Thesis

Survey of the quality of life after glaucoma surgery

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Affidavit

I hereby declare that the present diploma thesis and the work reported herein was originated and composed entirely by myself and without any assistance from third parties. Furthermore, I confirm that no sources haven been used in the preparation of this thesis other than those indicated in the thesis itself.

Finally, I declare that I have no conflict of interests.

Graz, 04.11.2021 Christian Pahljina eh.

Danksagung

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Abbreviations

ALT	argon laser trabeculoplasty
CPC	cyclophotocoagulation
CCT	central corneal thickness
DCT	dynamic contour tonometry
Fig	figure
GAT	Goldmann applanation tonometry
GSS	glaucoma symptom scale
IOP	intraocular pressure
M	musculus
MLT	micropulse laser trabeculoplasty
NTG	normal tension glaucoma
PACG	primary angle closure glaucoma
PEX	pseudoexfolation
PG	pigmentary glaucoma
POAG	primary open-angle glaucoma
QOL	quality of life
SD	standard deviation
SLT	selective laser trabeculoplasty

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Zusammenfassung

Hintergrund/Ziele: Vergleich der postoperativen Lebensqualität nach minimal invasiver Glaukomoperation (XEN® Gel-Stent) mit der postoperativen Lebensqualität nach Trabekulektomie.

Methoden: Eine Querschnittserhebung bei Patient*innen mit diagnostiziertem Glaukom, die sich entweder einer Implantation des XEN® Gel Stents oder einer Trabekulektomie im Zeitraum von 2014 bis 2018 an der Universitätsklinik Graz unterzogen haben. Die Lebensqualität wurde mit Hilfe des GSS (Glaucoma Symptoms Scale) - Fragebogens erhoben.

Ergebnisse: 157 Patient*innen wurden eingeschlossen. 80 Patient*innen unterzogen sich einer minimal invasiven Glaukomoperation (XEN®) und 77 einer Trabekulektomie. Nach einer Stratifizierung für die postoperativen Jahre hatte die Trabekulektomie-Gruppe im ersten postoperativen Jahr signifikant mehr Symptome (85.6 vs. 70.4; p=0.03). Dieser Unterschied verschwand jedoch in den folgenden Jahren. Die Gesamtzufriedenheit mit der Operation war bei Patient*innen, die unabhängig von der Art des Eingriffs keine weitere IOD-senkende Medikation benötigten, signifikant höher (p=0.001). Von 10 Punkten des Fragebogens war nur einer in der Trabekulektomie-Gruppe signifikant schlechter (verschwommenes Sehen; 75.5 vs. 60.8; p=0.01), was jedoch darauf zurückzuführen war, dass 92.5% der minimal-invasiven Glaukom-Operationen mit einer Phakoemulsifikation kombiniert waren.

Schlussfolgerung: Lebensqualität gemessen anhand der Glaukom-Symptomskala war zwischen minimal-invasiver Glaukomoperation und Trabekulektomie sehr vergleichbar, mit Ausnahme des ersten postoperativen Jahres, in dem die nicht-visuellen Symptome in der Trabekulektomie-Gruppe schlechter waren.

Abstract

Background/Aims: To evaluate quality of life after minimal invasive glaucoma surgery (XEN® Gel stent) in comparison with trabeculectomy.

Methods: A cross-sectional survey of patients diagnosed with glaucoma, who either underwent implantation of XEN® Gel Stent or trabeculectomy from 2014 to 2018 at the University Hospital of Graz. The quality of life was assessed by using the GSS (Glaucoma Symptoms Scale) – Questionnaire.

Results: 157 patients were included. 80 patients underwent minimal invasive glaucoma surgery (XEN®) and 77 trabeculectomy. When stratified for postoperative years the trabeculectomy group had significantly more symptoms in the first postoperative year (85.6 vs. 70.4; p=0.03), but this difference disappeared in the following years. The overall satisfaction with the surgery was significantly higher in patients who did not further need IOP lowering medication regardless of the type of procedure (p=0.001). Out of 10 items of the questionnaire only one was significantly worse in the trabeculectomy group (blurry/dim vision; 75.5 vs. 60.8; p=0.01), but this was due to the fact that 92.5% of minimal invasive glaucoma surgeries were combined with phacoemulsification.

Conclusion: Quality of life measured by Glaucoma Symptom Scale – Questionnaire was very comparable between minimal invasive glaucoma surgery and trabeculectomy except for the first postoperative year, when non-visual symptoms were worse in the trabeculectomy group.

1 Introduction

The term glaucoma refers to a variety of diseases affecting the eye, that lead to a potentially progressive neuropathy of the optic nerve. The most important risk factor for developing glaucoma is an elevated intraocular pressure (IOP). (4) Because glaucoma is among those eye diseases that are responsible for the majority of vision impairment worldwide, it´s treatment is essential. (17) Therefore, medical, laser and surgical treatment is available to lower the IOP and reduce or even stop the progression of the optic neuropathy. But these treatments also lead to side effects which can reduce the patient's quality of life. Symptomatic side effects are with forgetfulness, medication cost, poor health literacy and others, responsible for poor adherence to medical glaucoma therapy. (8,22) Quality of life is furthermore reduced by the patient's knowledge of the diagnosis itself, leading for instance to fear of blindness. (19)

Medical therapy, which either reduces the production of aqueous humor or improves its outflow, is commonly used to initiate the treatment of patients diagnosed with glaucoma or ocular hypertension. If medical therapy is not sufficient in achieving target pressure levels, laser (trabeculoplasty, cyclophotocoagulation) or surgical therapy is indicated. (7,9,94) Considered as the surgical gold standard is the trabeculectomy, which is also the most frequently performed glaucoma surgery. But recently minimal invasive glaucoma surgery (MIGS), like the XEN®-gel stent, has gained popularity and is rapidly expanding. (20,21)

Within the framework of this consecutive cross-sectional data analysis, the post-operative quality of life of patients treated with trabeculectomy is compared with the post-operative quality of life of patients treated with the minimal-invasive XEN®-gel stent. For this reason, patients diagnosed with glaucoma who underwent trabeculectomy or an implantation of the XEN®-gel stent to reduce IOP at the department of ophthalmology of the Medical University of Graz between 2014 and 2018 were asked to participate in this study.

2 Background

2.1 The Anatomy and function of the eye

The eye is part of the human sensory system and the stimulus for its light-sensitive sensory cells, called photoreceptors, is the visible light (electromagnetic radiation with wavelengths in the range of 400-750 nanometers). (59) It's probably one of the oldest sensory organs and was already used 600 million years ago by unicellular flagellates for orientation. (8)

The eyeball (bulbus oculi), of which only 1/6 is visible to the outside, measures about 24mm in length and is situated in the orbital cavity. (1,2) The osseous orbit has the shape of a four-sided pyramid, with its peak lying at the canalis opticus and enclosed to the front by the eyelids. Located in the canalis opticus are the ophthalmic artery and the optic nerve. With open eyes, the upper eyelid covers 2mm of the superior margin of the cornea, while the lower eyelid tangents the inferior margin. The eyelids are connected with the eyeball through the conjunctiva, which is a transparent mucous membrane. (8,10)

The tear film is produced by the lacrimal glands and the small accessory lacrimal glands. The lacrimal glands are positioned above the lateral corner of the eye and are divided into the Pars orbitalis, which is facing the bone and the Pars palpebralis, which is facing the eyelid, by the tendon of the Musculus levator palpebrae superioris. The tear film is composed of an aqueous layer, secreted by the lacrimal glands, a lipid layer, responsible for a reduction of humidification, secreted by the meibomian gland and a mucin layer to improve adhesion to the cornea, secreted by conjunctival goblet cells. (1,8,62)

The bulbus oculi is composed of the following three layers:

- The tunica fibrosa bulbi, consisting of the sclera and the cornea.
- The tunica vasculosa bulbi also known as uvea, consisting of the iris, corpus ciliare and the choroid.
- The tunica interna bulbi consisting of the pigmented epithelium and the retina. (1,2)

2.1.1 Tunica fibrosa bulbi

The cornea is the transparent, curved, anterior part of the tunica fibrosa bulbi. It covers the iris, the pupil and the anterior chamber. The cornea is responsible for 2/3 of the total refraction of the eye. In its center, the cornea is about 550 µm thick, which can have an impact on the accuracy of the measurement of IOP. The avascularity and its homogenous structure are responsible for the transparency of the cornea. Therefore, nutrients need to be transported via diffusion from the aqueous humor to the inside surface and from tear fluid to the outside surface of the cornea. (1,8)

The cornea is formed by 5 layers:

- Epithelium cornea: The epithelium cornea is composed of 5 to 6 layers of cells. Located in the periphery of the cornea between epithelial cells are Langerhans cells for immunity and melanocytes. Found in the basal epithelium at the border to the sclera (limbus cornea) are stem cells of the corneal epithelium.
- Anterior limiting membrane (Bowman´s layer): This acellular layer is about 8-14µm thick and composed of collagen fibers.
- Substantia propria: This layer, which is also called corneal stroma, makes up to 90% of the thickness of the cornea.
- Lamina limitans posterior: Also, Descemet's membrane, is the basement membrane of the corneal endothelium.
- Endothelium cornea: The mitochondria-rich endothelial cells forming a 3-4µm thick plate are important for active transport and protein synthesis. In the first year of life humans have 5000 corneal endothelial cells per mm^2. This number decreases over time and is at about 2000/mm^2 at the age of 80. The number of endothelial cells is important for the pump function (pumping fluid out of the cornea into the anterior chamber), which cannot be maintained sufficiently if its below 1000/mm^2, and then leads to corneal swelling. (1,58)

The sclera covers 4/5 of the eye, is in contrast to the cornea not transparent and is appearing white. It serves as insertion for the six extraocular muscles (M. rectus medialis, M. rectus lateralis, M. rectus superior, M. rectus inferior, M. obliquus superior and the M. obliquus inferior) that control movement of the eye. In the front, the sclera is limited to the cornea, which is suited into the sclera like a watch glass. (1,8)

The sclera is formed by 3 layers:

- The episclera: The outermost layer of the sclera, a vascular connective tissue layer containing elastic fibers, macrophages, melanocytes, and lymphocytes.
- Stroma: The scleral stroma consists of collagenous fibers arranged in bundles of varying thickness. These bundles are arranged in a diamond-shaped pattern, which besides the higher water content is the reason why the sclera is not transparent like the cornea.
- Lamina fusca: This layer is consisting of fine collagen lamellae and is attached to the choroid and respectively to the ciliary body. (1)

Located in the iridocorneal angle (angulus iridocornealis) is the trabecular meshwork, which works as a filter for the draining aqueous humor. The trabecular meshwork is made of an iridial part, which is it´s innermost part and consisting of meshed tissue strands and gaps, a corneoscleral part with filter network, which is narrowing to Schlemm´s canal and the cribriform meshwork, which is also a part of the internal wall of Schlemm´s canal and with the endothelial lining of Schlemm´s canal the location of the main outflow resistance of the aqueous humor. At the lamina cribrosa, where the sclera is formed into a mesh-like structure by elastic and collagenous fibers, the optic nerve fibers exit the eye. (1,8)

2.1.2 Tunica vasculosa bulbi

Located in this layer are many vessels, nerves, smooth muscles cells and connective tissues. It is important for the blood supply of the eye, the accommodation as well as for secretion and outflow of the aqueous humor. The posterior part of the tunica vasculosa bulbi is the choroid, which is located between the sclera and the retina.

