Ph.D. Thesis

MINIMAL INVASIVE SURGERY OF LESIONS OF SELLAR, PARASELLAR REGION AND SKULL BASE

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LIST OF PUBLICATIONS RELATED TO THE SUBJECT OF THE THESIS

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II. **Fülöp B.** & Bella Zs., Palágyi P., Barzó P.: Endoscopic removal of the tuberculum sellae meningioma through endonasal transsphenoidal approach Ideggyogy Sz. 2016 Mar 30;69(3-4):133-8. Hungarian

III. Barzo P, Zador Z, Bodosi M, Bella Z, Jambor D, **Fulop B,** Czigner J.: Combined Minimally Invasive Supraciliary and Transfacial Approach for Large Tumors with Skull Base and Sinonasal Involvement. World Neurosurg. 2018 Jan;109:1-9. doi: 10.1016/j.wneu.2017.08.162. Epub 2017 Sep 4

CONTENTS

ABBREVATIONS in the text:

AC	**adenocarcinoma**
CCRCC	**clear cell renal cell carcinoma**
c.s.	**cavernous sinus**
CSF	**cerebrospinal fluid**
EEA	**extended endonasal approach**
ENB	**esthesioneuroblastoma**
FESS	**functional endoscopic sinus surgery**
ICA	**internal carotid artery**
lg-	**low-grade**
M	**meningioma**
m-SP	**malignant sinonasal (Schneiderian) papilloma**
MR	**magnetic resonance**
NF	**neurofibroma**
NPAC	**nasopharyngeal papillary adenocarcinoma**
orb.	**orbital**
RMS	**rhabdomyosarcoma**
SNUC	**sinonasal undifferentiated carcinoma**

INTRODUCTION AND AIMS:

The surgical treatment of pituitary tumors has been performed for just over a century. Even though transnasal approaches were used during mummification procedures in ancient Egypt, the first pituitary surgery was performed via transcranial (transfrontal, transtemporal) exploration (1). Parallel to transcranial exploration, transfacial and transsphenoidal techniques with lateral rhinotomy and partial resection of the nasal and nasal cavities developed. In 1907, *Schloffer* (2) successfully removed a pituitary adenoma via the transsphenoidal route in Innsbruck. *Kocher's* modified (3) midline nasal route, sparing the frontal ethmoid and maxillary sinuses, radically reduced post-operative infectious complications. Cushing completed the first sublabial, transepteptic, transsphenoidal surgery in 1910. The endonasal transsepteal transsphenoidal technique, which is wide spread in Europe, is associated with the name of *Hirsch* from Vienna, a student of *Hajek*. In the past century, pituitary surgery has undergone tremendous development and interventions have seen a renaissance since then (4). Following in the footsteps of *Dott*, *Hardy* and *Guiot*, first introduced an operating microscope, which was supplemented by an X-ray illuminator for proper intraoperative orientation (5). In the 1980s, the rigid endoscopic technique of *Messerklinger, Stammberger*, and *Kennedy* became not only a basic element of ear-nose-throat diagnostics but also of rhinological surgery. The gradual expansion of the indication areas of endoscopic exploration, as well as the neurosurgical and ear-nose-throat areas, have allowed for the use of cranial and pituitary adaptations. Interestingly, with the introduction of the microscope, *Guiot* and *Apuzzo* used an endoscope for the first time in the sella and the parasellar lesions, but the first "pure" endoscopic transsphenoidal tumor removal was only published 20 years later by *Jankowski* (6) which, by the hands of *Jho* and *Carrau*, obtained routine application (7-10). Over the past 10 years, the procedure has become widespread throughout the world and many of its variants have been known for endoscopically assisted microscopy interventions through one or both nostrils (11). There is also a debate between the "endoscopic" and "microscopic" camps as to the advantages and disadvantages of the two interventions and as to which is the first choice to be made on the basis of them (12-16).

The introduction of transnasal microscopic surgery in Hungary is connected to the work of *Pásztor* and *Piffkó* et al. (17). Subsequently, *Czirják* used and further developed the paraseptal approach through the transsphenodial pathway. In addition, the work on suprasellar tumors is linked to the work of *Czirják,* with minimal invasive application of an eyebrow incision in Hungary.

Nasal diagnostics (1983) and later endoscopic surgery, at the oto-rhino-laryngology and head-neck-surgery department in Szeged were among the first to be introduced in Hungary. Thus, we were able to use it early on in the borderline work of the two professions and pituitary surgery (18).

The introduction of endonasal technique in Szeged is associated with the activities of *Bodosi* and *Czigner* (1986) and as a result of the co-operation between the neurosurgery and oto-rhino-laryngology and head-neck-surgery departments, tumor surgery with transsphenoidal surgery has been extended to the nasal cavity and the intracranium (19).

Due to the combined endoscopic and microscopic surgery of hypopsy tumors, which are routinely used and our endoscopic experience with surgery on cerebral ventricles, we have extended the use of the endoscope to the treatment of cranial base tumors. For neuroendoscopic interventions, the surgeon’s perfect anatomical orientation, excellent endoscopic practice (joint team training, gradual learning curve) and use of the latest technical equipment is essential. To do this, continuous education, knowledge of special endoscopic devices, and their proper knowledge of exploration is required. A presentation of the special endoscopic posterior transepteptic transsphenoidal surgical technique with a Live Cadaver Surgical Presentation at the Conference of the Hungarian Neurosurgery Society in Szeged in 2011, was complemented by a hands-on workshop. Regular practical training, including the specialty learning curve and professional consultations are provided at the annual SZERINA (Szegedi Rhinological Days) conference during lectures and special cadaver dissection exercises at the Institute of Pathology and Anatomy of the University of Szeged. Practical experience and regular training programs have enabled the development of new surgical combinations such as combined endo-microscopic pituitary surgery (CEMPS) and simultaneous multiportal skull base surgery (SMSBS), which have been introduced in everyday practice.

The treatment of sinonasal tumors involving the frontobasal area together with the nasal cavity and/or paranasal sinuses represents a major challenge because of the proximity of vital anatomical structures. The surgical resection remained the cornerstone of therapy, with a combination of transfacial and transcranial approaches for tumors invading both the sinonasal area and the anterior skull base. The general aim of the combined surgery is to achieve a tumor-free margin, i.e., an en bloc resection, together with a better scope and thus safer operative conditions for the resection of the intracranial extension. The extension of these tumors into the cranial vault, similarly to primary tumors of the anterior skull base, traditionally has been approached through pterional, subfrontal, or bifrontal craniotomy. These techniques are often complicated by iatrogenic injury induced by the extensive craniotomy and soft-tissue manipulation. A new combination of the limited transfacial approach and the minimally invasive eyebrow incision is described as an efficient and safe technique for the resection of tumors invading both the anterior fossa and the sinonasal area.

MY DUTIES AND AIMS IN THIS COMPLEX STUDY WERE:

1. How can we combine the use of a microscope and an endoscope in hypophysis operations, and how can we provide the technical background for this?
2. What innovation results from using an endoscope? What are the advantages and disadvantages of a pure endoscopic and purely microscopic technique? How can the benefits of both be highlighted if the two techniques are combined?
3. How can the technical background of purely endoscopic transsphenoidal skull base tumor removal be ensured?
4. How can the skull base team with the technical background of its design and education be accomplished?

I. INTRODUCTION

I.1. Introduction

The pituitary gland has come to be known as an independent glandular body since the 17th century (*Brunner*). Endocrine, a hormone-producing function in the study of acromegalic patients, was assumed only from the end of the 19th century (20.21), but its functioning was only confirmed by *Evans* and *Long* (22) in animal experiments. Surgical treatment of pituitary tumors has a history of just over a century. Even though transnasal approaches have been used to reveal the cranial cavity and remove the brain in mummification procedures in ancient Egypt, the first pituitary surgeries were performed via transcranial (transfrontal, transtemporal) exploration (1). Parallel to transcranial exploration and the transsphenoidal technique, which initially involved lateral rhinotomy and the partial resection of the nasal bone and nasal cavities, developed. In 1907 (2), *Schloffer* successfully removed a pituitary adenoma via transsphenoidal surgery in Innsbruck. *Kocher's* modified (3) midline, nasal approach, sparing the frontal ethmoid and maxillary sinuses, radically reduced postoperative, infectious complications. In 1910, *Cushing* completed the first sublabial, transseptal, transsphenoidal surgery, which was the most common method in the US until the end of the 20th century. The endonasal transsepteal transsphenoidal technique, which is wide spread in Europe, is associated with the name of *Hirsch* from Vienna, a pupil of *Hajek*. In the past century, pituitary surgery has undergone tremendous development and interventions have been experiencing a renaissance since then (4). First of all, when he started with the operating microscope in the footsteps of *Hardy, Guiot* and *Dott*, he supplemented his procedure with an X-ray illuminator for proper intraoperative orientation (5). Its application in Hungary is associated with *Pásztor* et al. (17). The introduction of this technique in Szeged is associated with the work of *Bodosi* and *Czigner* (1986). In the 1980s, the rigid endoscopic technique of *Messerklinger, Stammberger* and *Kennedy* not only became a basic element of ear-nose-throat diagnostics, but it also became a basic element of rhinological surgery. The gradual expansion of the indication areas of endoscopic exploration, the neurosurgical and ear-nose-throat areas, allowed the use of cranial and pituitary adaptations. Interestingly, with the introduction of the microscope, *Guiot* and *Apuzzo* used an endoscope for the first time in the sella and the parasellar lesions, but the first "pure" endoscopic transsphenoidal tumor removal was only published 20 years later by *Jankowski (*6) which was obtained during routine application (7-10) by the hands of *Jho* and *Carrau*. Over the past 10 years, the procedure has become widespread throughout the world and many of its variants have been known for endoscopically assisted microscopy interventions through one or two nostrils (11). There is also a debate between the "endoscopic" and "microscopic" camps as to the advantages and disadvantages of the two interventions and as to which should be the first choice to be made on the basis these views (12-16). We have been using the endoscope for two years in our clinic during hypophyseal surgery. In our study, we report on not only the experience gained during this time but primarily on the endoscopic tumor removal technique which we use and the resulting spontaneous learning process, comparing it with international literature and recommendations.

I.2. Introduction

With the development of transnasal transsphenoidal sella surgery, the use of an endoscope in skull base surgery first appeared in 1963, when *Guiot*, et al. (7), reported their experiences. In 1978, *Bushe* and *Halves* (23) described the combined use of an endoscope and a microscope for pituitary surgery and then the first purely endoscopic intervention was published in 1992 by *Jankowski* (6). With the development of both pituitary surgery and sinus surgery, endoscopic surgery has become more widespread as both the technical equipment and the application areas have evolved and widened. In our institute, the combined endoscopic and microscopic surgery of pituitary tumors was introduced in 2007 and has routinely been used successfully in more than 200 cases (18). In this field, and as a result of our experience in the endoscopic surgery of cerebral ventricles, we have extended the use of the endoscope for the treatment of cranial base tumors. There have been reports of endoscopic endonasal surgical treatment of primary tumors of the frontal skull in recent years (24-39). When a tumor in the anterior skull base is close to the nasal cavity, it seems logical that the surgical excision should be transnasal instead of transcranial to minimize damage to the brain tissue surrounding the tumor. The aim of our case study is to extend the minimally invasive, endoscopic treatment option for operative diseases affecting the skull base, in addition to standard procedures.

I.3. Introduction

The treatment of sinonasal tumors involving the frontobasal area together with the nasal cavity and/or paranasal sinuses represents a major challenge because of the proximity of vital anatomical structures. During the past 50 years, the surgical techniques recommended for the treatment of these oncologically complex diseases have undergone considerable evolution. Inspired by the disappointing results of radiotherapy, in 1954 Smith et al.(40) were the first to introduce a combined transcranial (i.e., transbasal) and transfacial approach for the resection of sinonasal tumors, subsequently reporting a series of successful operations by using the elaborated procedure (41). Since then, surgical resection remained the cornerstone of therapy, with a combination of transfacial and transcranial approaches for tumors invading both the sinonasal area and the anterior skull base. The general aim of the combined surgery is to achieve a tumor-free margin, i.e., an en bloc resection, together with a better scope and thus safer operative conditions for the resection of the intracranial extension. To satisfy these criteria, a number of strategies have been developed to access this region, weighing the advantage of a wide exposure in association with an extensive facial decomposition (42,43) against the disadvantage of a narrower access with, however, significantly less cosmetic disfigurement (44). The extension of these tumors into the cranial vault, similarly to primary tumors of the anterior skull base, traditionally has been approached through pterional, subfrontal, or bifrontal craniotomy. These techniques are often complicated by iatrogenic injury induced by the extensive craniotomy and soft-tissue manipulation. In the effort to avoid the aforementioned complications, Donald H. Wilson introduced the idea of keyhole surgery (45). Subsequently, van Lindert et al.(46) further developed this concept and introduced the supraciliary exposure (i.e., through eyebrow incision), a minimally invasive modification of the subfrontal approach originally proposed for the surgical treatment of aneurysms. This approach, however, provides an excellent exposure of the anterior fossa as well as the supra- and retrosellar regions, making it a suitable technique to access not only aneurysms but also frontobasal, suprasellar, or parasellar tumors (47), and, as we propose, the intracranial extension of sinonasal tumors. In the present report, a new combination of the limited transfacial approach and the minimally invasive eyebrow incision is described as an efficient and safe technique for the resection of tumors invading both the anterior fossa and the sinonasal area. Our series of 11 patients demonstrate minimal mortality and morbidity with excellent cosmetic outcomes.

II. METHODS AND MATERIALS

II.1. Methods and materials

Between November 2006 and December 2010, at the Department of Neurosurgery of the University of Szeged, we operated on 61 patients using the transsphenoidal approach. After the interventions, we performed routine endocrinological check-ups (continuous postoperative hormone determination) as well as control head MRIs (6 to 8 weeks post-surgery). We recorded postoperative pituitary status, reduction or cessation of pathological hormone production, transient or permanent diabetes insipidity, success of tumor removal (residuum), duration of surgery, endoscopic versus microscopic proportion, histological examination of lesion, minor and major complications, such as: cerebral palsy, meningitis, epistaxis, and neurological symptoms observed during or after surgery. Initially, an endoscope was used exclusively to identify the anatomical structures during the preparation of the surgery and to clarify the developmental variations effecting the operation (i.e., the operation was performed exclusively by microscopy). The positive experiences gained in this regard have prompted us to endoscopy the endonasal phase first and then, almost invisibly, the sphenoidotomy and intrasellar tumor removal. The first operations lasted 2–2.5 hours, despite the fact that the intrasellar part was always microscopically. However, in six of the last 10 patients, total tumor removal was done only with an endoscope between 1-1.5 hours on average, with the shortest endoscopic intervention being 40 minutes. Since the endoscopic equipment is still not entirely optimal, we still have to undergo microscopic continuation of the operation from time to time during the intrasellar phase. The technique we currently use is described below.

