Aus der Klinik für Augenheilkunde
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DISSERTATION

# Clinical and morphological findings after canaloplasty

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von

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# Abstract

**Aim:** The present retrospective study reports two years results of the safety and efficacy of canaloplasty on phakic and pseudophakic eyes and phacocanaloplasty surgery in the treatment of open-angle glaucoma (OAG).

**Methods:** 100 eyes of 75 patients with OAG were included in this retrospective study, for which data was collected both preoperatively and postoperatively at 1day, and at 1, 3, 6, 12, 18 and 24 months. Assessment of clinical outcomes included intraocular pressure (IOP) reduction, visual acuity, medication use, as well as morphological manifestation after the surgery in the forms of bleb morphology, postoperative complications and further surgical intervention. Surgical failure was defined as a failure to meet specified IOP-related criteria.

**Results:** Forty-six phakic (Group 1A) and thirty-four pseudophakic (Group 1B) eyes underwent canaloplasty and twenty eyes underwent phacocanaloplasty (Group 2). The difference between preoperative and postoperative IOP at all time periods was statistically significant for all groups ($P \leq 0.05$). Canaloplasty on phakic eyes renders a 36% IOP reduction, while on pseudophakic eyes it renders a 42% reduction, and phacocanaloplasty renders a 51% reduction. At 18 months, the success rate (IOP at or below 15 mmHg with or without medication) in the phacocanaloplasty group was higher (75%) than in the canaloplasty group (50%). Preoperatively, the mean ±SD logMAR VA in Group 1, Group 2 and in total registered at 0.13 ±0.2, 0.20 ±0.1, and 0.14 ±0.2, respectively. Similarly, at 24-month the results registered at 0.26 ±0.5, 0.06 ±0.1, 0.23 ±0.5, respectively. There were 62% of the eyes in Group 1A, 64% of the eyes in Group 1B and 75% of the eyes in Group 2 without medications at 24 months. Postoperatively, 85.7% of the total eyes had a blebless appearance. Early complications such as 74% transient hyphema, 6% fibrin reaction, 2% elevated IOP, 1% choroidal effusion and 1% descemet membrane detachment with iris prolapse and late complications like 8% blebs and 6% elevated IOP were found. Only 14% of total eyes needed postoperative intervention, with 3% needing canaloplasty revision.

**Conclusion**: Canaloplasty surgery is minimally invasive, effective in reducing IOP, has a low complication rate, and can be offered as a first-line treatment in selected patients with OAG. The findings show also that the combined surgery, rather than canaloplasty alone is better in reducing the IOP and medication-use postoperatively, has a higher success rate, better visual acuity and lower complications and postoperatively interventions.

## Zusammenfassung:

**Ziele:** Diese retrospektive Studie berichtet über die zweijährigen Ergebnisse der Sicherheit und Wirksamkeit von Kanaloplastik in phaken und pseudophaken Augen sowie Phakokanaloplastik in der Behandlung des Offenwinkelglaukoms (OAG).

**Methoden:** Diese retrospektive Studie untersuchte 100 Augen von 75 Patienten mit Offenwinkelglaukom, für die Daten sowohl präoperativ erhoben wurden als auch postoperativ am ersten Tag nach der Operation sowie jeweils nach 1, 3, 6, 12, 18 und 24 Monaten. Zur Beurteilung der klinischen Ergebnisse wurden folgende Parameter herangezogen: Senkung des intraokularen Drucks (IOP), Sehschärfe, Medikation, morphologische Erscheinungen in der Form der Filterkissen-Morphologie, postoperative Komplikationen, Notwendigkeit von Folgeoperationen. Als erfolglos wurde ein Eingriff gewertet, wenn der erwartete Zieldruck nicht erreicht wurde

**Ergebnisse:** An 46 phaken Augen (Gruppe 1A) und 34 pseudophaken Augen (Gruppe 1B) wurde eine Kanaloplastik durchgeführt, und 20 Augen wurden mit Phakokanaloplastik behandelt (Gruppe 2). Der Unterschied zwischen dem präoperativen und dem postoperativen Augeninnendruck (IOP) war für alle Gruppen zu allen Untersuchungszeitpunkten statistisch signifikant ($P \leq 0.05$). Kanaloplastik an phaken Augen ergab eine durchschnittliche Verringerung des Augeninnendrucks um 36%, bei pseudophaken Augen verringerte er sich um 42%, und Phakokanaloplastik reduzierte den Augeninnendruck durchschnittlich um 51%. Nach 18 Monaten erreichten in der mit Phakokanaloplastik behandelten Gruppe 75% der Augen den Zieldruck von 15mmHg oder besser, mit oder ohne Medikation, während nach Kanaloplastik (Gruppen 1A und 1B) 50% diesen Wert erreichten. Der Mittelwert ±SD logMAR VA lag präoperativ in der Gruppe 1 (A und B) bei 0,13 ±0,2, in Gruppe 2 bei 0,20 ±0,1 sowie für alle Gruppen zusammen bei 0,14 ±0,2. Nach 24 Monaten lagen die respektiven Werte bei 0,26 ±0,5 (Gruppe 1A und 1B), 0,06 ±0,1 (Gruppe 2) und 0,23 ±0,5 (gesamt). Keine Medikamente benötigten nach 24 Monaten 62% der Augen in Gruppe 1A, 64% der Augen in Gruppe 1B und 75% der Augen in Gruppe 2. Postoperativ waren von allen operierten Augen 85.7% ohne Filterkissen. Als Frühkomplikationen traten 74% transientes Hyphäma, 6% Fibrinreaktion, 2% erhöhten Augeninnendruck und jeweils 1% eine Aderhauteffusion und Descemet-Membran mit Irisprolaps auf. Spätkomplikationen traten Filterkissen mit einer Häufigkeit von 8% auf, sowie erhöhter Augeninnendruck mit 6%. Nur 14 % der gesamten Augen benötigten Folgeeingriffe, davon 3% eine Revision der Kanaloplastik.

# Abstract

**Fazit:** Kanaloplastik kann bei ausgewählten Patienten mit Offenwinkelglaukom (OAG) als minimalinvasive Maßnahme zur effektiven Senkung des Augeninnendrucks bei niedriger Komplikationsrate als Behandlungsmethode der Wahl angeboten werden. Ein kombinierter Eingriff (Phakokanaloplastik) zeigt gegenüber alleiniger Kanaloplastik einen besseren postoperativen Verlauf in Bezug auf Senkung des Augeninnendrucks und Reduktion der Medikation, bessere Sehschärfe, weniger Komplikationen und Folgeeingriffe.

# 1. Introduction

Glaucoma is currently defined as “a progressive optic neuropathy involving characteristic structural damage to the optic nerve and characteristic visual field defects” [1].

The prevalence of glaucoma worldwide has become more pronounced, especially due to rapidly aging global population. In fact, by 2010 forecasts predict around 60.5 million people will have primary open angle glaucoma (POAG) and primary angle close glaucoma (PACG). Furthermore, these figures are due to increase to 79.6 million by 2020, of which 74% will have POAG. Similar forecasts show that by 2010 Bilateral blindness will be present in 4.5 million people with POAG and 3.9 million people with PACG, which also due to rise to 5.9 and 5.3 million people in 2020, respectively. In essence, glaucoma is the second leading cause of blindness worldwide [2].

Glaucoma can be classified roughly into two main categories, open angle and closed angle glaucoma. Primary open angle glaucoma (POAG) is considered the most common form of glaucoma. It is usually a chronic disease that progresses slowly as the increase in IOP causes high pressure to build up and the optic nerve becomes unable to resist, resulting in an enlargement of the optic disc cupping and atrophy of the nerve fiber layers. On the other hand, primary closed angle glaucoma (PCAG) is caused by a blockage in the drainage angle by the peripheral iris which results in an obstruction of the outflow of aqueous humor from the eye. When the drainage angle suddenly becomes completely blocked, pressure builds up rapidly causing painful symptoms, such as seeing halos around lights, red eye, very high intraocular pressure (>30 mmHg), nausea and vomiting, sudden decreased vision, and a fixed, mid-dilated pupil.

Current management of glaucoma is directed at lowering intraocular pressure, which continues to be the only risk factor for the disease that has been proven to be treatable. There are several variants of treatment for lowering intraocular pressure, including drugs, laser surgery, and incisional surgery. Typically, topical medical therapy and laser treatment are employed to lower the intraocular pressure (IOP). However, responses to this treatment have indicated possible inadequacies; for example, patients may be non-compliant with chronic medical therapy, there may be intolerable side effects associated with the drugs applied to treat glaucoma. Surgical approaches to reduce eye pressure are primarily achieved to improve aqueous fluid outflow, thereby reducing the IOP. There is some evidence that primary surgical treatment is superior to primary medical treatment in patients with open angle glaucoma [3].

# Introduction

Severe complications and the need for an intensive postoperative treatment regimen by the standard filtering surgery have encouraged glaucoma surgeons to develop less invasive non-penetrating procedures that avoid filtering blebs [4, 5].

With the recognition of the juxtacanalicular meshwork and the inner wall of Schlemm's canal as the common sites of major resistance to outflow [6], procedures were directed to selectively remove these tissues, leaving a thin trabeculo-descemetic membrane intact.

Having advanced from viscocanalostomy [7], canaloplasty successfully deals with problems associated with that earlier procedure, such as the recollapse of Schlemm's canal and closure of the ostia. In this case, canaloplasty enhances the natural outflow in three main ways [8]: firstly, transtrabecular flow is augmented in part by tensioning the meshwork and opening up the trabecular layers; secondly, circumferential viscodilation of Schlemm's canal maintains IOP lowering; and, finally, viscodilation of Schlemm's canal also opens up the collector channels. The application of a scleral lake and a Descemet's window gives an additional insurance, maintaining sustained IOP reduction over the long-term. By dealing with all of the possible sites of resistance, including potentially occluded collector channels, postoperative pressures in the range of low-to-mid teens are achieved through canaloplasty surgery, similar to that achieved with trabeculectomy. As canaloplasty gains more interest among surgeons and patients, it should find its own place in a plan of glaucoma surgery.

# 2. Background

## 2.1 Aqueous humor dynamics

### 2.1.1 Aqueous humor formation, composition and function

Aqueous humor is secreted by the non-pigmented ciliary epithelium lining the ciliary processes. Aqueous formation has several important processes that typically happen simultaneously: these include diffusion, ultrafiltration, and active secretion. The majority of aqueous production (80-90%) results from active transport, which is an energy-dependent process that selectively moves a substance against its electrochemical gradient across a cell membrane with participation of ATP and carbonic anhydrase [9]. The rate of aqueous humor turnover is 2.4 ± 0.6 μl/min (mean ± SD, day time measurements in adults aged 20-83 years). The diurnal variations using fluorophotometry were observed in aqueous humor turnover rates which are also known as the circadian rhythm of aqueous humor flow. Aqueous humor in the flow is higher in the morning than at night. Aqueous humor flow is normally about 3.0 μl/min in the morning, 2.4 μl/min in the afternoon, and drops to 1.5 μl/min at night [10].

The major components of the aqueous humor are carbohydrates, glutathione, urea, amino acids, organic and inorganic ions, and proteins, oxygen, carbon dioxide and water [11]. The composition of aqueous differs from that of plasma, the greatest differences are the low protein and high ascorbate concentrations in the aqueous humor relative to plasma (200 times less and 20 times greater, respectively) [12].

Aqueous humor is a colorless, transparent fluid, which constitutes an important component of the eye's optical system between the cornea and the lens. During its passage through the eye, aqueous humor has a number of important functions: It provides nutrition to the cornea and the lens, and maintains intraocular pressure (IOP), both of which are important for the structural and optical integrity of the eye. The presence of specialized proteinous factors in the aqueous humor again emphasizes the fine interplay between the angiogenic and anti-angiogenic factors that probably helps to maintain the avascular nature of both the cornea and the lens which is crucial for the transparency of these tissues [13].

