Diploma thesis

Transnasal endoscopic decompression of the optic nerve
A retrospective data analysis

submitted by

Isabella Viktoria Leitner

In fulfilment of the requirements for the degree of

Doktor(in) der gesamten Heilkunde

(Dr. med. univ.)

at the

Medizinischen Universität Graz

conducted at the

Department of Otorhinolaryngology

under supervision of

Assoz. Prof. Priv.-Doz. Dr.med.univ. Peter Valentin Tomazic, PhD

Ass. Prof. Dr.med.univ. Wolfgang Köle

Graz, 30.06.2020

Statutory Declaration

I declare that I have authored this thesis independently, that I have not used other than the declared sources / resources, and that I have explicitly marked all material which has been quoted either literally or by content from the used sources.

Graz, 30.06.2020 *Isabella Viktoria Leitner eh.*

Acknowledgements

I would like to thank my supervisor Assoz. Prof. Priv.-Doz. Dr.med.univ. Peter Valentin Tomazic, PhD for the opportunity to write this diploma thesis, especially for his constant availability, patience and solutions he could offer for my concerns. My thanks also go to Ass. Prof. Dr. med. univ. Wolfgang Köle for his support.

At this point I would like to thank my parents Mag. Meinrad and Mag. Ingrid Leitner, who were always there for me, who supported me with my decisions and enabled my studies. Special thanks go to my mother for proofreading my thesis.

I would also like to thank my sisters Mag. Rebekka Leitner and Lena Leitner for their emotional support.

Furthermore, I would like to thank my friends and all people who supported me during my studies for the unforgettable time.

Zusammenfassung

Einleitung
Die transnasale endoskopische Dekompression des Nervus opticus ist ein Operationsverfahren, mit dem der komprimierte Nerv entlastet und weitere Schäden durch Verletzungen verhindert werden können. Die Hauptursachen für eine Kompression sind Unfälle, die zu Schädelfrakturen führen und expansive Eingriffe, wie zum Beispiel Tumore. Neben der konservativen Therapie, der Gabe von Steroiden und intrakraniellen Zugängen ist die endoskopische Dekompression eine etablierte Methode. In der internationalen Literatur divergieren die Meinungen stark, welche Parameter das postoperative Sehvermögen der Patientinnen und Patienten beeinflussen. Ziel dieser Studie war es, mehrere Parameter zu analysieren und Schlussfolgerungen zu ziehen, die helfen können, die Behandlungsmöglichkeiten für zukünftige Fälle zu verbessern und anzupassen.

Material und Methoden
In dieser Studie wurden Daten von Patientinnen und Patienten an der Abteilung für Hals-Nasen- und Ohrenheilkunde der Medizinischen Universität Graz gesammelt, die zwischen dem 1.6.2001 und dem 18.11.2018 einer Optikusdekompression unterzogen wurden. Insgesamt erfüllten 62 Personen die Einschlusskriterien und an 32 Fällen wurde eine endoskopische Dekompression durchgeführt. Diese wurden für die Hauptanalyse berücksichtigt. Nach retrospektiver Erhebung der Daten folgte die statistische Analyse, um die Parameter zu vergleichen, die eine Sehverbesserung nach der Operation begünstigen.

Ergebnisse
Die Verwendung von Steroiden zeigte keinen Vorteil am visuellen Ergebnis. Im Gegenteil, von den Fällen ohne Steroidbehandlung verbesserten mehr (66,67%) ihr Sehvermögen als in der Gruppe mit Steroidbehandlung (31,25%) (p=0,049).
Die Personen, bei denen in der radiologischen Bildgebung vor der Operation eine Verletzung des Sehnervs nachgewiesen werden konnte, hatten eine höhere Heilungsrate (66,67%) im Vergleich zu der Gruppe mit einem unversehrten Sehnerv (28,57% verbessert) (p=0,033).

Schlussfolgerungen
In Anbetracht der Erfolgsrate der Visusrehabilitation (50%) nach endoskopischer Operation wäre die Erstellung einer Standardleitlinie für Sehnervenkompressionen ein wichtiges zukünftiges Ziel zur Verbesserung der Erfolgsrate. Schlussfolgend aus den Ergebnissen

könnte der radiologische Befund als Indikator für eine Operation dazu beitragen, nicht vorteilhafte Operationen zu vermeiden. Auch die Verwendung von Steroiden sollte sorgfältiger erwogen und mit weiteren Studien zur Analyse ihrer Durchführbarkeit untersucht werden.

Überraschenderweise wurde keine starke Korrelation hinsichtlich des Zeitpunkts der Operation beobachtet. Da unsere Studiengruppe klein war und von mehreren Autoren ein chirurgischer Eingriff innerhalb eines kurzen Zeitfensters empfohlen wird, sollte die allgemeine Empfehlung für eine sofortige Operation gültig bleiben.

Abstract

Introduction

The transnasal endoscopic decompression of the optic nerve is a surgical method which can decrease pressure on the nerve and prevent further damage after injury. The main causes for a compression are accidents which lead to skull fractures and expansive procedures such as tumors.

Besides conservative therapy such as steroids and intracranial approaches, endoscopic decompression is a well-established method. In the international literature opinions on which parameters influence the visual outcome of the patients differ a lot. The objective of this study was to analyze several parameters and draw conclusions which may help to improve and adapt treatment options for future cases.

Material and methods

In this study, data from patients at the Department of Otorhinolaryngology at the Medical University of Graz were collected who underwent an optic nerve decompression between 1 June 2001 and 18 November 2018. In total, 62 patients fulfilled the inclusion criteria and 32 underwent an endoscopic decompression. They were considered for the main analysis. Retrospectively collected data were statistically analyzed to compare parameters that favor visual improvement after surgery.

Results

The use of steroids did not show a benefit in visual outcome. On the contrary, in the group of patients with no steroid treatment more patients (66.67%) improved in vision as in the group with steroid treatment (31.25%) ($p=0.049$).

Patients with an injury of the nerve proven in radiological imaging before surgery had a higher recovery rate (66.67%) in comparison to the group with a normal optic nerve (28.57% improved) in their scans ($p=0.033$).

Conclusion

Considering the success rate of vision recovery (50%) after endoscopic decompression surgery, the establishment of a standard guideline for optic nerve compressions would be an important future target to improve the success rate. As a conclusion, the radiological findings as indicator for surgery might help to avoid non-beneficial surgeries. Moreover, the use of

steroids should be considered more carefully and investigated with further studies analyzing their feasibility.

Surprisingly, no strong correlation was observed regarding the timing of surgery. Since our study group was small and immediate surgery in a short time frame is recommended by several authors, the general recommendation for immediate surgery should remain valid.

Table of contents

Glossar and abbreviations

AION	anterior ischemic optic neuropathy
CRP	c-reactive protein
CSF	cerebrospinal fluid
CT	computed tomography
ENT	ears, nose and throat
ICP	intracranial pressure
MRI	magnetic resonance imaging
NASCIS	national spinal cord injury study
NF 1	neurofibromatosis type I
RAPD	relative afferent pupillary defect
RCT	randomized controlled trial
TBI	traumatic brain injury
TON	traumatic optic neuropathy
UK	United Kingdom
VEP	visual evoked potentials

Table of figures

Tables

1 Introduction

The transnasal endoscopic decompression of the optic nerve is the gold standard method for decompression of the optic nerve due to damages of trauma, tumors or inflammations. The results after the operation are not always clear, as many different factors influence the visual outcome of the patients. The aim of this study is to analyze the impact of these factors and to determine under which preconditions the best result can be achieved. The indication and success rates of the ENT Department of the Medical University of Graz are used to create a treatment algorithm with the best results with patient data from 2000 to 2018.

1.1 The paranasal sinuses

1.1.1 Anatomy and development of the paranasal sinuses

The paranasal sinuses are pneumatized appendices in the human skull and are created differently during fetal development. The maxillary sinus and the frontal sinus have a common drainage. They develop from the ethmoid infundibulum or also from an ethmoid cell or a frontal recess. Only the sphenoid sinus develops independently from an expansion of the nasal mucosa. This takes place at the end of the third month. The development of the sinuses starts within the cartilaginous structures which is called the primary pneumatization. Later, the secondary pneumatization of the bone follows which replaces the cartilage. (1)

An adult usually has four pairs of paranasal sinuses. The ethmoid cells and the maxillary sinus exist since birth, but the frontal sinus and the sphenoid sinus develop later and they also show a higher variability in form and size. (1)

1.1.2 Function and physiology of the paranasal sinuses

Because of the paranasal sinuses the skull becomes much lighter due to the air-filled spaces. They also act like a resonance body, so they have an influence on the voice. An important, if not vital function is also the protection of nerves and vessels. Like an airbag, external force can be buffered in the same way as in a punch or accident. Also they are important for the regulation of temperature. (5)

The paranasal sinuses are lined by a similar epithelium as the nose has, called the Pars respiratoria, but smaller in height. Histologically there are also not so many goblet cells and the epithelial cells carry cilia (ciliated epithelium). With their movement, secretions and foreign bodies can be transported out of the cavities. The mucus transport (mucociliary clearance) is genetically targeted towards the natural ostia / outflow tracts of the respective sinuses. (5)

1.1.3 The sphenoid sinus

The sphenoid sinus is located posterior to the other paranasal sinuses, above the nasopharynx and in front of the sella turcica. In most cases the ostium of the sinus can be found medial to the upper concha, in some cases lateral to it. (6)

Usually separated through a septum (or several), it develops between the age of 6 and 7 years a pneumatization which also includes the corpus of the sphenoid bone. (1)

The sphenoid sinus develops as a posterior expansion in the area of the sphenoethmoidal recess. (7)

Varying in size and shape the volume can reach between 0,3 and 11cm³. Through the sphenoethmoid recess, it is connected with the upper nasal meatus (demonstrated in figure 1). (1)

The roof of the sphenoid sinus is formed by the sella turcica. The sphenoidal conchae form a part of the anterior wall of the sinus. Its bony walls separate the sinus from the brain (above), the pharynx (below) and the nasal cavity (in front). (7)

Boundaries of the sinus are the septum medially (with variations), the lateral wall of the sphenoid bone (lateral border) with the carotid canal and the internal carotid artery. The dorsal border is formed by the clivus (a part of the sphenoid bone), the upper wall by the sella turcica and the bone of the anterior cranial fossa. Special attention during surgery should be paid to the optic chiasm which is located above the sinus. The floor is the thickest bone of the borders. Through the natural ostium the sphenoidal sinus is connected to the sphenoethmoidal recess and to the upper/common nasal meatus. (5,7)

