tools as well as new modern surgical techniques and approaches on the prognosis of patients with pituitary adenomas, the authors analysed patients who had surgical therapy for pituitary adenomas at their clinic in the years between 1963 and 2014 retrospectively.

2. Material and methods

2.1. Patient population

We performed a retrospective analysis on selected 277 patients [133 women and 144 men] operated at the department of Neurosurgery, at Saarland University between 1963 and 2014. The average age of the overall patient population was 51.2 years [SD ± 13.9 years].

Three groups of patients were selected according to the time interval, in which they were treated: we selected a first group of patients (group A) who was treated in the time period from 1963 until 1980. This collective was surgically treated mostly via transcranial approaches. Additionally, CT imaging was introduced in 1985 and MRI in the early 1988s at the Saarland University clinic. In order to allow a direct comparison between the time period in which the treatment was performed without modern imaging methods and the time at which it was already available, we selected this group in comparison to the two following collectives: the second group of patients (group B) was treated in the time period from 1990 until 2000. These patients underwent mainly sublabial/transseptal microsurgical procedures. The last group of patients (group C) treated in the time period from 2011 until 2014 underwent purely endoscopic endonasal procedures.

Inclusion criteria consisted of a minimum patient age of 18 years, the diagnosis of a histologically proven pituitary adenoma and a complete health record of our department, including surgical report, histology, medical report and perioperative imaging after 1985. All patients with incomplete data were excluded.

The retrospective study was authorized by the ethical committee of medical association of the Saarland.

2.2. Tumor size

Pituitary adenomas were classified in microadenomas (diameter < 10 mm), macroadenomas (diameter ≥ 10 mm) and giant adenomas (diameter ≥ 40 mm) according to previous literature [15,21,22,28]. Thereby, the classification was based on preoperative imaging in group B and C and on the intraoperative finding and description of tumor size in the surgical report in group A.

2.3. Tumor extirpation

Gross total resection (GTR) of tumors was established on the basis of the operation report and of the postoperative imaging, if available (group A: n = 4, group B: n = 38, group C: n = 96). In cases of secreting adenomas a serologically proven normalization of the hypersecretion also needed to be evident according to the endocrinological definition at the assigned time.

2.4. Perioperative complications

Complications were analysed on the basis of the operation report, the medical report, the postoperative imaging and the follow up. Perioperative complications consisted in:

Epistaxis, meningitis, CSF fistula, amaurosis, postoperative hemorrhage, postoperative hydrocephalus, diabetes insipidus, postoperative panhypopituitarism and exitus letalis.

2.5. Follow-up

The patients were investigated in the neurosurgical outpatient clinic of the Saarland University either within routine follow-up appointments 4–6 months postoperatively and then on a yearly basis only, unless medical complaints appeared. Patients were mostly seen by an endocrinologist for medical treatment, or for regular serologic hormonal lab testing in cases of secreting adenomas, and for control of pituitary function.

Remission was defined by the normalization of the postoperative serum hormone levels (according to the definitions and the reference values of the lab as defined at the assigned time).

Recurrence was based upon evidence of tumorous tissue regrowth on CT or MRI imaging after previous GTR or increased hormonal serum levels in lab tests or occurrence of new clinical symptoms and resumption of treatment (resurgery or medical treatment), if no imaging was available in early decades.

Average follow-up time was 12.1 ± 9.3 years for group A, 10.1 ± 8.1 years for group B and 3.4 ± 1.9 years for group C (range 6 months–38 years).

Clinical data was obtained from the neurosurgical inpatient and postoperative follow-up records. Special attention was paid to tumor size, initial symptomatology, time period required for diagnosis, type of surgical method, extent of surgery, perioperative complications, endocrinological and ophthalmological outcome and tumor recurrence. Time of recurrence or time of death was obtained.

2.6. Statistics

The analysis of data was performed using SPSS, version 22, IBM Corporation, NY, US. The differences of the data of the two patient groups were compared using Whitney-U-Test, χ^2 -Test, Fisher's exact test. Survival curves were calculated by the life table (Kaplan-Meier) method to account for periods of follow up. Additionally, an uni- and multivariate cox-model analysis was performed. Significance level was set at $p < 0.05$.

3. Results

3.1. Overall results

A total of 93 patients met the inclusion criteria in group A (treated between 1963 and 1980), a total of 88 patients were included in group B (those treated between 1990 and 2000) and a total of 95 patients were included in group C (those treated between 2011 and 2014). In the first group, 52% (49/93) were of male and 48% (44/93) were of female gender. In the second group, 61% (54/88) were male and 39% (34/88) were female. In the third group, 42% (40/95) were male and 58% (55/95) were female.

The average age of the patients in group A was 46.4 years [SD ± 11.3 years], whereas in group B it was 53.7 years [SD ± 14.9 years] and in group C is was 51.3 years [SD ± 17.2 years]. There was no statistically significant difference between the age and gender distribution of these cohorts. Details see Table 1.

3.2. Tumor histology

In the group of adenomas diagnosed before the year of 1980, 67 cases were endocrine inactive pituitary macroadenomas and 26 adenomas were hormone-secreting (14 growth hormone, 10 prolactinomas, 1 TSH secreting, 1 STH/prolactin secreting). In