### 2.1.2 Aqueous humor circulation and outflow

The aqueous humor flows around the lens and through the pupil into the anterior chamber (AC). Convection flow exists in the AC downward close to the cornea, where the temperature is cooler and upward near the iris where the temperature is warmer [14].

It leaves the eye through two routes, conventional and unconventional pathways: 80% of aqueous humor flows conventionally through the trabeculum into Schlemm's canal into 20 to 40 collector canals after which it is drained away by the episcleral veins (conventional pathway). The other 20% of aqueous humor leaves the eye unconventionally through the uveoscleral route, which is the aqueous pass across the ciliary body into the suprachoroidal space and episcleral tissue (unconventional pathway) [15]. Unlike the conventional pathway, the outflow through the unconventional pathway is relatively independent of the intraocular pressure [16]. From the trabecular meshwork (TM), fluid movement takes place down a pressure gradient into and through the inner wall of the Schlemm's canal, following the conventional route, and appears to be a passive pressure-dependent transcellular mechanism, frequently associated with paracellular routes, such as giant vacuoles and pores acting as one-way valves [6].

From Schlemm's canal, the aqueous humor enters the episcleral veins, where the pressure is approximately 8-10 mmHg [17] and the resistance of the conventional aqueous drainage tissues is approximately 3-4 mmHg/µl/min. This results in an average IOP of 15.5 ± 2.6 mmHg (mean ± SD) for the general population [18]. In humans, 75% of the resistance to the aqueous humor outflow is localized to the TM, and 25% occurs beyond Schlemm's canal [19]. The major site of resistance resides in the juxtacanalicular portion [20].

The uveoscleral outflow pathway is an accessory system, first described by Bill [21]. This pathway allows free access from the anterior chamber to the supraciliary and suprachoroidal spaces via the collagen containing spaces between the ciliary muscle bundles. From there the fluid egresses the sclera and uveal vascular system.

## 2.2 Anatomy of the conventional outflow system

### 2.2.1 The trabecular meshwork

The trabecular meshwork is a triangular structure, a sieve-like band of connective tissue about 750 μm in width at the angle of the anterior chamber [22]. The thickness of the trabecular meshwork in glaucomatous eyes ranges between 50-70 μm in the anterior region and between 100-130 μm for the posterior portion [23]. It is important to note that eyes with primary open angle glaucoma suffer from an accumulation of elastic fibers sheath material called "sheath derived plaques" (SD-plaques) and a significant decline in trabecular meshwork cells, the latter which often causes a fusion and thickening of the trabecular lamellae [24].

The trabecular meshwork consists of three portions as follows:

a. The uveal meshwork is adjacent to the anterior chamber which consists of cord-like meshes with irregular 25-75 μm openings extending anteriorly into the region of Schwalbe's line and posteriorly into the ciliary body and iris root [25]. The intertrabecular spaces are relatively large and offer little resistance to the passage of aqueous.

b. The corneoscleral meshwork is the middle portion which consists of sheets-like meshes with elliptical openings ranging from 5-50 μm in diameter that extend from the Schwalbe line to scleral spur [25]. Here, the intertrabecular spaces are smaller than in the uveal meshwork.

c. The juxtacanalicular connective tissue (JCT) is approximately 2-20 μm thick, typically adjacent to the inner wall endothelium of the canal of Schlemm. The JCT largely consists of extracellular matrix (ECM) that is loosely arranged and contains a small amount of embedded cells [26]. As such, depending on the expression of many ECM molecules, the JCT mostly consists of two independent zones. These two zones include the inner JCT zone, which is 2-10 μm in size and can be found near the inner wall of Schlemm's canal, and the outer JCT zone that is 11-20 μm in size and that forms a transition between the inner JCT zone and the trabecular lamellae [27].

### 2.2.2 Schlemm's canal (Friedrich Schlemm 1795-1858)

#### 2.2.2.1 Overview

It is a circumferential vascular sinus, located at iridocorneal angle and surrounded by sclera, trabecular meshwork, and the scleral spur. Generally Schlemm's canal (SC) has a cross-sectional area that varies between 4064 to 7164 $\mu m^2$, with many branched aqueous channels [28]. The total circumference is 36 mm [29] and the length in radial plane is 190-370 µm [30]. The diameter of the canal lumen is IOP-dependent and the space can be absent at high pressures or very large at low pressures [31]. The SC is lined by a continuous endothelium with tight junctions, which is divided into an outer and inner wall (Figure 1). The SC endothelium that lies directly adjacent to the juxtacanalicular trabecular meshwork is known as the inner wall. The remaining endothelial cells line the outer wall. The endothelial cells of the inner wall differ from those of the outer wall in morphology, cell-specific marker expression, specialized cellular organelles and functions [28].

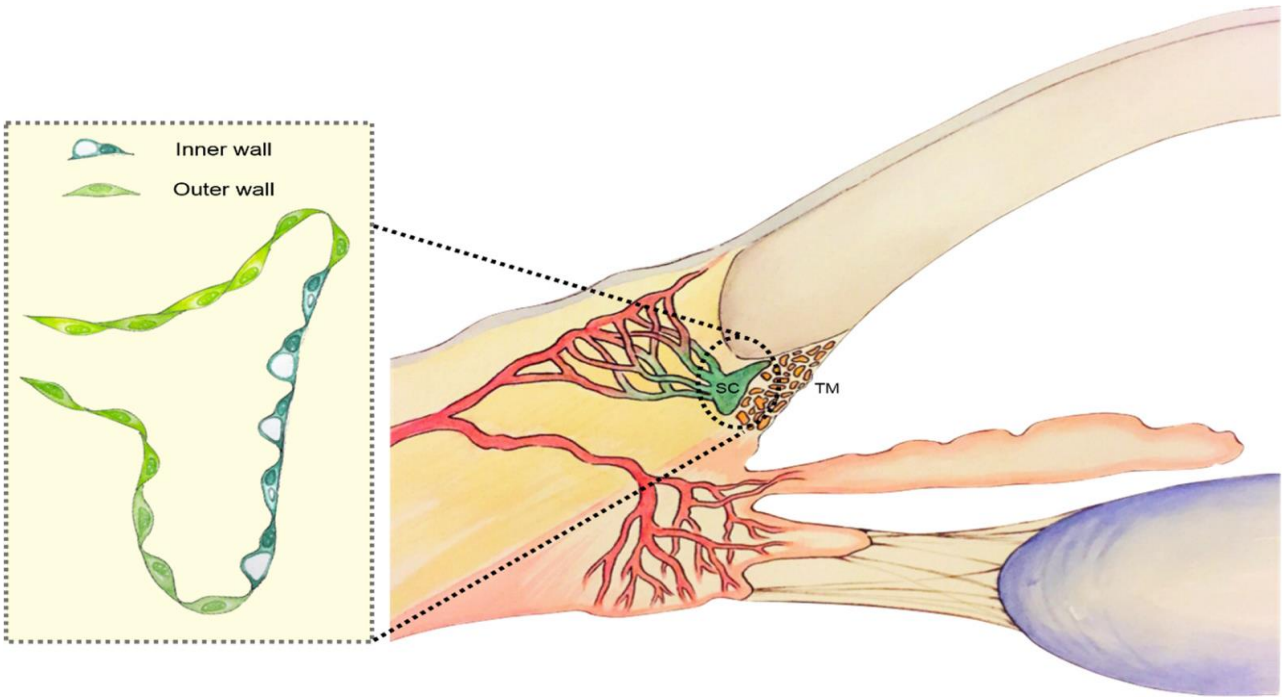



**Fig. 1.** Schematic view of the conventional outflow pathway. The left inset shows an expanded view of the Schlemm's canal's microanatomy detailing the cell morphology of the inner and outer walls [28].

#### 2.2.2.2 Schlemm's canal inner wall endothelium

The inner wall is lined by a continuous monolayer of long, slender endothelial cells; their long axis is parallel to the canal lumen. The cells have an average diameter of 8-12 μ and in a many parts a thickness of 0.2 μ. They rest on an incomplete basal lamina, which are in considerable areas not supported by ECM, but are in direct contact with the open spaces of the JCT, these cells are also attached to one another by zonulae occludentes and desmosomes represented by a tight junction between the cells which represent physiologic barriers to perfusion of fluid and particles. A characteristic aspect of the SC inner wall endothelium is the formation of cellular outpouchings (so-called giant vacuoles) in response to the pressure gradient associated with aqueous humor flow. The vacuoles are delineated by a distinct single membrane; the size varies considerably with a diameter of up to 2.5 μ. The frequency of the vacuoles shows a great variation from one area to another [32]. The pressure-induced cellular distention causes these invaginations to form and recede in a cyclic fashion, causing transient transcellular pores, which can grow up to 1 μm, to form in the distending wall [33]. As such, the canal of Schlemm can be considered to have the highest hydraulic conductivity rate within the whole body [34]. The pore density of the inner wall endothelium of glaucomatous eyes is less than one fifth that found in normal eyes. This may be the cause of the elevated intraocular pressure associated with glaucoma [35]. The endothelial cells lining the outer wall of SC attached one to another by zonulae occludens lying on a basal lamina, which are more consistent than the one of the SC inner wall [36].

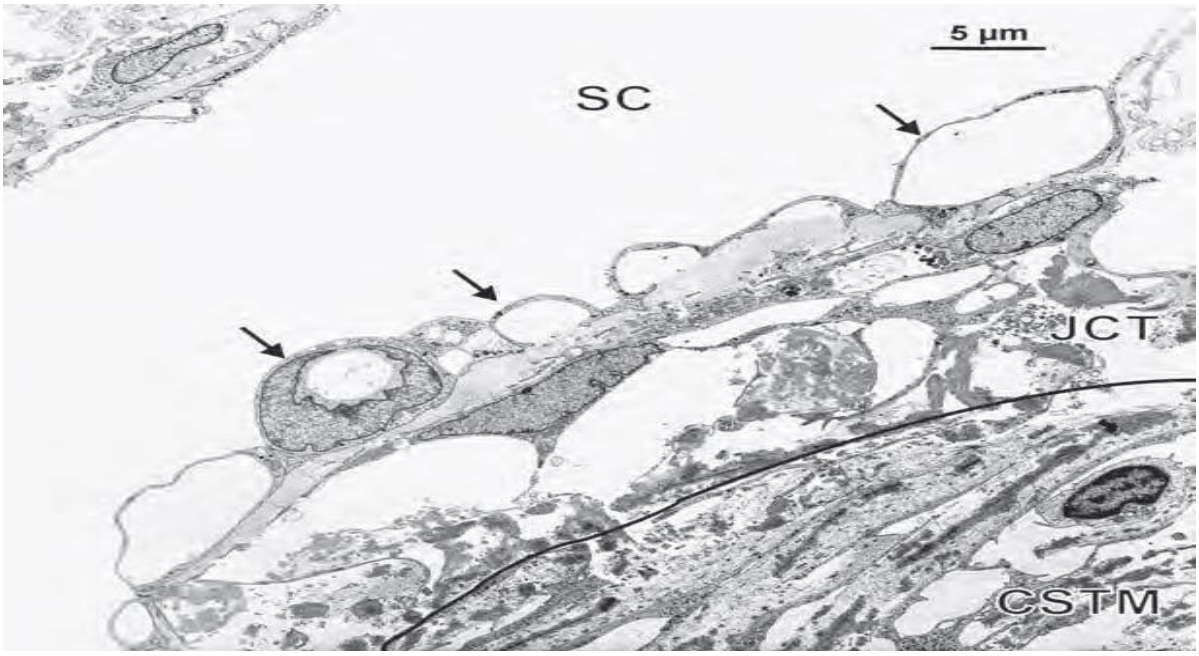



**Fig. 2.** Electron micrograph of the inner wall region of Schlemm's canal (photography by Tamm E. R.). The black line separates the corneoscleral trabecular meshwork (CSTM) from the juxtacanalicular connective tissue (JCT). Arrows indicate the inner wall endothelium of Schlemm's canal (SC). The endothelium forms characteristic outpouchings ('giant vacuoles') in response to aqueous flow [37].