The choroid itself is made up of Bruch´s membrane, the lamina vasculosa and the suprachoroidea, which is the location of the uveoscleral outflow.

The pigment melanin, which is produced by melanocytes in the choroid, absorbs excess light and thereby prevents scattering and reflection of light within the bulbus oculi. (1,2)

The ciliary processes, which are linear folds that are projecting into the space behind the iris and the ciliary muscle are forming the ciliary body. In each eye the total surface area of the ciliary processes is about 6 square centimeters, due to its folded architecture.

The main structures of the ciliary processes are blood vessels and the secretory ciliary epithelium, which produces the aqueous humor in an average rate of 2 to 3 µL/min. The secretory ciliary epithelium forms the aqueous humor almost entirely as an active secretion.

The function of the ciliary muscle, which is composed of smooth muscle cells, is to change the shape of the elastically deformable lens, which is called accommodation and is the reason why we see sharp. The ciliary muscle itself is innervated by the parasympathetic nerve, which leads by stimulation to a contraction of the ciliary muscle and thereby to a relaxation of the lens ligaments, leading to a thicker lens and increased refractive power. (1,60)

The lens is located behind the pupil and the iris and separates the anterior cavity from the vitreous cavity. (2) The anterior cavity itself is divided into the anterior chamber, which is located between the cornea and the iris, and the posterior chamber, which is limited to the back by zonula fibers and the lens as well as to the front by the iris. (2)

The lens of the eye helps, along with the cornea, to transmit and focus light onto the retina and therefore contains very high concentrations of proteins making up 60% of its total mass. Surrounding the lens is a collagenous capsule, which functions as a barrier to diffusion and is important for the shaping of the lens during accommodation. The cells of the lens are, like cells of the cornea, depending on the aqueous humor for nutrition. (1,61) With age the elasticity of the lens decreases and focusing on close range is reduced (presbyopia). (59)

The iris of the eye functions as an aperture with the pupil as its opening. The neutral positioning of the pupil is a diameter of 4mm, which can be narrowed to 1.5mm and dilated to 8mm. The iris is thereby regulating the light intensity for the retina and setting the depth of field. This is achieved by two muscles. The Musculus dilatator pupillae, extending in the peripheral part of the iris between the stroma of the iris and the posterior iris epithelium, responsible for dilation, and the Musculus sphincter pupillae, which is arranged in a ring around the pupil, responsible for narrowing. Two layers of dark pigmented cells (stratum pigmenti iridis and pars iridica retinae) are located on the backside of the iris, which are blocking light, so not too much light is entering the eye. The front side of the iris is the only region of the human body where loose connective tissue, with its loose structure and many gaps, can be seen directly. (1,59)

The space between the lens, the posterior chamber and the retina is filled by the vitreous body. The vitreous body consists of 99% water but is very viscous due to hyaluronic acid complexes. Next to water, a loosely structured collagen fiber network, but hardly any cells, can be found in the vitreous body. It fills up to 65% of the eye and has a shock absorbing function and is responsible for an even attachment of the retina to the pigmented epithelium and layers following outside. (1,8)

2.1.3 Tunica interna bulbi

The pigmented epithelium contains the black pigment melanin and is important for exchange processes between the choroid, which is nourishing the outer third of the retina, and the retina. Apart from this, the pigmented epithelium is important for the photoreceptors of the retina, because it takes over the phagocytosis of the constantly renewing outer segments containing visual pigment. (1,60)
The retina is by function a part of the human brain, that consist of sensory cells and neurons. It is responsible for absorption as well as processing of the light stimulus and its transmission to the visual center of the brain. The photoreceptors, bipolar cells and ganglion cells are three retinal neurons which are connected in series. The photoreceptors are divided into rod cells and cone cells. The rod cells are responsible for night vision, while the cone cells are responsible for color vision.
The function of the Müller cells, which are specific retinal glial cells that are spanning vertically across all layers of the retina, is to maintain the retinal mechanical cohesion.
The fovea centralis, located in the center of the macula lutea, is the area with the highest visual acuity and is composed solely of cone cells. The fovea centralis is only about 0.3 millimeters in diameter. All axons of the ganglion cells extend to the optic disk from where on they form the optic nerve, optic chiasm and optic tract. The optic nerve is made of approximately 1.1 million axons of retinal ganglion cells and is located about 15 degrees nasally of the macula lutea and its fovea centralis. The axons of the optic nerve end in the lateral geniculate nucleus of the thalamus, from where on, the axons of the geniculate cells, known as optic radiation, carry visual information to the visual cortex in the occipital lobe of the brain. (1,8,60)
The retina itself can be divided into 9 layers, which are from the outside to the inside:

1. The photoreceptor layer: In this layer the outer segments of the photoreceptors are located, which contain disks filled with visual pigment, but not their perikaryons.
2. The external Limiting Membrane: In this layer the cell body of photoreceptors is linked to Müller cells via desmosomes.
3. The outer nuclear layer: Cell nucleus of photoreceptors are forming this layer.

4. The outer plexiform layer: Outer layer of synapses between axons of the photoreceptors and dendrites of the bipolar cells and horizontal cells.
5. The inner nuclear layer: Cell nucleus of bipolar cells, amacrine cells, horizontal cells, Müller cells and interplexiform cells.
6. The inner plexiform layer: Layer of synapses between the axons of bipolar cells and dendrites of ganglion cells and amacrine cells.
7. The ganglion cell layer: This layer is formed by the perikaryons of ganglion cells.
8. The retinal nerve fiber layer: This layer is formed by axons of ganglion cells leading to the optic nerve head.
9. The internal limiting membrane: This layer is the basal lamina of the retina and the boundary between the retina and the vitreous body. (1,87)

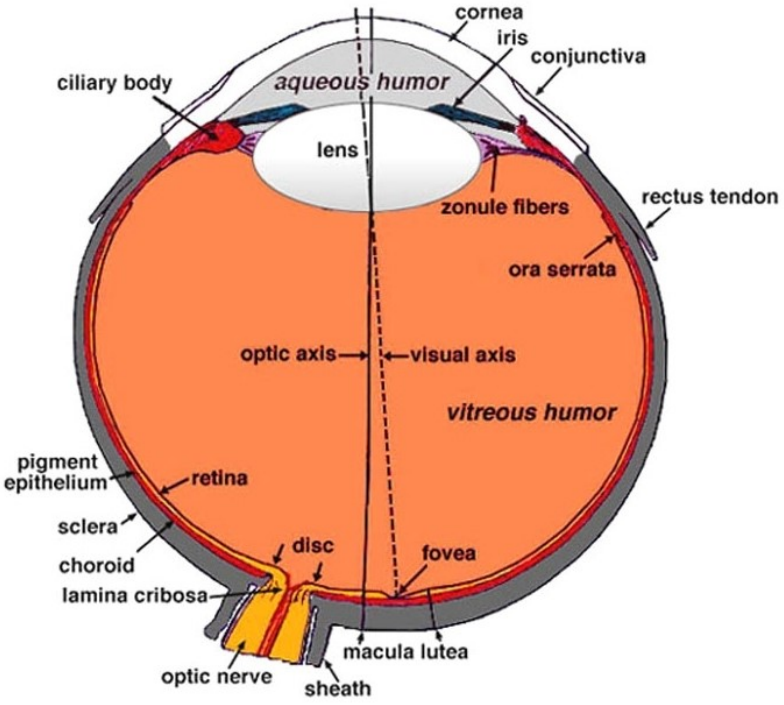


Figure 1: Illustration of the Anatomy of the human eye. (86)

2.1.4 Physiology

The dioptric system of the eye consists of the cornea, aqueous humor, lens and vitreous body, and works as a convergent lens. It produces a reduced and reversed image on the retina. The total refractive power of the resting eye is 59 diopters. (59) The light enters the eye through the lens system and then passes through the vitreous body, to enter the retina from the inside of the eye and therefore must pass firstly through the ganglion cells, the plexiform and other layers until it finally reaches the photoreceptors on the outer side of the retina. Since the passage through these layers decreases visual acuity, the inside layers are pushed to the side in the foveal region of the retina to allow the light to pass unhindered to the cone cells and so reducing the impact of these layers on the visual acuity.

The cone cells and rod cells are containing light-sensitive chemicals, the so-called cone pigments or color pigments in the cone cells and the rhodopsin in the rod cells. (60) The configuration of these light-sensitive chemicals is altered by light incidence, which is inducing the signal process of phototransduction converting light stimuli into electrical signals. (59)

The human eye possesses three different types of cone cells for color vision. Cone cells with blue-sensitive pigment showing peak absorbencies at light wavelengths of 445 nanometers, cone cells with green-sensitive pigment showing peak absorbencies at light wavelengths of 535 nanometers and cone cells with red-sensitive pigment showing peak absorbencies at light wavelengths of 570 nanometers. By mixing these three lights the eye is capable of detecting almost all gradations of colors. (60)

Visual acuity ($V = 1/\alpha$) is the reciprocal value of the eye´s resolution. On the retina, the centers of two separate points must be 2 micrometers apart from each other to be distinguished. Due to the fact that the diameter of the eye's fovea measures under 500 micrometers, only in 2 degrees of the visual field maximal visual acuity is available. (59,60)

Through the center of the optic nerve disc the central artery enters the eyeball from where on it divides to provide blood supply to the internal layers of the retina. The nutrition for the outer layers of the retina relies on diffusion from blood vessels of the choroid. (60)

After light has been transformed into electrical impulses by the retina, visual information is transported via the visual pathway to the lateral geniculate nucleus where the information is pre-sorted and transmitted to the primary visual cortex which is located in the occipital lobes. In the primary cortex an initial analysis of the picture is made and further processing like analysis of movement or object identification is accomplished by the secondary visual cortex. (8)

2.2 The Glaucoma

2.2.1 Definition

Glaucoma represents a variety of diseases with different etiologies, defined by a characteristic optic neuropathy. They all have damage to the optic nerve disk and visual field defects in common. Glaucoma proceeds progressively and its major risk factor is an elevated IOP. Annually approximately 1 million people worldwide lose their eyesight due to glaucoma, making it one of the most common causes of blindness worldwide. It´s pathology is not yet fully understood, but a relation between the level of the IOP to retinal ganglion cell death was found. Mechanisms leading to this retinal ganglion cell death are direct mechanical damage and ischemic damage. According to the mechanical theory retinal nerve fibers are damaged as they pass through the cribriform plate. The vascular theory claims, that chronic ischemic injury to the optic nerve results from compression of capillaries due to elevated IOP. (4,7,8,9,37)

2.2.2 Epidemiology

Globally 2-3% of the population over 40 years are living with glaucoma and approximately 50% of them are undiagnosed. (4) The prevalence of glaucoma increases with age and while in 1.5% of all humans over the age of 40 years the IOP lies above the statistical standard limit, it rises to 7% above the age of 70. (8) The most common type of glaucoma in Caucasian, Latinos and Africans (the latter having the highest prevalence) is the primary open-angle glaucoma. (4,5)

The highest prevalence of angle-closure glaucoma occurs in the Inuit, but it is also very common within people of Asian descent. (4,5) Angle closure glaucoma is mainly diagnosed in the age between 60-80 years and women are affected twice as often as men by an acute angle closure. (8) The most common secondary glaucoma is the pseudoexfoliation glaucoma. (7)

