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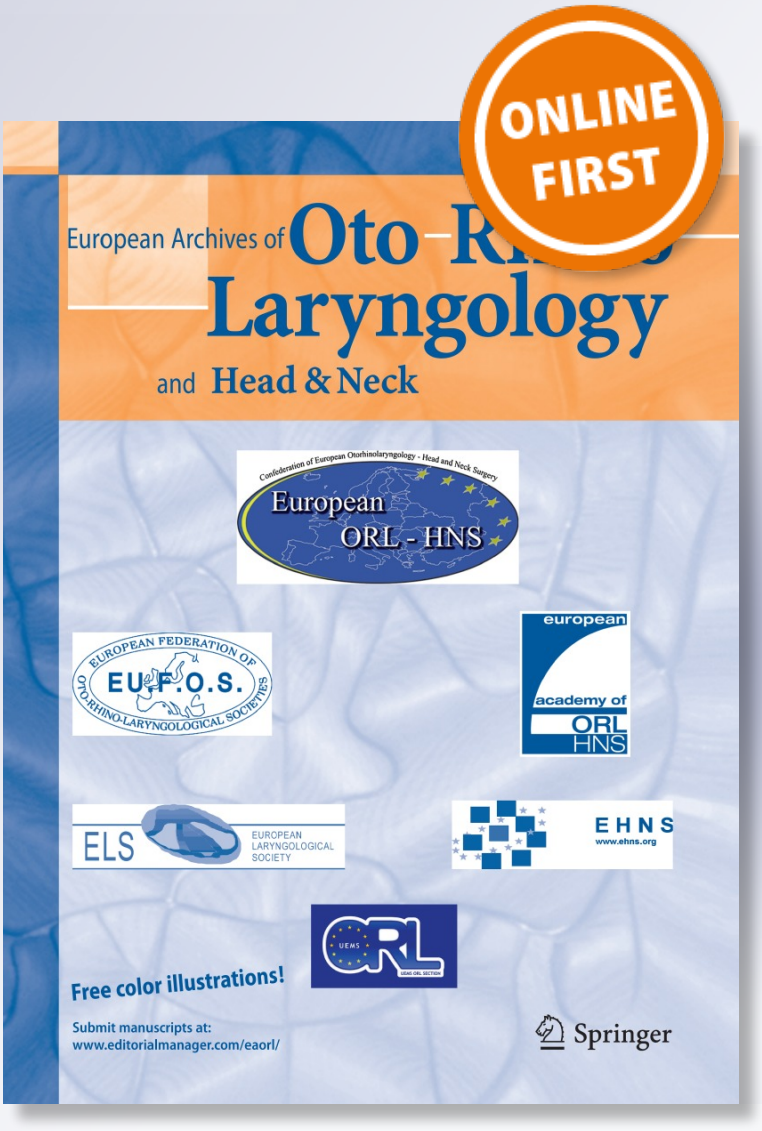

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RHINOLOGY

Initial experiences with endoscopic rhino-neurosurgery in Amsterdam

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Abstract Endoscopic surgery of the skull base has been on the rise for several years. Endoscopic access for surgery can be achieved from the frontal sinus anteriorly along the skull base to the odontoid process posterior inferiorly. An endoscope is inserted through one nasal corridor and allows visualization of the working field and up to three surgical instruments can be used to address the lesion. This is called the "two nostrils–four hands technique". This is a retrospective study of 67 cases. Setting of the study is an Amsterdam University hospital. Cases were identified in the department of otorhinolaryngology and department of neurosurgery database. All patients operated between 1 January, 2008 and 1 February, 2012 with pituitary tumours that extend beyond the sella, sinonasal tumours and all non-pituitary skull-base tumours were included. Mean tumour diameter was 3.8 cm. We performed a near-to-gross total resection in 92 % of cases where we intended to perform a total resection. The most frequent complication was CSF leakage. This study demonstrates that this technique is safe and reliable. What is needed is a dedicated team, which includes a dedicated anesthesiologist, endocrinologist, ophthalmologist, and radiation oncologist.