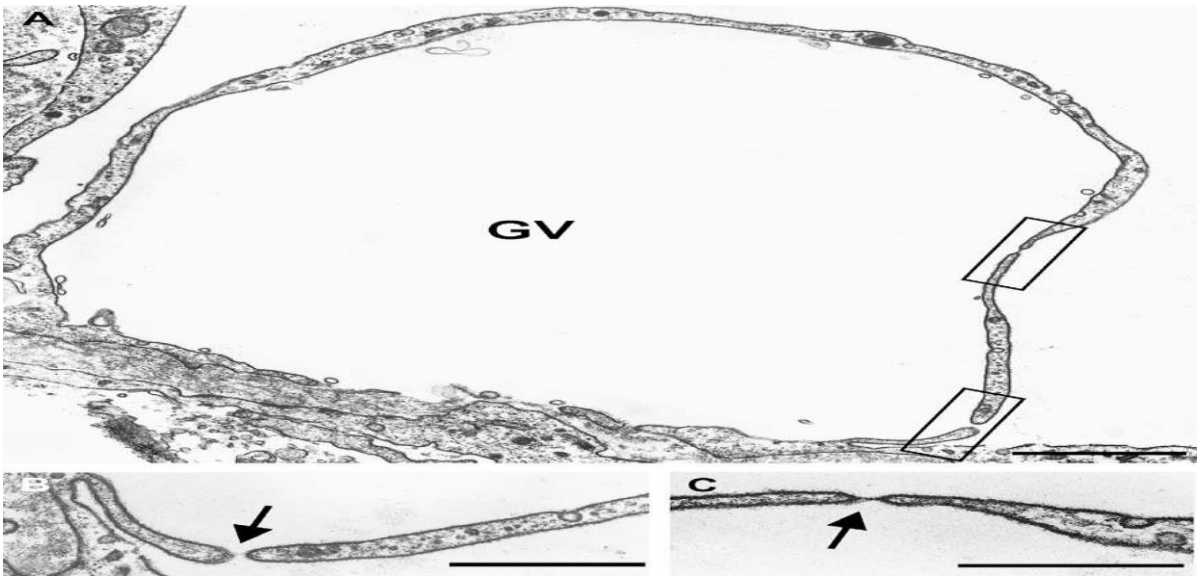



**Fig. 3.** Electron microscopic image of an inner wall giant vacuole (GV) that forms two intracellular pores (boxed areas in A). Both boxed areas are shown in (B) and (C) at higher magnification. While the pore in (B) is largely open and only covered by very fine filamentous material (arrow), the pore in (C) is covered by a diaphragm (arrow). Magnification bars: 1 mm (A), 0.5 mm (B), and 0.5 mm (C) [26].

### 2.2.3 Collector channels, aqueous veins and episcleral veins

Schlemm's canal drains into a complex system of intrascleral, episcleral, and subconjunctival venous plexus through a series of collector channels [38].

There are two types of such collector channels, including the internal collector channels, which were first described in 1933 by Sondermann as simple digitations of the internal wall of Schlemm's canal; as well as the external collector channels, which were first described in 1942 by Ascher. Combined, there are a total of 25-35 collector channels that originate from the outer wall of Schlemm's canal. They are limited by the same endothelium lining surrounded by a fine connective tissue that runs in two directions [25]. Additionally, Battista et al., have shown that the collector channels play a key role in blocking aqueous outflow in POAG eyes, especially when inner wall tissue of the trabecular meshwork herniates into the collector channels, it blocks aqueous outflow [39]. Those vessels that reach the episcleral plexus directly are called aqueous veins (up to 8). Aqueous veins are thick and terminate in episcleral and conjunctival veins in a laminated junction called the laminated veins of Goldman. The other system consists of thinner vessels that drain indirectly into three stages venous plexuses, the deep and mid-scleral plexus (intrascleral plexus) and the episcleral plexus. The latter receives blood from the perilimbal conjunctival veins and drains into the cavernous sinus via the anterior ciliary and superior ophthalmic veins. Conjunctival veins drain into superior ophthalmic or facial veins via palpebral and angular veins [25].

## 2.3 Aqueous humor outflow resistance

In glaucoma, the increased IOP is caused by an increase in aqueous outflow resistance within the drainage pathways, and not by an increase in secretion of aqueous humor [10].

The mechanism by which outflow resistance is generated in the normal eye and is increased in the glaucomatous eye is still not understood. Aqueous humor passes through the outflow pathway as a bulk flow driven by a passive pressure-dependent transcellular mechanism and does not involve active transport. Histologic, experimental, and theoretical studies of the aqueous outflow pathways point toward the juxtacanalicular region and inner wall of Schlemm's canal as the likely site of aqueous outflow resistance in the normal eye. At least 50% of the aqueous outflow resistance in the normal eye and the bulk of the pathologically increased resistance in the glaucomatous eye reside in the trabecular meshwork and the inner wall of Schlemm's canal [40].

### 2.3.1 Potential role of Schlemm's canal collapse (partial and total)

Aqueous humor outflow through the canal of Schlemm plays a predominant role in maintaining a constant level of intraocular pressure (IOP) which is important for the maintenance of the eye's normal visual functions and for the nourishment of its avascular tissue. There are many studies that have investigated the influence of intraocular pressure on the morphology of the aqueous outflow system and the effect of the canal collapse on the flow resistance through the aqueous outflow network. Most interesting is the work of Johnstone and Grant who studied the Schlemm's canal morphology at different intraocular pressure levels, and found that the endothelial cells stretch to form progressively larger hemispherical vacuoles into the canal lumen as IOP increases. In other words, these vacuoles, which contained aqueous humor and sometimes erythrocytes, increased in number and the size depending on IOP. The study also found that the trabecular meshwork and the endothelium appeared to expand progressively further into Schlemm's canal, reducing its lumen, which appeared occluded at 50 mmHg. Increasing differences in appearance were found in eyes at progressively higher pressures (Figures 4 and 5) [41]. Partial collapse of the canal, probably of its anterior portion, can play a part in reduction of filtering space and can increase canal resistance to circumferential flow and thus be a mechanism of glaucoma [42]. Similarly, Tandon has concluded that a progressive occlusion of Schlemm's canal with apposition of its opposing walls might contribute to outflow obstruction, and this forms part of the mechanism of the increase in outflow resistance observed in some cases of glaucoma [43].

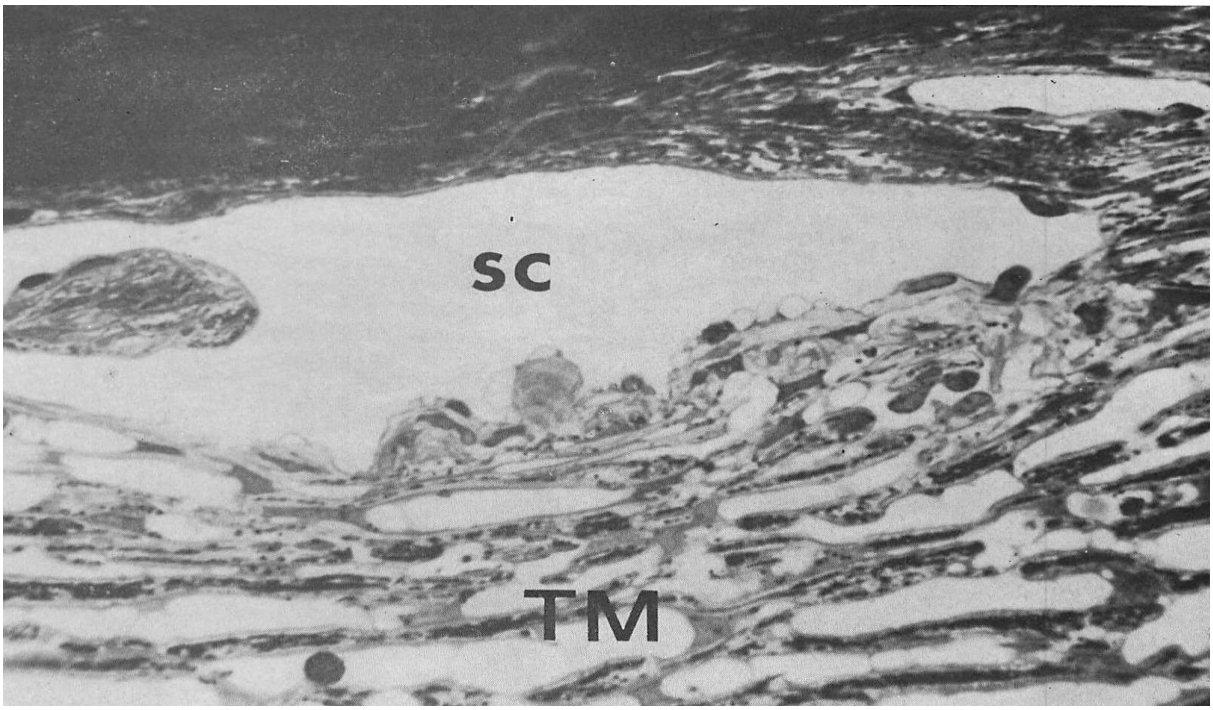



**Fig. 4.** Schlemm's canal (SC) of enucleated eye fixed at 5 mmHg IOP. Schlemm's canal (SC) remains moderately large, and there is space between the lamellae of the trabecular meshwork (TM) [41].

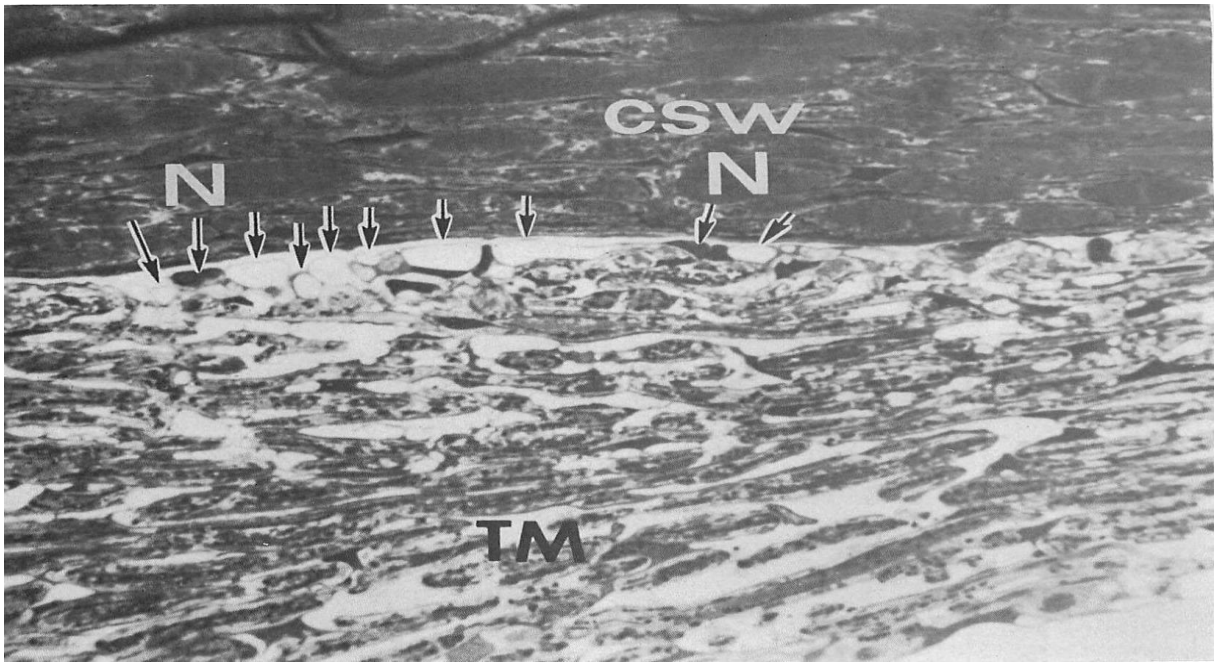



**Fig. 5.** Schlemm's canal (SC) of enucleated eye fixed at 50 mmHg IOP, showing nuclei (N) and vacuoles (arrows) of the endothelial cells lining the inner wall of Schlemm's canal in opposition to the external corneoscleral wall (CSW). The canal has been reduced to a potential space [41].