In Austria roughly 80.000 people suffer from glaucoma. Quigley and Broman estimated the number of people worldwide diagnosed with open angle glaucoma or angle closure glaucoma to be 60.5 million in the year 2010 and calculated that this number will rise to 80 million by 2020. In 2010 more than 8,4 million people diagnosed with primary glaucoma were bilaterally blind and with that number rising to 11.1 million people by 2020, glaucoma remains a major cause of blindness worldwide. (23,25)

2.2.3 Risk Factors

The main risk factor for developing glaucoma is an elevated IOP. Further risk factors are age, ethnicity and myopia. First degree relatives of patients diagnosed with glaucoma have an increased risk of developing glaucoma themselves. Other risk factors associated with glaucoma are vascular diseases, smoking, diabetes mellitus, oral contraceptive, translaminar pressure gradient, reduced ocular perfusion pressure and an enlarged optic disk. (3,4,8)

2.2.3.1 IOP

The physiological IOP lies between 10 and 21 mmHg, is not a constant value and fluctuates throughout the day. (6,27,30) The regulation of the IOP is accomplished by a balance between the secretion and drainage of aqueous humor. (63) The production of the aqueous humor is carried out by the ciliary epithelium through active and passive secretion of the blood plasma. (4)

The IOP causes the smooth curvature of the cornea and a constant distance between cornea, lens and retina. It is also responsible for a uniform positioning of retinal photoreceptors and the pigmented epithelium on Bruch`s membrane, which is important for the optical image. (6,27,30)

The aqueous humor floats intermittently pulsating through the pupil from the posterior chamber into the anterior chamber. This is due to the iris lying on the lens causing the aqueous humor to remain in the posterior chamber until the pressure is high enough to lift off the iris and produce a little gap. 85% of the aqueous humor floats then from the chamber angle of the anterior chamber through the trabecular meshwork into Schlemm´s canal and further into collector channels, aqueous veins and from there into episcleral veins. The other 15% enter, by passing through the uvea and the ciliary body, the bloodstream through uveoscleral vasculature. (6,24)

If the IOP is too low, vision impairment can result in distortion of cornea, lens and retina and if the IOP is too high it can lead to glaucoma. (6,24)

There are two main pathologies, that can lead to glaucoma. An increased resistance in the trabecular meshwork causing a reduced outflow of the aqueous humor and therefor a higher IOP, or an increased pupil flow resistance which causes a pressure increase in the posterior chamber that moves the iris in front of the trabecular meshwork which occurs in angle-closure glaucoma. (6)

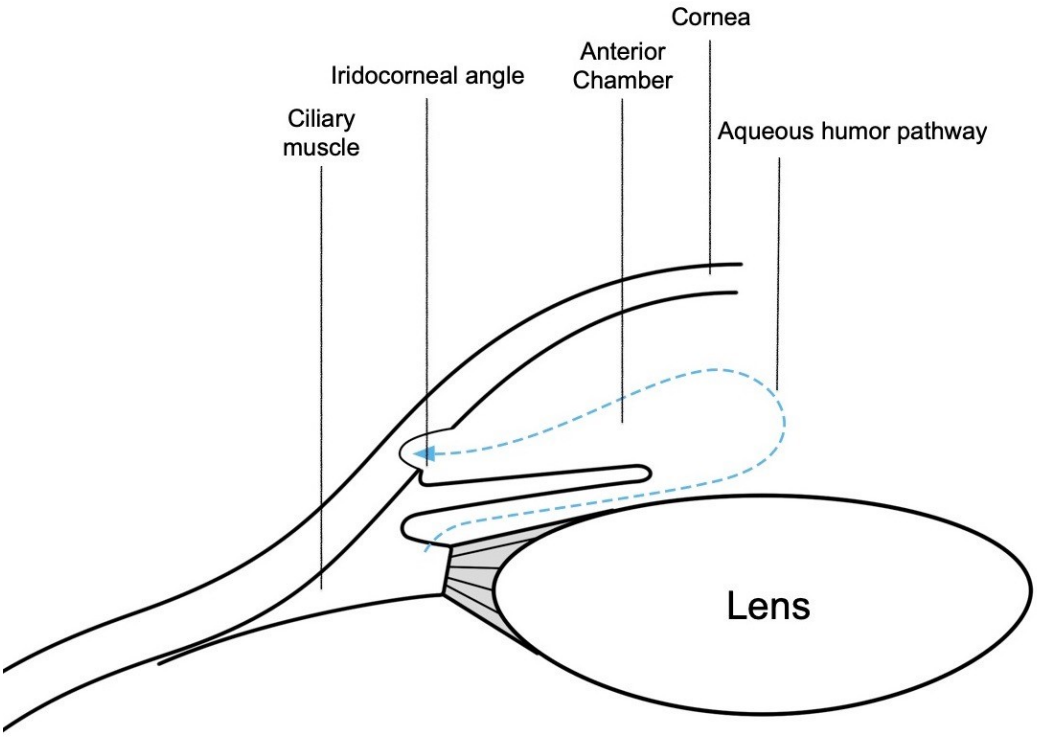


Figure 2: Pathway of the aqueous humor from its secretion in the ciliary process in the posterior chamber surpassing the lens to enter the anterior chamber and leaving through the trabecular meshwork in the anterior chamber angle.

2.2.4 Diagnosis

Patients usually don’t recognize primary open angle glaucoma in its early stages, because it proceeds painlessly and without symptoms. In early stages patients are not recognizing visual field defects which are irreversible. Thus, early diagnosis of glaucoma is important, enabling early intervention and preventing the progression of the disease and loss of eyesight. (25) For diagnostic and monitoring purposes the physician is able to use the following methods. (8)

2.2.4.1 Tonometry

The tonometry is the measurement of the IOP. The physiological IOP is situated between 10 and 21 mmHg and can be measured with different non-invasive methods. (8)

- Goldmann applanation tonometry (GAT): This method is the most accurate procedure to measure the IOP of the patient and is performed with the slit lamp whilst the patient is sitting. A tonometer head is brought in contact with the anaesthetized cornea, until an area of 3.06 mm in diameter is flattened. The pressure leading to this flattening is corresponding with the IOP of the patient. (8,9)

  Inaccurate values can occur due to a tight collar, breath-holding, Valsalva's maneuver, the physician touching the eyelids and squeezing the eyelids. An important factor in the accuracy of the measurement with GAT is the central corneal thickness, which should especially be measured in normal tension glaucoma, since a thinner cornea can lead to falsely measured lower values of the IOP. (8,9)

- Non-contact-tonometry: During this procedure an air blast flattens the cornea, which then results in an alteration of the reflection. This alteration is used for measuring the IOP. The advantages of this method compared to the applanations-tonometry are that the cornea does not have to be anaesthetized, no germ transmission can occur and there´s no risk of damaging the cornea. The disadvantages are that the measuring accuracy is lower than with the applanations-tonometry and it cannot be performed on patients with scarred cornea. (8)

- Rebound tonometry: Used in this method is a simple portable device with a magnetized steel wire shaft, covered with a round plastic tip at the end that hits the cornea and bounces back. The higher the IOP, the faster the probe bounces. This movement is used to calculate the IOP. It´s used in children and self-tonometry. (6,12,9)

- Dynamic contour tonometry (DCT): In DCT a concave shaped measuring body containing a piezoelectric pressure sensor, which is mounted to the slit lamp, is brought in contact with the cornea. This method is independent from corneal thickness and other biomechanical corneal properties. (4,8)

- The IOP can also be estimated by palpation of the bulbus oculi, which is carried out by palpating the bulbus oculi through the upper eyelid. (8) This very inaccurate method is particularly helpful for the general practitioner, who doesn't have any accurate instruments for measuring the IOP and in this way is able to palpate an acute angle-closure, whereby the bulbus is hard as stone. (8)

However, not only an elevated IOP can lead to a progression of glaucomatous damage, increased fluctuation of the IOP also poses risks. For that reason, it can be important to measure the IOP over the course of the day. This can be accomplished by measuring the IOP with the Goldmann applanation tonometry at predetermined times throughout the day and in the future continuously with for instance contact lens sensors (CLS) like Triggerfish. (28, 29, 31)

2.2.4.2 Ophthalmoscopy

The ophthalmoscope enables the physician to view the fundus of the eye, with its optic disc, retina, macula, fovea and the posterior pole. Since the retina is transparent to allow light to reach the photoreceptor, basically only the retinal vessels, structures of the choroid, causing the reddish color of the fundus, and the pigment epithelium are visible. (8)

In glaucoma the physician pays attention to the size and excavation of the optic disc. The excavation is the cupping in the center of the optic disc, which can indicate glaucoma, if it is appearing very big. The cup-to-disc ratio compares the diameter of the excavation to the diameter of the optic disc. Suspicious for glaucoma is a difference of the vertical cup-to-disc ratio between both eyes of more than 0.2. (4) Furthermore, the shape of the excavation is evaluated. Since at first the nerve fibers of the superior and the inferior papilla pole perish in glaucoma, the shape of the excavation is high oval in contrast to the physiological transverse oval excavation. Signs of a progressive glaucoma can be optic disc hemorrhages, which are also often seen in normal-tension glaucoma. Optic atrophy leads to alteration of vessels, like change of position and a sharp turning into the cup (bayoneting). (3,4,8,11)

(A) (B)

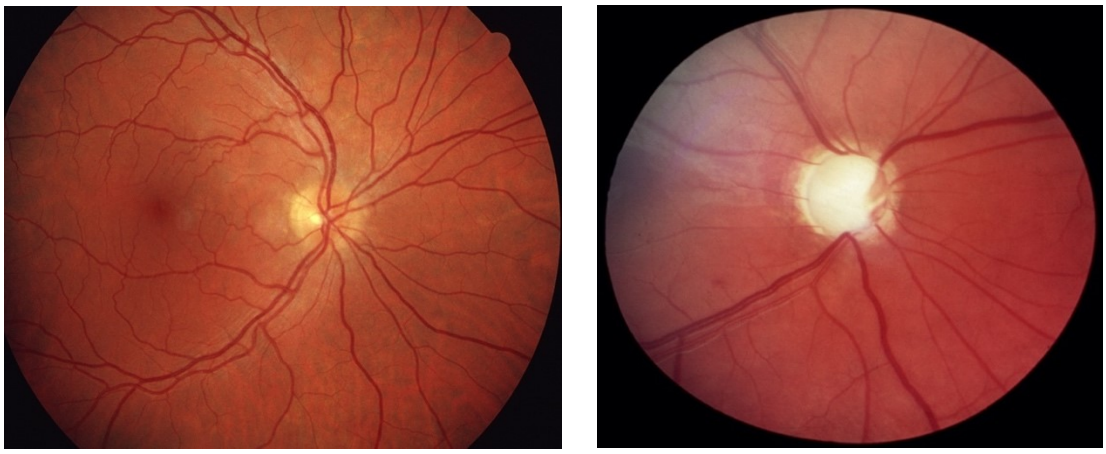


Figure 3: Normal retina (A) and severely damaged optic nerve in advanced glaucoma as seen with the ophthalmoscope (B). (87,88)

2.2.4.3 Optical coherence tomography (OCT)

This non-invasive imaging technique produces high-resolution sectional images of the posterior segment of the eye. Its functional principle is similar to ultrasound imaging but uses near infrared light instead of sound waves. (4)

The OCT can be very useful for follow-up during early-stage glaucoma to identify glaucomatous progression because it measures the thickness of the retinal nerve fiber layer and inner macular retinal thickness very accurately. (8,9)