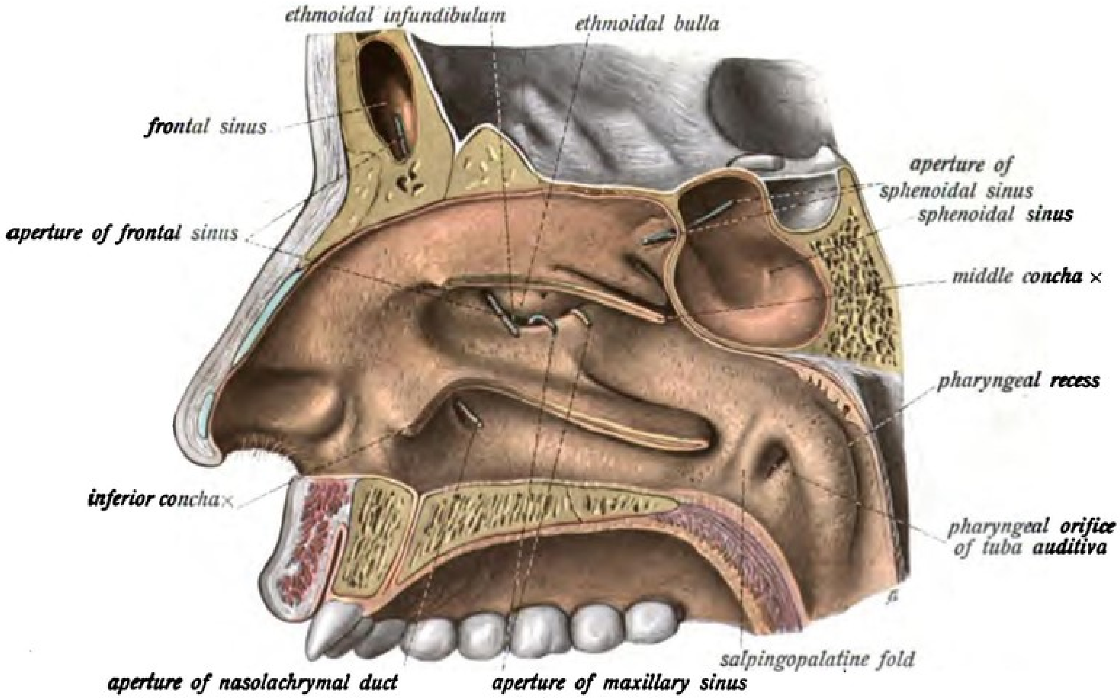

Figure 1:The nasal cavity and the sphenoid sinus (1)

1.2 The optic nerve

The optic nerve is not a real cranial nerve, more a continuation of the brain which connects the retina with the lateral geniculate nucleus. It consists of more than one million axons of retinal ganglion cells. The central retinal artery and vein pass through the nerve to the bulb of the eye. The following parts can be described: intrabulbar (approx. 1mm), intraorbital (24-30mm), canalicular (8-10mm) and intracranial (approx. 15mm). The nerve can be compressed especially in the canalicular section (because of bony confinement) and the nerve cannot evade due to its attachment to the dura mater. In reverse, the intracranial part is protected by the surrounding bone and the intraorbital part by soft tissue. In its canalicular part, the nerve is accompanied by the ophthalmic artery (Figure 2) and parts of the sympathetic nerve system. During surgery, special attention must be paid to this artery because of its immediate proximity to the nerve. Both structures can pass through the sinus without coverage if the pneumatization is well-developed. (5,7–9)

The intraorbital part is usually not straight, the nerve runs curved. The intrabulbar/intraocular part is composed of non-myelin sized nerve fibers, so its circumference is smaller than in the other parts and the fibers are transparent. This part is also called the optic disc, which

forms a hole in the retinal pigment epithelium and the choroid. (7,9)
Blood supply is varying between the parts, the posterior ciliary arteries with their anastomoses, the pial and choroid plexus are covering the intraocular part followed by branches of the cranial arteries for the intracranial and canalicular part. (7)
The optic channel is not completely covering the nerve in 4% of patients. The normal length is about 10mm and the width 4-5mm. (10)
In coronary CT scans, the normally circular shape of the channel can be compared with the opposite side after a trauma. (9)
If the sphenoid sinus is sufficiently pneumatized a “bulge” of the nerve´s bony channel can be seen. Between the optic nerve bulge and the carotid bulge lies the so-called optico-carotid recess. (11) According to several anatomical studies, this recess is an important marker for surgical procedures in the area of the sphenoid sinus. It also helps to identify the internal carotid artery and the optic nerve. Special attention should be paid to anatomical variations. (11–15)

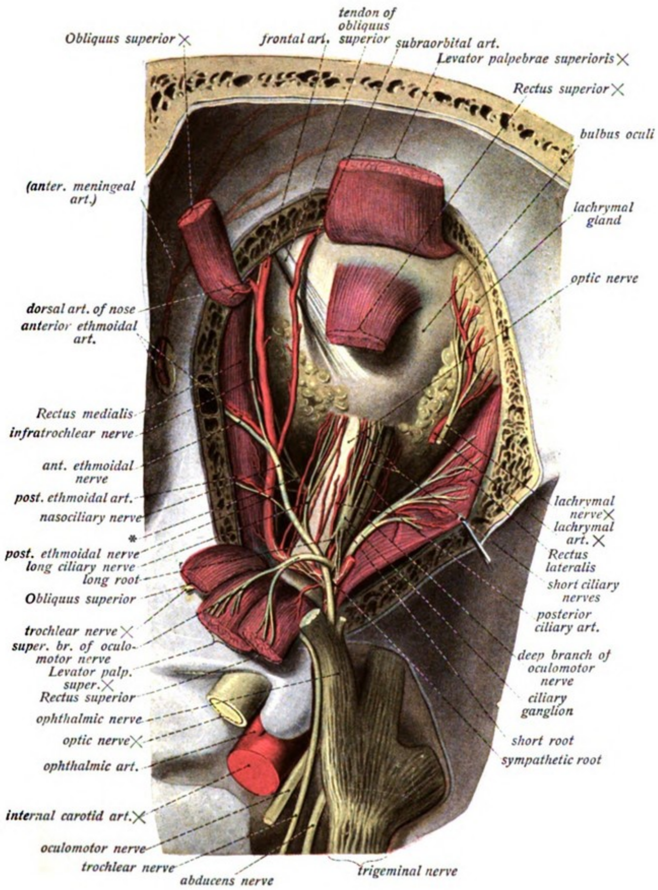

Figure 2:The optic nerve entering the globe (2)

1.2.1 The nerve sheaths

The nerve sheaths of the optic nerve originate from the meninges of the brain. A distinction is made between an external (equivalent to the thick membrane of the brain) and an internal sheath (equivalent to the soft membrane and arachnoid membrane). There is an intervaginal space between those membranes. (7)

While slitting the nerve sheaths, the subarachnoid space located under the internal layer can be opened. It has a connection to the liquor space. This can lead to a CSF leak, which could be avoided by incising only the external layer. Connective tissue makes it difficult to separate the membranes. (9,16)

1.2.2 The anulus of Zinn

The anulus of Zinn or common tendinous ring is the origin of the extraocular muscles at the end of the optic nerve canal. The muscles form a cone surrounding the optic nerve with accompanying vessels and nerves (Figure 3):

Muscles:
- Superior rectus muscle
- Inferior rectus muscle
- Medial rectus muscle
- Lateral rectus muscle
- Superior oblique muscle

Only the inferior oblique muscle originates from the floor of the orbit.

Nerves:
- Optic nerve (II)
- Oculomotor nerve (III)
- Abducent nerve (VI)
- Nasociliary nerve (V1a)

Vessel:
- Ophthalmic artery

(5,7)

This area is also the fusion point of the pia mater (soft membrane of the brain) and arachnoid mater (thick membrane of the brain), where the nerve can get compressed easily. Usually, the anulus gets incised too during an optic nerve decompression. (16)

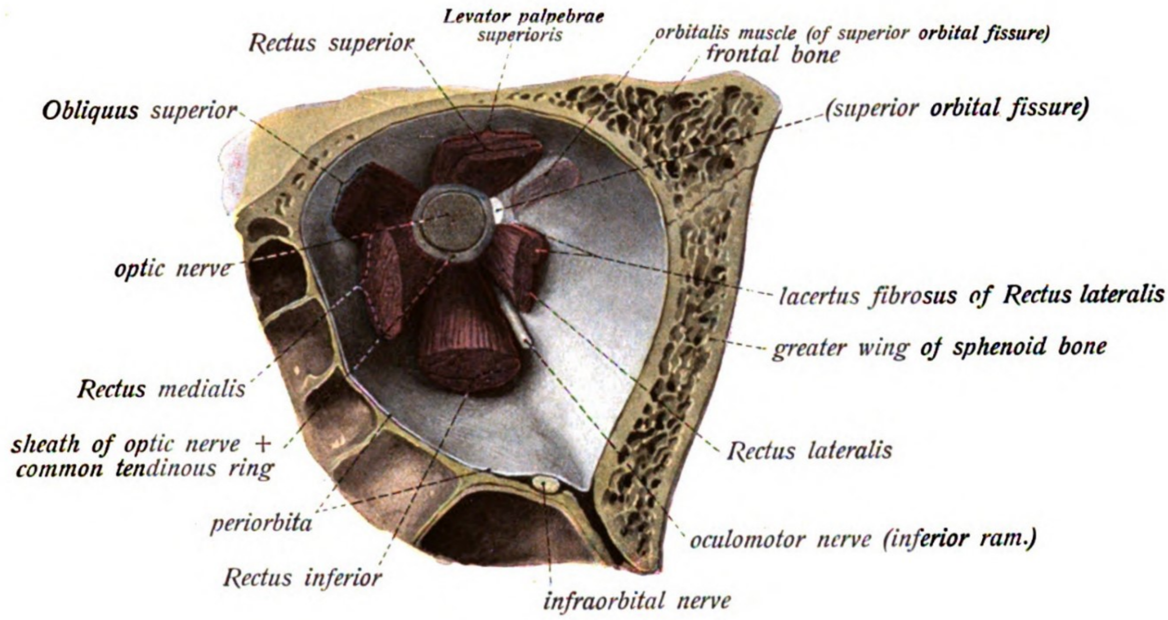

Figure 3:Scheme of the orbit, showing the common tendinous ring (3)

1.2.3 Optic nerve injuries

1.2.3.1 Traumatic injuries

A traumatic optic neuropathy (TON) is the result of direct or indirect trauma, usually an unrecoverable condition. A differentiation is also made between primary (immediately after injury, e.g. concussion, avulsion, contusion, transection, etc.) and secondary (after surgery, e.g. edema, ischemia, etc.) trauma which caused the injury. Iatrogenic damages can be caused by medical interventions (e.g. surgery). TON is very common with a young age and affects around 5 of 100.000 people. Pathophysiological, the retinal ganglion cells, which are important for the neurological transmission from the retina to the brain, may die due to insufficient blood supply. It can happen with up to 3% of all traumatic brain injuries (TBI) and mid-face fractures. A closed skull trauma may lead to TON in 0.5-5% cases. Two of three head traumas go along with an optic nerve injury. The cause of an injury can be any object from an accident (bullets, iron bars, etc.), bone fragments or a surgery close to the optic nerve which can affect it directly. Direct traumas have a lower rate of recovery. Most of the time, the intracanalicular and the intraorbital part may get injured, due to the tight fixation to the surrounding tissue (periosteum, dura mater).Other reasons leading to indirect trauma are general accidents (traffic or domestic accidents, external force, etc.). If the optic canal gets injured and the nerve sheath hemorrhaged, the nerve is no longer adequately supplied with blood. Approximately one third of the patients with TON have fractures of this canal. Blindness is often the result. Very typical are bicycle accidents with an injury of the frontal or temporal area where the nerve gets disjointed or avulsed. Also, multiple face/skull base fractures can affect the optic canal. (8,9,17–22)

1.2.3.2 Orbital fractures

Orbital fractures (happen with 3% of facial fractures) can lead to a damage of the optic nerve when it gets compressed or bruised by edema or injuries of the bone. Therapeutic approaches are steroids or a surgical decompression. Hemorrhage, transection and stretching of the nerve can lead to blindness or progressive visual loss. Initial stabilization and treating damaged contents of the orbit are also important (e.g. sclera, retina, lens). (23)

Those complex fractures can be classified by the damaged part of the orbit (walls, floor and roof), mostly by the surgeons. It depends on the clinical setting and profile of the risk whether a surgery has to be performed. There are different surgical approaches, e.g. endoscopic surgery is especially used for medial wall fractures. (24)

1.2.3.3 Chronic injuries

A slow deterioration of vision is typical for a compression of the optic nerve. Fast vision loss is more common with an optic neuritis or an anterior ischemic optic neuropathy (AION). An injury in the orbital part of the nerve can lead to swelling, exophthalmos, retinal detachment, papilledema, etc. Causes can be a tumor, Grave ´s Disease (typical is an asymmetric progressive loss of vision), sarcoidosis, tuberculosis, fungal infections, mucoceles, fibrous dysplasia, aneurysm, pseudotumor and other expansive processes.