# 3. Treatment Modalities

## 3.1 Overview

Before beginning treatment of glaucoma, it is necessary complete a full and accurate glaucoma diagnosis. Results published by the multicenter Early Manifest Glaucoma Trial have confirmed that therapy is necessary when damage has occurred to the optic nerve or visual field [44]. The main goal of treatment is to reduce IOP to an appropriate level (also called target pressure) compatible with preservation of the optic nerve's normal function and stability of visual fields, most multicenter studies prospectively select an end-point percentage for pressure reduction as the research target e.g., a 30% reduction in the Normal-Tension Glaucoma Study [45], 25% reduction in the Early Manifest Glaucoma Trial [46], or 20% reduction in the Ocular Hypertensive Treatment Study [47]. There are two basic ways to achieve a reduction of IOP; it can be done either by inhibiting aqueous humor production or by improving the aqueous outflow. Lowering IOP via various pharmaceuticals and/or surgical techniques is currently the most common form of glaucoma treatment.

## 3.2 Surgical anatomy

The glaucoma filtering surgery is typically performed at the area of the surgical limbus. The anatomical limbus is a well-demarcated zone which is situated where the peripheral cornea externally meets the sclera. It is a bluish-grey, broad transition zone of ~1 mm in width from peripheral cornea to sclera in the deeper layers, The bluish-grey appearance of the surgical limbus is due to the extension of the deeper corneal lamellae beyond the external margin of the peripheral cornea, which is illustrated by viewing the scleral bed of a 1/3 thickness scleral flap at the limbus. In the upper part of the scleral bed, there are transparent corneal lamellae through which the brown iris is visible. In the scleral bed, posterior to the cornea, is a grey band which is the trabecular meshwork, and at the posterior border of this grey band dense scleral tissue is visible. The junction of the posterior limit of the grey band and the sclera is the external landmark for the scleral spur and canal of Schlemm. Deeper dissection at this landmark will lead directly to the canal of Schlemm. The scleral spur expands slightly posterior to this junction. It is important to recognize these landmarks, particularly when performing non-penetrating filtration surgery [48].

## 3.3 Evolution of non-penetrating filtration glaucoma surgery

The main idea behind non-penetrating filtering surgery is to surgically enhance the natural aqueous outflow channels, rather than create a new and possibly overly effective drainage site. Due to complications with established surgical approaches such as trabeculectomy, alternative non-penetrating filtering surgery has been developed. The avoidance of penetration into the anterior chamber should allow the anterior segment to recover more quickly, with less risk of hypotony and/or related complications. The evolution of NPGS started with the original works of Epstein [49] and Krasnov [50] in the late 1950s and early 1960s.

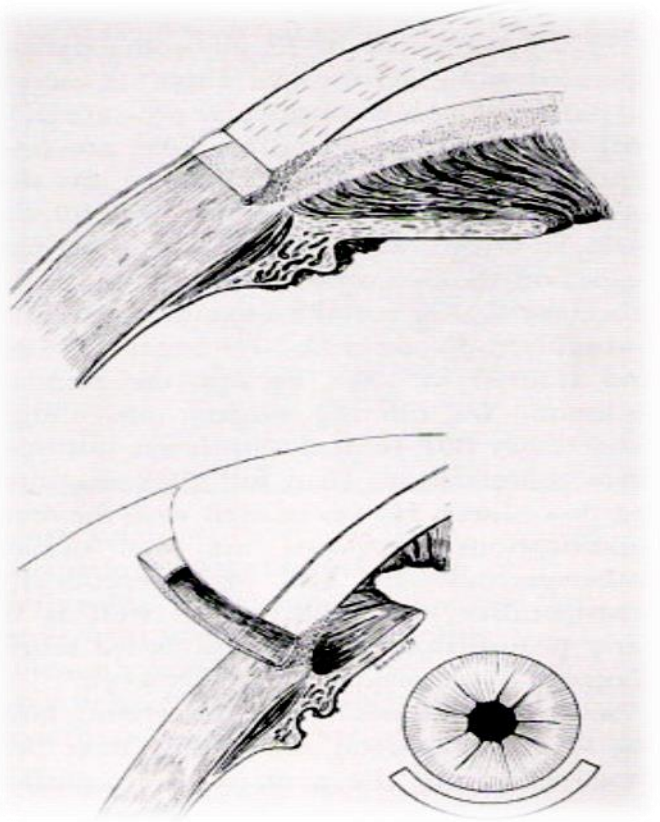


**Fig. 6.** Schematic representation of sinusotomy. Schlemm's canal is unroofed. There is no superficial scleral flap to cover the sclerectomy. Inner wall is untouched [51].

Epstein noticed the percolation of fluid in the paralimbal sclera by a dissection of deeply seated pterygiae. He described a paralimbal deep sclerectomy operation in which a narrow band of scleral tissue is removed over Schlemm's canal for 180º without anterior chamber penetration. The deep sclerectomy was then covered with conjunctiva. Epstein performed this operation on South African black patients with severe progressive glaucoma [49]. Krasnov theorized that the outflow resistance is situated intrasclerally beyond the outer wall of Schlemm's canal and not in the trabeculum; therefore he developed a safe non-penetrating filtering surgery, leaving in place the trabeculum and the inner wall of Schlemm's canal. In 1962, he performed the first sinusotomy, in this operation a narrow 1.5 mm wide lamellar band of sclera was removed and a "deroofing″ of Schlemm's canal over 120º from 10 to 2 o'oclock without touching the inner wall of the canal was created. Sustained IOP reduction after sinusotomy was usually associated with a more diffused filtering bleb, which tends to disappear with time. Sinusotomy was

actually safer than full thickness procedures that were the standard filtering surgery at that time. However, sinusotomy never become popular, because it was a difficult operation that needed a surgical microscope that was nevertheless less efficient in identifying the Schlemm's canal. When it was recognized that the juxtacanalicular meshwork and the inner wall of Schlemm's canal were the site of major resistance to outflow, new procedures were designed to selectively remove tissue in a procedure called ab-externo trabeculectomy [51].

### 3.3.1 Ab-externo trabeculectomy

Ab-externo trabeculectomy is similar to sinustomy surgery except for the presence of a superficial scleral flap and the removal of the inner wall of Schlemm's canal and the juxtacanalicular meshwork, while leaving the corneoscleral and the uveoscleral intakt [51]. In a study by Rossier et al. [52], the outflow facility of the remaining membrane after the trabeculectomy ab externo increased from 0.21 ± 0.6 to 2.03 ± 1.43 μl/min/mmHg after the removal of 4 mm of membrane consisting of the endothelium of SC and the juxtacanalicular TM. Tanihara et al. reported a 90% of well-controlled (IOP < 21mmHg) and 81.7% of "overall success" in "at least 1 year follow-up" study [53].

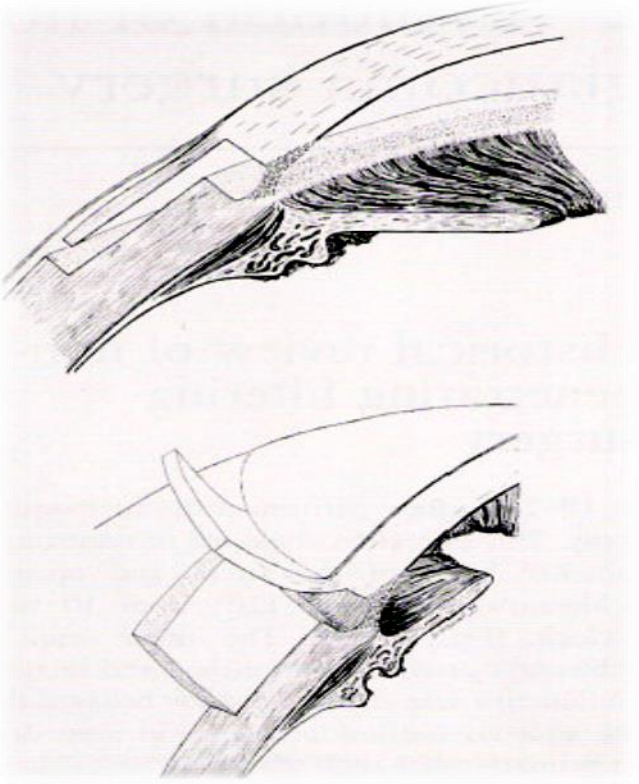


**Fig.7.** Schematic represention of ab externo trabeculectomy. A deep sclerectomy unroofing Schlemm's canal is covered by superficial scleral flap. Schlemm's canal inner wall and juxtacanalicular trabeculum are removed [51].

Another way to increase the aqueous outflow in a patient with restricted posterior trabeculum outflow is through the procedure called deep sclerectomy whereby the corneal stroma behind the anterior trabeculum and Descemet's membrane is removed causing the main aqueous outflow to occur at the level of the anterior trabeculum and Descemet's membrane, otherwise known as the trabeculo-descemet's membrane (TDM).

### 3.3.2 Deep sclerectomy

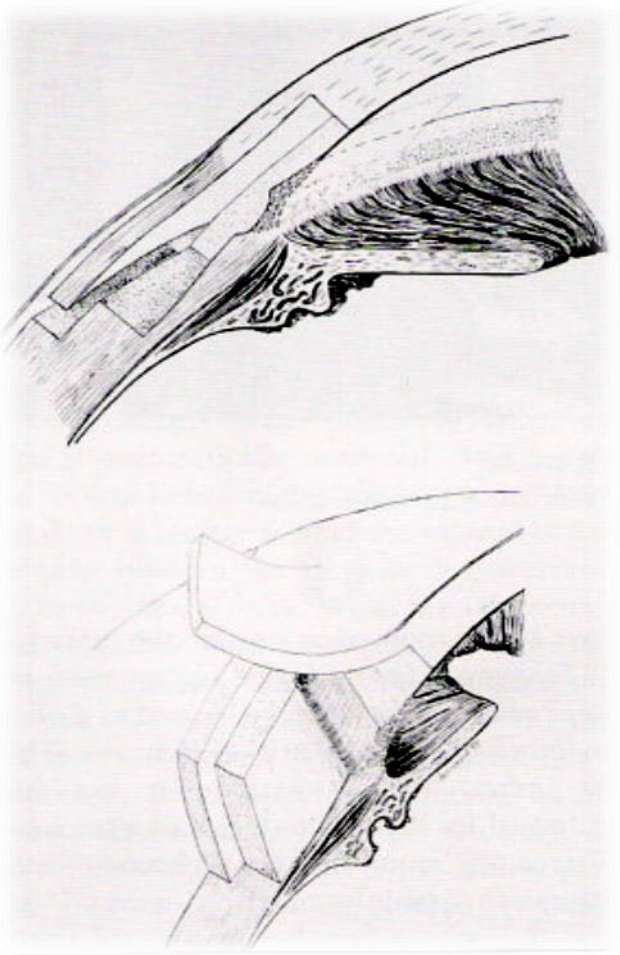


**Fig. 8.** Schematic representation of deep sclerectomy. Under a superficial scleral flap, deep corneosclerectomy, unroofing Schlemm's canal, is performed. Corneal tissue behind anterior trabeculum and Decemet's membrane are removed [51].