2.2.4.4 Perimetry

Perimetry is the examination of the visual field and is another important examination for the diagnosis, follow-up and management of glaucoma. The visual field is the area someone is able to see whilst focusing on one point without moving the head. Physiologically its limited superiorly at 50°, nasally at 60°, inferiorly at 70° and temporally at 80°. Visual acuity is highest at the fovea and decreases progressively to the periphery of the visual field. (8)

With static computerized perimeters like the Humphrey perimeter or the Octopus perimeter the central 30° of the visual field are examined in glaucoma. During this examination the patient sits in a dimmed room with his eye looking into the center of the perimeter. At a certain spot in the perimeter a dim light is presented and if the patient is capable of seeing it, he or she presses a button, if not, the light will get brighter until it´s visible to the patient. This will go on at other spots as long as the visual field of the tested eye is examined. With the perimetry alone glaucoma can only be recognized in an advanced stage, since visual field defects (scotoma) first occur if more than 30% of nerve fibers have perished. In patients diagnosed with glaucoma visual field defects occur firstly paracentral and if untreated extend progressively. At the same time, advanced glaucoma visual field defects can go unrecognized by the patient due to compensation through the other eye. Nevertheless, visual acuity of patients with glaucoma remains well for a long time because the fovea is usually spared out until terminal stages. (8)

In newly diagnosed glaucoma, the patient should undergo perimetric examinations three times a year in the first two years to assess the progression rate. To analyze the progression the physician pays attention to a number of values like the Mean Defect (MD), which is a representation of the overall depression of the visual field, or the square root of loss variance (sLV), which provides information about if the loss is diffuse or localized.
Sources of error might be a poor compliance of the patient, uncorrected refractive error, ptosis or rim artefacts of the refractive lenses. (8,9,32-35)

In glaucoma the visual field loss processes in 6 phases:

1. Relative paracentral scotoma
2. Isolated absolute paracentral scotoma
3. Absolute scotoma with connection to the blind spot
4. Sector scotoma
5. Total loss except for the central visual field and periphery rests
6. Total loss of the central visual acuity

In untreated primary open angle glaucoma patients will go through these phases within 10 to 15 years. (8)

2.2.4.5 Gonioscopy

The ophthalmologist using a gonioscope is able to assess the iridocorneal angle, which should be done in every glaucoma patient. He or she can in this way differentiate between an open, narrow and blocked angle. Structures of the iridocorneal angle visible with gonioscopy are:

- Schwalbe´s line: The border between the corneal endothelium and the trabecular meshwork.
- The trabecular meshwork: Consisting of an anterior unpigmented part and a posterior pigmented part. It is the location of Schlemm´s canal.
- The scleral spur: Appearing as a white line
- The ciliary body: Visible with the gonioscope is the foremost part of the ciliary body, which is appearing as a brownish ribbon and serves as the insertion of the root of the iris.

To evaluate angle anatomy, to compare findings at different times and for classification between different patients, it's helpful to use a practical grading system like Shaffer or Kanski. Furthermore, the ophthalmologist looks out for an increased pigmentation of the trabecular meshwork, neovascularization, adherences of the iris called synechia and the opening distance of the chamber angle. (4,8,9,13)

2.2.4.6 Pachymetry

The corneal thickness is measured with pachymetry. (8) The thinnest area is the center of the cornea with around 550 µm. the cornea is gaining thickness to the periphery up to around 660 µm. (89)

Central corneal thickness (CCT) can have an impact on the accuracy of the measurement of the IOP. The IOP measurement in patients with thin central corneal thickness leads to falsely lower IOP values while in patients with thicker CCT the IOP is measured higher than the actual IOP. (8,36,89,90) But CCT also has an impact on the risk of developing glaucoma itself leading to an increased risk up to 70 % if CCT decreases by 40 µm. (91)

2.2.5 Types of Glaucoma

Glaucoma can be divided into primary glaucoma, if it occurs spontaneously and not as a consequence of another disease, and secondary glaucoma, which results from identifiable causes like the use of glucocorticoids or the pseudoexfolation-syndrome. (8)

Further it's important to differentiate between the open-angle glaucoma, with an open chamber angle and outflow resistance in the trabecular meshwork and the angle-closure glaucoma, characterized by a closed chamber angle and outflow resistance caused by the iris. (8)

2.2.5.1 Primary open-angle glaucoma (POAG)

The primary open-angle glaucoma mainly occurs within elderly people and is the most common glaucoma type, making up to 90% of glaucoma. (6) In general, it affects both eyes, the chamber angle is open, and it is characterized by a slow progression with atrophy of the optic nerve resulting in a vertical-oval excavation of the optic disk. The pathophysiology behind this type of glaucoma is the deposition of hyaline material in the trabecular meshwork resulting in a reduced outflow of the aqueous humor causing the IOP to rise, which results in damage to the fibers of the optic nerve. (8)

It is important to differentiate the open-angle glaucoma from **ocular hypertension**, where the IOP is above 21 mmHg, but without damage to the optic disk and no defects in the visual field. (4) Ocular hypertension occurs in 4-10% of the population over 40 years. (4). A study by Kass et al. implies that ocular hypertension has a cumulative risk of 9.5% to develop a primary open angle glaucoma within 5 years if untreated. (83)

We also have to differentiate **the normal-tension glaucoma**, where the IOP is below 21 mmHg, but with damage to the optic disk and corresponding restriction of the visual field. (8)

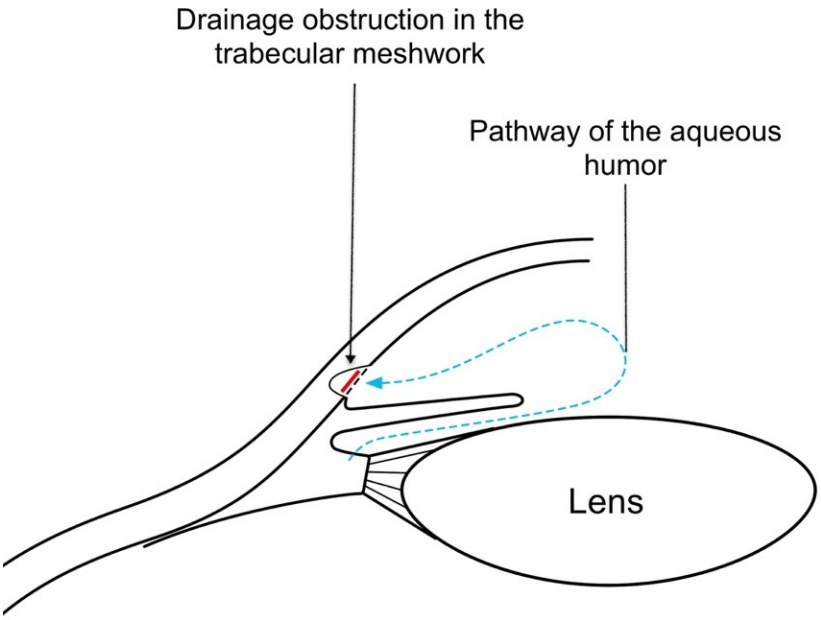


Figure 4: Drainage obstruction of the aqueous humor in the trabecular meshwork in primary open angle glaucoma.

2.2.5.1.1 Therapy

The aim of therapy of open-angle glaucoma is the reduction of elevated IOP, which is the only treatable risk factor in glaucoma. This can be accomplished by medical therapy, laser treatment or surgery. (8,63) The goal of the IOP-reduction is to reduce the progression rate of visual field defects. To retain quality of life in patients diagnosed with glaucoma for their expected life span by reducing the progression of the disease, the IOP is adjusted individually in every patient and every eye (target IOP). To evaluate the individual target IOP, the stage of glaucoma, the height of the IOP prior to the therapy, age and life expectancy, progression rate, other risk factors, side-effects and risks of therapy, as well as the patient's preference must be considered. (94)

2.5.1.1.1 Medication

Generally, the first attempt to reduce the IOP is medical therapy. Therefore, various substances which are used in monotherapy or in combination exist. The efficiency of the therapy should be controlled at regular intervals. (8)
It's important to increase the adherence to the therapy by giving patients precise description of the disease and its treatment. The prescribed medical therapy has to be explained to the patient, with emphasis on timing and technique of application to ensure maximum effectivity. (4)

- Prostaglandin derivative: Examples are Latanoprost, Travoprost or Tafluprost which open the uveoscleral outflow path and in this way reduce the IOP. Prostaglandin derivatives lower the IOP more than any other medical ocular antihypertensive therapy and are generally prescribed as first-line therapy. The IOP lowering effect of prostaglandin derivatives lasts for several days and a single application per day is recommended. Significant side-effects may be intensified lash growth, thickening and hyperpigmentation, darkening of the color of the iris due to irreversible hyperpigmentation and a reversible hyperpigmentation of periocular skin. A frequently occurring side-effect is a conjunctival hyperemia. Prostaglandin derivatives hardly have any systemic side-effects, which may be headache, triggering migraine or feeling of illness. (8,4,14)

- Parasympathomimetics: Pilocarbin and Carbachol are improving the outflow of the aqueous humor through the trabecular meshwork and thereby reduce the IOP. They used to be prescribed frequently in open angle glaucoma but are applied nowadays mainly in angle closure glaucoma. A significant side-effect of this therapy is the myosis, which can make it difficult to drive at night and reduces the vision of older patients with primary stage cataract. (8,4,14)

- Beta-blockers: Agents like Timolol, Betaxolol or Levobunolol lower the IOP by throttling the production of the aqueous humor. This effect decreases in 10% of patients and the IOP has therefore to be reduced by other options. Beta-blockers should not be applied at night, because the production of the aqueous humor is more than halved at night and the IOP lowering effect would decline. Furthermore, Beta-blockers applied at night can lead to an aggravation of the visual field by reduction of the perfusion of the papilla due to massive drop in blood pressure during sleep. Beta-blockers are preferred in patients with cystoid macular edema, inflammation or herpetic keratitis. They hardly lead to any ocular side effects but can lead to many systemic side effects like fatigue, headache or disorientation. However, these substances must not be applied in patients with bradycardia, bronchial asthma or atrioventricular block, because they can aggravate these diseases which could have fatal consequences. (8,4)

- Carbonic anhydrase inhibitors: For instance, Dorzolamid and Brinzolamid, which like beta blockers lead to a reduction of the production of aqueous humor and might have a neuroprotective effect. They should be applied three times a day if prescribed as monotherapy or two times a day when combined with other medical antihypertensive substances. Side effects may be burning, an allergic blepharoconjunctivitis or a bitter taste after application. (8,4)

- Sympathomimetics: Alpha 2 receptor agonists like Clonidin or Brimonidin, which reduce the production of aqueous humor by affecting the ciliary epithelium. They also increase the uveoscleral outflow and might have a neuroprotective effect as well. Local side effects may be an allergic conjunctivitis or a granulomatous anterior uveitis and systemically a dry mouth and fatigue can occur. (8,4)

2.5.1.1.2 Laser treatment

Trabeculoplasty:

This therapy is indicated in patients who have an elevated IOP which cannot be reduced appropriately with medical therapy but who have no indication for surgical treatment. It can also be indicated as first line therapy by noncompliance of the medical therapy or as adjuvant therapy to prevent polypharmacy. It´s performed in patients with open-angle glaucoma, pigmented glaucoma, ocular hypertension and pseudoexfoliation glaucoma. During this treatment 50-100 laser spots are spread over the anterior part of the trabecular meshwork leading to an improved outflow of the aqueous humor. The full effect of this treatment can be seen after 4-6 weeks and leads to an IOP reduction of 6-8 mmHg for approximately 2 years. There are three types of trabeculoplasties: the selective laser trabeculoplasty (SLT), the argon laser trabeculoplasty (ALT) and the micropulse laser trabeculoplasty (MLT). (8,4,6)