Chronic compression of the nerve leads to a venous congestion - the blood supply to the nerve and retina through the capillaries decreases and may cause blindness. (19,25–27)

An injury to the optic nerve can lead to complete ablation or necrosis. This can result in permanent blindness. Rehabilitation depends on the severity of the injury.(8)

Orbital hematoma which are a frequent condition can cause an orbital department syndrome (OCS). Local injections and trauma are the main reasons, but also infections can raise the orbital pressure. Lateral canthotomy is the first treatment option but if this is not sufficient, an optic nerve decompression might also be necessary. Applying acetazolamide and elevating the head can be a try for a conservative approach. (8,19,28,29)

1.2.3.4 Tumor compression

The most frequent tumors compressing the optic nerve are gliomas,: there are anterior (affecting the nerve) and posterior optic nerve tumors (affecting the chiasm). Usually, the posterior tumors cause more symptoms. Prognosis is better for young people than for older patients. In general, there is a high variability in tumors and there is a frequent association with neurofibromatosis type 1. Most of the time, children or adolescents are affected. Typical symptoms are a progressive loss of vision and depending on the localization, a unilateral anopsia or e.g. a bitemporal hemianopsia (chiasm is affected). If the hypothalamus or the suprasellar region above are involved, behavioral changes and endocrine manifestations are possible and the ICP can rise. The nature of these tumors varies from slowly growing and high aggressive. In general, the prognosis is good if the tumor is not extending to other structures of the brain. (30)

Meningiomas can also affect the visual structures and are related to the dura. They are more frequent with women and can also originate from the optic nerve sheath. Other origins are the optic foramen, the planum sphenoidale or the tuberculum sellae. They may also affect the hypothalamic function and extent to the cavernous sinus. Prognosis is worse than for optic nerve gliomas. (30)

Other tumors affecting the optic nerve are craniopharyngiomas which develop from remnants of Rathke´s Pouch. Typical of the tumor, besides a vision loss, are growth disturbance with children and endocrine disturbance (amenorrhea, galactorrhea, hypopituitarism) with women and men. Frequently those tumors have calcifications which can be detected by means of CT scans or even X-rays. (30)

The optic nerve can also develop tumors, the most frequent one is the optic nerve glioma. Those mostly benign tumors are also associated with NF 1 and cause symptoms like visual deterioration, changes of the optic nerve head (swollen, pale), vascular pathologies, strabismus or they are asymptomatic. Usually, the tumor is slowly growing and not intracranially expanding. Opinions diverge, whether they should be excised or observed because the risks of these tumors are still unclear. (31)

Malignant optic nerve gliomas are more likely in adulthood. Depending on the location of the tumor, proximal tumors can cause a bilateral visual loss and distal tumors typically affect only one side. Unlike benign tumors, the treatment options are not highly effective. Other tumors of the optic nerve are gangliogliomas, medulloepitheliomas and hemangioblastomas. There are primary nerve sheath tumors from the arachnoid and secondary tumors which are of intracranial origin.

Symptoms of the primary tumors vary depending on the location of their origin. They may cause a vessel obstruction, can grow intracranially and surround the optic nerve. Optic neuropathy, vision loss, proptosis and strabismus are possible signs in patients. Typical radiological findings are calcifications, an expanded nerve and hypodense tissue encircled by a hyperdense structure. Due to the difficult location and connection to the optic nerve, radiation therapy is more often recommended than surgery. Craniotomies can be performed for primary and secondary optic nerve sheath meningiomas to remove intracranial components. (31)

1.2.4 Diagnostics

After an injury, a detailed examination by an ophthalmologist should be carried out. A problem with these patients is the survey of medical history and the visual examination which is limited by comatose conditions, analgesics, injuries in the surroundings of the eye or injuries of the pupil (due to lesions of the 3rd cranial nerve). The reason is very often a serious accident. (8,16,18)

Diagnosis includes measurement of the visual acuity, pupillary light reaction, fundoscopy and perimetry. The capacity of vision should be frequently determined to see changes during the hospital stay. Usually, the central visual acuity is decreased when there is an inflammation or compression of the optic nerve. This is an important parameter for the diagnosis, as well as the missing pupillary reaction. In the unconscious patient, the presence of the afferent pupillary reaction is a sign that there is remaining visual function. RAPD is a sign for an injury. If both eyes are affected, the sign may not be there. The swinging-flash-light-test is a sensitive test for evaluation, the promptness of the pupillary reaction is a measurement for the extent of the damage. The examination of the visual field helps to localize the injury to a region along the optic tract (e.g. optic chiasm) which can be performed with perimetry or by a confrontation test for a less precise assessment. Typical of a tumor are bitemporal or homonymous hemianopia by compressing the optic nerve or chiasm.

In addition, imaging of the skull (CT, MR) should be performed. Slices of the axial plane are obligatory (Figure 3 is showing an axial MRI of the eyes). A coronal scan can detect injuries of the anterior skull base. (8,9,16,18,27)

Preoperative CT scans may also help to identify the exact location of the optic nerve, defects of the bone and the relationship to the sphenoid and ethmoid sinus to avoid injuries of the optic nerve. (12) Further, the detection of anatomical landmarks, such as the optico-carotid recess can be useful for surgery. (11)

A CT scan is favored to detect optic canal fractures, which is important to plan surgery. Other advantages of CT scans are: they can be used with foreign bodies (ferromagnetism is a contraindication for MRI), they are fast and they show lesions interior and exterior to the orbit. CT scans are considered as the best option to detect orbital fractures, the radiologist should examine the anterior and posterior chamber of the orbit and the position of the lens. The orbital veins and nerves should also be evaluated. (32,33)

Fundoscopy can help to assess the injury of the nerve. If an atrophy is detected, there is no indication for surgery. To examine the optic disc, direct or indirect ophthalmoscopy is performed. Normally, it is sharply limited, with a rosy color (because of capillaries) and with a central excavation (Figure 4 shows a healthy optic disc). Four to six weeks after a trauma an atrophic optic nerve leads to a pale optic disc. If a tumor is the cause, the damage is less visible in fundoscopy despite a severe vision deterioration. The compression inhibits the conduction of axons but does not destroy them quickly. The measurement of color vision can also show a decrease when the optic nerve is affected. To evaluate this, both eyes or the visual fields get assessed in their perception of an object of intensive color. Another, more precise option is the Farnsworth-test. It is also important to measure the intraocular pressure of the eye to detect edemas or hemorrhages which come with high pressure and an open globe (low pressure). (8,9,16)

Visual evoked potentials (VEP) belong to advanced diagnostics. They allow to read reactions of the visual tract by recording an EEG from the occipital lobe and are therefore an objective measurement for visual acuity. They are useful especially in unconscious patients. Reductions of more than 66% of VEP favors the indication of surgery. In general, patients with a TON due to a trauma have multiple injuries and need to be examined by an interdisciplinary (trauma) team. With a carotid sinus fistula or an aneurysm of the intern carotid artery, angiography must be performed. Ultrasound can help to determine a hematoma of the orbit or the optic nerve sheath. (8,9,16,18)

Figure 4: Fundoscopy showing a normal optic disc (4)

1.3 Surgery

The transnasal approach for optic nerve decompressions is considered "gold-standard" and has been the preferred method at the ENT University Hospital of Graz since 1991.
Benefits include reduced mortality, faster recovery of patients and the minimal invasive approach (which results in a better cosmetic outcome). (16)

1.3.1 Indications

Surgery should be performed when there is a decrease in visual acuity after an injury (which usually shows that the afferent optic nerve is affected) when the optic nerve is still intact.(16) This surgery allows to avoid further damage to the nerve which is caused by edema. Furthermore it is possible to liberate the nerve from bony pieces. (34)

In general, a traumatic injury, mucoceles, pseudotumor cerebri, fibrous dysplasia, ischemic optic neuropathy, endocrine orbitopathy, meningiomas and others are indications for an optic nerve decompression. (16)
There are different opinions on the timing of surgery. On the one hand, Yang et al. achieved in 96 patients suffering from TON the best results within a time frame of less than 3 days between injury and surgery. (35) On the other hand, Tandon et. al recommend 1-2 weeks as an interval. (18) Levin et al. could not find a benefit from treating an optic nerve lesion

immediately after accident in their interventional study with 133 patients. (36) In their prospective case study of 20 patients, Gupta et. al observed the best results within a time frame of 72 hours to perform surgery. (17) Sarkies et. al could not find any association between vision recovery and time of surgery. (29,37)

Dhaliwal et al. sum up the controversial findings in a review of 24 articles regarding the timing of intervention. According to them, no specific point of time is favored, but even late interventions may help to improve vision. (38)

If the intracranial portion is affected, most of the time a craniotomy is indicated. (16)

1.3.2 Contraindications and limitations

Surgery should not be performed if the optic nerve is completely avulsed, (because the nerve will not recover) if the shape of the bulb has changed distinctly, if anatomical difficulties do not permit surgery or if the patient is not amenable for surgery in general. (8,16)

With the endoscopic method, only the medial and inferior part of the optic nerve canal can be reached (which are closely located to the sphenoid sinus). If the superior or lateral part is affected, a craniotomy is indicated. (39)

Contraindications for endoscopic sinus surgery (FESS) are infections like acute sinusitis, orbital abscess or frontal osteomyelitis. (6)

1.3.3 Technique

At the University Hospital of Graz, the Stammberger and Messerklinger method is used.

Before starting surgery, anesthesia (general anesthesia is preferred) is necessary.

