

Pituitary Surgery in Germany – Findings from the European Pituitary Adenoma Surgery Survey

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Key words

pituitary adenoma, pituitary surgery, survey

received 06.12.2022

revised 19.03.2023

accepted 23.03.2023

accepted manuscript online 23.03.2023

published online 12.05.2023

Bibliography

Exp Clin Endocrinol Diabetes 2023; 131: 362–366

DOI 10.1055/a-2061-1284

ISSN 0947-7349

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ABSTRACT

Background Surgery is, next to medical and radiation therapy, the mainstay therapy for pituitary adenomas. While scientific consensus regarding the key aspects of pituitary surgery exists among neurosurgeons, procedures are not standardized and might vary significantly between hospitals and surgeons.

Objective To provide an overview of how neurosurgical departments in Germany manage pituitary surgery.

Methods Responses from the European Pituitary Adenoma Surgery Survey were analyzed. The survey contained 60 questions regarding demographics, training, surgical and endocrinological aspects, and patient management.

Results Sixty neurosurgical centers from Germany responded to the survey. Among the centers, 35.3% (n = 18) exclusively use the microscopic and 31.1% (n = 14) the endoscopic technique; all other centers (n = 28) use both approaches. Of responding centers, 20% (n = 12) perform less than 10 transsphenoidal pituitary surgeries per year, and 1.7% (n = 1), more than 100 operations. The number of transcranial pituitary operations is significantly smaller, with 53.3% of centers performing only 0–2 per year, 35% performing 3–5, and only one center (1.7%) performing more than 15 transcranial operations per year. In 8 centers (13.3%), surgeries are always performed together with an ENT surgeon; in 29 centers (48.4%) ENT surgeons are never involved. In most centers (n = 54, 90%) intraoperative MRI is not available. Image guidance (with preoperative CT and/or MRI data) is used by 91.7% of respondents (n = 55). Forty-two centers (72.4%) routinely prescribe hydrocortisone after pituitary surgery, and 75% (n = 45) have pituitary board meetings with endocrinologists, radiologists, and radiosurgeons. Fifty-two (86.7%) respondents perform the first follow-up scan by MRI 3–4 months after surgery.

Conclusions The data showed differences as well as similarities between centers and could help to discuss the standardization of methods and the formation of networks and certification to improve patient care.

Introduction

Pituitary adenomas were first surgically approached transcranially at the end of the 19th century but the transsphenoidal approach was introduced at the beginning of the 20th century by Hermann Schloffer [1], and shortly afterwards, Oskar Hirsch described the endonasal technique [2]. With the introduction of antibiotics, cor-

tisone, and the microscope, complication rates dropped significantly, and the transsphenoidal approach became increasingly important for the treatment of pathologies of the sellar region.

The limits of the endonasal transsphenoidal approach have been significantly extended by the endoscope [3] and furthermore sophisticated techniques like nasoseptal flaps [4], neuronavigation

[5], intraoperative magnetic resonance imaging (MRI) [6] and the administration of intrathecal fluorescein [7] have been suggested and evaluated to improve the extent of resection and to reduce complication rates in recent years. While some colleagues reported the advantages of working in a multidisciplinary team together with ear-nose-throat (ENT) surgeons [8], others prefer to work exclusively with colleagues in their department. Most studies state that intrasellar lesions are removed equally effectively by endoscopic and microscopic techniques; however, some authors suggest that the endoscope offers advantages in treating pathologies with extra- and parasellar extensions [9].

Here, we present data analysis from an online Europe-wide European Pituitary Adenoma Surgery survey (EUPASS)[10–12] to obtain a detailed overview of the current practice of pituitary surgery among neurosurgical departments in Germany.

Material and Methods

The data presented were collected through EU-PASS, conducted between April 1st, 2019 and June 30th, 2019. For this survey, eligible departments of the 39 neurosurgical societies of the European Association of Neurosurgical Societies were either contacted by a study group member directly or via email to the department chairmen with an invitation to answer the questions of the online survey. The survey was created via a web-based platform (SurveyMonkey Inc., San Mateo, California, USA.) It consisted of 60 questions in three categories: 1) demographics, 2) adenoma types and treatment, and 3) techniques. For this manuscript, survey responses from Germany were converted into a dataset for further analysis.