Keywords Endoscopy · Skull base · Minimal invasive surgery

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Introduction

Endoscopic nasal and sinus surgery has been performed since the 1970s, initially for chronic sinusitis, but with advances in technique and equipment, also for removal of tumors and treatment of cerebrospinal leaks [1]. Around the same time Apuzzo, Bushe and Halves popularized the use of the endoscope as an adjunct in transsphenoidal surgery of the pituitary [2–4].

Jankowski and his team were the first to describe a purely endoscopic endonasal technique for operating on the pituitary gland, successfully operating on three patients [1]. Purely endoscopic endonasal surgery was consequently developed in various countries with the notable contribution of Jho and Carrau in the USA and de Divitiis & Cappabianca in Italy, developing new instruments and techniques while also starting to include tumors beyond the boundaries of the sellar region [5]. Nowadays the skull base is accessible from the frontal sinus to the foramen magnum, while removing the anterior arch of the atlas even allows for access to the odontoid process [6]. These approaches have been named expanded endoscopic endonasal approach, or maybe more appropriately endoscopic rhino-neurosurgery (ERN) [7].

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Endoscopic surgery offers a panoramic vision with a better view of the sella and surrounding structures and avoiding the need for brain retraction. Patient comfort is increased as there is no visible scarring and one can avoid the use of a transsphenoidal retractor and postoperative nasal packing. Complication rates, as well as resection rates appear to be comparable to conventional techniques [9–11].

As surgeons are getting more familiarized with this relatively novel technique and specialized instruments are developed, surgical indications are widened and more lesions are being treated with ERN [8, 12–15].

In our institution, otorhinolaryngology and neurosurgeons have a tradition of operating pituitary tumors transsphenoidally together, while since 2001 all pituitary tumors were fully endoscopically treated. With increased experience and training we started using the extended two nostrils—four hand approaches, initially for macro-adenomas and subsequently also for other skull base lesions. We have used this method for both rhinological, as well as for neurosurgical pathology. In this article we present our initial experiences with this technique. We report resection rates, clinical, visual, endocrinological and neurological outcome and complications.

Methods

Charts from all patients treated endoscopically with skull base pathology by otorhinolaryngology and/or neurosurgery between January 2008 and February 2012 were retrospectively reviewed. All patients with pituitary tumors that extend beyond the sella, sinonasal tumors and all non-pituitary skull-base tumours were included. Data on patient demographics, symptoms and signs, pre- and postoperative imaging, surgical approach, peri- and postoperative complications, and time until discharge were collected. If there was no reference of a certain symptom in the chart, the patient was assumed not to have that symptom. Patients were excluded if no follow-up data were found in patient charts or if no postopimaging was available.

Surgical procedure

We employ the "two nostrils–four hands technique". This technique is performed by two surgeons: an otolaryngologist and a neurosurgeon working simultaneously. This technique allows the surgeon to perform a bimanual dissection while the colleague holds the endoscope, moving it dynamically to improve visualization. Lumbar drainage was not routinely performed peri-operative.

Surgical technique has been described extensively elsewhere [8]. In short, the patient was placed in a supine position, with the head turned slightly towards the surgeon. Cocaine was used to vasoconstrict and shrinks the nasal mucosa. We used both Brainlab and Medtronic for registration of neuronavigation. When indicated, a part of the upper leg was draped for possible fascia lata and fat graft harvesting. Entering the nostril, the inferior as well as the middle turbinate were lateralized and mostly preserved [16]. If required, the middle turbinate was amputated in one side, to provide more space. Approach and amount of bony resection were tailored for each patient and pathology. In more recent cases, a mucoseptal flap was (partially) prepared in advance when indicated [17]. In selected cases of olfactory groove pathology we opted for a transcribiform approach, a so-called DRAF III procedure [18]. Tumour removal varied for different pathologies and is described in detail elsewhere [19–26]. We chose our closure by a graded system, devised by Esposito et al. [27]. If no mucoseptal flap was needed, it was replaced on the nasal septum. Initial CSF-leak rates were still too high when singly relied on the mucoseptal flap. Since we started using a multilayer technique, leakage has become a rarity. For large skull base defects, with open access to the cisterns, we now use a fat plug, fascia lata, a dura scaffold, and the mucoseptal flap. We support the flap with jelonet gauze instead of the balloon of the foley catheter. Two days bed rest without lumbar drainage is sufficient to get excellent closure results.