As initial step the middle turbinate may be injected with a mixture of lidocaine and epinephrine (1:100 000, 1%). Decongestive patties are deposited in the nasal cavity and in the middle meatus. A complete spheno-ethmoidectomy is performed in most cases. Alternatively, a paraseptal approach may be chosen depending on the anatomy and /or if an additional orbital decompression is required. The position of the superior turbinate helps to identify the natural sphenoid ostium. The ostium gets opened and enlarged with special attention to the internal carotid artery and the optic nerve to avoid injuries. After identifying the optic nerve canal, a diamond drill is used to thin out the bone which then can be gently removed by dissectors. The incision of the optic nerve sheath and the annulus of Zinn is performed afterwards, but not in every case. (6,16)

This procedure can reduce a compartmental syndrome after an injury. (40,41)
According to Luxenberger et al., the incision is indicated for patients with close injuries to the optic nerve channel (e.g. fractures of the bony canal, intrasheath hematoma, swelling of the nerve). Sometimes, an orbital decompression follows in the same procedure. At the end of the surgery the nostrils get a tamponade. (6,16)

1.3.4 Decompression for tumors

Tumors affecting the optic nerve, e.g. gliomas also lead to a deterioration of vision. If the optic chiasm is compressed, a bitemporal hemianopsia can often be diagnosed. Further, a raised ICP and the involvement of the hypothalamus are common. There may also be behavioral and endocrine abnormalities in patients. Usually a biopsy is performed to clarify the tumor entity. When debulking suprasellar craniopharyngiomas which are affecting the optic nerve, the hypothalamus and the third ventricle, a complete resection can cause damages to those structures. The qualities of the tumor (solid, cystic, calcifications or it enlarges the sella turcica) have an impact on the decision whether a complete removal should be performed. Remaining parts can be treated with radiation. (30)
Fibrous dysplasia, which has a low incidence, can also cause optic nerve decompression where surgery is the only curative intervention. Sometimes only a subtotal debulking/decompression can be achieved endoscopically (15)

1.3.5 Complications

There is always a risk of damaging the internal carotid artery (if it is not covered by bone) and the ophthalmic artery (when it is medial to the optic nerve; 15.5%). A mild CSF leak may occur because of the optic nerve slitting. Fibrin glue is usually applied to avoid this complication. (8,16)
If a CSF fistula occurs, it can be repaired by a re-operation. (6)
The optic nerve may be injured (during the opening of the sphenoid bone), as well as other bordering structures (apex of the orbit, cranial structures) and there is also a risk of infections of the sinus and meningitis. (16,42)

1.4 Conservative treatment

High spontaneous recovery rates are reported with patients who initially had a good vision after injury. (33) Also, if the compression is caused by a trauma. (39)

According to Carta et al, there are some parameters such as low visual acuity, hemorrhaged posterior ethmoid cells, older patients (>40 years) and unconsciousness after injury, which favor performing the surgery. (43)

1.5 Use of steroids

First tested in animal studies, corticosteroids are one of the main treatment options for optic nerve injuries. They can be given in combination with surgery or as a single therapy. Visual improvement was seen in patients who were treated within a short time frame after injury. In general, steroids should bring neuroprotection, be antioxidative and decrease edema. (22,44,45)

According to literature, steroids should achieve the best results when they are given within a time frame of 8 hours after an injury. Methylprednisolone is favored, because of its neuroprotective effects. (21,46,47)

An experimental study of Lew et al showed that a high-dose steroid therapy can increase the blood flow of the optic nerve in rabbits. (48)

For the use of steroids, there is a distinction between the dosages (methylprednisolone) per day:

- Low (less than 100 mg)
- Moderate (100 - 499 mg)
- High (500 - 1999 mg)
- Very high (2000 - 5399 mg)
- Megadose (more than 5400 mg)

The last two dosages are mainly considered for the treatment of traumatic optic neuropathy. (45)

The retrospective study about spinal cord injuries recommends the use of 30mg/kg methylprednisolone as a bolus and then 5.4mg/kg/h for 24 or 48 hours, which is considered as high-dose. (46,49)

Possible positive effects of steroids are suppression of immunological mediators, shorter hospitalization and a better recovery time. (50)

Reported harmful effects, especially due to high doses, are increased mortality, a worse survival rate and increased axonal loss. (28,44,49)

2 Material and methods

2.1 Patients and data

This study used data from 84 patients who underwent optic nerve decompression at the Department of Otorhinolaryngology at the Medical University of Graz between 1 June 2001 and 18 November 2018. The data were collected from MEDOCS system in an Excel file and pseudonymized by using a number code. Thus, no third party has access to sensitive data and the patients' identity remains secure.

84 patients fulfilled the criteria "optic nerve decompression" (which also include patients from the Department of Neurosurgery of the University Hospital of Graz) in the beginning, but those with insufficient data (n=9) and patients who underwent orbital decompression due to Grave´s disease (n=7) were excluded from the study. Six patients underwent more than one optic decompression (endoscopic and/or craniotomy), they were also not considered in the closer analysis. In the group of the 62 remaining patients, 30 had a craniotomy (33 in total, 30 with sufficient data) and 32 an endoscopic decompression. Only those 32 were used for the main analysis. A comparison of the outcome regarding visual improvement was made between the craniotomy and endoscopic cases.

By means of statistical analyses we wanted to show which parameters influence the visual outcome of patients in order to improve the current treatment algorithm of the ENT Clinic of Graz and to achieve even more positive results in the future.

The main analysis focuses on visual acuity. For this purpose, data from the eye clinic were collected since all the patients were examined by an ophthalmologist.

2.2 Limitations of data collection

Data collection for parameters regarding height and weight were partially incomplete, as well as visual acuity was not measured in a standard way: There are two different data systems available, one from the eye clinic and one from the main hospital, thus not every ophthalmological record was available. In many cases pre- and postoperative visual acuity was not available, only subjective improvement reported by the patients could be considered. It was not possible to determine the exact strength of visual improvement and therefore any reported improvement in visual acuity was evaluated as positive.

2.3 Statistics and parameters

For the statistical analysis, Microsoft Excel (2016) for descriptive frequencies as mean value and standard abbreviation and SPSS (IBM SPSS Statistics 25) for statistical tests as chi-squared, Fisher´s Exact and Man-Whitney U test were used.

Standard parameters such as age, height and weight were analyzed regarding their maximum, minimum, mean value, median and standard abbreviation as well as gender distribution and mean follow-up period (time of hospitalization until the last day of an examination which was related to surgery (by the ENT clinic or department of neurosurgery at the University Hospital of Graz).

The main parameters which are relevant for the study were collected from each patient and include:

-Visual improvement (yes/no):

Any improvement of vision after surgery.

-Steroid use preoperatively (yes/no):

If the patient was additionally treated with steroids before surgery.

-Steroid use postoperatively (yes/no):

If the patient was additionally treated with steroids after surgery.

-CRP level (mg/l), CRP <1mg/l, CRP >1mg/l:

Last lab parameter before surgery, total level and distributed into the groups <1mg and >1mg.

-Complications (yes/no):

Any complication during or after surgery such as bleeding, cerebrospinal fluid fistula (CSF), secretion, pneumocephalus externus.

-Radiological evidence (yes/no):

If the imaging used (CT/MR) shows a compressed or injured optic nerve (by an edema, bone fragment, hematoma, etc.)

-Time injury-surgery (<1day, 1-3days, 3days-1week, >1week):

Time which passed between the anamnestic point of time of the injury/vision deterioration and surgery, distributed in four groups.

-Fractures of the skull (yes/no):

Mid-face fractures, fracture of the frontal sinus, sphenoid sinus, orbital cavity and optic nerve canal.

-Progressive course (yes/no):
Worsening of the patient’s vision after surgery.
-Major cause (tumor/trauma):
Cause of the optic nerve´s compression.
-Nerve sheath incision (yes/no):
Incision of the optic nerve sheath during surgery.

CRP levels were distributed in values “<1mg/l” (normal levels) and “>1mg/l” (elevated levels). The time between injury and surgery was stratified into the following four groups: “less than one day”, “between one day and three days”, “between three days and one week” and “more than one month”. As a progressive course was considered, if the patient’s outcome had worsened again after surgery.

The main question was if there was a relation between visual improvement and those parameters. For this aim, a chi-squared test was used. Some parameters required the Fisher´s Exact test, because the counts in the crosstabulations were less than five. If p-value was <0.05 (the level of significance was defined by $\alpha= 0.05$), the result was considered as significant.

A Mann-Whitney U test was used to determine whether there is a difference in CRP level between the groups “visual improvement” and “no visual improvement”.

This study was approved by the institutional review board of the Medical University of Graz (approval number: 30-216 ex 17/18)

3 Results

3.1 Standard parameters of the study population

In the group of 32 patients considered in the main analysis, 20 (62.5%) were male and 12 (37.5%) female. Their age on the day of surgery was considered, which was on average 45.34 years (SD: ±19.37), with a range between 6 and 79 years.

The minimum height was 1.50 meters, the maximum 1.98 meters. The average height was 170.07 ± 9.96 and the average weight 71.81 ±15.5. The maximum weight was 118kg and the minimum weight 35kg.

The follow-up period ranges from 0.1 months to 88 months, the median is 1.18 months.

In the 32 cases, 30 had a unilateral affection of the nerve, two had both sides affected.

3.2 Main parameters

The main parameter of this study was visual improvement (yes/no). The results showed an equal distribution in 16 out of 32 (50%) persons who had visual improvement, the other 16 (50%) did not improve.

To see which parameters influence the visual outcome of patients, all of the following parameters were analyzed with the help of a crosstabulation and Pearson´s chi-squared test or Fisher´s exact test to evaluate differences and a statistical association between the groups. A p-value of <0.05 was considered statistically significant.

3.2.1 Gender distribution

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=32)				
Male (n;%)	20 (62.5%)	9 (28.13%)	11 (34.4%)		
Female (n,%)	12 (37.5%)	7 (21.88%)	5 (15.63%)		
				0.465	

Table 1: Gender distribution

9 (45%) of the male patients (n=20) and 7 (58.33%) of the females (n=12) had visual improvement.

Chi-squared test was used in order to establish a statistical relationship between the gender and the visual improvement. The p-value was 0.465.

Of 12 female patients, 3 (25%) got steroids before surgery and 6 (50%) after surgery. 5 (41.67%) patients had complications during surgery.
The time between injury and surgery was less than 1 day in 3 females , between 1 and 3 days in 1 patient between 3 days and 1 week in 2 patients and more than 1 week in 5 (45.45%). Four had a CRP level less than 1 mg/l, 3 between 1 and 10 mg/l and 2 had more than 10 mg/l. The major cause was equally distributed, 6 (50%) had a trauma and 6 a tumor. 4 female patients had fractures, 5 a progressive course and 5 a nerve sheath incision.

Of 20 male patients, 6 (30%) got steroids before and 10 (50%) after surgery. 4 (20%) had complications during surgery. 5 had surgery in less than 1 day after the injury/visual deterioration, 2 between 1 and 3 days, 5 between 3 days and 1 week. 7 persons had surgery after 1 week.
CRP levels were in 6 patients less than 1mg/l, in 4 persons between 1 and 10 mg/l and 4 had more than 10 mg/l.
14 (70%) patients had a trauma as major cause and 6 a tumor. A radiological evidence was found in 11 (55%) male patients. 13 (65%) had fractures, 3 (15%) a progressive course and 10 a nerve sheath incision.
The cases with a bilateral affection (n=2) were both male.

3.2.2 Use of steroids preoperatively

Characteristics	**Total**	**Vision improvement**	**No vision improvement**	**p-value (2-sided, chi-squared)**	**p-value (Fisher´s Exact, 2-sided)**
	(n=29)				
Preop. Steroids (n; %)	9 (31.03%)	2 (6.9%)	7 (24.14%)		
No preop. Steroids (n; %)	20 (68.97%)	13 (44.83%)	7 (24.14%)		
					0.050

Table 1: Use of steroids preoperatively

In 9/32 cases (31.03%), steroids were used before surgery, 20 persons (68.97%) were not treated (e.g. with prednisolone).
The results showed that 2 patients out of 9 (22.22%) who got steroids, had visual improvement. In the group without steroids (n=20), 13 (65%) showed improvement.