CURRENTLY USED SURGICAL TECHNOLOGY

Intratracheal anesthesia, as well as surface and infiltration anesthesia

The operation is performed using general anesthesia and orotracheal intubation. We do not use preventive antibiotics. The eyelids are closed after the eyesalve is applied, while a gauze strip is placed in the oropharynx to prevent possible blood aspiration during the extubation. Nasal decongestants (xylometazoline 0.1% or 2% ephedrine) or decongestants and anesthetic sprays [lidocaine (5%) -phenylephrin (0.5%) or tetracain (2%) -ephedrine] are used by giving 4 puffs into each nostril and then a soaked cotton roll is inserted into the nasal cavity for at least 10 minutes. Due to the vasoconstrictive effect, the mucous membrane breaks down, there is more space, less bleeding, and less pain after surface mucosal anesthesia. The patient also requires less pain relief and anesthesia during surgery. There are two ways to lay the patient:

1. The patient is in a backward, mild anti-Trendelenburg position, the head is not fixed in a headrest, but retains 15-30 ° retroflexion and centering. The surgeon and the assistant are behind the patient's head, with the scrub nurse on the right side of the patient, behind the endoscopic tower. The anesthesiologist is on the left side of the patient. This lineup is suitable for fast, smooth, intraoperative alternation of endoscopic and microscopic techniques as needed. (Position preferred by neurosurgeon.)
2. The head is not fixed in this position either, the patient is lying on their back, while the head is in an anteflexion of 15-30 °. The surgeon is on the right of patient with the assistant and the scrub nurse are on the left. After an intubation, the anesthesiologist, along with the ventilator (larynx) tube on the chest and the abdomen, as well as the elongated catheter, is located near the feet of the patient. (FESS operation-based line-up, preferred by ear-nose-throat surgeon. Switching to a microscope is more difficult.)

Instrumentation

Endoscopic Tower: 150 W Cold Light, [preferably a 180 W xenon light source (provides adequate brightness even in bleeding), camera head (lens) and camera unit, monitor, DVD writer]. As far as possible, three rigid endoscopes at 0 °, 30 ° and 45 ° (4/170 mm orthopedic for nasal, 4/300 mm for the skull section) and a fixation kit (for the table). In hand-held instruments, the septum and FESS (functional endoscopic sinus surgery) handpiece tray are complemented by a series of *Kerrison*, *Rongeur*, and *Curette* insturments. There are many known techniques for using the endoscope that require two, three, or four hands to be coordinated by the handler alone or with one or both hands of the assistant. Currently, the three-handed technique is used so that the assistant holds the camera or the suction device. In the intrasellar phase, the use of the suction device is difficult for the neurosurgeon to forgo since, ignoring the microscope, its excellent depth of field is eliminated, and the suction device, as a tactile tool, helps to accurately assess depth and tissue consistency.

SURGERY

Endonasal phase

First, we examine the nasal cavity and epipharynx on both sides with a 0 ° or 30 ° endoscope and then visit the sphenoethmoidal recessus. The next step is to identify the ostium sphenoidale, the location of which is quite variable. It is usually found after passing the septum about 1.5 to 2 cm above the choana frame. In half of the cases, a wide yet visible 50% mucus-sealed, suction or probe-sealed ostium often covers the upper nasal cavity. The surrounding area is infiltrated on both sides with a 1-2% lidocaine + 0.1% tonogen solution (*Stammberger* recently preferred using only a 1: 1000 adrenaline as a surface decongestant). Two-sided infiltration of the back third of the septum separates both the periosteum and mucosa together. If the recess is narrow, the middle and upper nasal cavities are moved laterally. Some authors also suggest the rear mole of the middle concha, or even the full resection of the upper concha, for better access. Usually, we prefer penetration from the right side for a right-handed operator. A vertical incision of about 1 inch (3 cm) is made on the septum mucosa in front of the sinus sphenoidalis front wall. The mucoperiosteum is separated in the posterior direction by a length of 1 to 2 cm (Figure 1), and the explorer is inserted (which separates the conchas and septum widening the nasal cavity and relieves bleeding, helps to introduce the operating instruments, and protects the septum mucosa). Opening the explorer at the height of the incision, breaks through the bony septum (vomer) and the mucous membrane of the opposite side, while maintaining its integrity, is also separated subperiosteally. The posterior truncation of the bony septum is taken between the retractor arms (Figure 2). We look for ostium, expand it to the medial size, and prepare a 2 × 2 cm window on the front wall of the sphenoidal sinus (Figure 3).

Intrasphenoidal phase

By exploring the sphenoidal sinus, we first seek to minimize its mucous membrane as much as possible. The mucosa is separated from the intrasphenoidal septum on two sides (often not possible in the case of a pierced tumor) and held aside, and if the septum/s is/are in the way, it is/they are broken. A sphenoidal sinus is performed with an endoscope at the nasal base, n. optics and sinus carotids are clearly visible (Figure 4.).

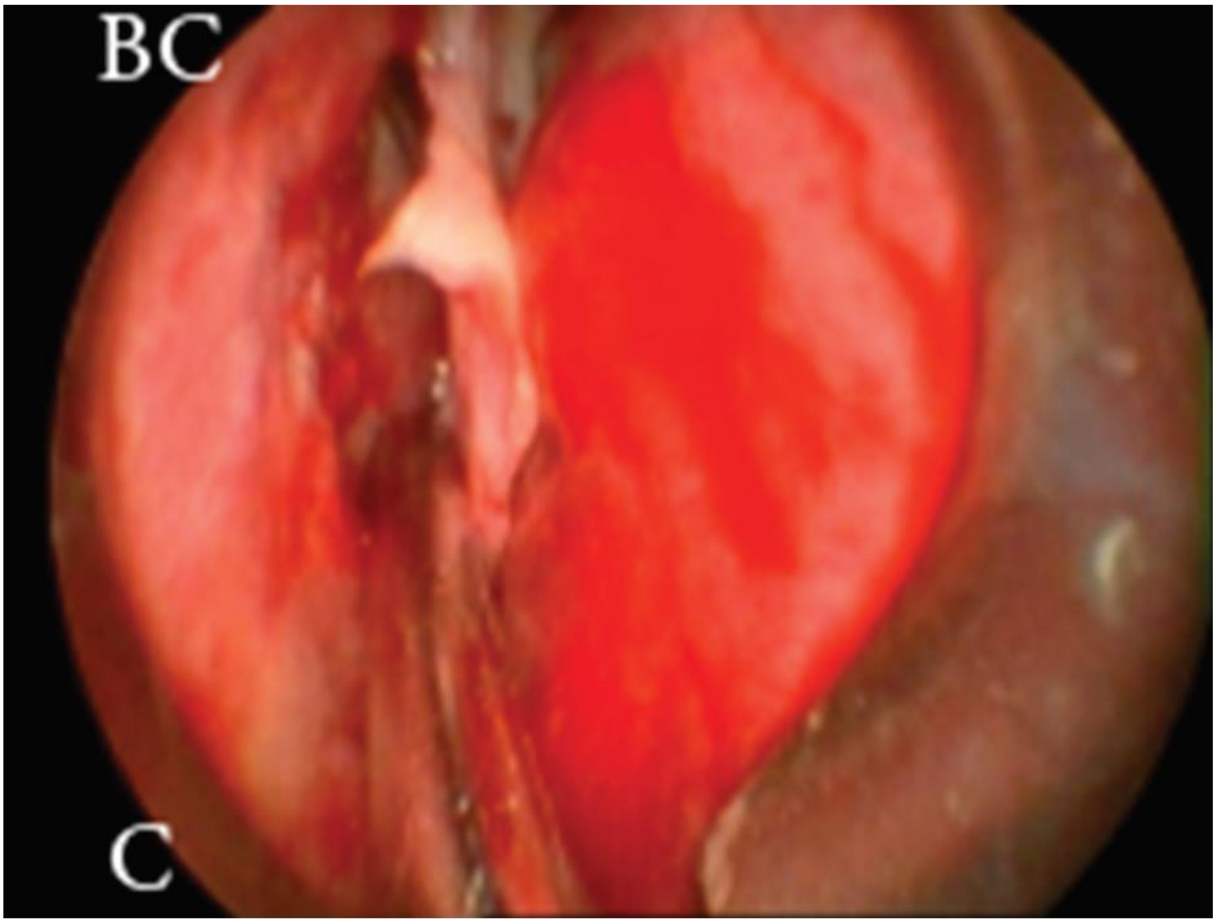

Figure 1. *Mucoperiosteal posterior septum lobe training, on the right side of the septum [the patient is lying on their back while the surgeon is behind the head of the patient, the cranial base (BC) is seen at the top of the picture and the calvarium at the bottom. (calvarium, C)]*

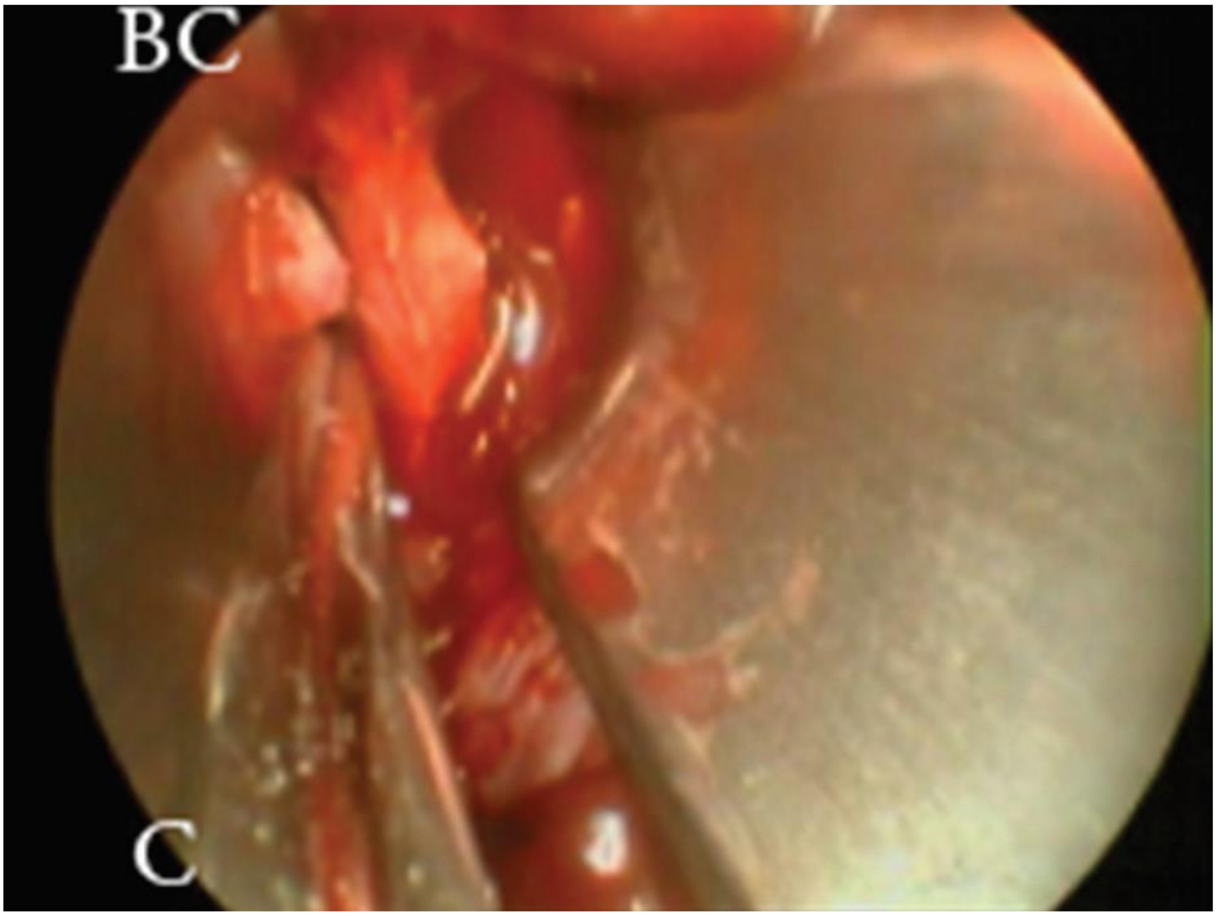

Figure 2. *Preparation of the vomer and insertion of the explorer*

Intrasellar phase, tumor removal

We switch to a longer endoscope (if possible) and fix the optics in an appropriate holder. We can open the front wall several different ways (with a small drill, *Kerrison*), but in many cases the pathological dislocation destroys the bone base and may even extend to the sphenoidal sinus (Figure 5). Opening the anterior wall of the sella in the direction of the dominant position of the lesion (planum sphenoidale, clivus, bilateral cavernosus sinus), taking care not to damage the dura. The dura is then opened on the center line. With a macroadenoma, this is harmless, but the microadenomas can damage the veins in the sella, which can cause violent bleeding or arachnoidea, which can cause CSF leakage. In rare cases, arterial hemorrhaging (ectasis carotid interna or primitive trigeminal artery) may also occur. For macroadenoma surgery, first the lower and then the lateral parts of the tumor are removed, leaving the suprasellar part till the end (Figure 6). The reason for this is, if we start the other way around, the sinking diaphragm and arachnoidea significantly narrows the surgical area, making it difficult or nearly impossible to remove the rest of the tumor. Following the removal of the intracapsular portion of macroadenoma, the pseudocapsule of the tumor was also separated from the surrounding area by being drawn into the already empty sella.

The operation can also be performed by means of hydroscopy (similar to arthroscopy). During this endoscopic examination or manipulation in the cavity of the sella, physiological saline is delivered with positive pressure, which is kept on the opposite side by continuous suction, so practically, we are working in the "aquarium" of the sella. Positive pressure against liquor pressure and the use of a 30 or 45 ° endoscope will help you review the cavity of the sella and remove the small residuum. At this step, we have the opportunity to extend the procedure and, if necessary, to examine the surrounding formulas, even using hydroscopy, ie gaining insight into the cerebral base, the formulas of the middle scala (Figure 7).