Deep sclerectomy differs from sinustomy and ab-externo trabeculectomy in that the postoperative drainage occurs at the level of anterior trabeculum and the Descemet's membrane, as described by Vaudaux and Mermoud [54] in an ex-vivo model of deep sclerectomy. They reported that the mean outflow facility after deep sclerectomy increased from 0.19 ± 0.03 to 24.5 ± 12.6 µL/min per mmHg. Demailly and co-workers added a collagen implant [55]. To enhance the filtration by avoiding secondary collapse of the scleral lake due to adhesion of the superficial scleral flap or contact of descemetic window, a collagen implant is placed within the scleral bed. This implant occupied the surgically created intrascleral bleb under the superficial flap during the early postoperative period where the healing process is at its peak. Shaarawy and Mermoud were able to show that deep sclerectomy with the collagen implant produced significantly better outcomes than that without the implant [56]. One month after the deep sclerectomy with collagen implant, the ultrasound biomicroscopy showed filtration around the scleral flap into the subconjunctival space and possibly some suprachoroidal filtration [57].

### 3.3.3 Viscocanalostomy

To emphasize the importance of injecting high-viscosity sodium hyaluronate (Healon GV) into Schlemm's canal as a means of improving aqueous drainage by this route, Stegmann et al. [58] described a variant of non-penetrating glaucoma surgery and termed it viscocanalostomy. It has been postulated that physiologic aqueous humor drainage may then be restored without formation of a filtration bleb because the superficial scleral flap is tightly sutured so that only aqueous humor regressing through trabeculo-descemet's membrane can reach the two surgically created ostia of Schlemm's canal, travel circumferentially within the canal, and enter the collector channel ostia and ultimately the aqueous veins. They also considered an increased outflow mechanism for the procedure's success: Aqueous humor that passes through the trabeculo-descemet's membrane window into the scleral bed can diffuse into the uveoscleral outflow system adjacent to it. The viscoelastic material is also placed in the scleral bed, this may prevent fibrin cross-linking and early scarring.

In the human eye, many studies have shown that the injection of viscoelastic into the canal of Schlemm leads to not only the dilation of the canal and associated collectors channels, but it also causes focal disruptions of the inner wall endothelium of the canal. This injection of viscoelastic into the Schlemm's canal also disorganizes the juxtacanalicular zone, resulting in direct communication of the juxtacanalicular extracellular spaces with canal's lumen. Furthermore, this may initially augment conventional outflow of aqueous humor. Disruption of the posterior wall of the Schlemm's canal may also cause direct communication between its lumen and the tissues of the ciliary body, thereby enhancing uveoscleral outflow [59].

In addition to the effects of viscoelastic material on dilating and disrupting the wall of Schlemm's canal, viscocanalostomy also has anti-inflammatory properties and may inhibit cellular migration, phagocytosis and cytokine production, and thus may interfere with wound healing [60].

The complications of canal re-collapse and the closures of the ostia of the collector channels have been found among the main causes for failure in viscocanalostomy [8]. Therefore, the recent development of a flexible microcatheter enabled 360º viscodilation of the SC ('enhanced' viscocanalostomy) [61].

### 3.3.4 Canaloplasty

#### 3.3.4.1 Canaloplasty with suture

Canaloplasty is a procedure using the microcatheter (iTrack, iScience, USA). The shaft of the microcatheter is 200 μm in diameter with an atraumatic distal tip approximately 250 μm in diameter. The device incorporated an optical fiber to give an illuminated beacon tip to aid in surgical guidance. During catheterization of Schlemm's canal, the illuminated tip was seen transsclerally to allow the surgeon in identifying the location of the distal tip of the microcatheter. The microcatheter had a lumen of about 70 μm with a proximal Luer Lock connector through which the ophthalmic viscosurgical device (OVD) could be delivered. The microcatheter was packaged with an OVD injector, which is a screw-driven syringe replacing the standard push syringe used to deliver OVDs to allow more precise injection of microliter volumes [62]. Surgeons followed traditional viscocanalostomy and deep sclerectomy approaches to perform a 2-flap dissection to the canal. To manipulate the microcatheter, a forceps was used and placed on the tip in alignment with the surgically created ostia of the canal. The microcatheter was advanced 12 clock hours within the canal while at the same time the surgeon observed the location of the beacon tip through the sclera and injected the OVD (sodium hyaluronate 1.4% [Healon GV]) as the tip was advanced. After catheterization of the entire canal length with the microcatheter and with the distal tip exposed at the surgical cut down, a 10-0 polypropylene suture was tied to the distal tip and the microcatheter withdrawn, getting the suture into the canal. The suture was cut from the microcatheter and tied in a loop, encircling the inner wall of the canal using a slip knot. The suture loop was carefully tightened to distend the trabecular meshwork inward, placing the tissues in tension, after which locking knots were added. A Descemet window was formed anteriorly just before or immediately after catheterization of the canal. The deep flap was cut and the superficial flap was sutured watertight to prevent bleb formation [63].

In essence, canaloplasty should be recommended in patients with mild to moderate glaucoma, in which the target IOP is not too low. Canaloplasty is also mostly recommended for eyes that have not undergone previous filtrating surgery for glaucoma, However Brusini P. and Tosoni C. [64] in their study confirmed that canaloplasty can be an option after failed trabeculectomy by a catheterization of the entire 360-degree circumference of Schlemm's canal in 5 eyes of their 6 eyes

included in the study. This procedure can be done in some cases where the Schlemm's canal has remained undamaged from previous filtrating surgery.

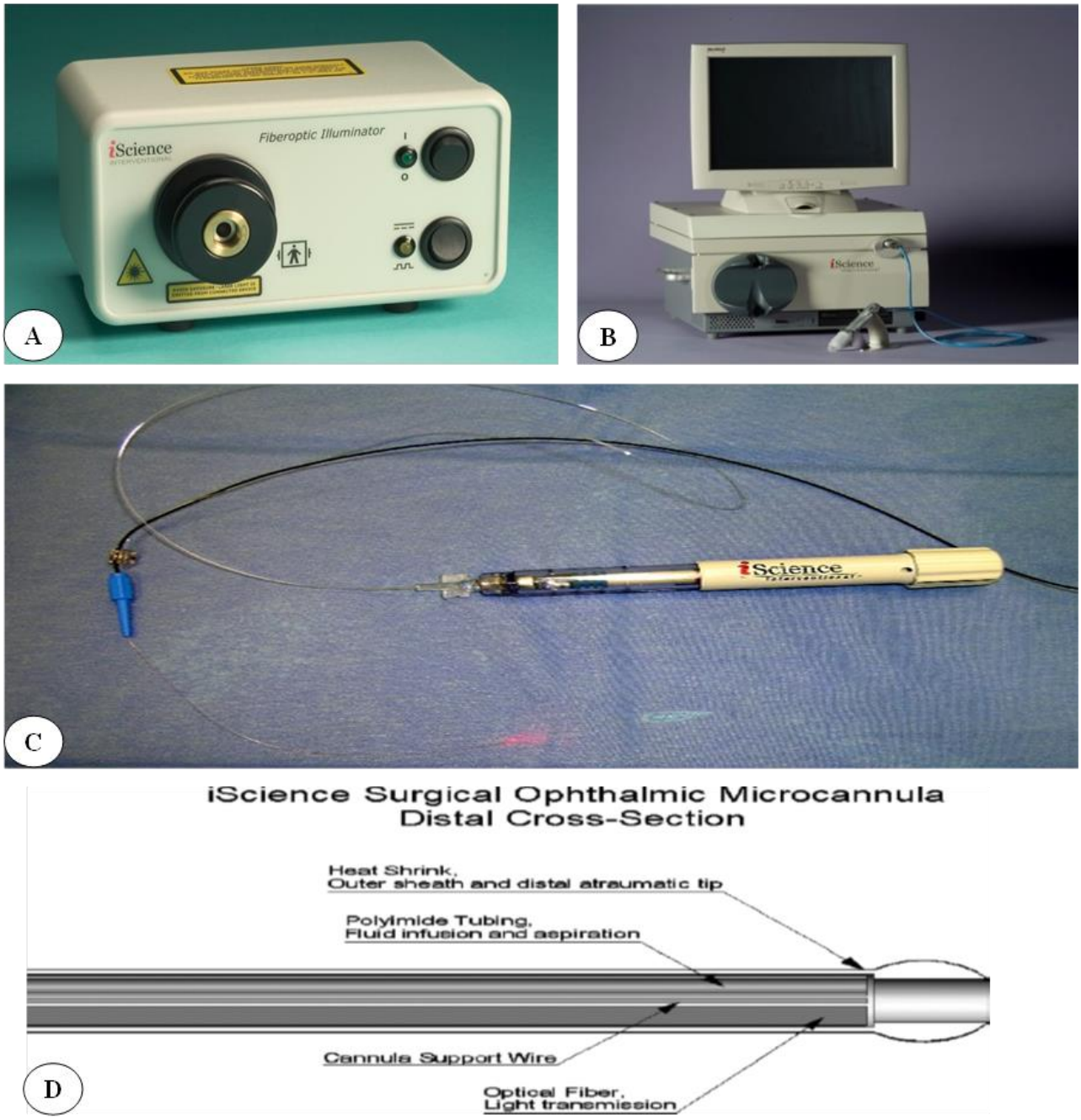



**Fig. 9.** i Science products: **(A)** Ophthalmic light source *i* Lumin ™, **(B)** Ophthalmic Imaging system *i* UltraSound ™, **(C)** Screw-driven syringe connected to the *i* Track ™ microcatheter, **(D)** Catheter design [65].

### 3.3.4.2 Canaloplasty with Stegmann Canal Expander (SCE)

The Stegmann Canal Expander (SCE; Ophthalmos GmbH, Schaffhausen, Switzerland) is a device to be implanted into Schlemm's canal during viscocanalostomy or canaloplasty. It is made of refined surgical polyimide and has an outer diameter of 240 μm. The device is loaded on to a 6-0 polypropylene thread connected to a torquer that facilitates implantation [66]. SCE has been developed to replace the suture stent, as proper suture tension is technically very challenging, cannot be measured, and has an inherent risk of cheese-wiring. Thus, through the development of SCE, canaloplasty becomes an easier and more reproducible procedure. SCE is implanted as follows: SC is deroofed by creating a superficial and a deep scleral flap, making a Descemet window like in viscocanalostomy and canaloplasty. After dilation of the surgical ostia of Schlemm's canal, the microcatheter is inserted into the canal to dilate it circumferentially with highly viscous sodium hyaluronate as described above for canaloplasty. After completed dilation, the catheter is withdrawn, and the SCE implant is placed inside both ostia of SC in order to establish a permanent distension of the TM. The superficial scleral flap is sutured watertight as in canaloplasty to prevent bleb formation and to force the aqueous humor to leave through the physiological outflow system [67].