For the statistical analysis we used a chi-squared test to evaluate a statistical relationship between the use of steroids preoperatively (yes/no) and visual improvement (yes/no) which was statistically significant (p=0.05).

3.2.3 Use of steroids postoperatively

Characteristics	**Total**	**Vision improvement**	**No vision improvement**	**p-value (2-sided, chi-squared)**	**p-value (Fisher´s Exact, 2-sided)**
	(n=31)				
Postop. Steroids (n; %)	15 (48.39%)	5 (16.13%)	10 (32.26%)		
No postop. Steroids (n; %)	16 (51.61%)	11 (35.48%)	5 (16.13%)		
				0.049	

Table 2: Use of steroids postoperatively

This parameter was analyzed to see if there is a difference in visual outcome (yes/no) between steroids before and after surgery (yes/no).

15 of 31 cases got steroids after surgery and 16 did not.

From a total count of 16, who showed visual improvement, 11 (68.75%) did not get steroids and in the group of patients who got steroids (n=15), visual improvement was achieved in 5 persons (33.33%). The result of Fisher´s exact test showed a p-value of 0.049 which is considered as significant.

3.2.4 Use of steroids in general

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=31)				
Steroids were used (n;%)	16 (51.61%)	5 (16.13%)	11 (35.48%)		
No steroids were used (n;%)	15 (48.39%)	10 (32.26%)	5 (16.13%)		
				0.049	

Table 3:Use of steroids in general

To see if it makes a difference if steroids were used in general, this parameter was analyzed. In total, 16 patients got steroids , 5 of these patients (31.25%) showed visual improvement and 11 (68.75%) did not. When no steroids were used, 10 out of 15 patients (66.67%) achieved improvement in vision and 5 (33.33%) did not.
A chi-squared test was performed with a p-value of 0.049.

3.2.5 CRP level

The highest count of CRP measured before surgery was 143.9 mg/l, the lowest 0.1 mg/l. The median was 1.1mg/l. To test for a significant relationship, three groups were formed:

a) CRP <1 mg/l
b) CRP 1 < x < 10 mg/l
c) CRP > 10 mg/l

In 23 analyzed cases, 40% of the patients in Group A (n=10) showed vision improvement, 71.43% in Group B (n=7) and 50% (n=3) in Group C (n=6).

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=23)				
CRP (mg/l) <1 (n;%)	10 (43.48%)	4 (17.39%)	6 (26.09%)		
CRP (mg/l) 1 <x <10 (n;%)	7 (30.43%)	5 (21.74%)	2 (8.7%)		
CRP (mg/l) >10 (n;%)	6 (26.09%)	3 (13.04%)	3 (13.04%)		
					0.500

Table 4: CRP levels

Since the p-value (p=0.500) of Fisher´s exact test was more than 0.05, no significance and relationship between CRP levels and vision improvement could be asserted.

In order to find out if there are differences in the absolute values of CRP levels between the group with visual improvement and without, a Mann-Whitney U test was calculated. The distributions did not differ between the groups (Kolmogorov-Smirnov p>0.05). No significance could be evaluated between both groups (U=57.000 mg/l, Z=-0.559, p=0.576).

3.2.6 Complications

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=31)				
Complications (n;%)	9 (29.03%)	4 (12.9%)	5 (16.13%)		
No complications (n;%)	22 (70.97%)	11 (35.48%)	11 (35.48%)		
					1.0

Table 5: Complications

Complications during surgery, or because of it, occurred in 29.03 % (n=9) of the patients (n=31). 44.44% of the patients (n=4), who had a complication showed visual improvement and 55.55% (n=5) did not. In the other group with no complications (n=22), half of the patients had vision improvement and the other half did not have any.

To test a relationship between complications and visual improvement, a Fisher´s exact test was performed (due to an expected count less than 5 in some cells of the cross table) with statistical significance (p=1).

The most frequent complication was a bleeding (3 male patients and 1 female patient), the second most frequent was a CSF fistula (2 females).

Complications	**Frequency**	**Percentage (n=31)**
Bleeding	4	12.9%
Nasal liquorrhea	1	3.22%
Secretions	1	3.22%
CSF fistula	2	6.45%
Pneumocephalus	1	3.22%
Total	**9**	**29.03%**
None	22	70.97%

Table 6: Distribution of complications

3.2.7 Time between injury and surgery

The time between injury/vision deterioration and surgery ranged between less than 1 day and more than 6 months. Therefore, to test a statistical relationship, the cases were divided into four groups.

a) <1day
b) 1-3 days
c) >3 days
d) >1week

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=30)				
Time injury – surgery <1 day (n;%)	8 (26.67%)	3 (10%)	5 (16.67%)		
1-3days (n;%)	3 (10%)	1 (3.33%)	2 (6.67%)		
>3days (n;%)	7 (23.33%)	3 (10%)	4 (13.33%)		
>1week (n;%)	12 (40%)	7 (23.33%)	5 (16.67%)		
					0.799

Table 7: Time between injury and surgery

Among all groups, Group D showed the most visual improvements with n=7 cases (23.33%). But Group D also had the most patients (n=12)
For the statistical analysis, Fisher´s exact test was used. Due to a p-value of 0.799 there is no significance.

a

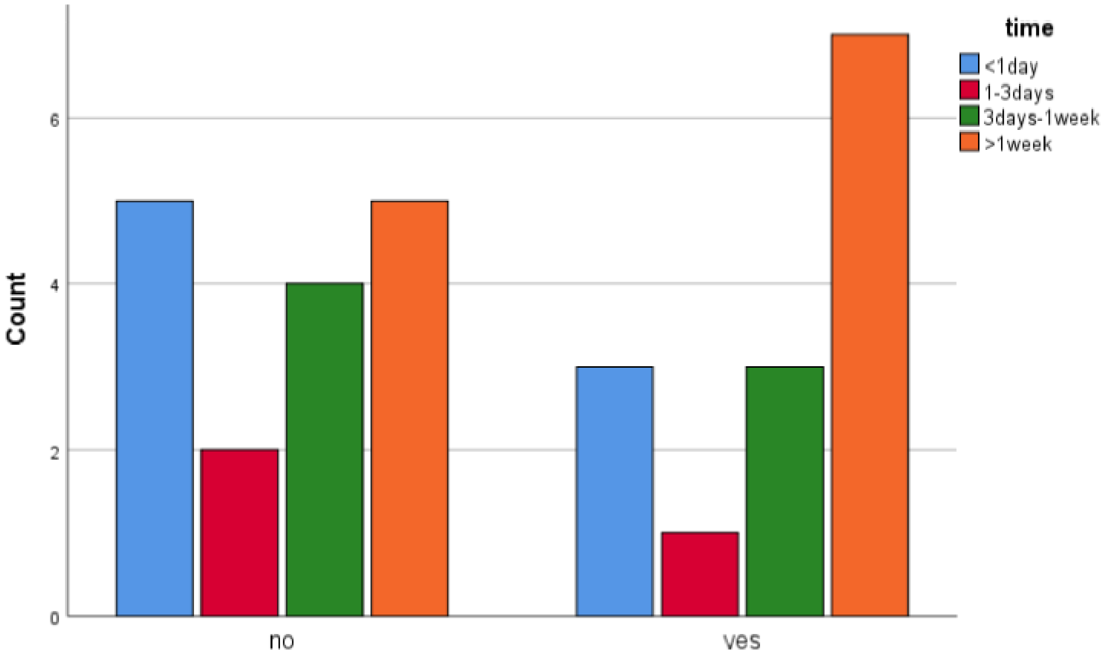

Figure 5: Time between injury and surgery; comparison

3.2.8 Radiological evidence

Preoperative imaging was used for all patients.

An affected optic nerve (compression, edema, hematoma, tumor compression, fracture of the optic channel, gas accumulation around the nerve) in CT or MRI scan leading to a compression could be seen in 18 cases (56.25%). 12 of those patients showed visual improvement (66.67%) and 6 (33.33%) did not improve.

Without the radiological evidence (n=14), 4 persons (28.57%) had better vision after surgery and in 10 (71.43%) no improvement was achieved

A chi-squared test was performed to evaluate whether there is a statistical relationship between radiological evidence and visual improvement.

With a p=0.033 there is a significance between the groups.

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=32)				
Radiological evidence (n;%)	18 (56.25%)	12 (37.5%)	6 (18.75%)		
No radiological evidence (n;%)	14 (43.75%)	4 (12.5%)	10 (31.25%)		
				0.033	

Table 8: Radiological evidence

3.2.9 Optic nerve lesions

According to the radiological records the optic nerve was in affected in 18 out of 32 cases. This table lists the frequency and distribution of the findings. A compression (38.89%) was the most frequent injury.

Optic nerve	Frequency	Percentage
Compressed	7	38.89%
Edema/ hematoma	3	16.67%
Tumor contact	4	22.22%
Thickening/swelling	1	5.56%
Fracture (optic canal/foramen)	2	11.11%
Gas accumulation	1	5.56%

Table 9: Etiology of optic nerve lesions

3.2.10 Fractures

Fractures of the orbit or the skull could be detected in 17 cases (53.13%). 8 (47.06%) of them showed vision improvement and 9 (52.94%) did not.

To test the level of significance, a chi-squared test was performed with p=0.723.

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=32)				
Fractures (n;%)	17 (53.13%)	8 (25%)	9 (28.13%)		
No fractures (n;%)	15 (46.88%)	8 (25%)	7 (21.88%)		
				0.723	

Table 10: Fractures

3.2.11 Progressive course

A progressive course could be observed in 8 patients. 5 of them (62.5%) had visual improvement and 3 (37.5%) did not have.

To test if there is a statistical association, a Fisher´s exact test (due to an expected count of less than 5 in cells of the cross table) was performed. The result was a p-value of 0.685.

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=32)				
Progressive course (n;%)	8 (25%)	5 (15.63%)	3 (9.38%)		
No progressive course (n;%)	24 (75%)	11 (34.38%)	13 (40.63%)		
					0.685

Table 11: Progressive course

3.2.12 Major cause

The study group was divided into patients with a traumatic injury, which led to surgery and those who had a tumor or other expansion in the area of the optic nerve.

Most of the time, traffic accidents or accidents at work (e.g. construction sites) are reported in the medical records.

Regarding the tumor entities, which are listed in Table 12, we have many different cases. The most frequent were fibrous dysplasia (3) and meningiomas (3) with an incidence of 25%

Tumor entity	**Frequency**	**Percentage**
Fibrous dysplasia	3	25 %
Inflammatory sinonasal polyps	1	8.33 %
Meningioma	3	25 %
Papillary endothelial hyperplasia	1	8.33 %
Sinonasal carcinoma	1	8.33 %
Sphenoid wing meningioma	1	8.33 %
Unknown malign neoplasm	1	8.33 %
Sphenoid sinus osteoma	1	8.33 %
Total	**12**	**100%**

Table 12: Distribution of tumor entities

In total, we had 20 cases (62.5%) who had a traumatic injury, 9 (45%) had visual improvement, 11 (55%) did not show any improvement.

In the group of the 12 tumor patients, 7 (58.33%) improved in vision and 5 (41.67%) did not.