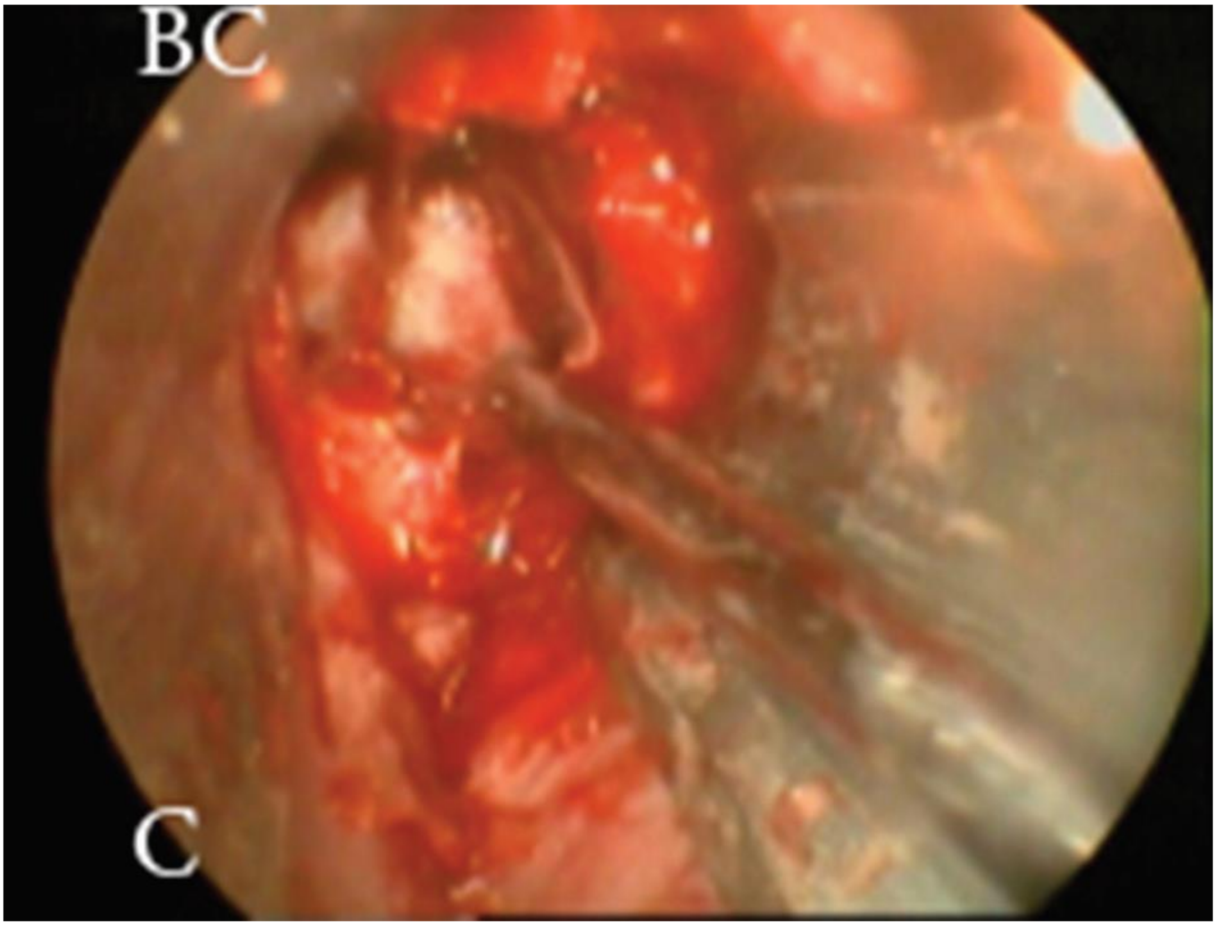

Figure 3. *A wide exploration of the sphenoidal sinus with partial removal of the front wall*

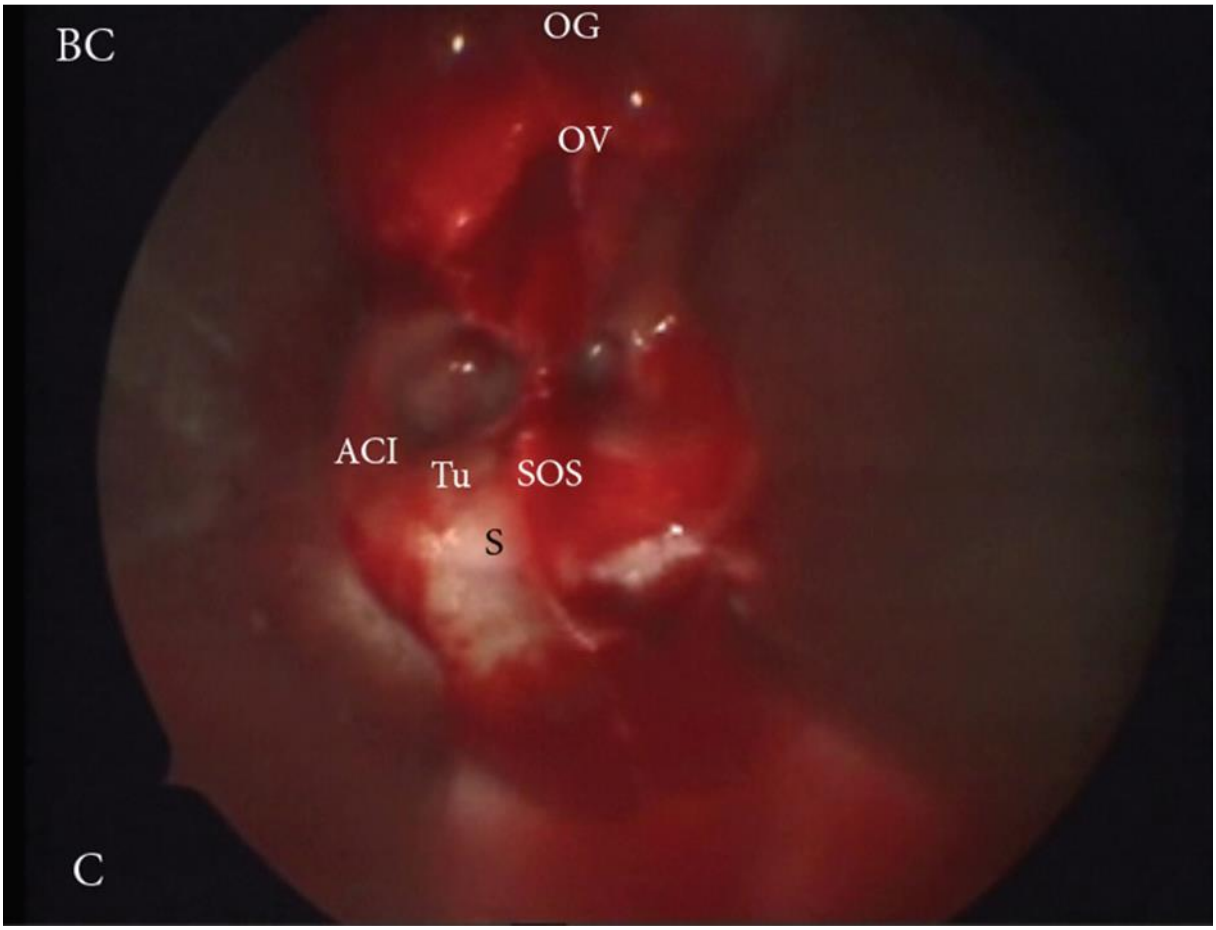

Figure 4. *The endoscope that leads to the sphenoidal sinus, the bottom of the sella (S), through the thin sella the transparent tumor (Tu), the septum of the bony sphenoid (SOS), the lower back of the vomer (OV), the nasopharynx (OG), and at the side the internal carotid artery (ACI) are clearly visible.*

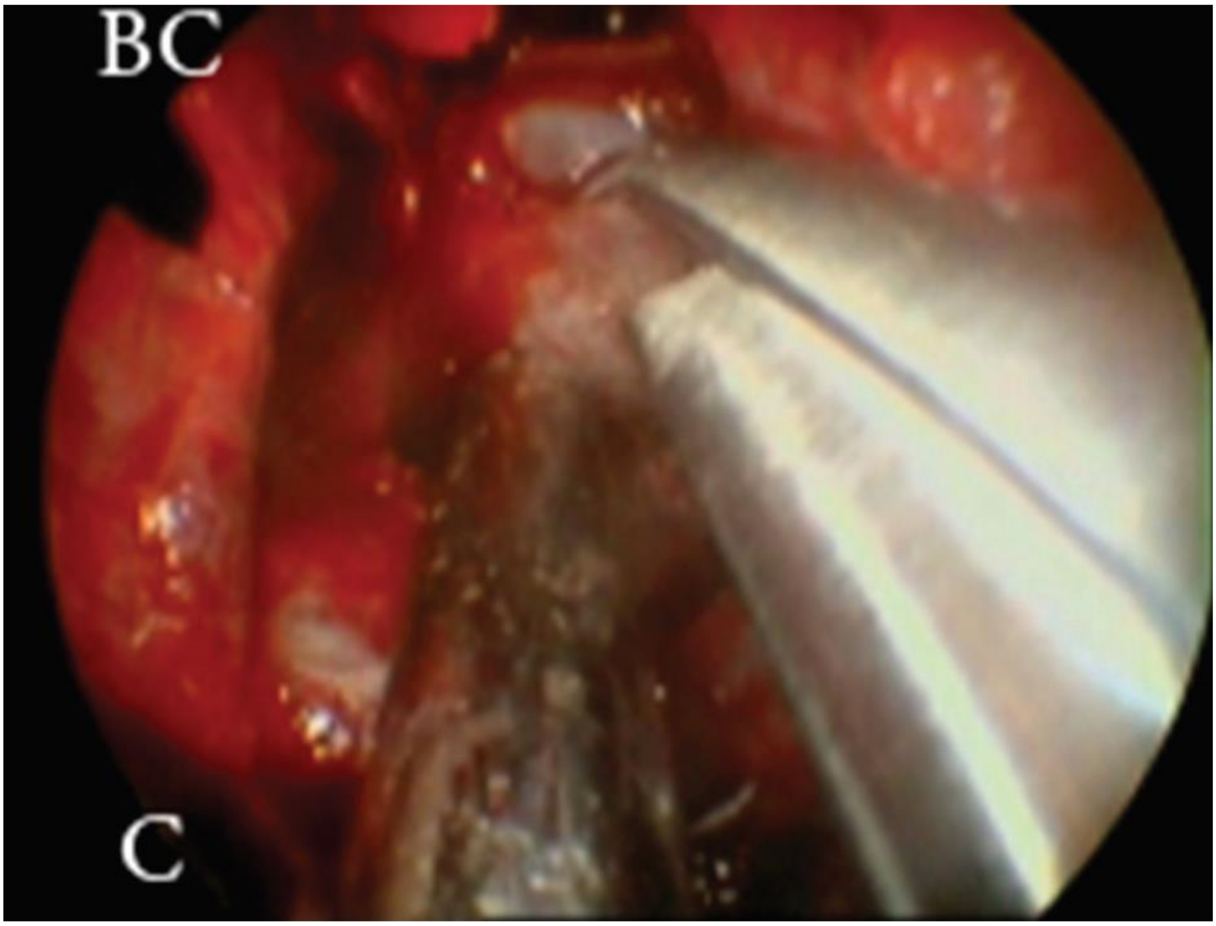

Figure 5. *Opening of the sella with removal of the posterior bony wall of the sphenoidal sinus*