Results

Demographics

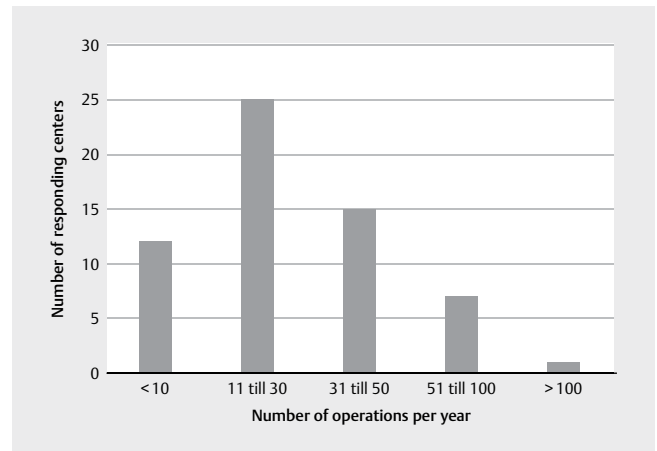
In total, 60 representatives of neurosurgical centers from Germany responded to the survey. Among these, 78.3% (n = 47) were academic centers and 21.7% (n = 13) were non-academic;

13.3% (n = 8) of respondents are working in centers in which annually, less than 1000 operations are performed, 16.7% (n = 10) in centers with 1000–1500 operations, 30% (n = 18) in centers with 1500–2000 operations, 5% (n = 3) in centers with 2000–3000 operations, and 10% (n = 6) in centers with more than 3000 operations are performed annually. ► **Fig. 1** shows the number of transsphenoidal pituitary surgeries per year. The number of transcranial pituitary operations was significantly smaller, with 53.3% (n = 32) reporting up to two cases per year, 35% (n = 21) between 3 and 5 cases, 6.7% (n = 4) between 6 and 9 cases, 3.3% (n = 2) between 10 to 15 cases and 1.7% (n = 1) with more than 15 transcranial operations per year.

The number of neurosurgeons performing transsphenoidal surgery in the responding centers was 1 in 23.3% (n = 14), 2 in 43.3% (n = 26), 3 in 20% (n = 12), 4 in 8.3% (n = 5), and 5 in 5% (n = 3) of the centers.

Training

At most centers (60%, n = 36), all residents assist in transsphenoidal surgeries, and only one respondent (1.7%) indicated that no



► **Fig 1** Number of transsphenoidal operations performed per year per center.

residents are involved in transsphenoidal surgeries. In the majority of centers (70%, n = 42), residents are not performing transsphenoidal surgeries under supervision during their training. In three centers (5%), 50% of residents, and in 14 centers (23.3%), 25% are trained in transsphenoidal surgeries. One center (1.7%) allows all residents to perform transsphenoidal surgeries under supervision.

Technical aspects

Among the centers, 35.3% (n = 18) exclusively use the microscopic and 31.1% (n = 14) use the endoscopic technique, while all other centers (n = 28) use both techniques and also microscopic endoscope-assisted transsphenoidal approaches. In eight centers (13.3%) surgeries are always performed in the presence of an ENT surgeon, while in 29 centers (48.4%), ENT surgeons are never involved.

The majority of respondents perform extended approaches either never (28.8%, n = 17) or only in 10% of cases (52.5%, n = 31). In most centers (n = 54, 90%), intraoperative MRI is not available. Image guidance (with preoperative CT and/or MRI data) is used by 91.7% of respondents (n = 55); 60% (n = 36) use it in all cases, and 31.7% (n = 19) use image guidance only in selected cases.