Outcome

Tumor size was calculated on the basis of preoperative MRI findings. Maximum diameter was measured manually and extension to various parts of the skull base was noted.

Gross total tumor resection was defined as 100 % macroscopic removal of the tumor mass, confirmed with postoperative imaging. Near-total resection was defined as <100 % removal, but ≥ 90 % and partial resection was defined as <90 % removal. Most patients received an MRI immediately postoperatively where the extent of removal was calculated; alternatively an MRI was performed at least 3 months postoperatively to avoid artifacts.

To determine visual outcome data from opthalmological examinations were collected. If no such examinations were available (i.e. if a patient had their ophthalmological follow-up in another hospital) patients charts were reviewed for subjective patient experience.

Neurological and endocrinological outcomes were determined by examining patient's charts.

Results

Patient characteristics

In the period of 2008–2012, 67 patients were operated using the expanded endoscopic endonasal approach. Three

patients were excluded because there was no follow-up imaging or data available in two cases, their operation had been too recent and no follow-up imaging had been made yet. One patient experienced complications, which did not allow her to undergo a follow-up MRI. We describe her case in the 'complications' section. Almost half of the patients were male (48 %) and the mean age at diagnosis was 49 years (range 4–77 years, SD 18.4).

Eleven patients presented with recurrent disease; three patients had undergone prior surgeries for meningiomas. Three patients had been treated medically with dopamineantagonist for prolactinomas. Two of these had also had previous surgery. Two patients had had prior surgery for null-cell adenomas. One patient had a tumor of the cerebellopontine angle which had been decompressed 10 years prior. One patient had a recurrence of an inverted papilloma that had transformed to a squamous cell carcinoma. One patient had had three previous operations for a recurring craniopharyngioma. One patient, a 6-year-old boy with an intranasal rhabdomyosarcoma had been treated with polychemotherapy and radiotherapy 2 years prior.

Symptoms

Median duration of symptoms before presentation was 8 months (interquartile range 26). Visual deterioration, visual field deficits, decreased visual acuity or both, was the most common presenting symptom (60.9 %).

Lesions

Mean tumor diameter was 3.8 cm (SD 4.9).

In total, 39 (60.9 %) tumors caused compression of the optic chiasm, 29 (45.3 %) extended to the sphenoid plane, 18 (28.1 %) extended to the prepontine region. Cavernous sinus involvement, unilateral or bilateral, was observed in 23 (35.9 %) of cases.

Therapy

In this series, 46 operations were performed by senior authors WvF and CG, 10 operations were performed by WvF and a different otolaryngologist, 3 operations were performed by CG and a different neurosurgeon, 4 by CG and another otolaryngologist and 1 operation was performed by a different otolaryngologist and a different neurosurgeon.

Median hospital stay was 8 days (interquartile range: 9).

Evaluation of postoperative MRI images showed gross-total resection in 28 cases (43.8 %), near-total resection was achieved in another 18 cases (28.1 %) and a subtotal resection was performed in 18 cases (28.1 %). However, complete resection was only intended in 50 operations, resulting in a near-to-gross total resection rate of 92.0 %. In three cases the intra-operative decision was made not to attempt a complete resection, because residual tumor was in a difficult location, which would increase the risk of intra-operative complications.

In only one case we attempted a complete resection, but had the postoperative MRI unexpectedly show residual tumor.

Intra-operative bleeding was observed in 17 cases (26.6 %). In 16 cases, it was venous in nature and easily stopped using Floseal or tamponnade and coagulation. In one case it concerned an arterial bleeding, this was a patient with an aggressive tumour of unknown pathology. Since the bleeding was hindering the operation, we decided to do a partial resection and, if the tumour turned out to be malignant, perform a second operation via a transbasal approach.

One patient experienced a postoperative hemorrhage (from the superior intercavernous sinus) that required emergency surgery; this resulted in a palsy of the oculomotor nerve, which had resolved completely at the time of follow-up. Another patient had a tumour recurrence after a complete resection of an intrasellar meningioma, but since he did not experience any symptoms and the lesion was very small, we decided to adopt a "wait and scan" policy.