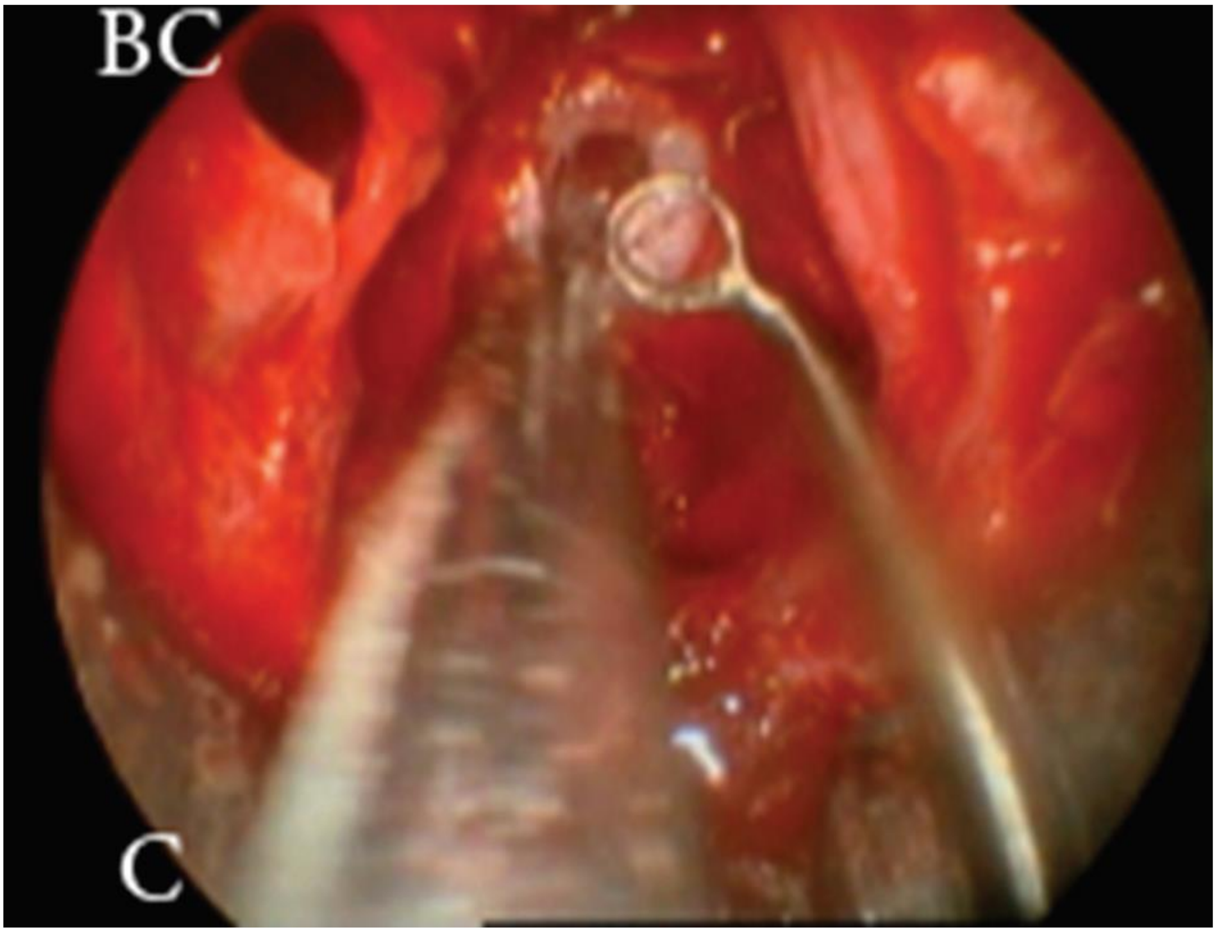

Figure 6. *Removal of pituitary tumor after incision of dura mater*

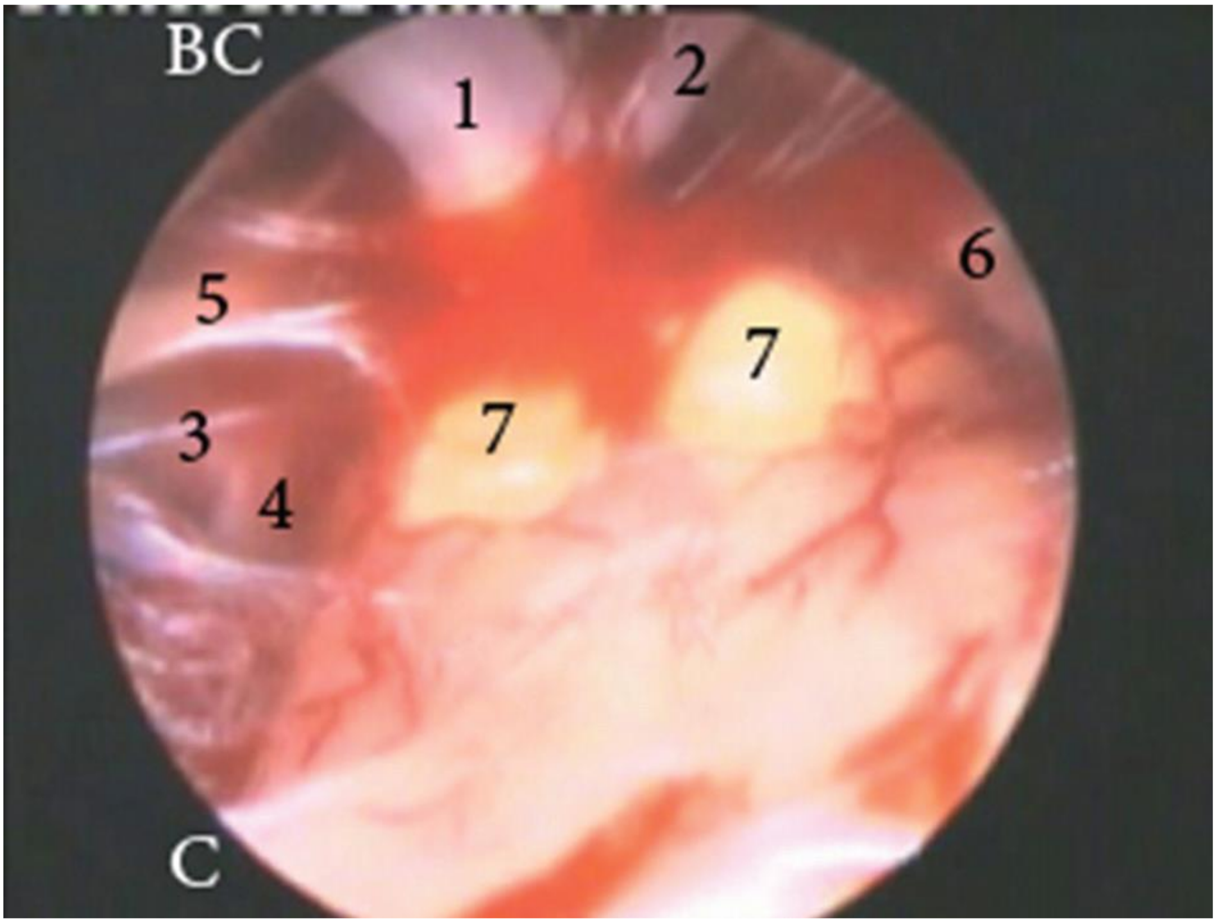

Figure 7. *Cranial base hydrocsopy*
1. basilar artery
2. superior cerebellar artery
3. posterior cerebral artery
4. posterior communicating artery
5. oculomotor nerve (n.III.)
6. posterior cerebral artery
7. bilateral mamillary bodies

Closure and Reconstruction of the Sella

A multi-layer closure is primarily required in case of either arachnoid injury or cerebrospinal fluid leakage due to suprasellar extended endoscopy. Usually, the lower third of the sella is filled with a fat graft, but if the leakage is significant, this can be reinforced by sealing the cavity with fibrin glue and fascia lata (Figure 8.). The sinus sphenoidal mucosa of the sinus is folded back. The septum from the opposite side is bluntly repressed to its original position and the mucoperiosteal lobe separated on the excision side is returned to the septum. You can loosely tamponize (for 3-5 and up to 7 days) with iodophoric, vaseline-filled gauze swabs, or even a spinal drain, depending on the degree of liquid permeation. The use of soft, self-thickening tampons or Sinufoam ® cellulose-containing foams for post-operative treatment of FESS can also be used to prevent mucosal adhesions. An endoscopic check-up is recommended two to four weeks post-surgery. (Figure 9).

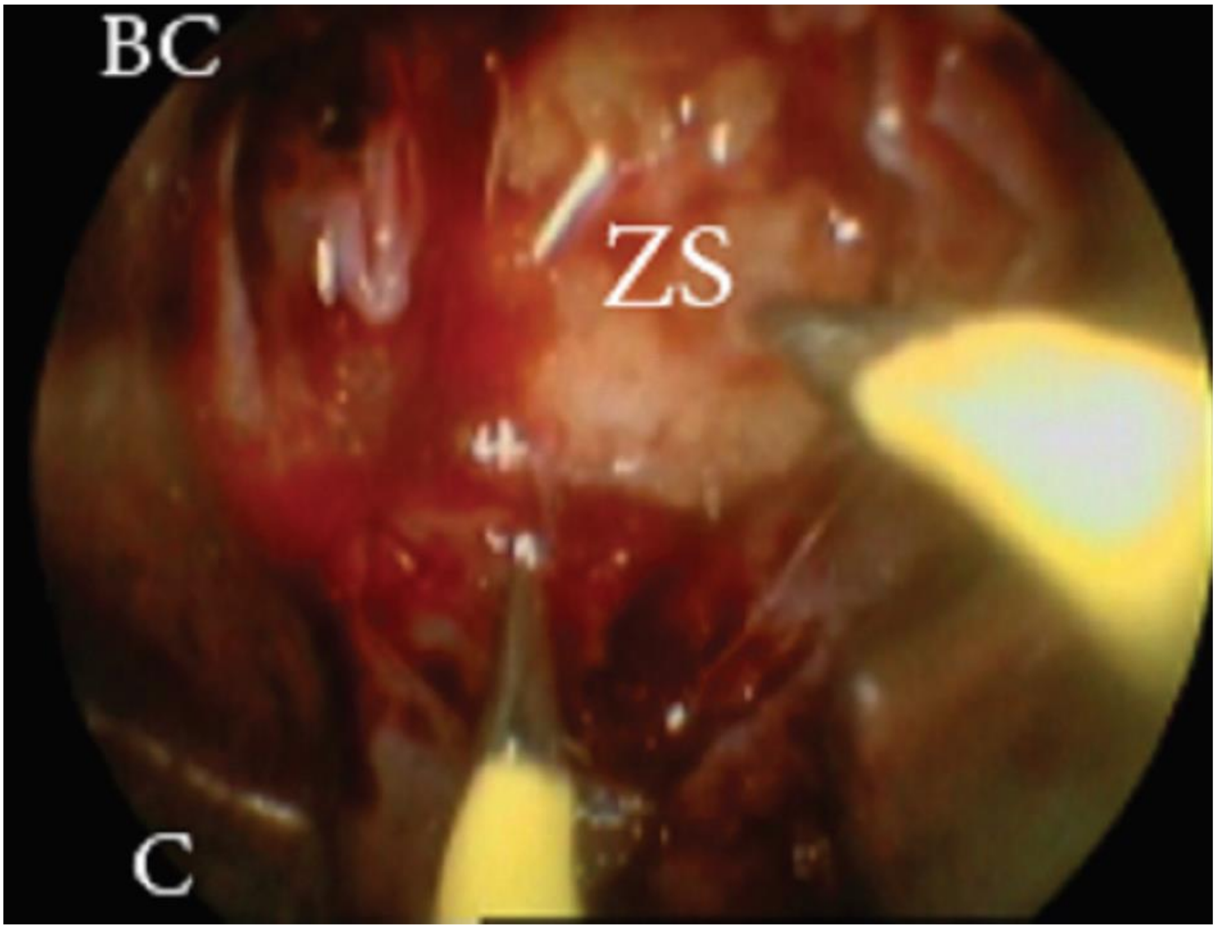

Figure 8. *Sella reconstruction with autologous fat (ZS), Surgicel® and, if necessary, with fibrin glue*

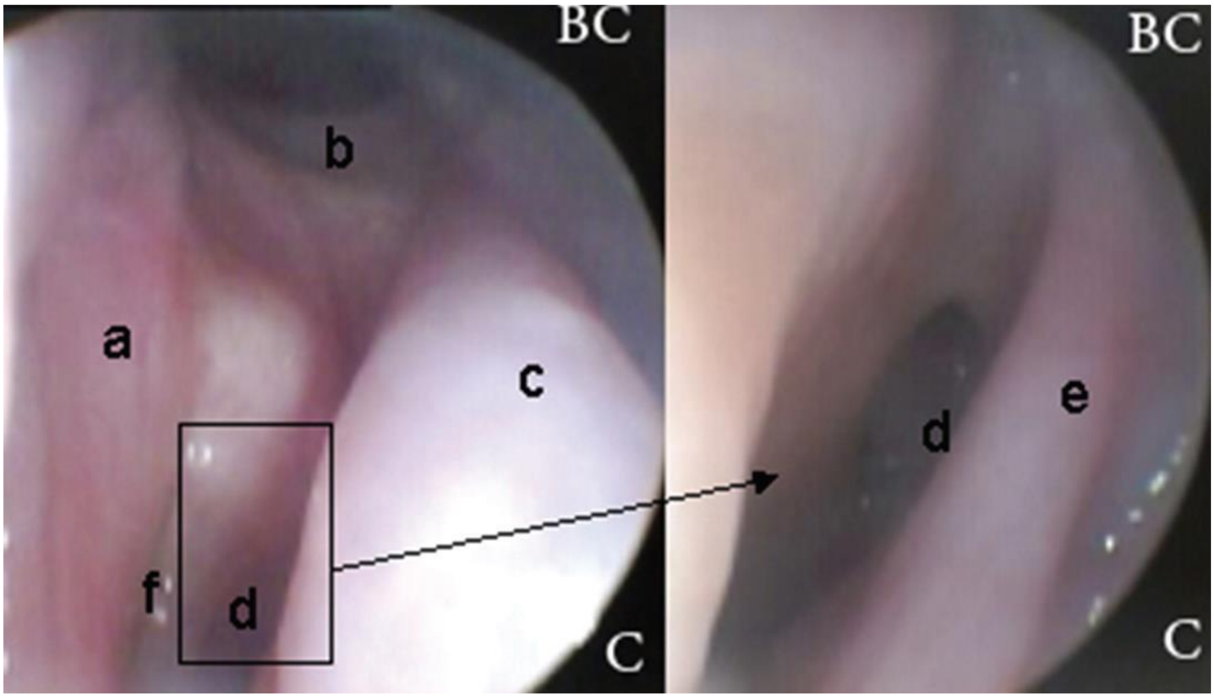

Figure 9. *Postoperative nasal endoscopic image, restitutio ad integrum (the patient is lying on their back, right nasal cavity)*
a. septum
b. choana frame
c. middle concha
d. sphenoid ostium
e. upper concha
f. surgical incision per primam healed

II.2. Methods and materials

Case Study

The 49-year-old female patient who was completely healthy, was subjected to several eye examinations over the course of several months due to vision problems. Based on the examination, a weaker papilla was found in her left eye as well as the discovery of a previous retrobulbar neuritis. However, VEP examination on the left side confirmed a functional impairment of her central optic fibers. As a result, the skull-MR scans (Figure 9.) showed a proliferative tumor that seemed to be tuberculum meningioma. The images showed the compression of both optic nerves and the optic chiasm due to the tumor. Neurological examination showed a visual impairment in the right eye also through confrontal visual field examination in addition to the impairment of the left eye.

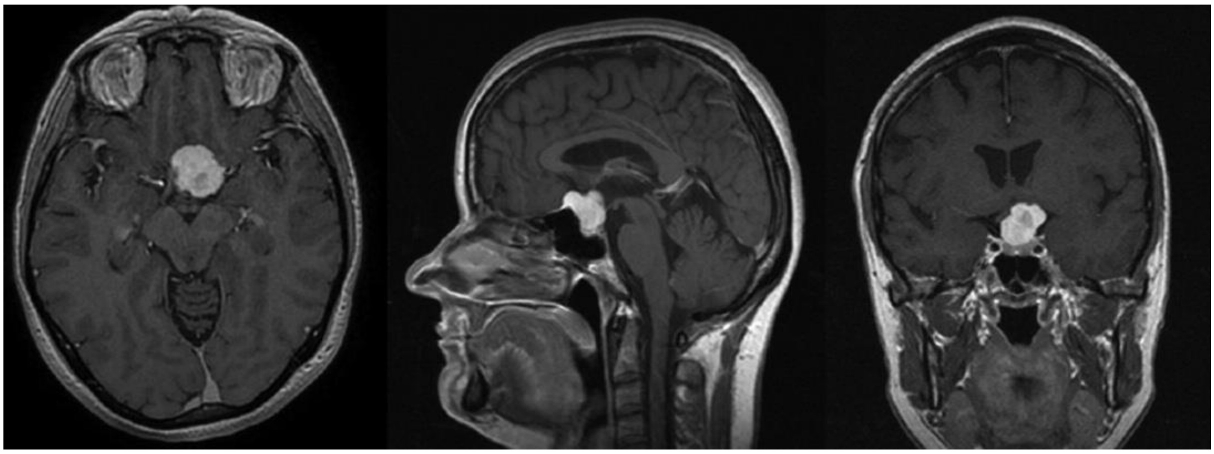

Figure 9. *Preoparetive contrast enhanced head MRI (T1 sequence, axial, sagittal and coronal) showed suprasellar spreading lesion like meningeoma, that was affected to sphenoid planum, tuberculum sella and intrasellar. Compression of both optic nerves and the optic chiasm was visible.*

SURGICAL TECHNIQUE

Surgical preparation

A detailed description of transsphenoidal endoscope assisted microscopic hypophyseal surgery, which involves the simultaneous use of 2-3 devices through the nose, is described in our previous publication (18). In our patient, the meningioma was removed via transnasal, transplanum endoscopic exploration with neuronavigation, which did not require the use of a microscope. The operation took place under general anesthesia with endotracheal intubation. The patient was laid on their back, the their head was fixed in a three-point Mayfield headset and navigation devices were attached to it. After the aseptic disinfection of the nasal, facial and femoral regions, we took fat from the subcutaneous layer of the thigh and then fascia lat graft.