Endocrinological aspects

Forty-two centers (72.4%) routinely prescribe hydrocortisone after pituitary surgery; the other centers follow cortisol levels in the early postoperative period and would substitute an existing deficit. Prolactinomas are treated surgically, if necessary, at all centers; 87.9% (n = 51) reported operatively treating 1–5 cases per year, while 6.9% (n = 4) operate on 6–10 prolactinomas and 5.2% (n = 3) on 11–20 prolactinomas per year. In 25 centers (42.4%), surgery is considered the primary treatment modality for prolactinomas in selected cases (e. g., apoplexy, acute vision loss). For pretreatment of pituitary adenomas, which is usually led by the referring endocrinologist/endocrinological center, dopamine agonists are used by 25.8% (n = 15) of respondents. In the case of acromegaly, first-generation somatostatin analogs (lanreotide and octreotide) are used by 37.9% (n = 22), second-generation somatostatin analogs (pasireotide) by 24.1% (n = 14), and growth hormone receptor antago-

nists (pegvisomant) are used by 13.8% ($n = 8$) of respondents; 23 (39.7%) do not use medication for pretreatment.

Management

Regular pituitary board meetings with endocrinologists, radiologists, and radiosurgeons are conducted by 16.7% ($n = 10$) of the centers once a week, 15% ($n = 9$) once a month, 43.3% ($n = 26$) conduct the meetings sporadically, and 25% ($n = 15$) never. Within the first 1–3 postoperative days, early MRI is performed routinely by 20% ($n = 12$) in all cases and by 50% ($n = 30$) in selected cases only. In cases of nonfunctioning adenoma remnants after surgery on the first follow-up MRI, 57 respondents (96.6%) underwent a watch-and-wait strategy for the patient. Using MRI, 71.2% ($n = 42$) of the centers assess anosmia; among these, 39% ($n = 23$) use MRI routinely, and 32.2% ($n = 19$) in selected cases. Nasal morbidity is assessed by 76.7% ($n = 46$) of the centers either through a clinical examination by themselves (38.3%, $n = 23$), by an ENT-doctor (35%, $n = 21$) or in combination with quality-of-life (QOL) questionnaires (3.3%, $n = 2$). 52 (86.7%) respondents perform the first follow-up scan by MRI 3–4 months after surgery. 93.3% of respondents ($n = 56$) follow up with their patients personally.

Discussion

With 60 centers responding to the questionnaire, to our knowledge, this is the largest survey on pituitary surgery in Germany, so far. The findings reveal that the caseload varies significantly, with the majority of centers (61.7%, $n = 37$) performing less than 31 transsphenoidal cases per year. The cases are shared between one (23.3%/ $n = 14$) or two (43.3%/ $n = 26$) surgeons in most centers. The debate continues on how many cases a center should treat per year to gain enough experience to offer sufficient care. While some advocate the creation of centers of excellence to centralize treatment, others argue that widespread expertise is needed to cover local demands. Another important parameter is the number of surgeons who perform pituitary surgery, as 13.3% of centers reported that 4 or 5 surgeons share the caseload, which might lead to a relatively low caseload per surgeon.

As a center, which annually operates approximately 60 pituitary adenomas per surgeon endoscopically, we believe that a certain caseload is necessary to enable the relevant learning process and create an interdisciplinary network to address the different aspects of this complex clinical condition. A certain level of experience with simpler cases is required to be able to address challenging cases with supra- and para-sellar extensions and use extended approaches. Several authors have shown the correlation between experience and complications [13]. So far, there is no consensus on how many cases per year are sufficient, and numbers between 25 [14] and 100 [15] cases per center or 50 cases [15] per surgeon are proposed.

Most centers only offer limited training in pituitary surgery for their residents, with 40% ($n = 24$) not allowing all of their residents to assist in transsphenoidal approaches and 70% ($n = 42$) not allowing surgical training under supervision. While education is a key area for defining a center of excellence [16], this also highlights the need for special programs and fellowships to allow neurosurgeons

with interest in pituitary surgery to receive adequate training to practice independently.