Thirteen patients underwent postoperative radiation therapy. Three patients had a clival chordoma, and there were three cases of olfactory neuroblastoma. One patient had a rhabdomyosarcoma and one a large chondrosarcoma. One patient had a GH secreting macroadenoma and had undergone a near-total resection that resolved her visual deficits completely, but unfortunately she still suffered from headaches and hormonal hypersecretion, and therefore a small residue in the cavernous sinous was treated with radiation. Two patients were referred for prophylactic radiotherapy of residual tumor. One patient had a prepontine meningioma, compression of the brainstem was effectively treated surgically and residual tumor was radiated to prevent regrowth. The other patient had an adenoma residue encasing the left carotid and middle cerebral artery.

Postoperative ICU admission was necessary in nine patients: five of these were pediatric cases, for which postoperative ICU is mandatory in our clinic. One patient remained intubated for one night because of fear for laryngeal swelling after a difficult intubation. One patient, a 70-year-old lady, was admitted for 1 day because of impending respiratory failure. One patient was slow to regain consciousness after surgery without any complications on CT scan. One patient had to be admitted to the ICU for 7 days. She was a 41-year-old woman with a history of schizoaffective disorder and nephrogenic diabetes insipidus brought on by lithium. Following resection of the craniopharyngioma she developed severe

hypernatriemia, probably as a result of a combination of central and nephrogenic diabetes insipidus. Mean ICU admission time for these four patients was 2.5 days.

Endocrinology

Twenty-one patients presented with endocrinological deficits: six patients had disturbances in one axis; five patients had disturbances in two axes, four patients experienced disturbances in three axes, two patients in four, and four presented with panhypopituitarism. Thirteen patients experienced transient postoperative diabetes insipidus, which was treated with DDAVP. One patient experienced transient SIADH. Nine of these 21 patients (42.8 %) experienced new pituitary dysfunction postoperatively. Two patients (9.5 %) experienced postoperative improvement.

Of 35 patients without preoperative endocrinological disturbances, 6 (18.2 %) experienced persisting postoperative pituitary dysfunction that was still present during follow up. The most common new pituitary deficit was diabetes insipidus.

Vision

Visual deterioration was the most common presenting symptom, and also the most important indication for surgery. Three patients presented without initial visual complaints, but at ophtalmological examination were proven to have visual deficits. Visual field deficits were observed most frequently. Of 25 patients without preoperative visual symptoms, one patient showed to have new visual field deficits at follow-up. Out of 39 patients with preoperative visual symptoms, 2 patients (5.1 %) experienced postoperative worsening of visual functions, 3 patients' (7.6 %) deficits remained stable, 32 patients' (87.1 %) visual functions had improved and 2 patients experienced a complete recovery Table 1.

Neurological deficits

Preoperative cranial nerve deficits other than optic nerve pathology were present in nine cases, (Table 2). One patient had direct postoperative improvement; none experienced worsening of their symptoms. Two patients, who had not exhibited cranial nerve deficits preoperatively, did suffer from cranial nerve palsy (III and VI respectively) immediately after surgery, which had resolved almost completely at follow-up. At follow-up, of nine patients who had exhibited non-optic cranial nerve deficits, three had resolved completely, two experienced improvement and four remained unchanged.

One patient presented with frontal syndrome, which at follow-up had resolved completely.

One patient had a large clival meningioma, which compressed the brainstem, and she suffered from left-sided hemiparesis. She experienced a period of tetraplegia in the immediate postoperative period, CT scan showed a small location of recent ischemia in the pons. During her hospital stay her condition improved to a hemiparesis. After discharge, she was admitted for rehabilitation in an inpatient setting for 6 months, after which she was able to return home. At follow-up she was walking without a walking aid, and her cranial nerve deficits had resolved completely.

Complications

Postoperative CSF leakage was the most frequent complication; surgical intervention for CSF leakage was needed in ten cases (15.6 %). However, one must take into account the learning curve involved in this type of surgery. In the past year (22 cases), we observed only one case of CSF leakage that required surgical intervention (4.5 %).

Meningitis was observed in three cases (4.7 %), in two other cases patients were treated with antibiotics without a definitive diagnosis of meningitis. One patient presented with severe meningitis 12 days after discharge, with an impaired consciousness and neck-stiffness and had to be admitted to the ICU for 3 days.