Nasal phase

Nasal decongestans and anesthetic [lidocaine (5%) -phenylephrin (0.5%)] sprays were used, in the form of 4 puffs in both nasal passages, then soaked cotton rolls were inserted into the nasal cavity for at least 10 minutes. Subsequently, *Tonogen-Lidocain* was injected to separate the mucoperiosteum from the back third of the septum on both sides (0 degrees, 170 mm rigid optics, 3CCD camera, video capture). On the right side of the septum, a *Hadad* lobe was created by lifting the mucoperichondrium and mucoperiostium pointing to the right side sphenopalatin artery, which was temporarily put in the nasal cavity (closure was made). The partial resection of the vomer and lamina ossis perpendicular to the rostrum sphenoidal, with ostium, was widely explored. By taking this route, we got into the sphenoid cavity to identify the sella (Figure 10).

(In one of the nasal passages is a camera and a surgical device, in the other is a suction device and another surgical device used during a four-handed technique).

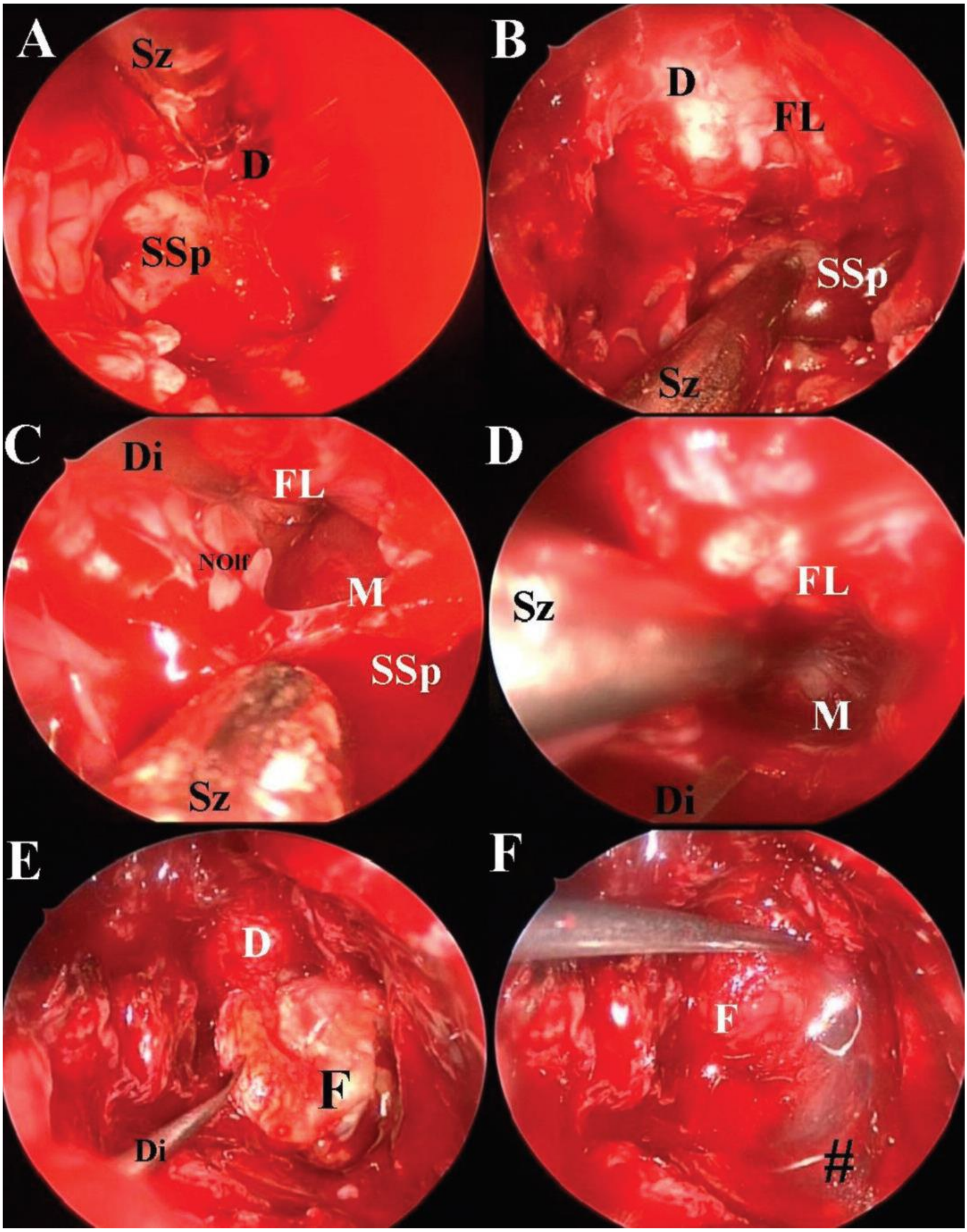

Figure 10. A: *Sella (transsellaris) and the upper wall (transplanum) of sphenoid sinus (SSp) was drilled at the base and after we started craniectomy by Kerrison-rongeur, dura mater was already identifiable (D) (S: suction).*

B: *Following the craniectomy on the base, after the initial opening of dura mater (D), the frontal lobe (FL) was visible.*
C: *Following the opening of the dura mater, the meningeoma (M) was in the field of vision between the right olfactory nerve (NOlf) and the base of the frontal lobe (FL). (Di: dissector)*
D: *Piecemeal removal of the meningeoma (Di: dissector).*
E: *We also used the fascia lata (F) autograft to close the dura mater.*
F: *The fascia lata (F) autograft is fixed with a tissue adhesive (#)*

Intracranial phase

The upper wall (transplanum) of sphenoid sinus and sella (transsellar) was drilled and a 2 x 1.5 cm craniectomy was made with a *Kerrison* rongeur. This included the rear third of the planum sphenoid and the upper part of the sella. Opening the dura with a scalpel, the tumor came into the field of vision, which was gradually removed completely. After the craniectomy and dural opening, due to this beneficial approach, the tumor was immediately deprived of blood supply, thus no bleeding was detected. After the complete removal of the tumor, the optic chiasm and the complete complex of the anterior communicating artery were revealed, which showed a relief of compression. To seal the dura, the fascia lata, the subcutaneous layer graft, *Surgicel* and *Gelfoam* were layered and fixed with a tissue adhesive. The epithelial and tissue deficiency of the skull was closed intranasally with a *Hadad*-lobe (Fig. 10). Silicone foil (not to be pulled out by the tampon when detamponing), and then a swab (Merocel, Betadine lubricant and solution) were inserted.

II.3. Methods and materials

Patients Characteristics

Eleven patients were diagnosed with a tumor invading both the anterior skull base and the nasal cavity and/or paranasal sinuses by means of contrast-enhanced magnetic resonance imaging. Intracerebral propagation or tumor size was not considered as exclusion criterion. The demography and clinical characteristics of patients enrolled in this study are presented in Table 1. All patients gave written informed consent before the operation.

Table 1. Clinical and Demographic Characteristics of the Patients

	Patient										
Characteristic	1	2	3	4	5	6	7	8	9	10	11
Age, years	44	49	32	17	58	61	72	21	7	6	41
Sex	M	F	F	F	M	M	F	M	M	M	M
Hospital stay, days	7	9	11	9	8	10	10	6	9	13	9
Reoperation *	+	-	-	-	-	-	-	+	-	+	-
Histology	AC	N	ENB	NPAC	Ig-AC	SNUC	M	NF	RMS	m-SP	CCRCC
Extension											
Intracranial	+	+	+	+	+	+	+	+	+	+	+
Intradural	+	+	+	+	+	+	+	-	+	-	-
Intranasal	+	+	+	+	+	+	+	+	+	+	+
Ethmoid sinus	+	+	+	+	+	+	+	+	+	+	+
Frontal sinus	+	+	+	+	+	+	+	-	-	+	+
Maxillary sinus	-	-	+	+	+	+	+	+	+	+	+
Sphenoid sinus	+	-	-	+	+	+	+	+	+	+	+
Retromaxillary	-	-	-	+	-	+	-	+	+	-	-
Other regional	orb.	orb.	orb.	c.s., orb.	orb.	orb.	c.s., orb.	clival	c.s., orb.	orb.	orb.

Intraoperative hemorrhage	-	-	-	-	-	+	-	+	-	-	-
Tissue glue use	-	+	-	+	-	+	-	-	-	+	-
Postoperative CSF leak	-	-	-	-	-	-	-	-	-	-	-
Postoperative hemorrhage	-	-	-	-	-	-	-	-	-	+	-
Survival	3 months, died	6,5 years, died†	6 months, died	8 years, alive	7 years, alive	2.5 years, died	10 years, alive	3.5 years, alive	5 years, alive	3 years, alive	1,5 years, alive
Postoperative radiotherapy	-	+	-	+	+	+	+	+	+	+	+
Duration of surgery, hours	3	3,5	4	4,5	1,5	4	2	1,5	3	2	1,5
Resectio	Subtotal	Total	Total	Total	Total	Total	Total	Total	Total	Total	Total

AC, adenocarcinoma; M, meningioma; ENB, esthesioneuroblastoma; NPAC, nasopharyngeal papillary adenocarcinoma; lg-, low-grade; SNUC, sinonasal undifferentiated carcinoma; NF, neurofibroma; RMS, rhabdomyosarcoma; m-SP, malignant sinonasal (Schneiderian) papilloma; CCRCC, clear cell renal cell carcinoma; orb., orbital; c.s., cavernous sinus; CSF, cerebrospinal fluid. M, male; F, female.
* Primary surgery in another institute.
† Unrelated cause of death.

Preoperative Care

All patients were administered a broad-spectrum antibiotic (a third-generation cephalosporin such as ceftriaxone via the intravenous route, initiated within 1 hour before surgery [1.5 g]) and continued for approximately 24-48 hours postoperatively (1.5 g twice a day). Antiepileptic drugs were not given routinely except for cases when the patient had a history of epileptic seizures or the intracranial propagation of the tumor was remarkable. Preoperative oral irrigation with antibiotics was used to reduce microbial flora. Standard disinfection procedure and isolation were performed.

Positioning of the Patients

After induction of general orotracheal anesthesia, the patients were placed in a supine position with the head fixed in a 3-pin Mayfield head holder and elevated approximately 15_ to facilitate venous drainage. The neck of the patients was retroflexed, resulting in an approximate 20_ angle between the plane of the anterior cranial base and the horizontal plane. This maneuver of retroflexion also supports the gravityrelated self-retraction of the frontal lobe. The most convenient access to the lateral paranasal sinuses requires a rotation of 10-30_ to the ipsilateral side. However, in the second part of the operation, during the surgery of the frontobasal intracranial lesion, rotation of the patient's head to the side opposite to the planned craniotomy might be necessary. Fine adjustments of the patient's position were achieved by tilting the operating table.

Transfacial Part of the Operation

Facial Skin Incision and Soft-Tissue Dissection. The skin incision was performed along the lateral aspect of the nose, corresponding with the traditional Weber-Ferguson approach (Figure 11) (48). Mimic muscles were cut and dissected in line with the planned maxillotomy.

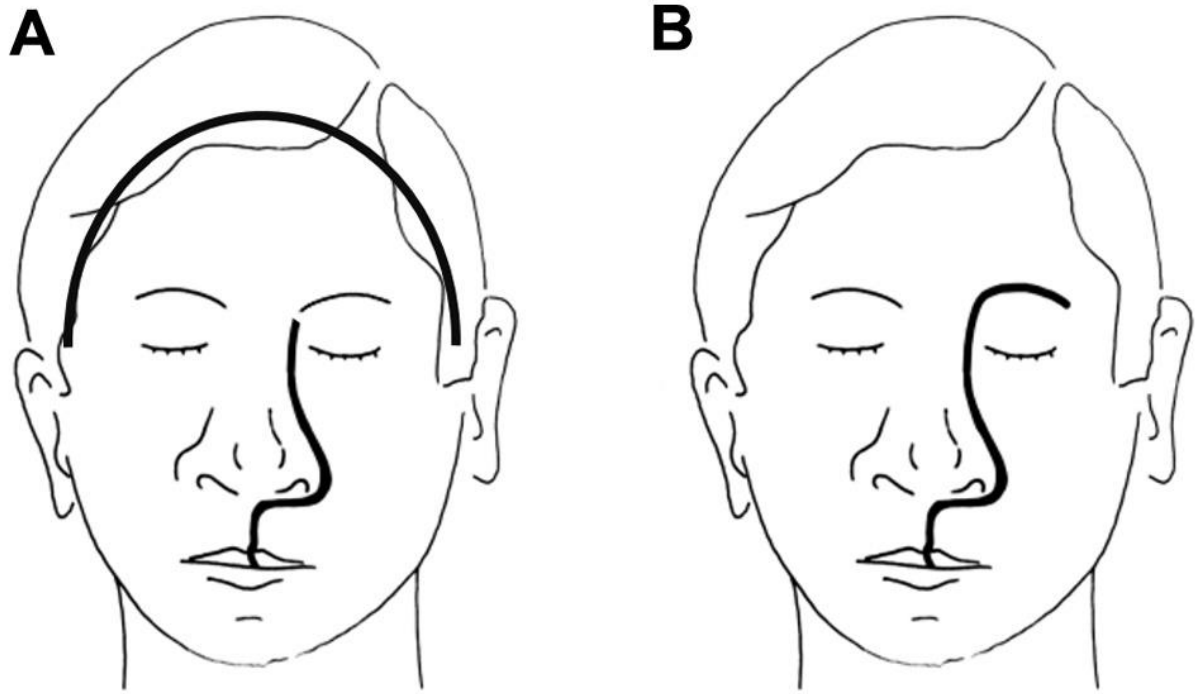

Figure 11. Schematic depiction of (A) the "classical" and (B) the hereby presented minimally invasive craniofacial approaches.