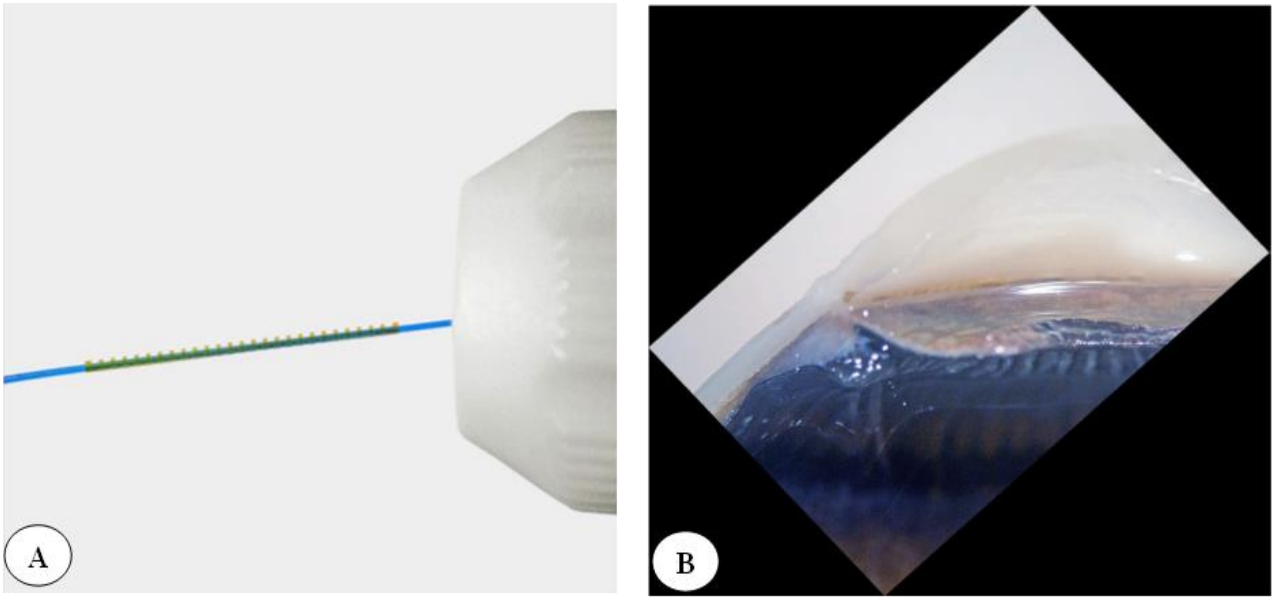



**Fig. 10**. Stegmann Canal Expander: **(A)** The Stegmann Canal Expander is loaded on a 6–0 polypropylene thread connected to a torquer. The device, made of polyimide, is 9 mm long and has multiple fenestrations. **(B)** Macroscopic view of the chamber angle showing Schlemm's canal and the Stegmann Canal Expander in place [66].

### 3.3.5 Canaloplasty combined with cataract surgery

Combining cataract and glaucoma surgery has gained popularity due to the frequent coincidence of the 2 conditions in older patients. The reduction in surgical trauma from 2 separate surgical procedures and the high incidence of cataract development after glaucoma surgery are factors supporting the application of a combined procedure in appropriate patients [68]. In addition, cataract surgery alone has been shown to lower IOP from 1 to 5 mmHg [69]. Furthermore, the combined procedure provides long-term lower IOPs than when cataract surgery is performed in a glaucomatous eye without filtration [70].

Phacocanaloplasty shows a lower IOP tendency than canaloplasty alone [71]. Phacoemulsification is a procedure that is mostly completed prior to canaloplasty using the techniques preferred by surgeons. A side corneal incision is made followed by the implantation of a posterior chamber IOL before beginning with the glaucoma procedure.

### 3.3.6 Canaloplasty and its potential application in glaucoma gene therapy

In recent years, ocular gene therapy has been a popular research topic, since it might provide a long-term treatment option for chronic ocular diseases. For glaucoma, various genes have been investigated (dominant negative Rho or Rho kinase, caldesmon, C3 transferase, matrixmetalloproteinases, and specific siRNAs) for efficacy in decreasing outflow resistance. These genes are thought to modify the structure of the TM that is responsible for outflow resistance. In Future, canaloplasty may be applied in glaucoma gene therapy. By using a transgene-containing cationic peptide-coated intracanalicular suture or injecting the non-viral transgene into Schlemm' canal during catheterization, it might be possible to achieve a significant transgene expression in the trabecular meshwork or Schlemm' canal without affecting the cornea, iris, and ciliary body [72]. Insertion of the microcatheter into each of the open SC ostia for only 1 clock hour to inject the vector/transgene might also be the easiest and least time consuming, as well as the safest approach, compared to circumferential cannulation. The most effective approach for IOP reduction might be to perform traditional circumferential canaloplasty and suture placement in combination with gene delivery [73].

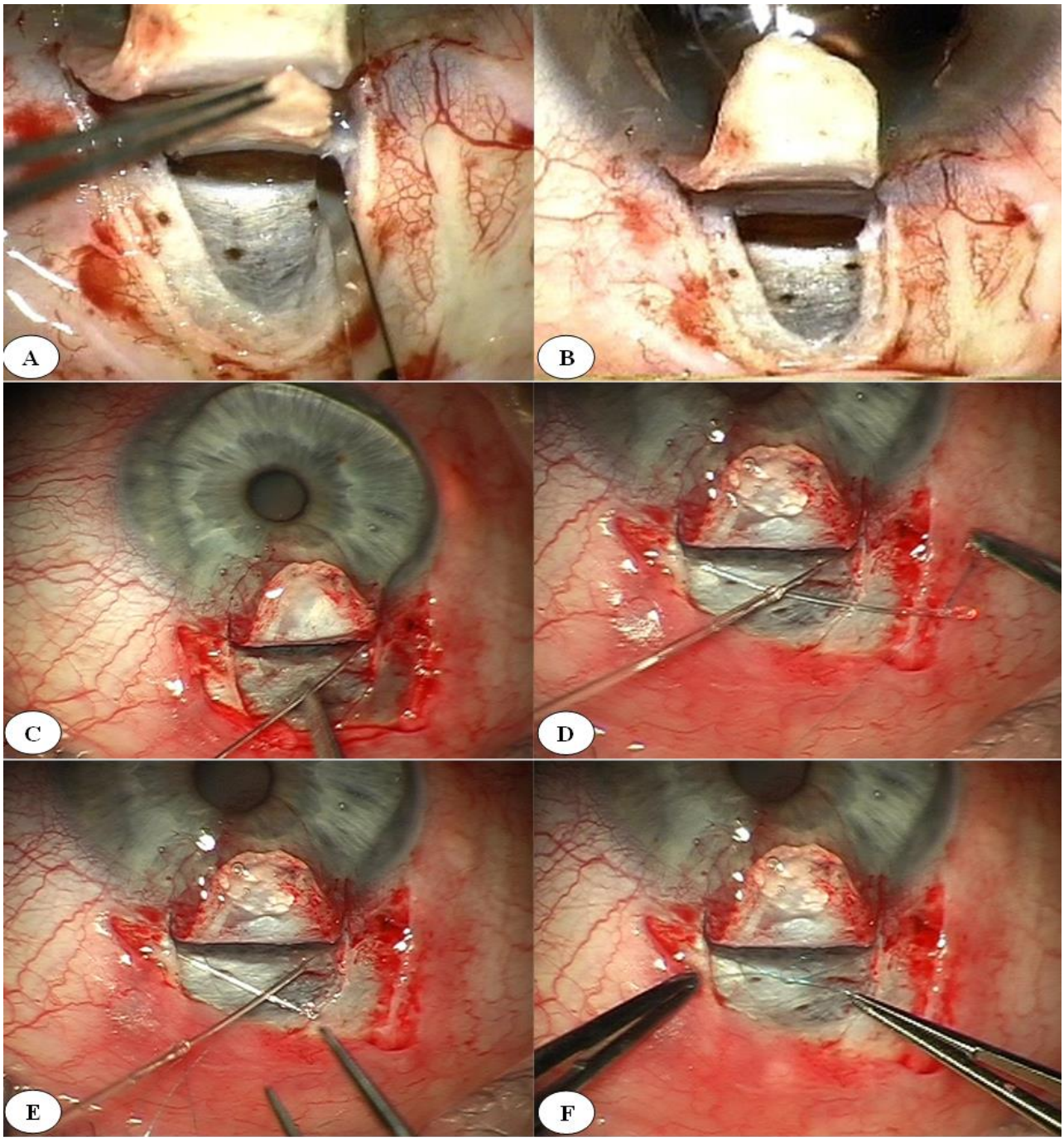



**Fig. 11.** Shows steps of canaloplasty: **(A)** Controlled preparation of the scleral flap using a mini crescent knife, **(B)** The deep scleral flap has been removed with angulated Ong scissors, **(C)** The micro-catheter is inserted into Schlemm´s canal and the correct advancement can be visualized by the red flashing laser light (circle), **(D)** A 10-0 polypropylene suture is affixed to the distal tip of the microcatheter, **(E)** The tubing is advanced into the surgical site, **(F)** The 10-0 prolene suture is tightened; the canal and meshwork are circumferentially stretched toward the center of the anterior chamber lake.

### 3.3.7 Postoperative care

Managing a canaloplasty patient postoperatively is simpler than managing a postop-trabeculectomy. Postoperative care begins on the first postoperative day, including checking the vision, IOP and the appearance of the eye. Topical medication used in the immediate postoperative period includes antibiotics and corticosteroids. A broad spectrum of antibiotic treatment is instead applied for 1-3 weeks as a theoretical prophylaxis against endophthalmitis. Corticosteroid, when used in adequate amounts, slows the rate conjunctival epithelialization, angiogenesis, and collagen synthesis, the influence of which is greatest during the inflammatory phase in the first 3 days after surgery. As the effect of steroids is dose-related, the initial high doses tapered off after a few weeks [74]. Even in some eyes with functioning filtering bleb, steroids may raise postoperative intraocular pressure (IOP), and their discontinuation may lower IOP [75]. Clark et al. studied the effect of dexamethasone on the outflow pathway in isolated human eyes and found a significant increase in IOP in approximately 30% of the dexamethasone-treated eyes. He also found that steroid treatment resulted in morphologic changes in the trabecular meshwork similar to those reported for corticosteroid glaucoma, the dexamethasone-treated hypertensive eyes had thickened trabecular beams, decreased intertrabecular spaces, thickened juxtacanalicular tissue, activated trabecular meshwork cells, and increased amounts of amorphogranular extracellular material, especially in the juxtacanalicular tissue and beneath the endothelial lining of Schlemm's canal [76].

### 3.3.8 Mechanisms of filtration after non-penetrating glaucoma surgery

Non-penetration focuses on allowing filtration via a membrane that occurs naturally and functions as a site for outflow resistance and avoids postoperative ocular hypotony by allowing progressive IOP drop [77]. This membrane is called the trabeculo-descemet's membrane; it is composed of both trabeculum and Descemet's membrane. To expose the membrane, a deep sclerokeratectomy should be performed thereby also providing a postoperative scleral space. Such a space has many functions, which decrease the risk of late-bleb-related endophthalmitis by acting as an aqueous reservoir and as a filtration site, thus avoiding the need for a large subconjunctival filtration bleb. As a consequence, the trabeculo-descemet's membranes function of resistance is both low enough to ensure a low IOP and high enough to keep both the anterior chamber depth intact as well as decrease and or completely avoid postoperative complication such as hypotony [78].