Characteristics	**Total**	**Vision improvement**	**No vision improvement**	**p-value (2-sided, chi-squared)**	**p-value (Fisher´s Exact, 2-sided)**
	(n=32)				
Major cause: trauma (n;%)	20 (62.5%)	9 (28.13%)	11 (34.38%)		
Major cause: tumor (n;%)	12 (37.5%)	7 (21.88%)	5 (15.63%)		
				0.465	

Table 13: Major cause

A chi-squared test was performed to evaluate if there is a difference in visual improvement between both groups with a p-value of 0.465.

3.2.13 Nerve sheath incision

During surgery, there had been a nerve sheath incision in 15 cases, 16 did not have one and 1 patient was not documented (=excluded).

In the group of patients with an incision (48.39%), 6 (40%) had vision improvement, 9 (60%) did not.

With no nerve sheath incision (51.61%), we have a result of 9 patients (56.25%) who improved and 7 (43.75%) who did not improve.

A chi-squared test showed a p-value of 0.366.

Characteristics	Total	Vision improvement	No vision improvement	p-value (2-sided, chi-squared)	p-value (Fisher´s Exact, 2-sided)
	(n=31)				
Nerve sheath incision (n;%)	15 (48.39%)	6 (19.35%)	9 (29.03%)		
No nerve sheath incision (n;%)	16 (51.61%)	9 (29.03%)	7 (22.58%)		
				0.366	

Table 14: Nerve sheath incision

3.2.14 Statistical association

As a summary, Figure 7 is showing the statistically interesting parameters. When using steroids in general, the number of visual improvements was lower than without.

If there was a radiological evidence, more vision improvement (38.71%) was detected and if the evidence was missing, the visual outcome was worse (12.9%).

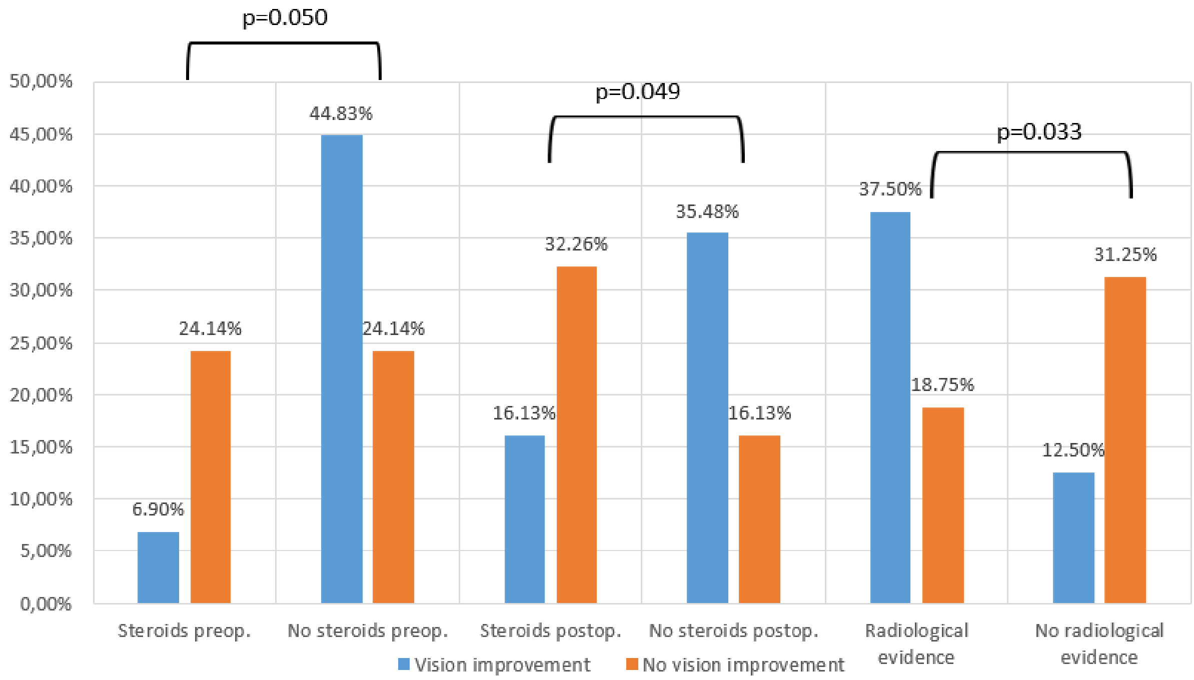

Figure 6: Statistical association of relevant parameters

3.3 Comparison to craniotomy

With the diagnosis "optic nerve decompression", 33 patients had a craniotomy and were excluded from the main analysis, which only concerns patients with an endoscopic surgery. To see if there is a difference in visual outcome, this group was also studied. 30 patients with a craniotomy had enough data to evaluate their visual improvement.

The patient population differs from the endoscopic population. Except for 2 patients, all had a tumor. The time span between visual reduction and surgery ranged from at least 10 days up to several years. Some patients were operated multiple times due to recurrences. The first surgery with optic nerve decompression was used for the evaluation.

To compare the visual outcome of both groups (craniotomy and endoscopic), a chi-squared test was performed with a p-value of 0.184.

In the group of the patients with a craniotomy, 20 (66.66%) had visual improvement, 10 (33.33%) did not have.

Characteristics	**Total**	**Vision improvement**	**No vision improvement**	**p-value (2-sided, Chi-Square)**	**p-value (Fisher´s Exact, 2-sided)**
	(n=62)				
Craniotomy (n;%)	30 (48.39%)	20 (32.26%)	10 (16.13%)		
Endoscopic patients (n;%)	32 (51.61%)	16 (25.81%)	16 (25.81%)		
				0.184	

Table 15: Comparison to craniotomy

:

4 Discussion

In this study, we wanted to analyze different parameters which influence the outcome of patients who underwent an endoscopic optic nerve decompression. The aim was to find positive influences on visual acuity to optimize the treatment process for patients and potentially achieve better postoperative results in the future.

There are many approaches to treat a compression of the optic nerve and every method has benefits and disadvantages. (51,52) We focussed on the transnasal endoscopic method, which is performed according to the method of Messerklinger and Stammberger at the Medical University of Graz. (16)

With consideration of our small case number (32 patients for the main analysis) we could identify two parameters which caused a significant difference in the visual outcome: the use of steroids and the radiological evidence of an affected / injured optic nerve. The aim was to optimize the treatment algorithms for future patients by considering these parameters.

In general, in our group of 32 patients, 16 (50%) benefitted from surgery with visual improvement. As a comparison, the prospective study of Gupta et al. showed an improvement of 80% (16/20 patients) after endoscopic nerve decompression, Rajiniganth et al. with 25% (11 of 44 patients). (17,53) Indications for surgery which are not clearly determined could be a reason for different results in improvement rates. (33)

In literature, there are also worse results reported: in the retrospective study of Zhen-Hua He et al. with 11 patients suffering from TON only 45.5% of the patients (after three months) had visual recovery. (54)

Surgery was performed on our patients because of vision deterioration after a trauma or due to a tumor.

4.1 Conservative treatment

We did not include conservatively treated patients in our study but according to the International Optic Nerve Trauma Study of Levin et al., steroid therapy or surgery do not bring a significant benefit in comparison to watchful-waiting. (18,36)

In general, a residual visual ability is considered as a good prognostic factor for a better outcome. Also, other studies show similar results in visual improvement in comparison to cases treated with steroids or surgery. But many patients who recover spontaneously usually have good baseline vision. This fact could bias the results. (18,33,38)

In our study, we did not analyze whether the residual visual ability influenced the outcome because the baseline vision was not properly reported in the medical records at the time of admission.

4.2 Gender differences

According to literature, traumatic optic neuropathies are more frequent in young male patients. Lee et al. described 121 patients including 79% male patients of an average age of 31 years. (18,55)
Also, orbital fractures which can lead to optic neuropathy are common with young men. (24)
In our study, 20 persons (62.5%) were male and 12 (37.5%) female. We could not find a significant difference in outcome related to gender, but we also had a higher percentage of male patients. This group may be exposed to more risks of a skull injury (motorcycles, construction sites, physical injuries, etc.)

4.3 Steroids

Corticosteroids for the treatment of traumatic optic neuropathy are used to improve or avoid edemas, swellings, vasospasm and to regain function. (17,56)
In this study, 16 of 31 patients (one was not documented) were treated with steroids, 5 of them showed improvement. In the group of 15 patients who did not get steroids, 10 patients improved in vision. Our results showed a significant difference between these groups, thus steroids may also have a negative effect on the recovery of vision.
We could not analyze the dosage of the corticosteroids, but Levin et al. could not show a benefit from steroids with a different dosage or timing in their interventional study. (36)
Saxena et al. mentioned two studies which examined the outcome of severe spinal cord and head injuries after treatment with steroids. In comparison to placebo, the study with spinal cord injuries stated a significant improvement due to steroids and the other study observed increased mortality with megadose treatment of corticosteroids. In their article, Saxena et al. pointed out the difficulty to compare the impacts on the spinal cord to the optic nerve. Since the difference between the studies was also the condition of severe head injuries with the second group, they have come to the conclusion that patients with brain injuries do not benefit from steroid treatment. (46,57,58)

Steinsapir et al. wanted to find out if there was a difference in visual outcome with a certain dosage of methyprednisolone and thus treated 38 rats with steroids or placebo after induced optic nerve injury. Results showed more axonal decline in the group treated with steroids. The theory was that methylprednisolone inhibits mechanisms that would normally prevent secondary injury to the nerve. (44)

Xu et al. reported one patient that might have died due to a fulminant intracranial infection after a mega-dose corticosteroid therapy. They stated that the surgery was not the reason for the infection so they related it to the steroids. (40)

Entezari et al performed a double-masked RCT in 31 patients who suffered from an indirect traumatic optic neuropathy. Sixteen received a steroid therapy, 15 a placebo. They could not show a significant difference in visual improvement between these groups (p=0.38). (59)

Yu-Wai-Man concluded in their sytematic review that steroids do not act beneficially in treatment. According to them, the possible disadvantages of those medications should be considered. They report that spontaneous improvement is also possible and therapy is not always necessary. (22)

In the study about optic nerve injuries in the UK, poor initial visual acuity is considered as a predictor for a worse visual outcome. (55)

Carta et al. recommend that patients should undergo surgery if they did not improve after receiving corticosteroids during 48h after injury. (43)

In a retrospective review of Ropposch et al., no beneficial effect of steroids could be found when they were given in addition to surgery. (60)

Since we do not include any cases with spontaneous recovery, our results could be biased because we could not compare those unknown patients to our surgically treated patients.

Overall, we agree that it should be considered in each individual case whether steroid therapy is appropriate. Further studies including a larger number of patients should be carried out to see whether steroids have an advantage.

4.4 CRP level

The last CRP level measurement before surgery was analzyed to see whether there is an impact on the postoperative result. Divided into three groups (CRP <1mg/l, $1<x<10$ mg/l, >10mg/l), we could not show a significant difference regarding vision improvement of the patients. So the hypothesis has to be rejected that higher CRP levels before surgery have negative effects on the visual outcome.