Maxillotomy

To approach the intra/paranasal portion of the tumor, a form of facial translocation was performed. The extent of the approach was dictated by the tumor size; however, in the vast majority of the cases, a mini-central facial translocation procedure was used as previously described by Janecka (49), in which the prepared composite unit was displaced laterally to provide surgical exposure. In selected cases, unit translocation was not necessary, and a standard lateral rhinotomy was performed with only a slight extension of the osteotomy. The paranasal extension of the tumor was debulked to provide a tumor-free margin at least in terms of the paranasal sinuses. In parallel with the last phase of the paranasal debulking, the supraciliary approach was initiated by the neurosurgeon.

Supraciliary Part of the Operation

Supraciliary Skin Incision and Soft-Tissue Dissection. The skin incision was made above the eyebrow, started from 5e10 mm lateral to the edge of the eyebrow, extended medially until reaching the upper end of the midfacial incision (Figure 11). The fascia and muscle were sharply cut and retracted 2e3 cm superiorly. Depending on the lateral extension of the skin incision, the temporalis muscle was stripped from its bony origin and retracted laterally.

Frontolateral Osteotomy, Extradural, and Intradural Dissections. A 3-5-mm burr hole was positioned immediately below the most anterior part of the superior temporal line. In general, when the frontal sinus was not extended too laterally and was not invaded by the tumor, a bone flap of 2.5 cm height and 3.5 cm width was created by making a linear (lower) and a C-shaped (upper) cut starting from the burr hole (Figures 12C, 13C, and 14C). After the removal of the flap, the dura was opened with a curved incision and reflected inferiorly. To avoid the use of instrumental frontal lobe retraction, a part of the orbital roof was drilled away, which was followed by the introduction of the surgical microscope. By approaching the carotid or chiasmal cistern, the arachnoid was cut, and a huge amount of cerebrospinal fluid (CSF) was allowed to egress to provide a more abundant access, further facilitating a completely retractor-free procedure.

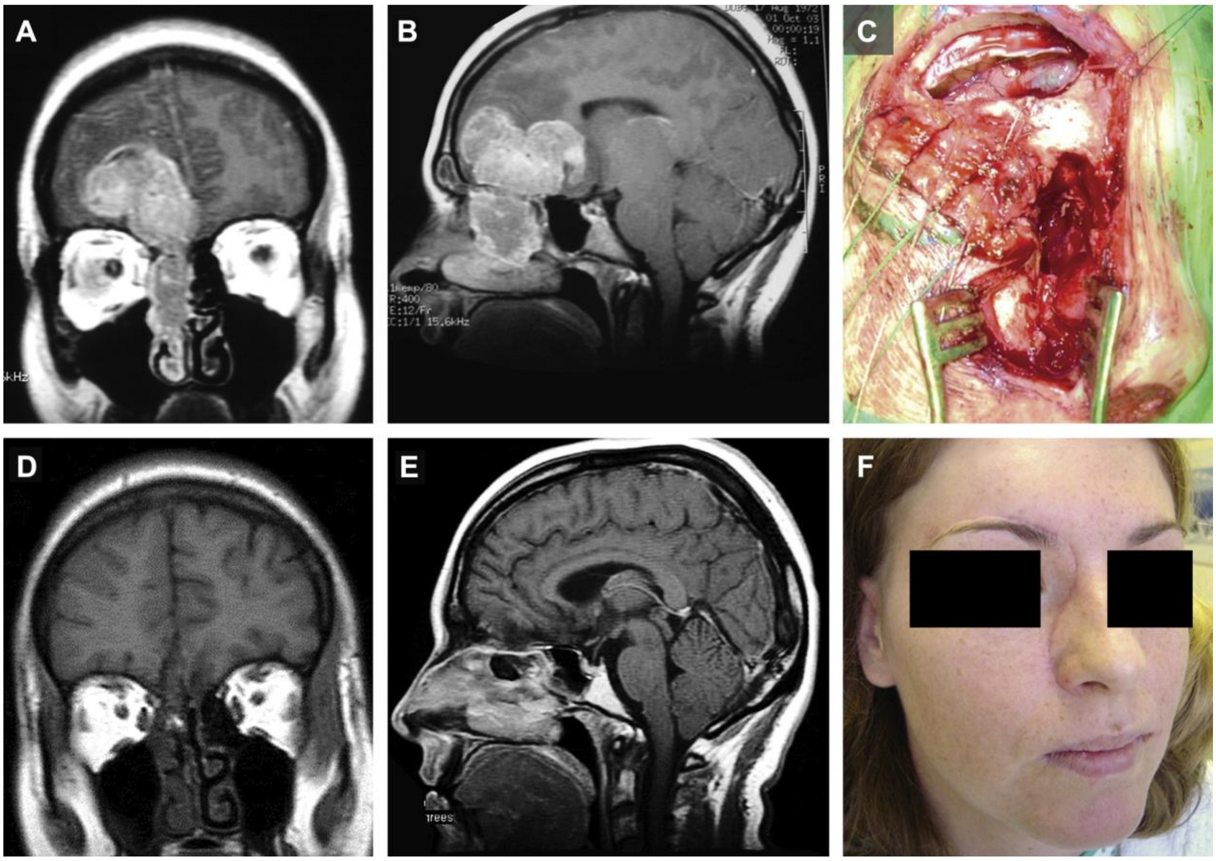

Figure 12. *Illustrative case 1 (patient 3). (A, B) A 32-year-old female patient presented with a contrast-enhancing lesion on magnetic resonance imaging (MRI) in the nasal cavity that extended along the right side of the nasal septum into the cranial space. The intracranial portion of the tumor stretched across the entire anteroposterior length of the anterior cranial fossa floor, displacing the orbital surface of the frontal lobe sup eriorly by 3-4 cm. (C) A combined supraciliary and paranasal incision was made as described above in the Methods section, followed by the gross total removal of the tumor mass. The patient's early postoperative course was unremarkable. Her neurologic examination showed no abnormality. (D, E) The postoperative MRI scan revealed a complete removal of the tumor. (F) The patient made an excellent recovery with great cosmetic results. The histologic diagnosis of the tumor was esthesioneuroblastoma. Unfortunately, despite our recommendation, the postoperative irradiation was not performed, and the patient eventually died due to multifocal distant intracranial metastases 6 months after surgery.*

In cases without dural involvement, the infiltrated part of the skull base bone was resected with a 5- to 10-mm margin, finalizing the removal of the tumor. In case the dura was infiltrated by the tumor, in addition to the resection of the bone as described previously, the affected part of the dura was resected with a 5- to 10-mm tumor-free margin. In cases with intradural propagation, first, the tumor vasculature was disrupted by the coagulation of the feeding dural arteries, when it was possible. The initial debulking of the tumor was achieved by piecemeal resection, and, eventually, the intracerebral extension of the tumor was removed entirely, mostly by suction without difficulty (Figures 12C, 13C, and 14C).

Closure and Reconstruction

After the end of the intracranial procedure, the subarachnoid space was filled with body-temperature saline. In cases without dural involvement, the dura was closed with continuous sutures to achieve a watertight seal. In cases necessitating dural resection (either with or without intradural propagation) a multilayer flap of fat and fascia previously prepared from the lateral thigh was used for a complete and watertight reconstruction of the anterior cranial base (supplemented with the occasional use of fibrin glue). In cases with huge dural dehiscence suggestive of postoperative CSF leakage despite all efforts described above, 5e7 days of spinal drainage was applied as well. Dural fixation was performed in each case by the use of a few stitches to the bone to prevent epidural bleeding. The bone flap was fixed by the use of titanium cranial fixation system or sutures running through w1-mm tunnels drilled in the bone flap and at opposite points in the cranium. The remaining bone gaps were filled with autologous bone dust and tissue glue to provide optimal healing results. After hemostasis was verified, closure of the muscle and the fascia was performed with interrupted sutures. The skin was closed with continuous sutures (Figures 12F, 13F, and 14F). During the reconstruction of the facial part, following the final verification of hemostasis, the retracted bone-muscle-skin composite unit was repositioned. Mini-plating was used for rigid fixation. Mikulicz tampons were inserted into the maxillary sinus and into the nasal cavity to absorb exuded fluids, especially blood, left in place for 3e4 days. Similarly to the supraorbital incision, the skin was closed with continuous sutures (Figures 12F, 13F, and 14F).

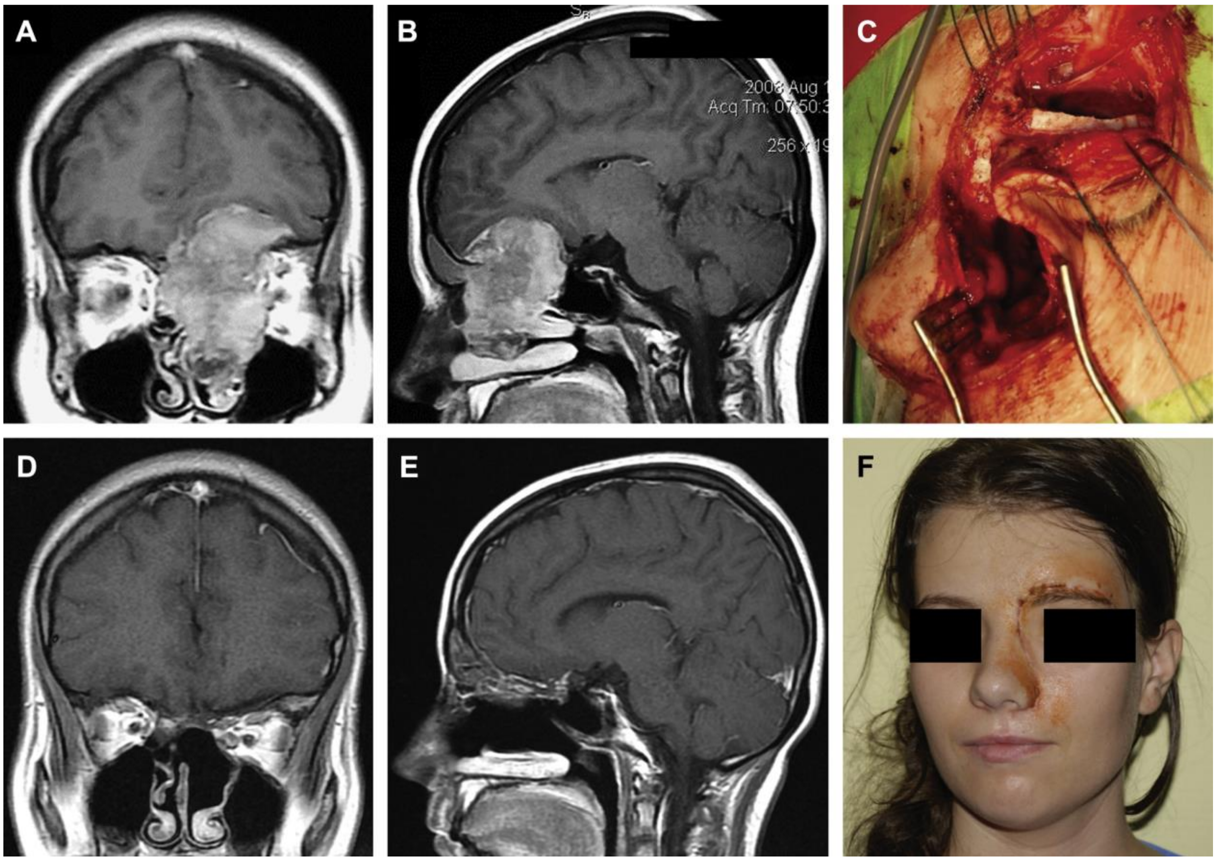

Figure 13. *Illustrative case 2 (patient 4). (A, B) A 17-year-old female patient presented with a contrast-enhancing lesion on magnetic resonance imaging (MRI) dominantly in the left nasal cavity extending along the left side of the nasal septum into the anterior vault, invading nearly all the paranasal sinuses. (C) A similar combined minimally invasive open approach was performed as described in the Methods. The patient's early postoperative course was unremarkable. Her neurologic examination showed no abnormality. (D, E) The postoperative MRI scan revealed a complete removal of the tumor. (F) The patient made an excellent recovery with great cosmetic results. The histologic diagnosis of the tumor was nasopharyngeal papillary adenocarcinoma. The patient received adequate postoperative radiotherapy and is still alive and well.*