- The selective laser trabeculoplasty uses a q-switched 532-nm Nd:YAG laser, which aims at melanin pigment in the cells of the trabecular meshwork without harming unpigmented cells and structures. In comparison to the ALT, the SLT doesn’t lead to thermal tissue damage and can be repeated. Complications may be mild inflammation, an increase of the IOP and the development of peripheral anterior synechiae. (8,4)

The use of SLT as primary therapy and as an addition to medical and surgical treatment of primary open-angle glaucoma and ocular hypertension has been increasing, because of lower cost and no significant difference in health-related quality of life and clinical outcome compared with medication used from the outset. (15,16)

- The argon laser trabeculoplasty reduces the IOP equally strong as the SLT but leads to thermal tissue damage and thus isn't repeated commonly. Complications may be an increase of the IOP, an anterior uveitis, the development of peripheral anterior synechiae and a cystoid macular edema. (4)

- The micropulse laser trabeculoplasty stimulates cells in the trabecular meshwork, without harming them. It's a new procedure with lesser damage to the surrounding tissue than the SLT or ALT. (4)

Cyclophotocoagulation:

Cyclophotocoagulation (CPC) is performed by using a diode laser and reduces the production of aqueous humor by inducing atrophy of the secreting ciliary epithelium. It may be indicated for pain relief in untreatable secondary glaucoma or in eyes with bad prognosis after invasive operations like trabeculectomy. (8,4)
Cyclophotocoagulative procedures used to selectively destroy the ciliary epithelium are transpupillary CPC, transscleral CPC, transvitreal endophotocoagulation and endoscopic CPC. The most frequently used procedures are the transscleral CPC and the endoscopic CPC. The transscleral CPC can be performed by either using a Nd:YAG laser or the semiconductor diode laser. Complications of cyclophotocoagulation may be hypotony, visual loss, postoperative pain, the need of retreatment, phthisis bulbi or intraocular haemorrhage. (71)

2.5.1.1.3 Surgical therapy

Surgical treatment of glaucoma can be divided into three major types. Among these three types are the penetrating operations, the non-penetrating operations and the minimal-invasive glaucoma surgery (MIGS). (8)

2.5.1.1.3.1 Penetrating Operations

Trabeculectomy:

The trabeculectomy was firstly described in 1968 by Cairns JE and has developed to the surgical gold standard for glaucoma therapy since then. (67)

Trabeculectomy is performed if neither medical treatment nor trabeculoplasty are successful in keeping the IOP in an adequate range. It´s a surgical procedure, whereby creating a fistula, the aqueous humor is able to drain out of the anterior chamber into the sub-tenon space. Firstly, an opening in the conjunctiva is created and then a flap in the sclera with its basis at the corneal limbus (the border of the cornea and the sclera) is made. After that, an opening through the trabecular mesh-work into the anterior chamber is created as well as an opening into the basis of the iris. Now the scleral flap is sutured in a way that the aqueous humor doesn't drain too quickly. Underneath the conjunctiva emerges a drainage bleb, which is covered and protected by the upper eyelid. From there the aqueous humor is absorbed by veins and lymphatic vessels. During the operation mitomycin c, which is an antime-tabolite, is applied to reduce the postoperative scarring of the scleral flap and the drainage bleb, which would lead to insufficient reduction of the IOP. (4,8)

Postoperative Complications:

- Flat anterior chamber: An excessive outflow, pupillary block and malignant glaucoma can lead to a flat anterior chamber. Often the anterior chamber regains its former shape, but if it doesn't, severe complications, like damages to the corneal endothelium, cataract and anterior synechiae, can develop. (4)

- Filtration failure: Bad filtration is characterized by an increasing IOP and a drainage bleb which is either flat without vascularisation, encapsulated

(Tenon´s cyst) or vascularised due to episcleral fibrosis. Treatment option may be cutting the sutures (for instance with an argon laser), needling and injection of 5-fluorouracil. (4)

- Blebitis: Blebitis is the infection of the drainage bleb which leads to a red, aching and clotting eye with photophobia. To analyze the blebitis a swab of the conjunctiva is indicated. Antibiotics like ofloxacin or cephalosporin should be used as its treatment. (4)

- Endophthalmitis: Resulting from a fistula, endophthalmitis has a very bad prognosis and can lead to blindness and loss of the eye. A rapid treatment with antibiotics applied locally, systemically and intravitreally is necessary.
  The most common pathogens for infectious postoperative complications are streptococci, staphylococci and haemophilus influenzae. (4)

2.5.1.1.3.2 Non-penetrating operations

These operations are more frequently performed in recent years, because the anterior chamber does not have to be opened and the inner trabecular meshwork remains intact, so they lead to less postoperative complications like hypotension. However, the reduction of the IOP is lower compared to the trabeculectomy and medical therapy often needs to be prescribed again. (4,8)
Counting to the non-penetrating operations are the deep sclerectomy, the viscocanalostomy, the canaloplasty and the trabectome. (4,8)

Deep sclerectomy:

By performing deep sclerectomy the ophthalmologist removes the inner wall of Schlemm´s canal and juxta-canalicular trabecular meshwork, which are responsible for the most outflow resistance in open angle glaucoma and thereby improves the outflow of the aqueous humor.
The management of the outflow of aqueous humor is accomplished by leaving an intact trabeculo-Descemet´s membrane. (66)

Viscocanalostomy:

At this procedure Schlemm´s canal is stretched with a viscoelastic, which leads to a development of micro-ruptures in the trabecular meshwork and thereby to a dosed outflow of the aqueous humor into the Schlemm´s canal. (68)

Canaloplasty:

Canaloplasty is aiming to reduce the IOP by draining the aqueous humor internally through reconstructed natural outflow by dilating Schlemm´s canal, which is collapsed in many patients diagnosed with primary open angle glaucoma. (68,69) Lewis et al reported that canaloplasty performed in combination with phacoemulsification leads to lower pressure values than if performed alone, which makes it an alternative of the penetrating glaucoma surgeries for the combined treatment of cataract and glaucoma. (68,70)

Trabectome:

This micro-electric surgical device is used by the ophthalmologist to remove a part of trabecular meshwork and inner wall of Schlemm´s canal whilst using a gonioscope. (4)

2.5.1.1.3.3 Minimal-invasive glaucoma surgery (MIGS)

Minimal-invasive glaucoma surgery is an operation for POAG, which is performed with minimal incisions. Stents used with these operations can drain the aqueous humor into suprachoroidal space, into subconjunctival space and through the trabecular meshwork into Schlemm´s canal. (8) Stents targeting the trabecular outflow like the iStent, are placed into the juxtacanalicular part of the trabecular meshwork which is usually the region of the greatest outflow-resistance in patients diagnosed with glaucoma. (18)

In stents targeting the suprachoroidal space, like the CyPass® micro-stent, the aqueous humor is absorbed by structures of the choroidea by creating a connection between the anterior chamber and the ciliary body. (8,18)

Stents targeting the subconjunctival space, like the Xen® gel stent, share the principle of filtration surgery by creating a new non-physiological pathway for the aqueous humor bypassing outflow resistances between the anterior chamber and the episcleral venous system. (8,18)

<u>XEN® gel stent:</u>

The XEN® gel stent is a subconjunctival stent that is made of porcine collagen cross-linked with glutaraldehyde with a length of 6 mm and a luminal diameter of 45 µm, 63 µm and 140 µm. It´s inserted through a small, self-sealing corneal incision and placed into the subconjunctival space, draining the aqueous humor as during filtration operations, into a subconjunctival drainage bleb. This stent is stiff when dehydrated becoming flexible when in contact with aqueous humor and works like a tube ordering the outflow to follow Poiseuille`s law of laminar flow with the length and diameter of the tube determining the rate of flow. The outflow resistance is precisely regulated by the luminal diameter preventing strong pressure drops. It can be combined with phacoemulsification or is done as stand-alone. To minimize the risk of scarring, antimetabolites like mitomycin c are applied locally. (8,18,72)

2.5.1.1.3.4 Postoperative Care in Glaucoma Surgery

Postoperative care is vital for the success glaucoma surgery by making sure, that the filtering bleb remains functioning in the longer term. Two important parts for the success of filtration surgery are the management of postoperative complications and of the wound healing in the area of the filtering bleb. The wound healing does vary from patient to patient and its modification with actions like subconjunctival injection of VEGF-inhibitors and cytostatics (5-Fluorouracil), needling, or enhancement of steroid medication can duplicate the success rate of the operation. If scarring can't be prevented with these methods' revision surgery has to be performed with removal of scar tissue. (38) The success of the operation can be divided into absolute successes and qualified success. In the case of absolute success, the target IOP can be reached without additional medical therapy whilst in the case of qualified success additional medication is needed. (38)

2.2.5.2 Primary angle-closure glaucoma

The angle-closure glaucoma is the other mayor subtype of glaucoma. The pathology behind the primary angle closure glaucoma is an obstruction of the anterior chamber angle, where the aqueous humor flows out of the anterior chamber. This can be caused by the iris or by synechia. (39,40). The primary angle closure glaucoma commonly has a more rapid progression than the primary open angle glaucoma and leads to more severe visual impairment. (4) The angle-closure glaucoma can be divided into acute angle-closure, intermittent angle-closure and chronic angle-closure glaucoma. Acute angle-closure results from an acute complete closure of the chamber angle by the basis of the iris. This can spontaneously happen to older people in dark surroundings, but it can also have iatrogenic origins like the use of mydriatics. It is an ophthalmologic emergency which needs rapid intervention, as it causes pain, vision deterioration, cardiac arrhythmia (due to vagus nerve stimulation), nausea and emesis. (8,9) It´s characterized by corneal edema, a mid-dilated unreactive pupil, a shallow anterior chamber, conjunctival hyperemia and an IOP that is commonly greater than 30 mmHg. (39)

The chronic angle-closure emerges from an untreated acute angle-closure, where adhesions in the chamber angle lead to an elevated IOP and damage to the optic disk. (7,8)

Mechanism of the angle closure:

The acute angle closure is most frequently caused by a pupillary block, with an obstruction of the flow of the aqueous humor through the pupil, which emerges in a narrow anterior chamber with the iris lying tightly on the lens.

This situation can lead to a complete pupillary block when the pupil is dilated, with the aqueous humor dammed up in the posterior chamber pressing the iris forward and thereby blocking the chamber angle. With the aqueous humor not able to exit the anterior chamber the IOP rises to values of 50-70 mmHg causing pain, visual disorder, nausea, emesis and bradycardia. (8,92)

Other causes are the plateau iris, where the chamber angle is obstructed by a thickened peripheral iris in dilated pupils and the ciliolenticular block, which emerges when the flow from the posterior chamber and the anterior chamber is blocked due to the ciliary processes attaching to the equator of the lens.