One patient suffered from apoplexia during anesthesia induction prior to surgery. This patient had a GH-producing macroadenoma, encasing the carotid artery. Prior to surgery, the patient had an angiogram while under anesthesia, to assess the possibility to sacrifice this carotid. At the start of the angiogram she had a dilated pupil. Subsequent CT scan showed hemorrhage in the tumor, and the operation proceeded as scheduled. Her N. III paresis had resolved completely at follow-up.

In one case we placed a lumbar drain peri-operatively. Unfortunately, this drain was left to drain 100 cc in the first postoperative hour. CT scan showed intracranial air and a subdural hygroma. Postoperative, she suffered from frontal syndrome with apathy and bradyphrenia. This patient was readmitted several months later for shunt placement because of hydrocephalus, which improved of her symptoms, but unfortunately she was unable to return home and now resides at a nursing home.

Two patients who suffered from anosmia postoperatively still had a reduced sense of smell 6 months after surgery. One patient is scheduled to undergo a new operation for synechiae and one patient developed epistaxis in the postoperative period for which exploratory surgery was needed.

Table 1 Patiënt characteristics

Pathology		Visual deficits		Endocrinological deficits		Cranial nerve deficits		Other symptoms	
Macroadenoma	37.5 %	Visual field defect	37.5 %	M. cushing	1.6 %	N.III	6.3 %	Headache	30 %
Meningioma	26.6 %	Visual impairment	42.2 %	Hyperprolactinemia	6.3 %	N. V	1.6 %	Diplopia	15.6 %
Chordoma	4.7 %	None	39.1 %	Acromegaly	3.1 %	N.VI	6.3 %	Hemiparesis	4.7 %
Craniopharynogioma	7.8 %			GH deficiency	6.3 %	N.VII	3.1 %	Cognitive impairment	4.7 %
Rathke's cleft cyst	4.7 %			Hypogonadism	15.1 %	N.VIII	1.6 %	Changed nasal passage	3.1 %
Chondrosarcoma	3.15			Hypocortisolism	6.3 %	N.IX	1.6 %	Difficulty swallowing	3.1 %
Esthesioneuroblastoma	3.1 %			Panhypopituarism	6.3 %	N.X	3.1 %	Epistaxis	3.1 %
Other	12.5 %			Hypothyroidism	15.1 %	N.XII	1.6 %	Vertigo	3.1 %
				Hyperthyroidism	1.6 %			Anosmia	3.1 %
								Hoarseness	3.1 %
				None	60.9 %			Frontal syndrome	1.6 %
								Nausea	1.6 %
								Rhinorrhea	1.6 %
								Urinary incontinence	1.6 %

Table 2 Patients with cranial nerve deficits

	Pathology	Location	Preoperative cranial nerve deficit.	Preoperative symptom	Postoperative deficits	Deficits at follow-up
M/30 yrs	Chondrosarcoma	Pituitary	N. III	Ptosis	Stable	Stable
F/10 yrs	Chordoma	Clivus	N.VI	Diplopia, nausea, vomiting, hemiparesis	Stable	Completely resolved
F/71 yrs	Meningioma	Clivus	N. VII and N. X	Hoarseness, facial palsy, hemiparesis	Worsened	Improved
M/50 yrs	Adenoma	Pituitary	N.III	Diplopia	Unchanged	Unchanged
M/34 yrs	Chordoma	Clivus	N.V and N.VI	Diplopia, facial hypesthesia	Improved	Improved
M/47	Meningioma	Sella	N.III & N. VI	Diplopia,	Improved	Improved
M/57	Adenoma	Pituitary	N. VI	Headache, diplopia	Improved	Complete recovery
F/33	Epidermoid	Petrous bone	N. V	Diminished facial sensitivity	Unchanged	Improved
F/67yrs	Chordoma	Clivus	N. III, VII, VIII, IX, X, XII	Diplopia, facial palsy, hoarse voice, difficulty swallowing, vertigo	Improved	Improved

Discussion

In this series of our initial 64 patients, the safety of the extended endonasal endoscopic approach for the resection of skull-base tumors is demonstrated.