Of the responding centers in Germany, 35.3% ($n = 18$) exclusively use the microscopic technique. As both techniques are safe and effective in removing pituitary adenomas, the advantages of each technique have to be considered. While the microscopic technique reportedly has shorter operation times and overall lower costs [17], the advantages of the endoscopic technique are discussed less uniformly. While some authors suggest that the endoscopic technique improves the extent of resection and reduces secondary treatments [17], results from a national database suggest similar rates of gross total resection and the need for adjuvant therapy [18].

Nevertheless, there is a worldwide trend towards endoscopic surgery, and while 31.1% ($n = 14$) of centers in Germany exclusively use the endoscopic technique, the majority ($n = 28$) implemented the microscopic and the endoscopic technique. These findings are comparable to the results from the European survey in which 56.8% reported using the endoscopic approach [10].

In recent years, the limits of the endonasal transsphenoidal route have been expanded, especially with the use of the endoscope. While in the beginning, almost exclusively small pituitary adenomas were resected, the approach has been used to successfully resect giant adenomas [19], craniopharyngiomas [20], and meningiomas of the anterior skull base [21] as well as pathologies extending into the maxilla and dens axis [22]. Although the results have been reported as promising, the learning curve is often flat [23], and suitable cases are rare, so it might be challenging to establish extended approaches even in centers with a high caseload. This is reflected in the results: Most centers in Germany reported either never (28.8%; $n = 17$) performing extended approaches for pituitary adenomas or only in less than 50% of cases (71.2%, $n = 42$).

If the approach is extended, the risk of cerebrospinal fluid (CSF) leak increases, and advanced closure techniques are necessary to keep complication rates low.

In regular cases (without extended approaches), the majority of respondents use multilayer techniques with some combination of fat, tissue glue, bone, and collagen sponges or dural substitutes. Only 10% ($n = 6$) of centers reported no closure of the sella if no intraoperative CSF leak was detected. Some authors have described the possibility of using intrathecal fluorescein to detect intraoperative CSF leaks [7, 24]. Fluorescein in pituitary surgery is not commonly used in Germany, and none of the centers reported using it. This result is in accordance with the results from other European centers, of which only two reported the use of fluorescein [10]. While a lumbar drain might reduce the risk of postoperative CSF leak, its routine placement is still discussed controversially due to associated complications and unclear effectiveness [25]. In case of an intraoperative CSF leak, the use of lumbar drainage varies between centers in Germany. Similar differences exist in the duration of lumbar drainage and whether it is combined with strict bed rest or not. Most respondents (63.8%) leave the drain for 4–5 days and keep the patients immobilized during that time (55%), and this must be evaluated critically, as recent publications came to the conclusion that LD does not provide significant advantages in the

treatment of CSF leaks [26], whereas prolonged immobilization poses a significant risk for thromboembolic complications. In accordance with other European countries [10], the use of intraoperative MRI and CT is only reported by a minority of centers (10%) in Germany. Although intraoperative MRI is available in only a few centers its use in pituitary surgery, especially in small adenomas is controversial. Image guidance, on the other hand, is used by the majority (91.7%) of respondents. 60% (n = 36) use it in all cases, which might be due to the wide availability of this technique and the fact that it is established and does not require a lot of time for set up.

There exists a consensus between large centers in Germany to perform MRI scans routinely after 3 months as the interpretation of earlier scans is often poor due to blood and hemostyptic products; therefore, many respondents (50%) perform early MRI only in selected cases. This attitude towards postoperative MRI exists throughout Europe [10].

Endonasal complications are most likely underreported and occur more frequently in cases with extensive damage to the mucosa (nasoseptal flaps, resection of the middle turbinate, binostril approaches). Nasal morbidity is assessed by 76.7% (n = 46), but the use of standardized quality-of-life questionnaires is relatively low, and only two respondents (3.3%) use them. Especially for research purposes, questionnaires like the sino-nasal outcome test (SNOT-22) might improve the comparability of different series.

Conclusion

Technical aspects of pituitary surgery vary between German centers. The data presented can help to lead to constructive debate about current clinical practice in Germany and support the effort to improve patient care by the formation of networks and certification.

Conflict of Interest

The authors declare that they have no conflict of interest.

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