The intermittent angle closure is characterized by episodes of increased IOP due to pupillary blocks, which resolve spontaneously. (8,92)

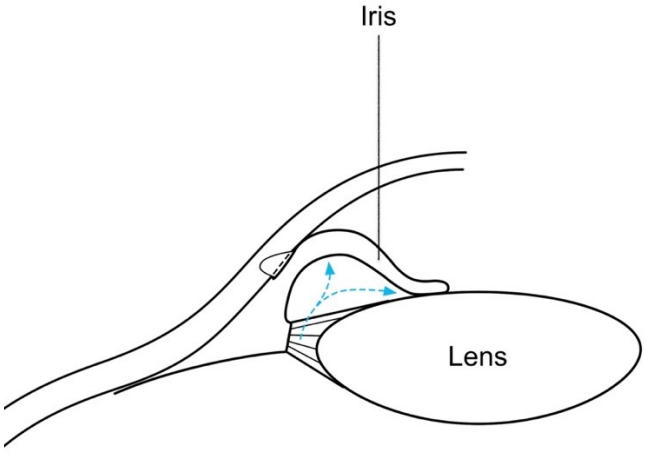


Figure 5: Pupillary block in acute angle-closure with the aqueous humor trapped behind the iris and obstruction of the anterior chamber angle.

2.2.5.2.1 Therapy

The acute angle-closure needs immediate treatment to reduce the elevated IOP and to prevent blindness. (8,39) Therefore, a combination of drugs consisting of carbonic anhydrase inhibitors, beta-blockers, mannit 20% and parasympathomimetics are applied at the same time. Followed by a peripheral iridectomy performed with laser (neodymium-YAG-laser) or surgery, which also needs to be performed on the unaffected eye to reduce the risk of developing acute angle-closure. Laser iridectomy should be performed if the IOP could be reduced into a safe range by medical therapy with declined corneal edema and an open anterior chamber angle. By laser iridectomy a hole in the outer edge of the iris is created, without damaging the cornea or the lens. In surgical iridectomy a hole in the iris is cut with micro scissors, which is performed if the IOP could not be reduced adequately with medical therapy. Iridectomy builds up a connection between the posterior and the anterior chamber, by removal of a small periphery part of the iris. (8)

2.2.5.3 Congenital glaucoma

Primary congenital glaucoma mostly occurs sporadically due to a developmental disorder which leads to an increased outflow resistance through the trabecular meshwork. (4) 10-40% of the cases are, mainly autosomal recessive, inherited. Genetic loci have been identified on the CYP1B1 gen and on the LTBP2 gen. (7) It's a rare disease with one newborn out of 10 000 – 18 000 in the European population being affected by this disease. (41)

Primary congenital glaucoma can be divided into three types based on the age of its onset.

- "real" congenital glaucoma: The IOP is elevated when the child is still in utero.
- Infantile glaucoma: Onset prior to the third year of age
- Juvenile glaucoma: Elevation of the IOP after the third year of age but prior to the 16th year of age. (4)

Symptoms of primary congenital glaucoma may be photophobia, epiphora, corneal enlargement and corneal clouding. (6)

Primary congenital glaucoma must be differentiated from an obstruction of the nasolacrimal duct, which also causes epiphora and photophobia, because misdiagnosis would lead to a delayed diagnosis and irreversible damage. (8)
Congenital glaucoma can also develop secondary to diseases like tumors (for instance the retinoblastoma), uveitis or persistent fetal vessels. (4)

2.2.5.3.1 Therapy

Medical therapy is insufficient in this type of glaucoma and therefore surgical treatment including drainage surgery, angle surgery and cyclophotocoagulation, is needed to normalize the IOP and prevent irreversible blindness. (8,41,84)

- Goniotomy: In goniotomy the abnormal trabecular meshwork is cut under direct gonioscopic view to lower the IOP. (4,84)
- Trabeculotomy: During this surgical procedure the ophthalmologist inserts a trabeculotome into Schlemm´s canal and tears through the trabecular meshwork into the anterior chamber. (84) It is indicated when the corneal edema is complicating the insight of the chamber angle and if multiple goniotomies failed. (4) A modification of the trabeculotomy is the 360° trabeculotomy where the whole circumference of the chamber angle is opened in a single session, whilst in the traditional trabeculotomy one third of the chamber angle is opened. (84)

If chamber angle surgery fails to achieve an adequate result, drainage implantation, trabeculectomy and cyclophotocoagulation can be further options to lower the IOP. (4)

2.2.5.4 Selection of Secondary Glaucoma

Pseudoexfoliation glaucoma:

The Pseudoexfoliation (PEX) syndrome is an age-related condition that is affecting both extraocular and intraocular tissues. The PEX glaucoma is the most important clinical finding of the PEX syndrome with occurring in 25%. Other clinical conditions associated with the PEX Syndrome are transient ischemic attacks, stroke, systemic hypertension and myocardial infarction. (42,43,92)

This glaucoma type, which is quite common in Scandinavian countries, is characterized by accumulation of microscopic fibrillo-granular fibers in the eye and the body. These fibers can be seen under the slit lamp on the lens and plug the trabecular meshwork, which increases the IOP. Typical for this type is an IOP which strongly fluctuates and reaches high levels. (7,8)

Neovascular glaucoma:

Diseases like diabetes mellitus or central retinal vein occlusion lead to retinal ischemia. Ischemic retina produces vascular endothelial growth factor (VEGF), which initiates vascularization on the iris and in the trabecular meshwork with fragile and permeable blood vessels. This develops a fibrovascular membrane, which covers the iridocorneal angle and decreases the outflow of the aqueous humor and thereby leads to an elevation of the IOP. (7,8,44)

In addition to the treatment of the vascular glaucoma with medical glaucoma therapy, panretinal photocoagulation and surgery, anti-VEGF therapy is used to treat intraocular neovascularizations. (45,46)

Steroid induced glaucoma:

Taking steroids locally or systemically over weeks can lead to an accumulation of mucopolysaccharides in the trabecular meshwork. This accumulation elevates the outflow resistance and results in ocular hypertension and secondary open-angle glaucoma. (6,8) Preventing steroid induced glaucoma by judicious use of steroids is very important.

Generally, the IOP decreases after discontinuance of the therapy, but in some cases the IOP remains permanently elevated and should be managed with treatment similar to that required for POAG. (47)

Pigmentary glaucoma:

The pigmentary glaucoma is characterized by excessive liberation and deposition of pigment on the back side of the iris. (4) The cause of the liberation is the rubbing of the iris on the zonula fibers, due to a higher pressure in the anterior chamber than in the posterior chamber. (8)

Medical therapy in pigmentary glaucoma is similar to in primary open angle glaucoma. If medical therapy is not sufficient, laser trabeculoplasty can be effective.

To prevent further irido-zonular contact and for the revision of the concavity of the iris and thus preventing further pigment liberation the ophthalmologist is recommended to perform laser iridotomy. In patients diagnosed with pigmentary glaucoma, filtration operation is more commonly performed to reduce the IOP than in patients diagnosed with primary open angle glaucoma. (4)

2.2.6 Quality of life of patients diagnosed with glaucoma

Quality of life (QOL) is defined by the world health organization as “an individual´s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person´s physical health, psychological state, personal beliefs, social relationships and their relationship to salient futures of their environment.” (26)

In patients diagnosed with glaucoma quality of life can be affected by many factors, like its treatment and the diagnosis itself. (48-50) More than 80% of the patients diagnosed with glaucoma experience negative emotions when firstly receiving their diagnosis and up to one third experience fear of losing vision. (48) Among patients diagnosed or suspected of glaucoma exists a statistically significant association with

depression and anxiety. (51,52) Furthermore there is an association between visual field loss and decline of QOL, by affecting the patients driving abilities and his or her vision-related dependency. (53) Patients diagnosed with glaucoma also have a higher rate of falls and motor vehicle collisions compared to individuals without glaucoma and because many people diagnosed with glaucoma are among the elder population, they are more vulnerable to falls and motor vehicle collisions with increased morbidity and mortality, leading to a decrease of their QOL. (54-57)

Patients in whom visual field loss has not developed yet, but who are experiencing side effects of antiglaucoma therapy might give up on the therapy, which is why patients should be educated on the possibility of the treatment´s side effects and the serious consequences of nonadherence. (51)

There are various questionnaires developed to assess quality of life of patients diagnosed with glaucoma. One of them is the Glaucoma Symptom Scale, which is a glaucoma-specific questionnaire surveying functional impairment and complaints in patients diagnosed with glaucoma. It specifically examines functional glaucoma-related disability and treatment-related symptomology. (64,65)

3. Materials and Methods

For this study, which was conducted according to the Declaration of Helsinki, we contacted 630 patients diagnosed with glaucoma, who either underwent trabeculectomy or minimal invasive glaucoma surgery with the Xen® gel stent (Xen45, Allergan CA, USA) between 2014 und 2018 at the department of ophthalmology at the university hospital in Graz Austria. The participants of the study were 18 years of age or older and men or women. Excluded were children, patients treated before 2014 and after 2018 and patients who were not able or willing to sign informed consent. After the study protocol was approved by the local institutional review board, we used the departments patient data management system, called EyMeD, to search for names and addresses of potential patients for our study. In June 2019 we sent envelopes to these patients consisting of an information sheet, giving knowledge about our intentions, our questionnaire, an example questionnaire how we expect the patients to fill in the questionnaire and a prepaid return envelope labelled with the address of the department of ophthalmology giving patients the ability to resend the questionnaire free of charge. These envelopes were sent to the patients addresses by the post office of the Medical University of Graz and costs were taken over by the department of ophthalmology. For this study we were using the Glaucoma Symptoms Scale (GSS) questionnaire, which consists of two domains including 10 items and was translated into German.

- For non-visual symptoms the domain Symp-6 was used, asking about burning/stinging, tearing, dryness, itching, soreness/tiredness and feeling of something in the eye.
- For visual symptoms the domain Func-4 was used, asking about blurry/dim vision, hard to see in daylight, hard to see in darkness and halos around the lights.

Patients who agreed to participate in our study were asked to evaluate only the operated eye, by scoring each of these 10 items between 1 to 6, where 1 means no symptoms at all and 6 meaning that symptoms are present all of the time. In addition to the GSS we asked about the patient's overall satisfaction of the operation on a scale from 0 not satisfied, to 10 very satisfied and if the patient applies no, equal, or more antiglaucoma eyedrop medications to lower the IOP than before the operation.

In advance of the operation every patient was examined with gonioscopy, slit lamp biomicroscopy, Goldmann Applanation Tonometry, standard automated perimetry (Interzeag Octopus 500, program G2), best corrected visual acuity (BCVA) and optical coherence tomography (OCT, Heidelberg Spectralis®). Both, trabeculectomy and the implantation of the Xen® gel stent, were performed in topical or retrobulbar anesthesia. All trabeculectomies these patients underwent were performed with fornix based conjunctival flaps and an application of the cytostatic mitomycin C (0.1mg/ml). Every Xen® implant was inserted in the patient's upper nasal quadrant of the affected eye. This implantation was either combined with phacoemulsification for co-treatment of cataract or done as a stand-alone procedure. After the operation, follow-ups at day 1, day 7, month 1, month 6 and month 12 were made, including the measuring of the IOP and performing slit lamp biomicroscopy. Furthermore, unpreserved topical steroids and antimetabolites were part of the postoperative management.

In autumn 2019 we created a file using Microsoft Excel™ consisting of data we received from the patients participating in our study and from clinical records. This file was then converted to the SPSS software version 25.0 (SPSS, Chicago, USA) to perform statistical analysis. For continuous variables the student´s t test or ANOVA was used, while for categorical variables the Chi-square test was used and p-values <0.05 were considered as statistically significant.

Name: .....

Geburtsdatum: ..... Operationsdatum: .....

Tropfen Sie nach der Operation des grünen Stars (Glaukom-OP) augendrucksenkenden Augentropfen?