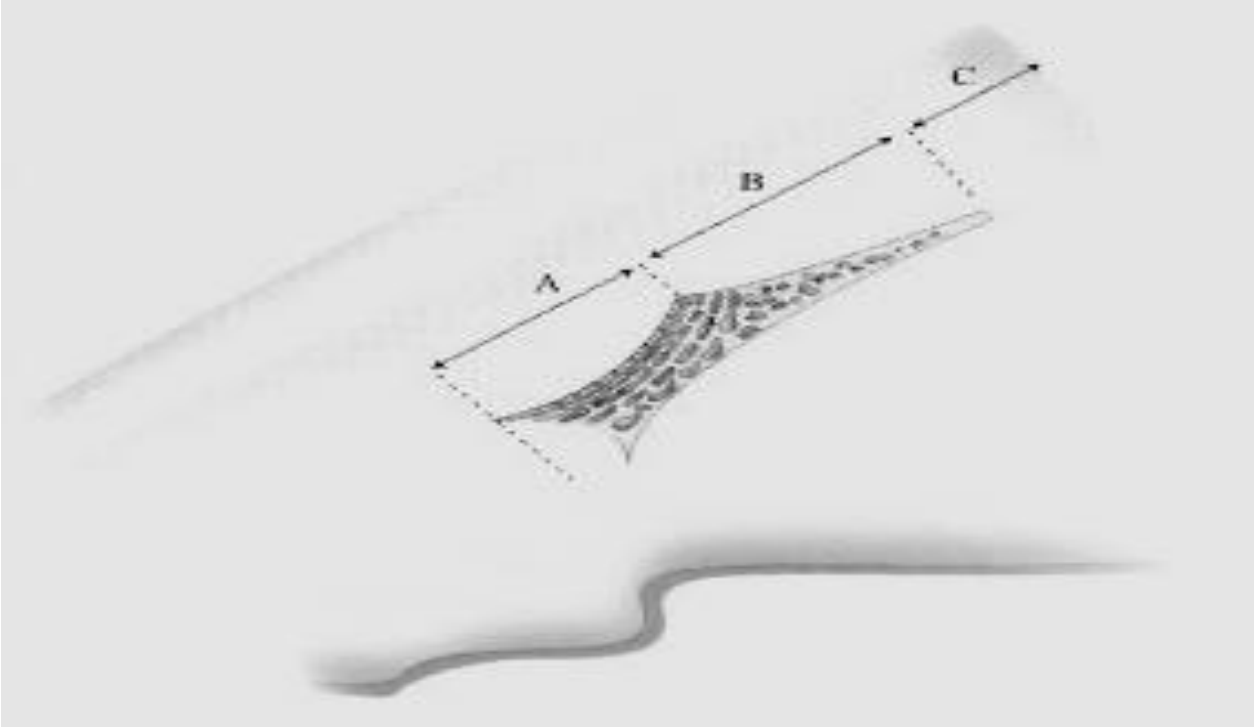



**Fig. 12.** Schematic representation of the trabeculo-descemet's membrane. (A) Posterior trabeculum, (B) Anterior trabeculum and (C) Descemet's membrane [79].

### 3.3.9 Ultrasound Biomicroscopic Imaging (UBM)

The Ultrasound Biomicroscopic imaging (UBM) method developed in the early 1990s introduced high-resolution cross-sectional imaging for assessment of the angle and ciliary body. In the normal eye, the cornea, anterior chamber and the retroiridal structures such as posterior chamber, iris, and ciliary body can be easily recognized. UBM systems use frequencies ranging from approximately 35 to 80 MHz. Ultrasound biomicroscopy systems are now produced by numerous companies, one of which is IScience Interventional (Menlo Park, CA, USA) that manufactures an 80-MHz scanner for high-resolution imaging of the angle and Schlemm's canal [80]. Imaging of the anterior chamber angle and Schlemm's canal can be assisted through the Ultrasound Biomicroscopy preoperatively, intraoperatively and postoperatively in canaloplasty. Imaging of all 4 quadrants of the postoperative eye can assist in the viscodilation of Schlemm's canal, in the distension of the trabecular meshwork from the tensioning suture and in evaluating general angle morphology [68]. The acquired UBM image is useful in analyzing whether there is a correlation between the trabecular meshwork distention and IOP results [62].

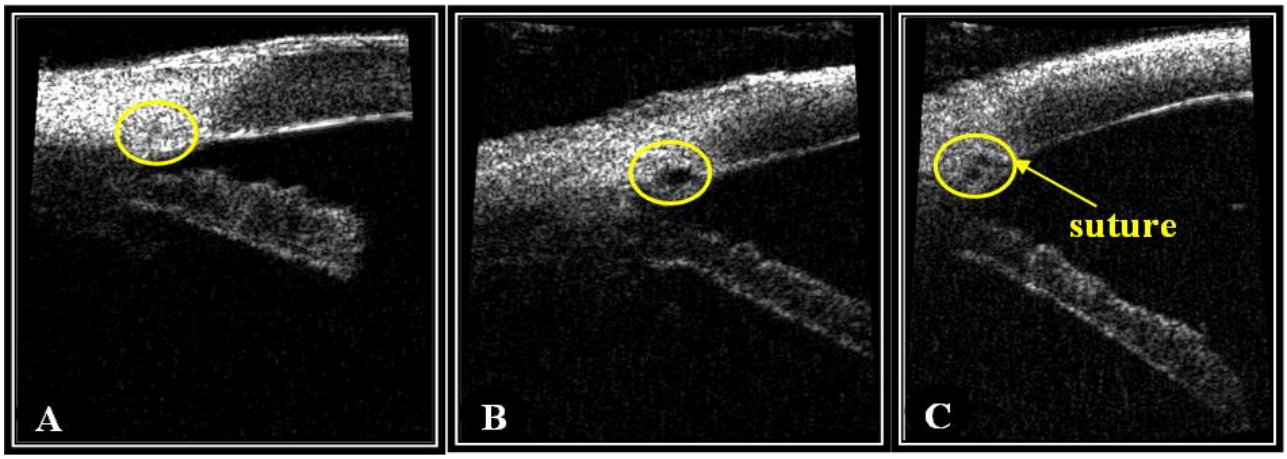



**Fig. 13.** High-resolution UBM images of anterior chamber angle before and after canaloplasty: **(A)** Preoperative, **(B)** Dilation of Schlemm's canal, **(C)** Dilation of Schlemm'canal and collector canals.

# 4. Aim of Work

Retrospective analysis of surgical cases performed from September 2007 to May 2010 addressing the following topics:

1. The assessment of the pressure-lowering effect, successes rate and safety of canaloplasty (circumferential viscodilation and tensioning of the inner wall of Schlemm's canal) in the managements of medically uncontrollable glaucoma.
2. The evaluation and comparison of the surgery's effectiveness in phakic eyes, pseudophakic eyes and when combined with cataract extraction by phacoemulsification (phacocanaloplasty) in management of medically uncontrolled glaucoma over a period of 24 months.
3. The assessment of the visual outcome after the surgery.
4. The assessment of the effect of canaloplasty on reduction postoperative use of medication.
5. The assessment of the morphological manifestations, complications and their management after canaloplasty.

# 5. Patients and methods

## 5.1 Design

Data were retrospectively reviewed for 100 eyes of 75 patients with uncontrolled primary open-angle glaucoma, who underwent either a canaloplasty or phacocanaloplasty operation over a 2 year period by the same experienced glaucoma surgeon. All procedures were performed under peribulbar anesthesia.

The mean preoperative IOP was 23.8 ± 6.8 mm Hg and the historical IOP 30-53 mmHg, with a mean of 2.1 ± 0.8 pressure-lowering medications. Mean age of the men and women was 64.4 ± 14.0 years.

All patients had been diagnosed with primary open-angle glaucoma (POAG), secondary open angle glaucoma including pigmentary glaucoma and exfoliation glaucoma, or POAG with narrowed but not occluded anterior chamber angle. There were no patients with a close angle, neovascular disease; uveitis; peripheral anterior synechiae; angle recession; developmental or secondary glaucoma with the exception of pigmentary and exfoliative glaucoma; and no patients with more than two laser trabeculoplasty procedures.

Preoperative and postoperative data were collected retrospectively from the electronic patient's files (computer Turbomed program). The preoperative collected data included diagnosis, years of treatment, number of topical medications, age, sex, ocular history, history of glaucoma, ophthalmic and systemic medication usage, IOP taken at most 60 days prior to surgery, best corrected visual acuity (BCVA) which was measured on decimal charts, gonioscopy, slitlamp and fundus examination, HRT, Papillary OCT, central corneal thickness and visual field testing using Humphrey 32-2 program automated field analyzer.

The postoperative data was collected from the follow-up examinations conducted 1 day and 1, 3, 6, 12, 18, and 24 months postoperative; they include tonometer measurement of IOP, best corrected visual acuity (BCVA), slitlamp examination, gonioscopy, medications, complications and secondary procedures reporting.

Whenever necessary, a further postoperative outcome value was obtained from the referring ophthalmologist. For efficacy analysis of the canaloplasty procedure, the patients were divided into groups. Group 1, represented patients who underwent canaloplasty alone "classic canaloplasty with suture", which was further divided in some of the statistical analyses into two subgroups; Group 1A

included canaloplasty operation on phakic eyes, and Group 1B included canaloplasty on pseudophakic eyes. Group 2, represented patients who underwent canaloplasty combined with cataract operation (phacocanaloplasty).

The primary endpoints included mean IOP and mean number of glaucoma medications at follow-up visits. The secondary endpoints included visual acuity, surgical-postsurgical complications and postoperative interventions.

Temporal clear corneal phacoemulsification with posterior chamber IOL implantation was performed surgically either before the glaucoma procedure or after the dissection of the sclera to access Schlemm's canal. The surgeon followed traditional viscocanalostomy and deep sclerectomy methods for surgical access to the canal, with the additional use of a microcatheter to dilate Schlemm's canal and install a trabecular tensioning 10-0 polypropylene suture (Prolene). A Descemet window was formed at the surgical site, followed by excision of the deep flap and watertight closure of the superficial tissues to prevent bleb formation.

Postoperatively, all patients were treated with topical 0.1% dexamethasone, 0.35% neomycin and 6000 U/ml polymyxin (Maxitrol) five times daily for 4 weeks, and then with topical non-steroid anti-inflammatory medication three times a day for 2-4 months.

## 5.2 Data analysis

All data were collected and entered into Microsoft Excel 2010. A pair-wise comparison of Student *t*-test was performed for IOP analysis in relation to surgical groups, to previous glaucoma surgeries and to hyphema, all the results at all postoperative time points compared with baseline values and for medication. Non-pairwise comparison of Student *t*-test was performed for IOP analysis in relation to age, to gender and to right and left eye, this test compared the results between groups at all postoperative time points. Kaplan-Meier survival model was used to determine the cumulative probability of an IOP over 21 mm Hg. The chi-square approximations for log-rank and Wilcoxon tests were chosen to compare the failure proportions between the surgical groups. A *P-value* of equal to or less than 0.05 was considered statistically significant. Values are shown as mean ± SD.

# 6. Results

## 6.1 Demographics

This study is based on 100 eyes of 75 patients, all of which were affected by uncontrolled glaucoma despite maximally tolerated medical therapy. These eyes underwent canaloplasty from September 2007 to May 2010 in the same eye-clinic and by the same experienced surgeon, in which the successful suture placement in Schlemm's canal was achieved in all cases. Out of the total of 100 eyes at the baseline, the number of eyes recorded post operation was 91 (91%) at 1 day, 87 (87%) at 1 month, 84 (84%) at 3 months, 82 (82%) at 6 months, 77 (77%) at 12 months, 36 (36%) at 18 months, and 29 eyes (29%) at 24 months.

The eyes were divided into two groups, "Group 1: classic canaloplasty with suture", which was itself divided in to two subcategories called "Group 1A: canaloplasty on phakic eyes" (including 46 eyes) and "Group 1B: canaloplasty on pseudophakic eyes" (including 34 eyes); and "Group 2: canaloplasty combined with cataract operation (phacocanaloplasty)" which included 20 eyes. The combined results of both groups were also considered in the analysis. One patient had a phakic eye and a pseudophakic eye, both of which underwent canaloplasty, and therefore this patient was included in both subgroups A and B.