4.5 Complications

We had a total complication rate of 29.03 % but with no significant relation to visual improvement. In comparison to that, Suzuki et al report a complication rate of 0.50% after FESS for chonic sinusitis / nasal polypes in Japan. According to them, complications are rare in general and the numbers vary a lot between studies. So they analyzed more than 50.000 cases who underwent one ore more sinus surgeries. Our higher rate can be explained by the small study group and the greater expansion of the surgery including the sphenoid sinus, since a key fact mentioned by Suzuki et al was the higher probability of complications with ethmoidectomy and sphenoidotomy. (67) Since we also included minor bleedings (unlike Suzuki et al) which did not require another surgery or blood transfusions, our rate is also higher.

4.6 Time

There are many different opinions regarding the right timing of surgery. Several studies suggest performing surgery within 3 days (72h) to get the most benefit. By keeping to this time frame, fewer long-term damages of the nerve (ischaemia, oedema) are reported. (17,35,38) Tandon et al recommend to undergo surgery between one and two weeks. (18)
As a comparison, Emanuelli et al showed a significant difference for beginning of medical or surgical treatment within 12h after injury. (47)
An animal study with mice reports about damages and changes on the molecular base of the nerve within 72h after an injury. (38,61)
In their systematic data review, Dhaliwal et al. analyzed more than 24 articles and concluded that more than 50% of the patients benefitted from surgery regardless of timing. (38)
We devided our patients in four groups: surgery in less than 1 day (3 of 8 improved), between 1 and 3 days (1 of 3 improved), between 3 days and one week (3 out of 7 improved) and more than one week (7 out of 12 improved). No significant impact of the timing of surgery could be observed.
On average, the tumor patients had a longer time span between their visual deterioriaton and surgery, but also after excluding the tumorgroup there was no relevant difference.

4.7 Radiological evidence and fractures

In a study of Gupta et al, they recommend to use CT scans, since it is easier to detect injuries of the bony optic canal. According to their results, if a fracture of the bony canal or a hematoma is causing the injury, the benefit of decompression can be high. (17)

Our study showed the following: 18 patients had an affected/injured optic nerve (compression, edema/hematoma, tumor contact, thickening, fracture of the optic channel/foramen, gas accumulation around the nerve) in their CT or MRI scans. 12 of them showed visual improvement after surgery. If there was no sign in the imaging, only 4 out of 14 improved. This is a significant difference, so we can conclude that surgery may bring more benefit if there is radiological evidence that the nerve is injured. It is possible that the nerve is not affected if the imaging is normal and the problem of visual loss is located elsewhere. In such cases, a wait- and- see strategy could be considered instead of immediate surgery.

Chen et al. reported in a retrospective review about case histories of 18/72 patients with a fibrous dysplasia who had an affected optic nerve channel in their CT scan. All of the 18 persons had clinically reduced (12/18) or absent vision (6/18). (26)

This is closely related to fractures, because Gupta et al. could show in their prospective study (including 20 patients) that in every case with a fracture (11/20) there was improvement in visual acuity after surgery. (17) The probability of recovery is 40% higher if there is a fracture of the optic channel or the bony orbita. Injuries due to blunt force and mid-facial fractures should also benefit more from surgery. (17)

Han et al. recommend to perform an early intervention, if any bone fragments or fractures are close to the optic nerve. (62)

On the contrary, Levin et al. mention in their study that optic canal fractures and resulting damages of the optic nerve will decrease the chance of recovery. Also, they could not observe that radiological evidence in a CT scan was in a relationship with visual outcome (under consideration that they did not have larger numbers of CT findings) (36).

In another study, Lee et. al state that orbital fractures are associated with poor visual outcome. (55)

In this study, we found no difference in the groups with or without fracture (we considered fractures of the orbit, optic canal fractures , mid-face fractures, frontal sinus and sphenoidal fractures). But if the fracture is obviosly affecting the optic nerve in the imaging, surgery should be considered immediately.

4.8 Progressive course

We analyzed the progressive course (if the outcome worsened after surgery or a revision was necessary) to compare the success of the study. 25% (n=8) of our patients had a deterioration during or after the hospital admission. We tested if there is an association with vision improvement, e.g. if the non-successful cases worsen more. The results were not significant. The follow-up time was very different between the patients (it ranged from 0.1 to 88 months) or they changed hospital and therefore not registered, so the progressive course is not a parameter which was exactly determined.

4.9 Major cause

Lee et al. mentioned domestic accidents, physical and traffic injuries as the most frequent causes of optic nerve compressions. (55) The majority of our patients, (62.5%) also had a trauma as cause.

In our patients, we could not show a significant difference in visual outcome after surgery between the tumor-group and the trauma-group. According to our results, we cannot take the main cause as a prognostic factor for better vision.

4.10 Nerve sheath incision

15 (48.8%) of 31 patients had a nerve sheath incison and 6 of them (40%) had visual improvement. Our results indicate that there is no statistical relationship between nerve sheath incision and visual improvement.

In literature, Xu et al (40) had a better visual outcome of 61.2% in the group with nerve sheath incision and 65.1% in the group without incision ($p>0.05$). This study claims that nerve sheath incision is not implicitly necessary for optic nerve decompression.

They analyzed 74 patients with traumatic optic neuropathy while comparing a group with surgery and nerve sheath incision (41.89%) and the other group without incision (58.11%).

Since it does not improve the visual outcome, Xu et al. mention the higher risk of damaging a vessel or causing a CSF-leak. In the group of patients who had a residual visual acuity before surgery, they found better outcome in patients without nerve sheath incision (64.2 and 74.1%, $p>0.05$). (40)

Thaker et. al. could show a controversial result: In their prospective study of 57 patients the improvement rate was significantly higher when nerve sheath decompression was performed additionally (improvement rate 46.6% with vs. 32.8% without incision, $p=0.10$). (63)

Two patients in our study had a CSF fistula as a complication but none of them had a nerve sheath incision, which should be considered as a possible cause, according to literature. (16)

We could not see any benefit from a nerve sheath incision, but also no disadvantages. Further studies with more patients would be necessary to obtain definite results.

4.11 Craniotomy

After our initial search, we had to exclude 30 patients because they underwent an open craniotomy in order to decompress the optic nerve. We could not compare them directly to our main group. The two groups (craniotomy and endoscopic cases) had different conditions: pre-existing diseases, cause of compression (only two of 30 patients had a trauma), time between surgery and occurrence of visual deterioration, multiple optic nerve decompressions.

We made a comparison of the main visual outcome, but the result is less conclusive due to the unequal groups. 32 patients underwent an endoscopic decompression, 16 patients (50%) improved, in the craniotomy group 20 of 30 patients (66.66%) showed improvement .No significant result was seen.

In order to obtain reasonable results it would be necessary to create very similar preconditions with both patient groups. However, the endoscopic method is considered as the less invasive method with faster recovery. (64)

Alokby et al report about several studies which tried to compare endoscopic and transcranial approaches. Although they also mention that results are influenced by unequal groups, the endoscopic method is considered as a safe alternative if patients are precisely chosen. (65)

In another study, Krischek et al mention a review of Kometor et al where they compared 47 studies with 453 patients treated for an esthesioblastoma with craniofacial, endoscopic or combined surgery. Their results where also biased by different malignancies of the tumors (more/less aggressive tumors where not equally distributed). But in general, they could not state a disadvantage in the outcome for endoscopic treated cases. (66)

5 Conclusion

Summarizing our results, we strongly recommend an exact documentation of visual acuity before and after surgery. The use of steroids should be evaluated carefully and individually for each patient. Disadvantages of these medications should be taken into account to avoid unnecessary use and overdoses.

A CT scan or MRI should be performed in every patient and the decision for surgery should be made according to the radiological findings. The therapy process should be more oriented towards the extent of the damage and also the baseline vision should be included as a relevant factor for further treatment. Without signs for an injury a conservative approach might be a better option. As a conclusion from our results, taking the radiological finding as indication for surgery might help to avoid non-beneficial surgeries.

Other than expected, no strong correlation was observed regarding the timing of surgery. Since our study group was small and immediate surgery within a short time frame is recommended by several authors, the general recommendation for immediate surgery should remain valid, unless a conservative treatment is approached.

Further, the results about nerve sheath incision do not show a strong correlation with a potential benefit. Since there is a risk for CSF leaks, a potentially lower complication rate could be achieved if more studies show the missing benefit.

Considering the general outcome of patients (their vision recovery) (50%) after endoscopic decompression surgery, the establishment of a standard guideline for optic nerve compressions would be an important future target to improve the success rate.

6 References

1. Sobotta J. Sobo 1906 424, marked as a public domain [Internet]. Wikimedia Commons. Available from: https://commons.wikimedia.org/wiki/File:Sobo_1906_424.png
2. Sobotta J. Sobo 1909 546, marked as a public domain [Internet]. Wikimedia Commons. Available from: https://en.wikipedia.org/wiki/User:CFCF/Sobotta#/media/File:Sobo_1909_546.png
3. Sobotta J. Sobo 1906 760, marked as a public domain [Internet]. Wikimedia Commons. Available from: https://upload.wikimedia.org/wikipedia/commons/0/0a/Sobo_1909_760.png
4. Häggström M. Medical gallery of Mikael Häggström 2014 [Internet]. WikiJournal of Medicine. 2014. Available from: https://en.wikiversity.org/wiki/WikiJournal_of_Medicine/Medical_gallery_of_Mikael_Häggström_2014
5. Anderhuber F, Pera F, Streicher J. Waldeyer Anatomie des Menschen. 19. Auflag. Berlin/Boston: Walter de Gruyter GmbH & Co.KG; 2012.
6. Patel A. Functional Endoscopic Sinus Surgery (FESS). [Internet]. 2016. p. 1–8. Available from: https://emedicine.medscape.com/article/863420-print
7. Hafferl A, Thiel W. Lehrbuch der topographischen Anatomie. 3. Auflage. Heidelberg: Springer-Verlag Berlin Heidelberg; 1996.
8. Reiß M. Facharztwissen HNO-Heilkunde. Heidelberg: Springer Medizin Verlag; 2009.
9. Grehn F. Augenheilkunde. 31st ed. Berlin, Heidelberg: Springer-Verlag; 2012. 300–303 p.
10. Berhouma M, Jacquesson T, Abouaf L, Vighetto A, Jouanneau E. Endoscopic endonasal optic nerve and orbital apex decompression for nontraumatic optic neuropathy: Surgical nuances and review of the literature. Neurosurg Focus. 2014;37(4):1–9.
11. Adrianakis A, Tomazic PV, Wolf A, F. A, Gerstenberger C, Pilsl U, et al. Optico-carotid recess and anterior clinoid process pneumatization – proposal for a novel classification and unified terminology: an anatomic and radiologic study. Rhinology. 2019;57(6):444–50.