□ Keine □ Gleich viel □ Weniger als vor der Operation

Wie zufrieden sind Sie mit dem Ergebnis der Operation auf einer Skala von „0“ (gar nicht zufrieden) bis „10“ (vollkommen zufrieden)? Bitte zutreffendes Ankreuzen.

0 1 2 3 4 5 6 7 8 9 10

Welche Symptome haben Sie nach der Operation?

Bitte zutreffendes Ankreuzen: „1“ (trifft nie auf) bis „6“ (tritt immer auf)

	1	2	3	4	5	6
Brennendes Auge						
Tränendes Auge						
Trockenes Auge						
Juckendes Auge						
Müdes Auge						
Verschwommenes Sehen						
Fremdkörpergefühl						
Blendung durch Tageslicht						
Erschwertes Nachtsehen						
Lichtschein um Lichter						

Figure 6: Example of the questionnaire we sent to the patients participating in our study.

4. Results

Out of 630 patients we contacted, 321 responded (50.95%). Of these 321 questionnaires, we were able to use 157 for our study (48.91%), 164 (51.09%) were incompletely filled in and therefore not useful. Of these 157 patients, 77 had undergone trabeculectomy (49.04%) and 80 patients had undergone minimal invasive glaucoma surgery with the XEN® gel stent (50.96%). 42 patients, who had undergone minimal invasive glaucoma surgery with the Xen® gel stent, were male (52.5%) and 38 patients were female (47.5%). 43 patients, who had undergone trabeculectomy, were male (55,84%) and 34 were female (44,16%).

Table 1 shows characteristics of the patients participating in our study grouped for XEN® and trabeculectomy. Patients who underwent minimal invasive glaucoma surgery with XEN® gel stent were overall older than patients operated with trabeculectomy (75.7 years vs. 71.1 years; p=0.007). Patients who had undergone trabeculectomy had in general been diagnosed with glaucoma that was in a more advanced stage than patients who had undergone implantation of the XEN® gel stent, indicated by visual mean defect (13.8 dB vs. 10.5 dB; p=0.01). 9 patients out of the XEN® group (11.25%) and 5 patients out of the trabeculectomy group (6.49%), had also been diagnosed with diabetes. Systemic hypertension was diagnosed in 37 patients operated with XEN® gel stent (46.25%) and 28 patients operated with trabeculectomy (36.36%). The average corneal thickness measured with pachymetry was 544.7µm in patients out of the XEN® group and 545.3µm in patients out of the trabeculectomy group. Primary open angle glaucoma was the most common subset of glaucoma diagnosed in our study patient groups with 51 patients in the XEN® group (63.75%) and 32 in the trabeculectomy group (41.56%). The second most common subset behind POAG was the secondary glaucoma subset pseudoexfoliation glaucoma, which was diagnosed in 22 patients treated with XEN® gel stent (27.50%) and in 19 patients treated with trabeculectomy (24.68%).

In the trabeculectomy group significantly more patients were diagnosed with primary angle closure glaucoma and secondary glaucoma than in the XEN® group (12 vs. 3 and 7 vs.2; $p<0.05$). Seventy-four of 80 minimal invasive glaucoma surgeries with XEN® gel stent, were combined with phacoemulsification for co-treatment of cataract (92.50%), leading to postoperative visual acuity significantly better than in patients who had undergone trabeculectomy.
Hyphema did occur postoperatively in 9 patients of the XEN® group (11.25%) and in 4 patients out of the trabeculectomy group (5.19%). In 21 patients who had undergone minimal invasive glaucoma surgery with XEN® gel stent postoperative needling was performed (26.25%), which was performed in 23 patients who had undergone trabeculectomy (29.87%).

Figure 7A is showing the course of the IOP over the first 12 months after glaucoma surgery. In patients who underwent trabeculectomy the preoperative IOP was significantly higher than in patients out of the XEN® group (28.71 mmHg vs. 23.24 mmHg; $p<0.001$). After the operation the IOP in the trabeculectomy group was lower at all post-operative follow up visits than in the XEN® group.

The number of IOP lowering medication patients required to apply in the first 12 months after operation are presented in figure 7B. Preoperatively there was no significant difference concerning the use of topical IOP lowering medication between the two groups, but it was statistically significant at the first four postoperative visits ($p<0.05$). After these first four visits this difference in requiring topical IOP lowering medication decreased and was not significant anymore at month 12 after surgery. There was no significant difference between patients who had undergone trabeculectomy and patients who had undergone XEN® in the number of patients requiring equal, less or no antihypertensive drugs after the operation compared with before operation.

The scores of the Glaucoma Symptom Scale are shown in table 2A. There was no significant statistical difference in the scores of burning/stinging, tearing, dryness, itching, soreness/tiredness, feeling of something in the eye, hard to see in daylight, hard to see in dark places and halos around light. But there was significant difference in blurry/dim vision (75.5 vs. 60.8; p=0.01).

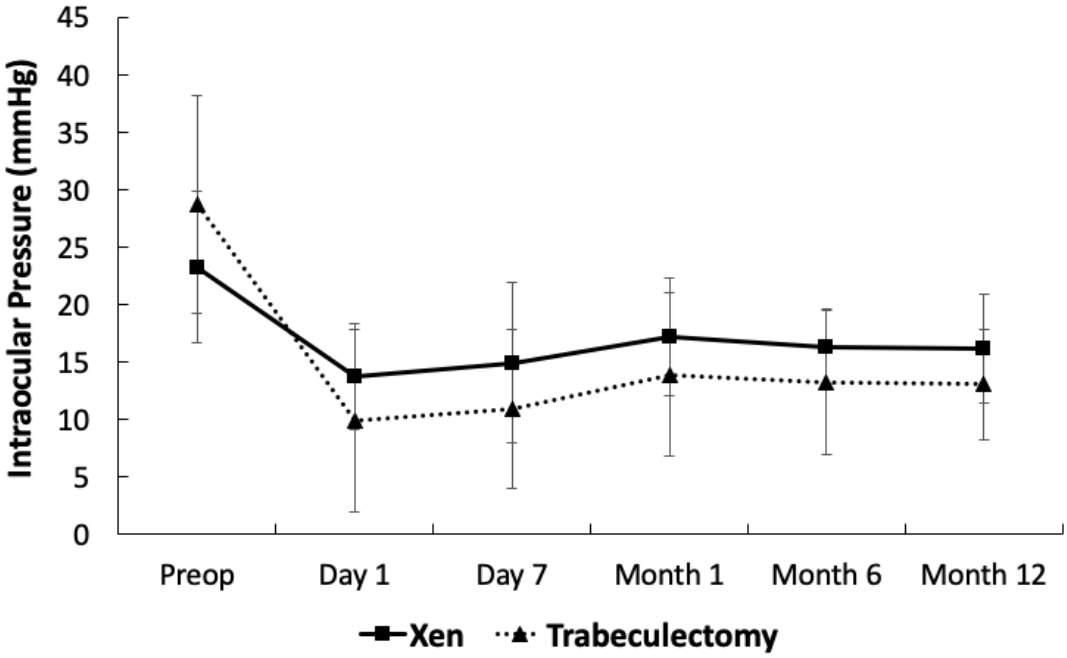
In table 2B it´s visible that the Symp-6 domain was significantly worse in the first year in patients treated with trabeculectomy (85.6 vs. 70.4; p=0.03). This difference decreased over the following years and became not significant when compared with the XEN® group.

Figure 8 shows the overall satisfaction patients had for their operations. It shows that there was no difference in satisfaction between patients who had undergone minimal invasive glaucoma surgery with XEN® gel stent and patients who had undergone trabeculectomy. However, satisfaction was lower when the operation did not lead to a reduction of the number of medications lowering the IOP patients were required to apply (7.27 vs 8.58; p=0.001).

	Xen	Trabeculectomy	p-value
Sex (male) n(%)	42 (52.2)	43 (55.8)	0.67
Age (years, SD)	75.7 (9.0)	71.1 (11.8)	0.007
Diabetes n(%)	9 (11.3)	5 (6.5)	0.30
systemic Hypertension n(%)	37 (46.3)	28 (36.4)	0.23
Pachymetry (µm, SD)	544.7 (37.8)	545.3 (44.6)	0.96
Cup to Disc Ratio (SD)	0.74 (0.20)	0.78 (0.18)	0.19
Visual Field Mean Defect (dB, SD)	10.5 (5.9)	13.8 (6.5)	0.01
OCT Global Index (µm, SD)	66.5 (18.8)	56.4 (20.1)	0.01
preoperative IOP (mmHg, SD)	23.24 (6.58)	28.71 (9.43)	<0.001
IOP 1 year postoperatively (mmHg, SD)	16.17 (4.78)	13.06 (4.79)	0.01
preoperative number of topical antihypertensive drugs required (SD)	2.49 (1.20)	2.58 (1.15)	0.62
number of topical antihypertensive drugs required 1 year postoperatively (SD)	1.59 (1.50)	0.97 (1.32)	0.07
type of Glaucoma			0.03
POAG n(%)	51 (63.8)	32 (41.6)	
PEXG n(%)	22 (27.5)	19 (24.7)	
PACG n(%)	3 (3.8)	12 (15.6)	
PG n(%)	1 (1.25)	4 (5.2)	
NTG n(%)	1 (1.25)	3 (3.9)	
Secondary Glaucoma n(%)	2 (2.5)	7 (9.1)	
combined with Phacoemulsification n(%)	74 (92.5)	0 (0.0)	<0.001
preoperative Visual Acuity (LogMAR, SD)	0.25 (0.27)	0.28 (0.32)	0.61
Visual Acuity (LogMAR, SD) 1 year postoperatively	0.20 (0.31)	0.30 (0.31)	0.05
postoperative Needling	21 (26.3)	23 (29.9)	0.62
postoperative Hyphema	9 (11.3)	4 (5.2)	0.17

Table 1: Characteristics of patients participating in the study grouped for Xen® and trabeculectomy. SD: Standard Deviation; POAG: Primary Open Angle Glaucoma; PEXG: Pseudoexfolation Glaucoma; PACG: Primary Angle Closure Glaucoma; PG: Pigmentary Glaucoma; NTG: Normal Tension Glaucoma

(A)



(B)

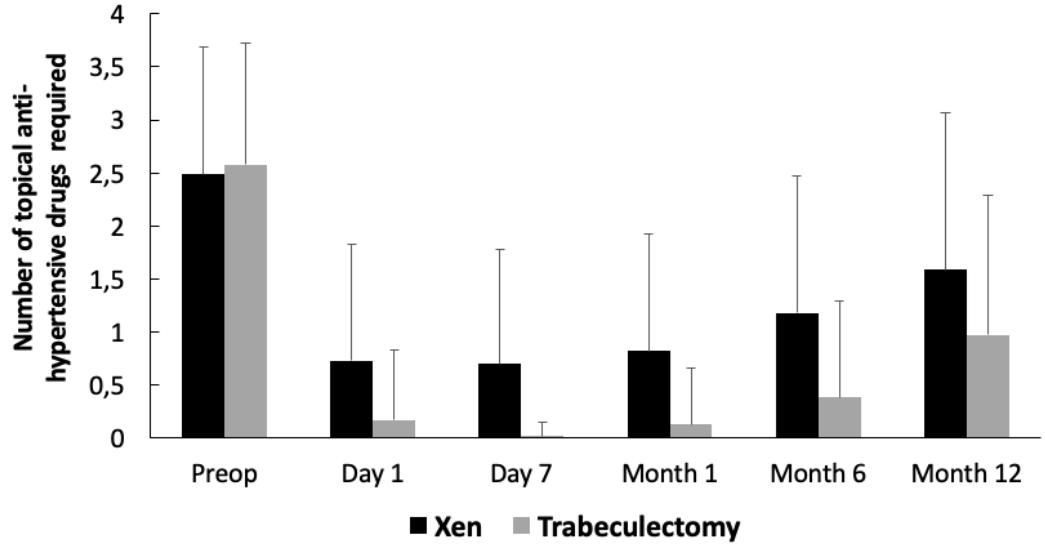


Figure 7: Course of the IOP (A) and the number of IOP lowering drugs in the first 12 months after operation (B). Bars, dots and triangles indicate means with standard deviation.