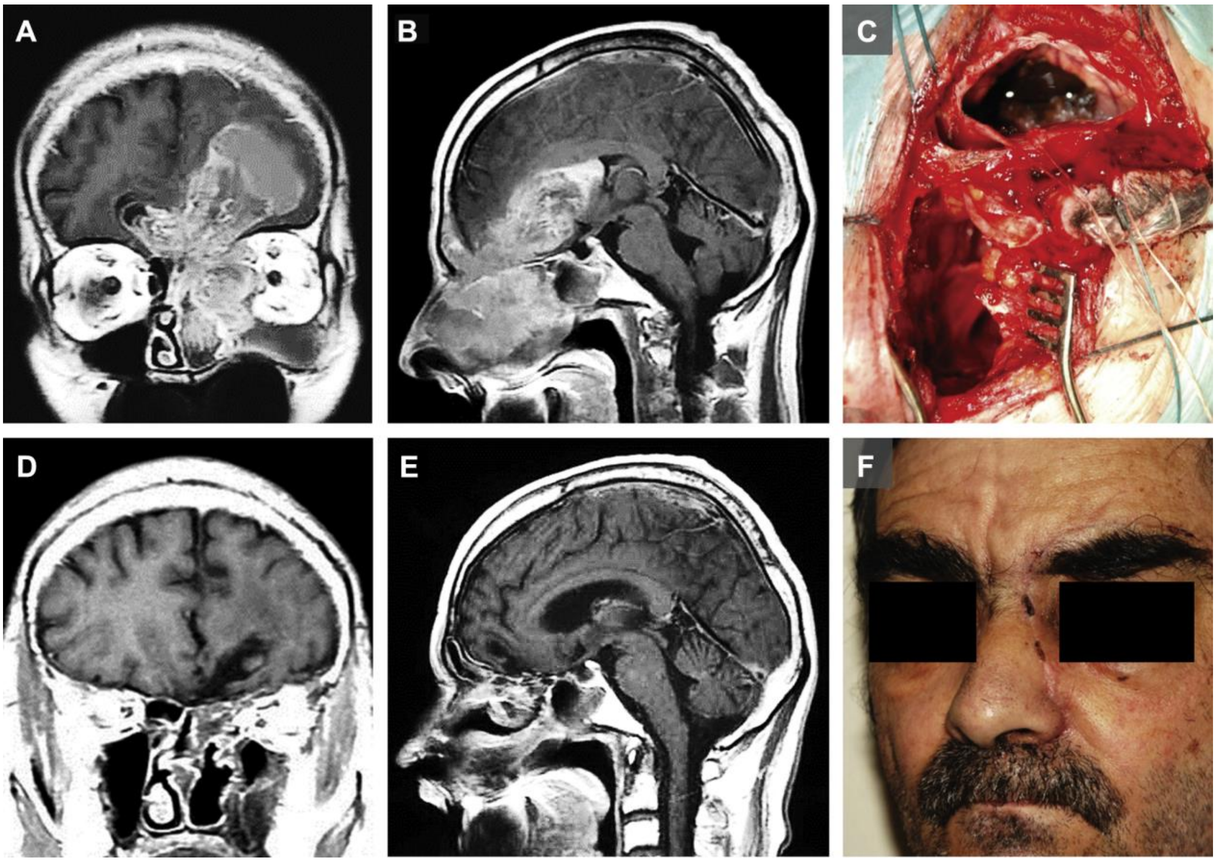

Figure 14. *Illustrative case 3 (patient 6). (A, B) A 61-year-old male patient presented with a contrast-enhancing lesion on magnetic resonance imaging (MRI) dominantly in the left nasal cavity extending along the left side of the nasal septum into the anterior vault, invading nearly all the paranasal sinuses. The intracranial portion of the tumor extended suprasellarly into the third and lateral ventricles. (C) A combined approach was performed similarly to that described in the Methods. The patient's early postoperative course was unremarkable. His neurologic examination showed no abnormality. (D, E) The postoperative MRI scan revealed a complete removal of the tumor. (F) The patient made an excellent recovery with great cosmetic results. The histologic diagnosis of the tumor was sinonasal undifferentiated carcinoma. The patient received adequate postoperative radiotherapy. The patient was lost to our follow-up 2 years after surgery and died half a year later due to unidentified reason (no autopsy is available).*

III. RESULTS

III.1. Results

Of the 61 endoscopic patients, 25 had complete endoscopic removal of their tumor. In the first 20 cases, only the endoscope was used three times, while 10 in the last 20 cases alone. In the examined group of patients, postoperative bleeding was observed (4.9%) in the form of minimal postnasal epistaxis. Postoperative MRI examinations showed clear tumor residuum in five cases, but due to its silent and non-spatial nature, no further surgery was required. During operation, 12 cases of CSF leakage (19.6%) were observed, spontaneously or spinal drainage was almost completely eliminated with the exception of one patient who had their fistula closed with intranasal endoscopy (fat, surgycel, fastia lat, fibrin glue). As a side effect, mucormycosis was confirmed in the histological sample removed from the sealed sphenoid sinus. Intraoperative removal of the mass, systemic fluconazole, and postoperative polyvinyl pyrollidone-iodine rinsing and local mometasone furoate, no local steroid use, showed no signs of relapse or invasion. Four weeks after surgery, 54 patients were excellent, three patients were good, and two patients reported satisfactory nasal breathing. Perforation of the back third of the septum was detected in four cases. (All of the cases were reoperations, and after the previous operation, the scarred mucoperiosteal septum lobe was damaged due to separation or insertion of nasal expander into the nasal passage.) In one case, on the second day after surgery, the patient suffered a stroke and accordingly, right hemiplegia, anisocoria developed. Despite intensive treatment, after a temporary improvement, the patient died on the 10th postoperative day. Pathological examination revealed a pons haemorrhage and lung microembolisation. One patient died due to a complication not at all related to the surgery (the patient fell three weeks after surgery and fractured their skull, resulting in a severe brain contusion). There were four cases of transient (<5 days) diabetes insipidus, but a sustained, hormone replacement condition developed in three cases. Abnormal hormone production was completely abolished in 59 cases, except for two acromegalic patients, although the decrease was significant, the daily GH level normalized and no further treatment was required, but the level of insulin-like growth factor binding protein remained elevated. Immediately after surgery, almost all patients were given cortisol and L-thyroxine supplementation to their home and endocrinological care. In sixteen cases (26.2% of the patients), substitution was completely abandoned later.

III.2. Results

Postoperative phase

In the post-operative period, spinal drainage was used to prevent transient nasal liquorrhoea for four days, with no CSF leakage. Only one time, due to diabetes insipidus, there was a need for desmopressin because of the divergence and ion displacement. In addition to these, there were no signs of fever and no clinical signs of meningitis appeared. Histopathological examination confirmed chordoid meningoma (grade II). When the patient came for the control examination, they reported reduced vision in the right eye and a decreased sense of smell. Six months later, the control head MRI showed no residual tumor and compression of both optic nerves and the optic chiasm ceased (Figure 15).

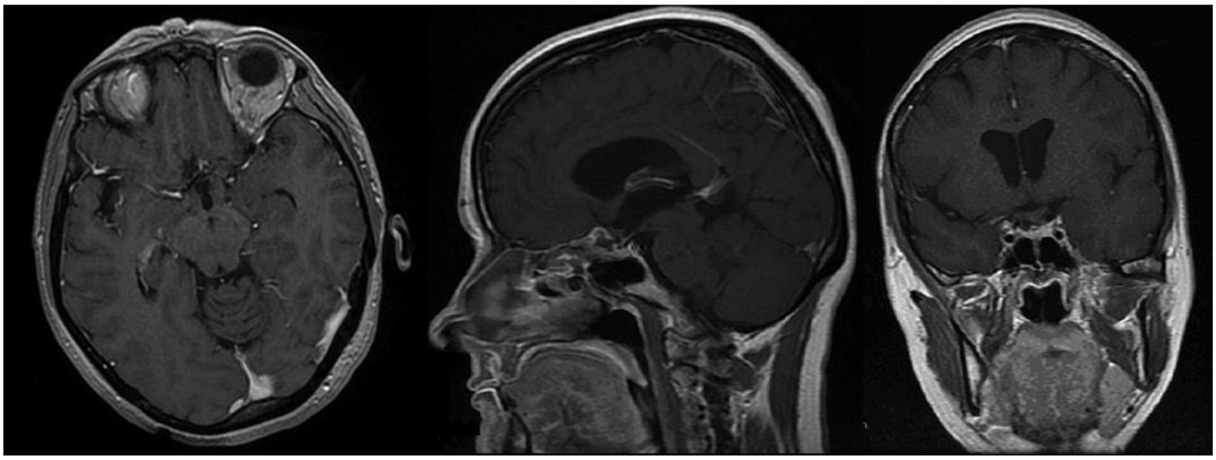

Figure 15. *Six months after surgery, contrast enhanced lesion on controll head MR images was not visible at the site of surgery*

III.3. Results

Table 1 summarizes the invaded regions, time of surgery, extent of resection (gross total or subtotal), postoperative morbidity, histopathological diagnoses, recurrences, and survival time of the 11 patients presented (Table 1). All patients had intracranial, intranasal, and ethmoid sinus (plus at least one additional paranasal sinus) involvement, 9 had intradural extension, and 9 presented with orbital, and 3 with cavernous sinus extension. The mean duration of surgery was 3.0 ± 0.9 hours. No case required orbital exenteration. Intraoperative and postoperative approach-related mortality was zero. Postoperative meningitis occurred in 2 cases, both healing to vancomycin or meropenem within a couple of days. Postoperative CSF leak rate was zero.

Only few patients required 1 or 2 days in the intensive care unit, and all patients were discharged from the ward within 2 weeks (mean hospital stay was 9.2 _ 1.9 days). Although, as an open technique, this approach may inherently be associated with a relatively greater risk of postoperative wound infection as compared with fully endoscopic approaches, no such event occurred in our case series. The esthetic outcome was excellent in all cases, as represented by the illustrative cases (Figures 12F, 13F, and 14F). The histological diagnoses included, sinonasal adenocarcinomas of different types and grades, esthesioneuroblastoma, rhabdomyosarcoma, malignant Schneiderian papilloma, neurofibroma, meningioma, and in one case a clear cell renal cell carcinoma, suggestive of an unusual distant metastasis. Only 3 of 11 patients had a histologically benign neoplasm. Among patients alive at the time of publication, 1 patient has less than 3 years of follow-up. Three patients died within 3 years, corresponding to a 3-year survival rate of 70%, 2 of them were the only patients not having received postoperative irradiation, whereas the third suffered of an anaplastic (undifferentiated) carcinoma. The cause of death was local recurrence in all 3 cases. One patient died years after the operation as the result of an unrelated condition. In 3 patients, local recurrence due to insufficient primary surgery in another institute necessitated the reoperation, 2 of them being still alive and well.

IV. DISCUSSION

IV.1. Discussion

We were among the first clinics in Hungary to introduce nasal diagnostics (1983) and later, intranasal endoscopic surgery in the oto-rhino-laryngology and head-neck-surgery department, thus we were able to take part in early neurosurgery of the pituitary surgery, thus combing the two fields. Initially, without any prior commitment to any of the procedures, we sought to find out how the endoscope could be more beneficial than conventional microscopic techniques. In order to judge this, the endoscope was first used exclusively in the preparation of the operation to identify the anatomical structures and to clarify the developmental variations affecting the operation, and the positive experiences gained with this, prompted us to first enter the endonasal section and almost unnoticably the sphenoidotomy and finally intrasellar tumor removal wass also performed with an endoscope. Perhaps we were able to complete the removal of the tumor completely by endoscopy in the case of the 8th patient, and we did not break the relative surge that followed then because we did not feel the need to introduce the new technique. The first operations lasted 2–2.5 hours, despite the fact that the intrasellar part was always microscopically, which is also very favorable in international comparisons, since in the largest centers, at the beginning, 3.5–4 hours of surgery was achieved after 30-40 patients reduce to 2-2.5 hours (12). However, in the last 10 patients, total tumor removal was done with only endoscope in six patients, with an average time of 1 to 1.5 hours (the shortest endoscopic intervention was 40 minutes). The shorter surgical time, in international comparisons, is probably also due to the fact that we do not feel compelled to use the endoscope at all costs and, if the operation becomes cumbersome, we can easily and quickly use the well-proven microscope technique. This is probably also due to the fact that the endoscopic equipment is still not optimally optimized, especially in the instrumentation of the intrasellar phase. In order to maintain this level of safety, we have not been able to ignore the continuous use of the retractor, although this is likely to be the next big step in the learning process. The benefits of the endoscopic removal of the pituitary adenoma are mainly questioned by former large pituitary centers, often rightly. Classical microscopic operations also show further development, and intrusions by transeptal or ostium sphenoidal expansion are also considered minimally invasive, which is an alternative to the endoscopic technique (16,50). However, most believe that while the potential for further development of the classical microscope is very limited, whereas the endoscopic technique has a very bright outlook (51). However, a proper comparison of different surgical methods can only be credible in those centers where, after a large number of microscopic (sublabial transseptal) interventions, they have gained significant experience with endoscopic techniques (52-55). Our experiences mainly support the statements that support the equivalent practice of microscopic and endoscopic techniques, since the alternate use of the two interventions, at each stage, allows for the most appropriate exploration for the given anatomical and pathological situation. Introducing the use of the endoscope is a great help in mapping the pre- and intraoperative anatomy, by bringing the operative area "near the instrument", and lateral recesses can be seen with the use of angular optics. Endoscopic techniques (56) involving the removal of the back of the septum and the front wall of the sphenoid sinus with the mucosa are widespread. In the method we use, the multilayer closure with sparing the mucoperiosteal lobes of the front wall of the septum and the sphenoid sinus and the mucous membrane of sinus result in restitution ad integrum healing (Figures 8, 9). In addition to the introduction of the new endoscopic technique, and using the microscope as needed, we have retained the unique benefits of binocular (stereo) vision and superior depth of field. In addition, hydroscopy in the sinus cavity provides the possibility of viewing 180 ° for minor bleeding, and for finding residual tumor parts. Introducing the device intradurally, it provides insight into the parasellar skull base through minimally invasive gates for transnasal techniques (Figure 7). The extension of endoscopic techniques may mean the possibility of further advancement primarily for the endoscopically assisted removal of tumors affecting the anterior skull base. In our cases, with the introduction of endoscopic technique, the operative time and intraoperative blood loss significantly decreased. Although we are not yet able to disregrard the use of nasal tampons, but gradually reducing the tampon period and using soft tampons, hospital stay can be reduced, and patient satisfaction is also gradually improving. The intervention is further minimally invasive, significantly modifying the size of the intranasal exploration, enabling early mobilization of the patient, which significantly improves the patient's perioperative comfort. As a result, nasal breathing problems detected by previous interventions have drastically decreased, as the integrity of the cartilage and bone of the septum remains largely in tact, and the development of possible post-operative intranasal connective tissue contractions can be eliminated by endoscopic revision.