With growing experience—and confidence—we were able to expand the range of our operations and now have operated the entire skull-base via the endonasal route. We have yielded similar rates of near-to-gross total resection, complications and postoperative outcome rates as found in literature [8, 21–23, 28–33].

The advantages of ERN have been described extensively [34–36]. The most direct pathway, panoramic view that cannot be attained with transcranial or endonasal microscopic approaches, no visible scarring and last, but certainly not least: no need for retraction of neurovascular

structures. Disadvantages of this approach are increased risk of CSF leak, a small surgical field and a decreased ability to cope with intra-operative hemorrhage.

At this moment there is no proof whether resection of pituitary tumors is better than microscopic resection, though there are some indications it may provide better visual outcome where it concerns tuberculum sellae meningiomas.

Our learning curve was largely a practical one. All surgeons were skilled in working with an endoscope, but the two nostrils–four hands technique requires the surgeons to work with multiple tools in a small space. In our first cases our experience in working solo was actually a minor hindrance because each surgeon has his own 'modus operandi'. As we got more and more acquainted with each other's modus operandi we were able to predict each other's moves and anticipate where to move, look, etc.

Where "sword fighting" with endoscopic instruments was common in the early stages of our experience with ERN, we now enjoy the benefits of having a colleague handling the endoscope, providing dynamic vision and being able to employ another surgical instrument when needed [37]. This relative disadvantage of having a small working space can be overcome by adequate bony resection. In the two nostrils–four hands technique, this is usually performed by the otorhinolaryngologist whereas the intracranial resection of the tumor is performed by the neurosurgeon. But when the occasion calls for it, it can be necessary for them to switch roles.

For closure, we use the vascularised nasoseptal flap described by Hadad-Bassagasteguy [17]. Over the years we have also incorporated the intra-operative grading system devised by Esposito et al. [27]. Application of this system allows for a better-tailored closure and better assessment of the risk of delayed CSF leaks.

For grade 0 leaks we do not use the nasoseptal flap, it is replaced on the nasal septum.

For grade 1 leaks we used to apply a dura scaffold supported by tissue glue. However, because of some late post-operative CSF leakages, we have started to also close Grade 1 leaks with a mucoseptal flap. For Grade 1, no other layers are needed.

For grade 2–3 leaks we use a fascia lata and fat graft with an onlay nasoseptal flap. We support the flap with dissolvable spongostan glued with tissuecol and cover it with antibiotic-impregnated vaseline gauze. For grade 3 leaks, we also insert merocel tampons in both nasal cavities and instruct the patient to stay in bed for 4–5 days.

What we found to be crucial for the multilayered closure technique is lowering the anterior wall of the sphenoid sinus to the level of its floor, so that the flap can be directly layered.

Postoperative CSF leakage is a common and dangerous complication. Our experience is that conservative measures are usually sufficient to reduce intracranial pressure to let the flap heal and close the leak. Lumbar drains are a potential entry port for infections and, as we have illustrated, can have even more serious complications, which is why we do not routinely use them. However, lumbar drains are useful when these conservative measures are insufficient. If lumbar drains are placed, they must be placed by experienced neurosurgical personnel. They must be managed by trained staff and the patient must be instructed to follow strict orders about pressure-increasing moments and the necessity to stay in bed. Obviously, the patient must be capable of understanding and following these orders.

In this series, we performed a near- to gross-total resection in 50 % of cases with Cavernous Sinus invasion. This is in accordance with results by other authors' reports [38–41]. Complete tumor removal in the case of Cavernous Sinus invasion is complex because of its complex anatomical structure. The relative high frequency of Cavernous Sinus tumor residual is also partly due to our learning curve and will likely be lower in subsequent series.

We started resecting the tumour invading the cavernous sinus after experience of over 400 pituitary cases, of which more than 100 with the current team. Particularly the innovative hemostatic agents, flowseal (Baxter) or Surgiflo (J&J), allow for excellent and rapid hemostatis, even with brisk venous bleeding from the cavernous sinus. We routinely use these new hemostatic agents to create a dry surgical field, which improves visual recognition of tumour remnants and therefore radicality [42].

Cavernous sinus tumour surgery is today rarely indicated. Stereotactic radiation is a safer alternative, with proven efficacy [43]. The main exception is for hormone producing pituitary tumors; in case of cavernous sinus invasion resection of this part can be the difference between cure and persisting disease [44].