12. Li J, Wang J, Jing X, Zhang W, Zhang X, Qiu Y. Transsphenoidal Optic Nerve Decompression: An Endoscopic Anatomic Study. J Craniofac Surg. 2008;19(6):1670–4.
13. Ozcan T, Yilmazlar S, Aker S, Korfali E. Surgical limits in transnasal approach to opticocarotid region and planum sphenoidale: An anatomic cadaveric study. World Neurosurg. 2010;73(4):326–33.
14. Yilmazlar S, Saraydaroglu O, Korfali E. Anatomical aspects in the transsphenoidal-transethmoidal approach to the optic canal: An anatomic-cadaveric study. J Cranio-Maxillofacial Surg [Internet]. 2012;40(7):e198–205. Available from: http://dx.doi.org/10.1016/j.jcms.2011.10.008
15. DeKlotz TR, Stefko ST, Fernandez-Miranda JC, Gardner PA, Snyderman CH, Wang EW. Endoscopic Endonasal Optic Nerve Decompression for Fibrous Dysplasia. J Neurol Surgery, Part B Skull Base. 2017;78(1):24–9.
16. Luxenberger W, Stammberger H, Jebeles JA, Walch C. Endoscopic optic nerve decompression: The Graz experience. Laryngoscope. 1998;108(6):873–82.
17. Gupta D, Gadodia M. Transnasal Endoscopic Optic Nerve Decompression in Post Traumatic Optic Neuropathy. Indian J Otolaryngol Head Neck Surg. 2018;70(1):49–52.
18. Tandon V, Mahapatra A. Current Management of Optic Nerve Injury. Indian J Neurosurg. 2017;06(02):83–5.
19. Bloching M. Indications and surgical technique of the endonasal decompression of the optic nerve from an otolaryngological point of view. Klin Monbl Augenheilkd. 2004;221(11):927–32.
20. Anderson RL, Panje WR, Gross CE. Optic Nerve Blindness Following Blunt Forehead Trauma. Ophthalmology [Internet]. 1982;89(5):445–55. Available from: http://dx.doi.org/10.1016/S0161-6420(82)34769-7
21. Volpe NJ, Levin LA. How should patients with indirect traumatic optic neuropathy be treated? J Neuro-Ophthalmology. 2011;31(2):169–74.
22. Yu-Wai-Man P, Griffiths PG. Steroids for traumatic optic neuropathy. Cochrane Database Syst Rev. 2013;(6).
23. Lipkin AF, Woodson GE, Miller RH. Visual Loss due to Orbital Fracture: The Role of Early Reduction. Arch Otolaryngol Neck Surg. 1987;113(1):81–3.
24. Boyette JR, Pemberton JD, Bonilla-Velez J. Management of orbital fractures: Challenges and solutions. Clin Ophthalmol. 2015;9:2127–37.

25. Augustin AJ. Augenheilkunde. 3. Auflage. Philipp M, editor. Heidelberg: Springer-Verlag Berlin Heidelberg; 2007.
26. Chen Y-R, Breidahl A, Chang C-N. Optic nerve decompression in fibrous dysplasia: indications, efficacy, and safety. Plast Reconstr Surg. 1997;99(1):22–30.
27. Behbehani R. Clinical approach to optic neuropathies. Clin Ophthalmol. 2007;1(3):233–46.
28. Lima V, Burt B, Leibovitch I, Prabhakaran V, Goldberg RA, Selva D. Orbital Compartment Syndrome: The Ophthalmic Surgical Emergency. Surv Ophthalmol [Internet]. 2009;54(4):441–9. Available from: http://dx.doi.org/10.1016/j.survophthal.2009.04.005
29. Sarkies N. Traumatic optic neuropathy. Eye. 2004;18:1122–5.
30. Ater J, Tarbell N, Laws, Jr. E. Optic nerve, chiasmal, and hypothalamic tumors [Internet]. 2002. p. 158–70. Available from: http://soc-neuro-onc.org/levin/Levin_ch05_p158-170.pdf
31. Miller NR. Primary tumours of the optic nerve and its sheath. Eye. 2004;18(11):1026–37.
32. Kubal W. Imaging of orbital trauma. Radiographics. 2008;28(6):1729–39.
33. Kumaran AM, Sundar G, Chye LT. Traumatic Optic Neuropathy: A Review. Craniomaxillofacial Trauma Reconstr. 2015;08(01):31–41.
34. Kong DS, Shin HJ, Kim HY, Chung SK, Nam DH, Lee J Il, et al. Endoscopic optic canal decompression for compressive optic neuropathy. J Clin Neurosci [Internet]. 2011;18(11):1541–5. Available from: http://dx.doi.org/10.1016/j.jocn.2011.02.042
35. Yang QT, Zhang GH, Liu X, Ye J, Li Y. The therapeutic efficacy of endoscopic optic nerve decompression and its effects on the prognoses of 96 cases of traumatic optic neuropathy. J Trauma Acute Care Surg. 2012;72(5):1350–5.
36. Levin LA, Beck RW, Joseph MP, Seiff S, Kraker R. The treatment of traumatic optic neuropathy: The International Optic Nerve Trauma Study. Ophthalmology. 1999;106(7):1268–77.
37. Warner N, Eggenberger E. Traumatic optic neuropathy: a review of the current literature. Curr Opin Ophthalmol. 2010;21(6):459–62.
38. Dhaliwal SS, Sowerby LJ, Rotenberg BW. Timing of endoscopic surgical decompression in traumatic optic neuropathy: a systematic review of the literature. Int Forum Allergy Rhinol. 2016;6(6):661–7.
39. Pletcher SD, Metson R. Endoscopic optic nerve decompression for nontraumatic

optic neuropathy. Arch Otolaryngol - Head Neck Surg. 2007;133(8):780–3.
40. Xu R, Chen F, Zuo K, Ye X, Yang Q, Shi J, et al. Endoscopic optic nerve decompression for patients with traumatic optic neuropathy: Is nerve sheath incision necessary? ORL J Otorhinolaryngol Relat Spec. 2014;76(1):44–9.
41. Pletcher S, Sindwani R, Metson R. Endoscopic orbital and optic nerve decompression. Otolaryngol Clin North Am. 2006;39(5):943–58.
42. Maegele M. Reversal of isolated unilateral optic nerve edema with concomitant visual impairment following blunt trauma: A case report. J Med Case Rep. 2008;2: 50:1–5.
43. Carta A, Ferrigno L, Salvo M, Bianchi-Marzoli S, Boschi A, Carta F. Visual prognosis after indirect traumatic optic neuropathy. J Neurol Neurosurg Psychiatry. 2003;74(2):246–8.
44. Steinsapir, Kenneth D, Goldberg RA, Sinha S, Hovda DA. Methylprednisolone exacerbates axonal loss following optic nerve trauma in rats. Restor Neurol Neurosci. 2000;17(4):157–63.
45. Yu-Wai-Man P. Traumatic optic neuropathy-Clinical features and management issues. Taiwan J Ophthalmol. 2015;5(1):3–8.
46. Bracken M, Shepard M, Collins W, Holford T, Young W, Baskin D, et al. A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal-cord injury. Results of the Second National Acute Spinal Cord Injury Study. N Engl J Med. 1990;332(20):1405–11.
47. Emanuelli E, Bignami M, Digilio E, Fusetti S, Volo T, Castelnuovo P. Post-traumatic optic neuropathy: our surgical and medical protocol. Eur Arch Otorhinolaryngol. 2015;272(11):3301–9.
48. Lew H, Lee S, Jang JW, Kim HY, Kang SJ, Kim SJ. The effects of high-dose corticosteroid therapy on optic nerve head blood flow in experimental traumatic optic neuropathy. Ophthalmic Res. 1999;31(6):463–9.
49. Steinsapir KD. Treatment of Traumatic Optic Neuropathy with High-Dose Corticosteroid. J Neuroophthalmol. 2006;26(1):65–7.
50. Sauerland S, Nagelschmidt M, Mallmann P, Edmund AM. Risks and Benefits of Preoperative High Dose Methylprednisolone in A Systematic Review. Drug Saf 2000. 2000;23(5):449–61.
51. Horiguchi K, Murai H, Hasegawa Y, Mine S, Yamakami I, Saeki N. Endoscopic endonasal trans-sphenoidal optic nerve decompression for traumatic optic

neuropathy. Neurol Med Chir (Tokyo). 2010;50(6):518–22.
52. Cook MW, Levin LA, Joseph MP PE. Traumatic Optic Neuropathy: A Meta-analysis. Arch Otolaryngol Head Neck Surg. 1996;122(4):389–392.
53. Rajiniganth M, Gupta AK, Gupta A, Bapuraj J. Traumatic optic neuropathy. Arch Otolaryngol Head Neck Surg. 2003;129 (11):1203–6.
54. He ZH, Lan ZB, Xiong A, Hou GK, Pan YW, Li Q, et al. Endoscopic decompression of the optic canal for traumatic optic neuropathy. Chinese J Traumatol - English Ed [Internet]. 2016;19(6):330–2. Available from: http://dx.doi.org/10.1016/j.cjtee.2016.03.004
55. Lee V, Ford RL, Xing W, Bunce C, Foot B. Surveillance of traumatic optic neuropathy in the UK. Eye. 2010;24(2):240–50.
56. Chen F, Zuo K, Feng S, Guo J, Fan Y, Shi J, et al. A modified surgical procedure for endoscopic optic nerve decompression for the treatment of traumatic optic neuropathy. N Am J Med Sci [Internet]. 2014;6(6):270—273. Available from: http://europepmc.org/articles/PMC4083528
57. Saxena R, Singh D, Menon V. Controversies in neuro-ophthalmology: Steroid therapy for traumatic optic neuropathy. Indian J Ophthalmol. 2014;62(10):1028–30.
58. Edwards P, Arango M, Balica L, Cottingham R, El-Sayed H, Farrell B, et al. Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury - outcomes at 6 months. Lancet. 2005;365(9475):1957–9.
59. Entezari M, Rajavi Z, Sedighi N. High-dose intravenous methylprednisolone in recent traumatic optic neuropathy ; a randomized double-masked placebo-controlled clinical trial. 2007;1267–71.
60. Ropposch T, Steger B, Meço C, Emesz M, Reitsamer H, Rasp G, et al. The effect of steroids in combination With optic nerve decompression surgery in traumatic optic neuropathy. Laryngoscope. 2013;123(5):1082–6.
61. Mabuchi F, Aihara M, Mackey MR, Lindsey JD, Weinreb RN. Optic nerve damage in experimental mouse ocular hypertension. Investig Ophthalmol Vis Sci. 2003;44(10):4321–30.
62. Han SR. Why do we need optic nerve decompression of traumatic optic neuropathy patients? Interdiscip Neurosurg Adv Tech Case Manag [Internet]. 2014;1(3):66–7. Available from: http://dx.doi.org/10.1016/j.inat.2014.07.006
63. Thaker A, Tandon DA, Mahapatra AK. Surgery for optic nerve injury: Should nerve

sheath incision supplement osseous decompression? Skull Base. 2009;19(4):263–71.
64. Peng A, Li Y, Hu P, Wang Q. Endoscopic optic nerve decompression for traumatic optic neuropathy in children. Int J Pediatr Otorhinolaryngol [Internet]. 2011;75(8):992–8. Available from: http://dx.doi.org/10.1016/j.ijporl.2011.05.004
65. Alokby G, Casiano RR. Endoscopic Resection of Sinonasal and Ventral Skull Base Malignancies. Otolaryngol Clin North Am [Internet]. 2017;50(2):273–85. Available from: http://dx.doi.org/10.1016/j.otc.2016.12.005
66. Krischek B, Godoy BL, Zadeh G, Gentili F. From craniofacial resection to the endonasal endoscopic approach in skull base surgery. World Neurosurg [Internet]. 2013;80(1–2):56–8. Available from: http://dx.doi.org/10.1016/j.wneu.2013.01.106
67. Suzuki S, Yasunaga H, Matsui H, Fushimi K, Kondo K, Yamasoba T. Complication rates after functional endoscopic sinus surgery: Analysis of 50,734 Japanese patients. Laryngoscope. 2015;125(8):1785–91.