(A)

	Xen Mean (SD)	Trabeculectomy Mean (SD)	p-value
Burning/stinging	82.3 (24.2)	80.8 (28.0)	0.73
Tearing	77.5 (26.9)	75.1 (29.6)	0.60
Dryness	75.5 (33.5)	72.5 (35.1)	0.88
Itching	80.5 (25.8)	77.4 (28.9)	0.48
Soreness/tiredness	83.0 (27.9)	79.5 (30.9)	0.46
Blurry/dim vision	75.5 (33.4)	60.8 (35.0)	0.01
Feeling of something in your eyes	81.0 (28.3)	79.7 (29.5)	0.79
Hard to see in daylight	65.3 (36.8)	65.2 (35.3)	0.99
Hard to see in dark places	68.0 (37.2)	62.1 (38.1)	0.33
Halos around light	76.8 (35.2)	78.4 (31.6)	0.75

(B)

		Xen Mean (SD)	Trabeculectomy Mean (SD)	p-value
Func-4				
	1st year	72.7 (24.5)	57.2 (25.9)	0.17
	2nd year	70.3 (24.9)	67.8 (26.4)	0.74
	3rd year	71.6 (29.2)	76.4 (19.5)	0.69
	4th year	71.9 (28.6)	67.9 (24.0)	0.68
	5th year	71.7 (49.1)	65.6 (25.1)	0.72
Symp-6				
	1st year	85.6 (13.2)	70.4 (16.5)	0.03
	2nd year	82.3 (13.7)	77.7 (19.4)	0.35
	3rd year	74.6 (19.1)	84.3 (14.9)	0.23
	4th year	81.2 (15.2)	82.7 (11.6)	0.77
	5th year	65.3 (54.1)	74.7 (23.0)	0.57

Table 2: Scores of the Glaucoma Symptom Scale (GSS). Shown in (A) are scores of all single items with means and standard deviation. Shown in (B) are scores stratified for postoperative year 1 to 5 divided into Func-4 summarizing 4 visual items and Symp-6 including 6 symptoms.

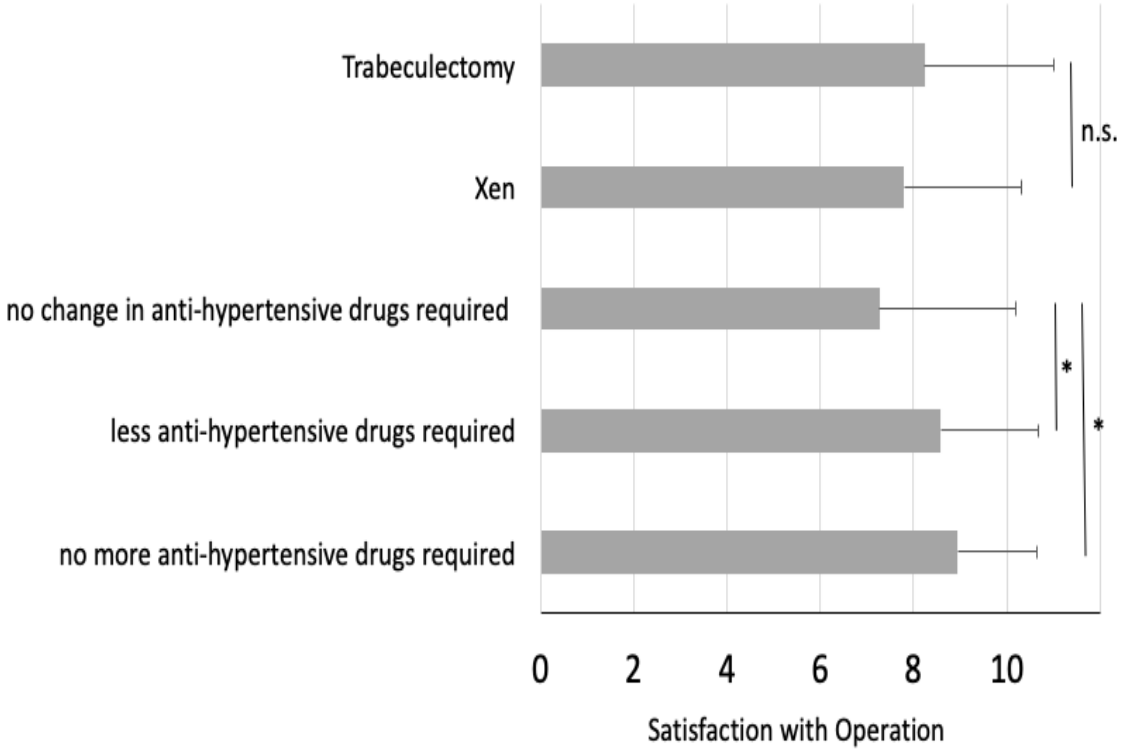


Figure 8: Showing the satisfaction of patients with the operation. 0 represents not satisfied at all, 10 represents total satisfaction. Bars indicate means with standard deviation. N.s.: $p>0.05$, *: $p<0.05$.

5. Discussion

Diagnosis and therapy of glaucoma have a great impact on the patient´s quality of life and might be even more important than parameters like IOP or visual field from the patient's perspective. (73) Therefore, the measurement of the quality of life in patients treated for glaucoma is very important in the assessment of treatment, especially with newly introduced surgical devices. Until today, few studies have been published on the difference in quality of life between trabeculectomy and minimal invasive glaucoma surgery. (74-76,82) In this study we have compared the quality of life after minimal invasive glaucoma surgery with XEN® gel stent with trabeculectomy up to 5 years after the operation using the Glaucoma Symptom Scale questionnaire and we are able to describe differences in non-visual ocular complaints in the first postoperative year.

We have chosen the Glaucoma Symptom Scale due to its short and simple structure giving good patient adherence and because it´s including visual and non-visual symptoms for comparison.
In this study we found no difference in the scores of the Glaucoma Symptom Scale for the two groups, which are similar to results obtained by Basilio et al. (74) Pahlitzsch et al compared the minimal invasive glaucoma surgery approaches iStent (Glaucos Corporation, Laguna Hills, CA, USA) and Trabectome (NeoMedix, Inc., Tustin,CA, USA) to trabeculectomy and likewise did not find any statistically significant different findings in quality of life. (93) We found differences between the two groups in the item "blurry/dim vision" which can be attributed to the fact that almost every minimal invasive glaucoma surgery with Xen® gel stent in this study was performed in combination with phacoemulsification for co-treatment of cataract.
In our study population we have seen that patients who had undergone trabeculectomy had more non-visual symptoms in the first postoperative year than patients who had undergone minimal invasive glaucoma surgery with the Xen® gel stent. This difference of non-visual symptoms between our two study groups diminished in the following years, which was also described by the collaborative initial glaucoma study. (50)

The characteristics of patients participating in this study are showing that patients who had undergone implantation of the XEN® gel stent were older and had been diagnosed with glaucoma in a less advanced stage compared to trabeculectomy, which is obvious since glaucoma is a progressive disease and trabeculectomy leads to lower IOP values than the XEN® gel stent, which are required in more advanced glaucoma stages. (81)

The results of this study showed that trabeculectomy leads more effectively to a lower IOP than the XEN® gel stent, which was seen up to 12 months after surgical intervention, with means between around 10 to 15 mmHg for trabeculectomy and between 15 to 20 for the XEN® gel stent. Similar results were obtained by Wagner et al. (75) in a retrospective cohort study showing that trabeculectomy was more efficient in lowering the IOP with a mean reduction of 10.5 mmHg at the 12-month follow-up compared to the XEN® gel stent with a mean reduction of 7.2 mmHg at the 12-month follow-up. Schlenker et al. compared in a multicentre retrospective interventional cohort study trabeculectomy with the XEN® gel stent and did not find any difference in success rates. (82) This might be due to the fact that in the study of Schlenker et al. reaching an IOP between 6 and 17 mmHg was taken as success, while in our study means of IOP were compared. (82)

Difference between the use of topical IOP lowering medication was seen in the first 4 follow-up visits and diminished at month 12 after operation, with no difference between the study groups. Parra et al. (76) investigated 91 patients diagnosed with open-angle glaucoma and concluded, that the implantation of the XEN® gel stent, either performed in combination with phacoemulsification or as stand-alone, lead to a reduction of the number of IOP lowering medication similar to that in patients after trabeculectomy. Furthermore, Parra et al. found similar results concerning the reduction of the IOP, with the trabeculectomy leading to a higher reduction of the IOP and significant lower IOP values at every follow-up visit.

In this study we also included the survey of the overall satisfaction patients had for their operation and we were able to find that the overall satisfaction did not depend on whether they underwent trabeculectomy or implantation of the XEN® gel stent, but on how the operation lead to a reduction of the number of topical IOP lowering medications patients were required to apply. This is not surprising since several studies have shown the impact of topical IOP lowering medications on quality of life. For instance, Balkrishnan et al. (77) found that a significant decrease in quality of life was associated with difficulties in the use of topical IOP lowering medication. Rossi et al. (79) described that the use of topical IOP lowering medication is a risk factor for the development of ocular surface diseases, like dry eye syndrome, which was also reported by Fechtner et al. (80), while Baudouin et al. (78) were able to find that ocular surface diseases have a harmful impact on patients' quality of life.

Study Limitations:

Limitations of this study are that it is single centred and has a cross-sectional design, which is commonly a source of bias and confounding. Questionnaires provide the risk of misinterpretation and misunderstanding of questions and subjectivity. With 164 questionnaires out of the 321 that we received filled in incompletely and therefore not useful for integration in this study, we must consider that our instructions for patients participating in this study weren't as comprehensible as we would have wished. Furthermore, more detailed questionnaires could have been useful for the detection of further differences between trabeculectomy and the XEN® gel stent, which might have been undetected in this study due to the short and simple structure of the glaucoma symptom scale questionnaire.

Conclusion:

In conclusion, we were able to find that quality of life in patients who underwent trabeculectomy was similar to patients after minimal invasive glaucoma surgery with the XEN® gel stent, with the exception of non-visual symptoms. These scored higher in the glaucoma symptom scale and thereby represent a worse outcome for trabeculectomy, however this result became irrelevant after the first postoperative year. In addition, we report that the overall satisfaction of the operation is strongly affected by the postoperative reduction of topical IOP lowering medication.

It still remains debatable if minimal invasive glaucoma devices like the XEN® gel stent will replace conventional filtration surgery in the future and further studies are needed to weigh up advantages and disadvantages, like the cost-effectiveness of minimal invasive glaucoma surgery devices. It will also become more important to evaluate the postoperative quality of life of new approaches of glaucoma management to attain the actual needs of glaucoma patients.

We recommend that in the future, further studies with a larger number of participating patients and a longitudinal approach should be conducted.

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