Cavernous sinus invasion is commonly in the posterior, inferior segment of the medial wall of the cavernous sinus. Tumor resection is done with blunt, hooked curretes and low intensity suction. Venous bleeding typically indicates removal of cavernous sinus tumor.

As for resection marges: operating such benign tumors is an issue of judgment, even more than an issue of skill. As we say to all our patients "we can always completely remove the tumor—what varies is the price one has to pay for it". And sometimes the price is too high. We have not have had any devastating complications until now, and we feel that this is the result not only of skill or ability, but also of correctly balancing the risks and benefits. Normally speaking, resection margins are not required in benign tumors—complete resection is enough. In the case of meningiomata, one has always to look out for the tail

sign—and remove the part of the dura that seems to be involved, if possible. Meningeoma resection is graded according to Simpson, with grade 1 indicating total removal, including removal of the dura from which the tumor originated. Endoscopic transnasal resection of meningeomas allows much better for Simpson grade 1 tumor removal, than traditional approaches, since the affected skull base is completely removed. Recurrence due to inadequate tumor margin has not yet occured, but follow up is relatively short.

Finally, we would like to share some notable characteristics about some of the most common tumors in the region. As is common with meningioma surgery, first debulk the tumor, than sharp dissect it from vital structures. Almost always an arachnoidal plane will be present between tumor and structures, which helps with the tumor removal. Arachnoidea is part of the patient, not of the tumor. Always try to drill more anteriorly in cases of tuberculum sellae meningioma, as the anterior extension of the tumor (dural tail) is always further than one would imagine.

While most pituitary adenomas are soft, one should always look out for the harder to remove tumors; firm pituitary tumors can be a real challenge, because the risk of optic nerve damage is real. Sometimes a CUSA, or similar power tool, can help to centrally decompress these firm tumors. Partial resection may be the safest strategy.

In cases of clival chordomas, complete removal is almost always impossible; however, one should aim for subtotal excision, to be followed by proton bean therapy. Calcifications in a chordoma on a CT may be an indicator of fibrous, difficult to remove tumor—and should prepare the surgeon for a case harder than normal to remove.

Craniopharyngeomas are among the hardest to resect tumors. The tumor can be large, have multiple lobular extensions, and may have an invasive growth pattern at the level of the thalamus. Again, calcification can make tumor resection particularly difficult. We use the CUSA to fragmentize the harder tumor parts, followed by piece meal removal. Pulling of tumor outside field of vision is strongly dissuaded; small arteries may be attached to tumor capsule, which may not withstand pulling. If enlarging of bony opening is not an option, leaving tumor behind may be the best strategy.

With resection rates, postoperative outcomes and complications similar to those reported in literature, this report—in addition to adding to the growing body of literature on endoscopic endonasal skull base surgery—shows that midline skull base surgery can be mastered almost in its entirety by "endoscopic skull-base surgeons". Other reports have shown that endoscopic reoperations can be performed without additional morbidity, because the nasal corridor is typically well preserved aside from occasional synechiae formation [8, 13].

What is critical for safe and successful ERN are a number of things. First of all a dedicated team with appropriate training and experience is essential. In our series every patient was operated by both an otorhinolaryngologist and neurosurgeon simultaneously. Although having two surgeons operate at the same time is costly, we believe the specialties are complementary in this procedure and having the benefit of input from both sides has been a contributing factor in the safety and success of our initial series. Other team members include a dedicated anesthesiologist, endocrinologist, ophthalmologist, and radiation oncologist. The case load of our center allowed us to get experienced in a relative limited number of years. We now do over 70 ERN cases per year, of which a third is for non-pituitary cases, with the volume going up each year. This has allowed us to invest in the dedicated equipment, which is also critical for these procedures. ERN is a highly specialized treatment that should be reserved for those centers where the settings allow this sub-specialization. Although ERN is not for everybody, it is here to stay. It is a safe and effective treatment, with clear benefits for our patients. Of course, case selection remains an important aspect in this kind of pathology and there will always be cases where a different approach will be better.

Conflict of interest None of the authors report a conflict of interest.

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