IV.2. Discussion

Surgical treatment of lesions affecting the skull base can be challenging for both neurosurgery and oto-rhino-laryngology and head-neck-surgery. Due to the common work of these professions, a close co-operation has been developed in our departments since the work of *Bodosi* and *Czigner* in the mid-1980s. As a result of the collaborative work of the different fields, many transcranial, transacial explorations have been created, with which, we can achieve tumor remove at almost any localation (57,58). In recent decades, a new area of endoscopic skull base surgery (39) has emerged as a result of the recent co-operation of the oto-rhino-laryngology and head-neck-surgery and neurosurgery departments. Using endoscopic techniques, lesions affecting the center of the skull are most likely to occur through the nasal routes (59). Recently, we may include these interventions in increasingly popular, minimal-invasive interventions, compared to transcranial excerpts requiring much greater invasiveness in some cases. However, we should not forget that the skull is opened the same way as in endoscopic skull base surgery, but in contrast to standard microsurgical approaches, we always perform a craniectomy and are aware of the unique complications (liquid flow, meningitis) that can arise from these interventions. In other literature, there is an increasing number of experiences from case studies and major centers (24-39, 59) in endoscopic skull base surgery. There are a number of studies to group and simplify these interventions, but there is still a lack of consistency between these studies, which can be confusing for the reader. In tumor surgery, the advantage of the endoscope over standard microbial surgery is to bring the "hidden places" into the field of vision, aiming at both the complete removal of the tumor and the protection of critical nerve elements. To do this, the optics provided at different angles by rigid endoscopes, provide a high degree of freedom and flexibility (18). It is not easy to compare the various sugical and approach techniques, as their indication and outcome vary widely depending on the nature and location of the disease. The advantages of endoscopic skull base surgery were found to have lower surgical burden, shorter hospitalization time in the post-operative period, minimal post-operative discomfort and the cosmetic advantage of open skull surgery (28-30, 33-35). An additional benefit of endoscopic exploration is that craniectomy in rhinobase does not require the brain to be held (57). In transcranial surgery, to get to the intracranial pathology, up to the center of the skull, after the opening of the dura, the basal cisterns must be opened and the brain must be held slightly, even without the use of retractor blade. In transnasal routes, nasal meatus and paranasal sinuses do not require brain maintenance to achieve basal lesion, thus avoiding brain retractor induced ischemia, intra- or post-operative brain swelling. For neuroendoscopic interventions, the surgeon's perfect anatomical orientation, excellent endoscopic practice (common team training, gradual learning curve) (39) and the use of the latest technical equipment are essential. With these abilities and opportunities, it is possible to overcome the difficulties of endoscopic surgery: monocular vision (unless a three-dimensional endoscopic device is available), visually impaired viscosity in massive bleeding, manipulation with critical vascular and nerve formulas at high depth, or vascular complication the above-mentioned aggravating circumstances of the fast solution options (57,59). Recently, the popularity and widespread use of the terms minimally invasive or minimally exploratory surgery may be misleading. In endoscopic skull base surgery, in contrast to transcranial microneurosurgery, the majority of cases are craniectomy. Despite the fact that there is no visible surgical damage on the skull, a very extensive skull defect can occur on the skull base, depending on the surgical procedure. Similar methods can be seen in transsphenoidal pituitary approaches as well, unless we compare the cranial defects of endoscopic transeptal and endoscopic posterior transseptal applied in our clinic. Although special attention needs to be paid to careful reconstruction and skull base plastics in standard skull base operations, which is extremely important for transnasal surgery, as it can only minimize the risk of complications of endoscopic surgery, post-operative liquorrhoea and subsequent meningitis. Endoscopic surgery, in addition to being minimally invasive, has maximum aggressive interventions. For the treatment of skull base tumors, we refer to the indications (24.59) and the indications used in other literature: the size of the tumor is small or medium sized, the vascular formulas should not be filtered as much as possible, and there should be no excessive lateral extension, but it is very advantageous if the blood supply of the tumor can be eliminated first thing during the approach. In the case of the operation indicated in our case report, the endoscopic transnasal transsphenoidal exploration could be visualized by planum sphenoid, sella, optic and carotid protuberance, as well as clivus. When a meningoma affecting planum sphenoidal, tuberculum sella and sella was confirmed in our patient, we were sure that the lesion could be removed by endoscopy. We agreed with the patient on the endoscopic procedure, as well as other surgical techniques because, in the case of the prefixed optic chiasm on the imaging images, there was a higher chance of optic nerve damage in the transcranial exploration, while in the case of transnasal route the optic nerve could remain intact. On the basis of the MRI images, it was evident that in the present case the patient had extensive sphenoid sinus, which made the endoscopic exploration considerably easier. After exploration of the sphenoid sinus, the bone was drilled into and then a craniectomy was performed with a *Kerrison* rongeur. In the course of revealing the tumor, it was deprived of its blood supply, so its practical removal was in avascular form, greatly helping the further removal of the tumor, as massive bleeding during endoscopic interventions complicates and slows the operation considerably as identifying the source of the bleeding itself can sometimes become difficult. By removing the tumor, both the vascular and nervous structures were releaved. One of the main aspects of the surgery planning was the avoidance of possible CSF leakage, so we used a fascia and fat graft to close the dura (multilayer dural closure - intradural, extradural intracranial, extracranial, subperiosteal). Reconstruction can be enhanced by using a fibrin / tissue adhesive, but spinal drainage was also used for four days to relieve the plastic.

IV.3. Discussion

History of Craniofacial Surgery

A general trend in the development of neurosurgical techniques is to minimize the extent of surgical exposure and iatrogenic injury while maintaining the greatest therapeutic efficacy. The first descriptions of a combined transcranial and transfacial (i.e., craniofacial) approaches are generally attributed to pioneering neurosurgeons such as Dandy (1941) (60) as well as Ray and McLean (1943) (61), for the resection of invasive orbital tumors. A recent paper from John Hopkins Medical School (62), however, published material from the operative notes of their famous predecessor, Harvey Cushing, who precisely documented the craniofacial approaches he applied on 3 patients with anterior skull base involvement as early as 1902e1909. More than half a century later, in 1963 Ketcham et al. (41), discussing the experience of a method previously reported in 1954 by Smith et al. (40), also described a combined method of transfacial and transcranial (subfrontal) exposure, with the latter aiming at the better staging of the intracranial extension and achieving a safer basal craniotomy for en bloc transfacial tumor removal. Later, in 1990 Janecka et al. (43) described a set of techniques for transfacial exposure of paranasal tumors by means of the preparation, temporary translocation, and, eventually, reposition of different sizes of composite anatomical units of the face (a.k.a. facial translocation). The authors likewise proposed that complementary craniotomies may be added to these approaches to aid in 3-dimensional tumor removal. The anterior cranial fossa in such cases used to be accessed traditionally via a standard pterional or bifrontal approach, extended from the cheek incision. This combined approach granted a surgical view from the contralateral Eustachian tube to the ipsilateral geniculate ganglion, together with the nasopharynx, clivus, sphenoid sinus, and the cavernous sinus. Although such a generous exposure allows extensive tumor resection, it is weighed against the challenge of restoring critical barriers as well as that of providing functional and cosmetically satisfactory reconstructions. Such heroic exposures eventually carry a considerable burden of complications, as reviewed by Ketcham et al. (43).

Toward Minimally Invasive Approaches

With the aim to reduce the extent of transfacial incision and facial osteotomies, in 2003 Liu et al. (44) proposed a set of minimally invasive approaches to the skull base and to the paranasal sinuses. They introduced 3 distinct exposures: 1) the standard and extended transbasal approaches, 2) the transmaxillary and combined transmaxillary-transsphenoidal approaches, and 3) the transsphenoidal and extended transsphenoidal approaches. The authors also suggest a combined use of standard transbasal and either transmaxillary or transnasal transsphenoidal approaches when the tumor invades sinonasal regions that are “blind spots” for the standard transbasal approach alone; however, the proposed and described transbasal (bifrontal) approach are in fact still not minimally invasive. Indeed, the different variants of traditional transbasal approaches (i.e., pterional, subfrontal, and bifrontal craniotomies) provide a large surgical exposure of the anterior fossa; however, such approaches are frequently complicated by retraction injury, intraparenchymal hemorrhage, and edema of the frontal and temporal lobes. The extensive skin incision and muscle retraction applied carry considerable risks of wound infection, subgaleal hematoma, facial or supraorbital nerve injury, as well as postoperative scarring and atrophy of the temporalis muscle. The introduction of the keyhole concept was a major step in the evolution of neurosurgery (46). This minimally invasive technique uses a small (3- to 5-cm sized) surgical incision and craniotomy, positioned after careful preoperative planning to optimally expose the intracranial lesion. As part of this concept, the supraciliary approach (eyebrow incision) was developed to access the anterior and middle fossa for the surgical treatment of aneurysms, frontobasal, suprasellar, or parasellar tumors (47). Since its introduction, several authors have described their positive results taking advantage of this technique (63-67). In our Institute, the supraciliary approach was introduced in the beginning of the 2000s for frontobasal tumors and aneurysms of the Willis-circle. Based on the excellent results experienced, we gradually widened the indications for this approach. As we found, the supraciliary exposure provides adequate access to intracranial extensions of tumors invading both the sinonasal area and the anterior fossa. This resulted in the development of a combined method of the supraciliary and transfacial exposure as a minimally invasive approach for the treatment of such surgically complex tumors. Even though in the hereby proposed combined technique (where the supraciliary incision is connected to the facial incision) the nerves passing through the supraorbital notch are necessarily divided, in our experience, the majority of the function comes back within a few months in most of the patients. We experience that this technique provides a convenient anatomical access for a reliable, watertight sealing of the dura even in such a difficult site as that above the lamina cribrosa. In selected cases, with relatively simpler anatomical situation, an isolated lateral (thus nerve-saving) supraciliary incision would be sufficient and thus also can be recommended in conjunction with the proposed limited transfacial approach.

Extended Endoscopic Approaches

With the emergence and expanding experience in the field of endoscopic endonasal approaches, it has become increasingly possible to access multiple previously endoscopically less accessible intracranial regions, including the anterior fossa, via techniques referred to as extended endonasal approaches (EEAs) (19, 39). Accordingly, EEA, as a minimally invasive approach, can be suitable in experienced hands for the treatment of tumors invading both the anterior fossa and the sinonasal area. However, the use of EEA is limited by the locoregional extension of the pathology. Indeed, according to the European Position Paper of the European Rhinologic Society, absolute contraindications for EEA as an alternative for a transcranial approach include an extension of the tumor lateral to the mid orbital roof or the optic nerve, an anterior and/or lateral involvement of the frontal sinus, and sinonasal tumors with brain parenchymal invasion (39). Similarly, an endoscopic approach is not recommended as an alternative for open transfacial surgery when the resection of a sinonasal tumor requires orbital exenteration, skin excision, or maxillectomy (apart from that of the medial part) (39). Furthermore, the rate of postoperative CSF leak, as the most common complication after EEA, has been reported to be remarkably greater compared with open transcranial surgical procedures, especially in reports before the development of endoscopic reconstructive skull base techniques (39). Our team has more than 10 years of experience with endoscopic endonasal approaches (18) and has increasing experience with EEA for the resection of tumors of the anterior fossa (19). To our observation, the duration of the surgical procedure with an EEA may be remarkably greater compared with the craniofacial approach presented here, especially in cases in which dural reconstruction is needed. The position paper of the European Rhinologic Society highlights the clear need of incremental experience in the field of endonasal endoscopic reconstructive surgery before the selection of an EEA as an option for skull base tumors as a prerequisite for its superiority over open surgical approaches (39). This, however, evidently necessitates high-volume centers. Especially for such rare and anatomically complex conditions that invade both the sinonasal area and the anterior fossa, our proposed combined minimally invasive open craniofacial approach might be a suitable technique for a broader range of rhinologic and neurosurgical communities, even for centers with limited patient volume.

V. CONCLUSIONS

V.1. Conclusion

Based on our experience, the foundation of the success of the operation include, careful endocrinological preparation and post-operative care, as well as intraoperative alternation of microscopic and endoscopic techniques as needed. The combination of the two techniques and the use of posterior transeptal-transsphenoid exploration, fully complies with the minimally invasive principles and thus provides the surgeon with continuous, ideal adaptation to the current situation, while providing the patient with the surest healing opportunity.

V.2. Conclusion

In our case study, we report on our experience with endoscopic removal of a skull base tumor located in the frontal skull base, discussing its benefits and potentially dangerous complications. In general, we can conclude that endoscopic skull base surgery cannot yet replace standard microsurgery. But with correct indication, in some cases, it can replace or complete the existing surgical repository of the underlying pathological lesions affecting the skull base. After reviewing the data from different literature, this is the first reported case in Hungary for the endoscopic transsphenoidal removal of a skull base meningoma and the nasoseptal *Hadad* lobe skull base reconstruction.

V.3. Conclusion

The main goal in sinonasal and skull base surgery include being radical, while at the same time, being as minimally invasive as possible, while retaining functionality. Our results, presented as a whole, indicate the successful application of the novelty of the minimally invasive and time-saving combination of supraciliary keyhole surgery and limited facial translocation. The resulting being: an overall low mortality rate, a good 3-year survival rate, a high frequency of gross total tumor removal, along with satisfactory results in secondary outcome measures, such as post-operative complications, hospital stay, and esthetic results. Based on these, we highly recommend this combination technique for widespread use in the surgical treatment of tumors involving both the sinonasal area and the anterior cranial fossa, especially in extensive cases falling out of evidence for wholly endoscopic surgery, and for neurosurgical units in centers with limited patient volume.

NEW RESULTS (according to the aims of this thesis)

1. In the pituitary surgery, we had an early opportunity to use the endoscope, thanks to the start of the nasal endoscopic surgery in the oto-rhino-laryngology and head-neck-surgery department here, in Szeged. In the initial period, we used only an endoscope to identify anatomical structures and developmental variations in the first phase of surgery. Based on our positive experiences with this, the use of the endoscope was gradually extended to sphenoidotomy and then to intrasellar tumor removal.

2. Introducing the use of an endoscope is a great help in mapping pre- and intraoperative anatomy, as it brings the operative area "near the instrument" and lateral recesses can be seen with the help of angular optics.
   In addition to the introduction of the endoscopic technique, the unique advantages of binocular (stereo) vision and excellent depth of field, were preserved by using a microscope as needed. In addition to these, the hydroscopy applied in the sinus cavity also offers the possibility of a 180 ° view for residual tumor parts, even in cases of minor bleeding.
   The alternate use of the two interventions at every stage, with maximum adaptation to the given anatomical and pathological situations, allows for the most appropriate exploration.

3. Expanding the endoscopic techniques of pituitary surgery, is an opportunity for advancement, especially for the endoscopically assisted removal of tumors affecting the frontal skull base. The combined endoscopic and microscopic surgery of pituitary tumors, used routinely, and with our endoscopic experience with surgery on intracranial ventricules, we have extended the use of endoscope to the treatment of cranial base tumors.
4. For neuroendoscopic interventions, the surgeon's perfect anatomical orientation, excellent endoscopic practice (joint team training, gradual learning curve) and the use of the latest technical equipment, are essential.
   To this end, necessary and further training, as well as cadaver exercises for level courses, have been developed.

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ATTACHEMENT – REPRINTS OF PUBLISHED PAPERS

APPENDIX I.

APPENDIX II.

APPENDIX III.