Most of the patients were female (62.6%) affected by open angle glaucoma under maximally tolerated medical therapy (82 primary open angle glaucoma, 3 pigmentary glaucoma, 12 pseudoexfoliation glaucoma and 1 normal pressure glaucoma) or POAG mixed with another mechanism. These patients also have high risk factors such as old age, high intraocular pressure (IOP), elevated papillary excavation, visual field defects and thin corneal thickness. Many patients on maximally tolerated medical therapy had an IOP higher than the target pressure determined on the basis of functional and structural damage. Thirty four (34%) were pseudophakic at the baseline, forty six (46%) were phakic and twenty (20%) with visually significant cataract had canaloplasty combined with cataract surgery (phacocanaloplasty). Demographic data are summarized in Table 1.

**Table 1. Demographic characteristics**

| Parameters | Group 1 Canaloplasty | | Group 2 Phacocanaloplasty | Total |
|---|---|---|---|---|
| | A) ph* eyes | B) ps eyes | | |
| **General** | | | | |
| Patients [n] | 31***** | 30 | 15 | 75 |
| Eyes [n] | 46 | 34 | 20 | 100 |
| Age [y]: | | | | |
| Mean ± SD | 53.2 ± 13.6 | 73.3 ± 7.7 | 70.5 ± 6.8 | 64.4 ± 14.0 |
| Range | 18 - 72 | 58 - 90 | 55 - 82 | 18 - 90 |
| Gender [n (%)]: | | | | |
| Female | 20 (26.6) | 18 (24) | 9 (12) | 47 (62.6) |
| Male | 10 (13.3) | 12 (16) | 6 (8) | 28 (37.3) |
| Eye: | | | | |
| OD | 25 (54.3) | 17 (50) | 8 (40) | 50 (50) |
| OS | 21 (45.6) | 17 (50) | 12 (60) | 50 (50) |
| Glaucoma diagnosis, [n (%)]: | | | | |
| Primary open-angle | 42 (91.3) | 24 (70.5) | 16 (80) | 82 (82) |
| Pseudoexfoliative | 1 (2.1) | 7 (20.5) | 4 (20) | 12 (12) |
| Pigmentary dispersion | 2 (4.3) | 1 (2.9) | 0 | 3 (3) |
| Mixed mechanism | 1 (2.1) | 1 (2.9) | 0 | 2 (2) |
| Normal pressure glaucoma | 0 | 1 (2.9) | 0 | 1 (1) |
| **Baseline** | | | | |
| Intraocular pressure IOP (mmHg): | | | | |
| Mean ± SD | 22.5 ± 5.1 | 25.2 ± 7.4 | 24.6 ± 8.8 | 23.8 ± 6.8 |
| Range | 16 - 44 | 13 - 48 | 14 - 44 | 13 - 48 |
| Medications: | | | | |
| Mean n of med ± SD | 2.1 ± 0.8 | 1.8 ± 0.9 | 2.5 ± 0.6 | 2.1 ± 0.8 |
| Range | 1 - 3 | 0 - 4 | 0 - 4 | 0 - 4 |
| Previous antiglaucoma surgery/eye [n (%)]: | | | | |
| With | 4 (8.6) | 7 (20.5) | 3 (15) | 14 (14) |
| Without | 42 (91.3) | 27 (79.4) | 17 (85) | 86 (86) |
| Papillary excavation (clinical C/D-ratio) Mean ± SD | 0.7 ± 0.2 | 0.8 ± 0.1 | 0.9 ± 0.1 | 0.8 ± 0.2 |
| Pachymetry [µm] Mean ± SD | 526.1 ± 41.8 | 538.5 ± 28.1 | 534.1 ± 47.2 | 531.3 ± 39.6 |

* ph: phakic, ps: pseudophakic, n: number, y: year, med: medication, 31: clarified in the text

All patients were 18 years old or older. Of all patients, the majority (40%) were part of the age group of “66-75 years”, followed by 21.3% who were in both age groups “under 55” and “56-65 years”, 13.3% who were in the age “group 76-85 years” and 4% who were “over 85”.

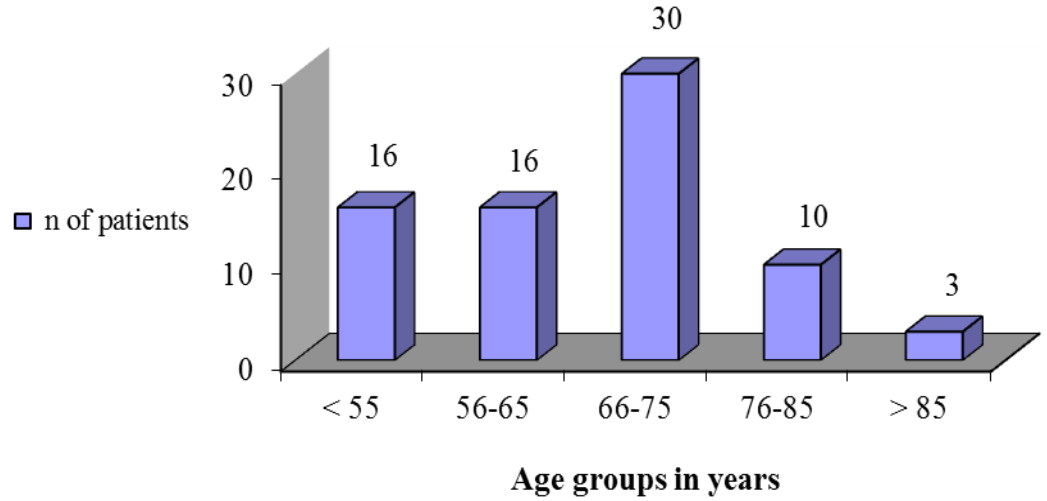



**Fig. 14.** Age distribution.

The baseline IOP of most eyes (59%) was between 20-30 mmHg, otherwise 29% of all eyes recorded a baseline IOP of between 13 and 19 mmHg.

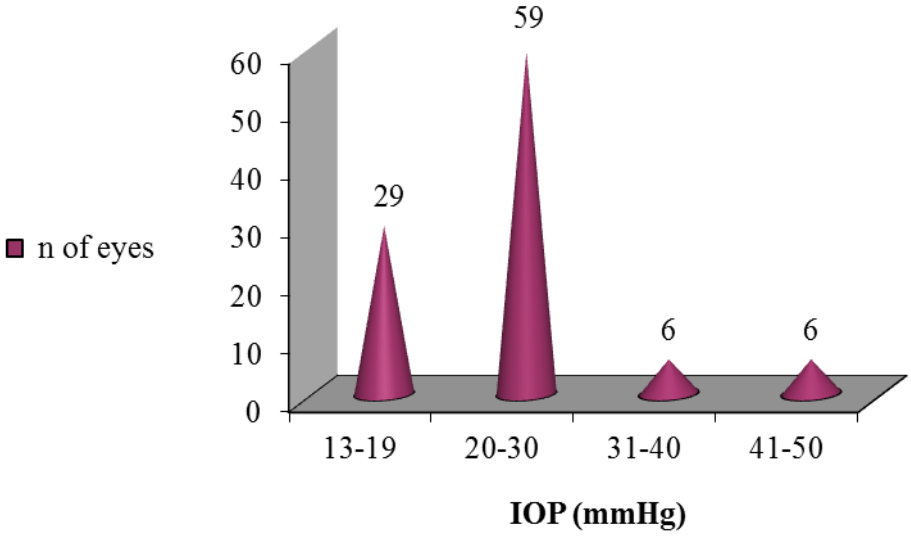



**Fig. 15.** Numbers of eyes in relation to preoperative IOP.

While 91 eyes were on 1-4 medications at the baseline, 9 eyes were not on any medication. Moreover, 38% of the eyes were on 3 medications.

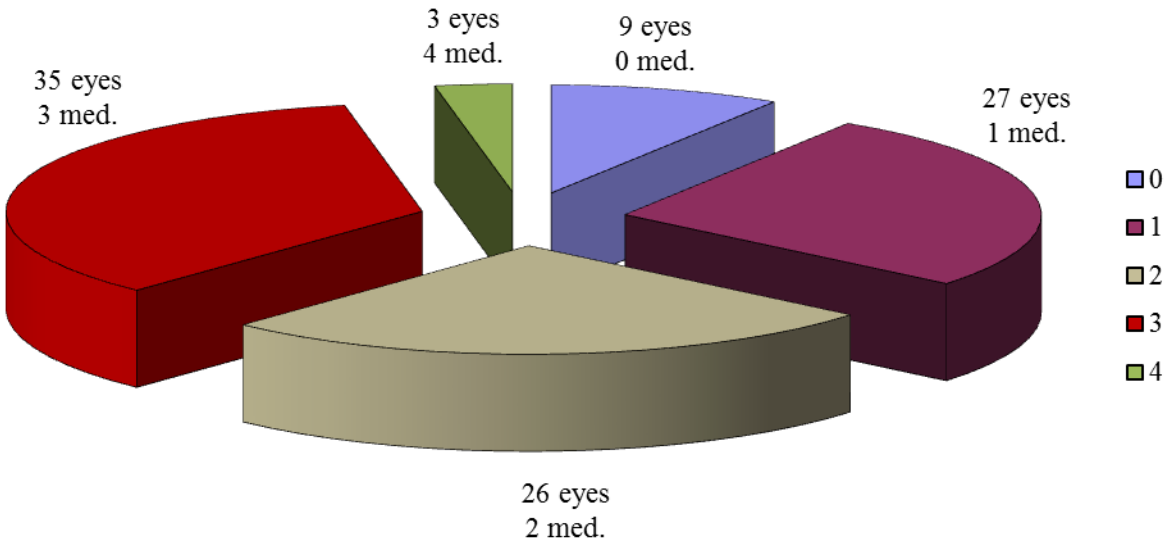



**Fig. 16.** Preoperative medications.

The most common use of medication was as prostaglandin analogue eye drops, either taken alone or combined with other medication, followed by ß blocker, and then the less commonly used miotic as illustrated in the following Figure:

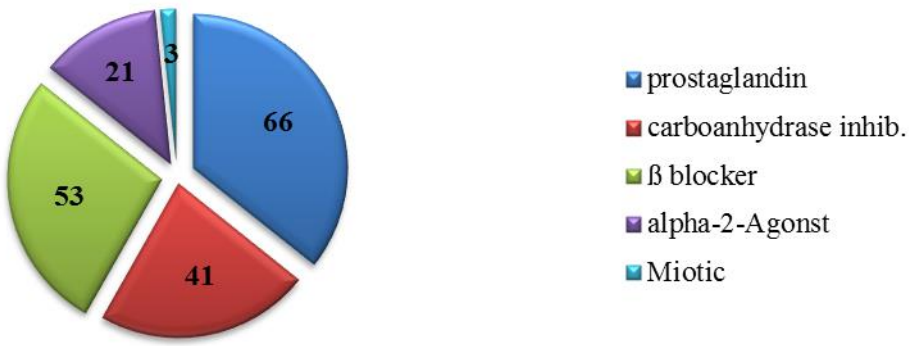



**Fig. 17.** Preoperative medication types.

Thirty four eyes had a previous cataract surgery and were included in this study as subgroup "Group 1B: canaloplasty on pseudophakic eyes", which along with the other surgical groups, are illustrated in the following table:

**Table 2. Previous ocular surgery**

| | Group 1 Canaloplasty | | Group 2 Phacocanaloplasty | Total |
|---|---|---|---|---|
| | A) ph* eyes | B) ps eyes | | |
| Eye, n | 46 | 34 | 20 | 100 |
| Cataract surgery, n (%) | 0 (0) | 34 (100) | 0 (0) | 34 (34) |
| Laser trabeculoplasty, n (%) | 2 (4.3) | 4 (11.7) | 2 (10) | 8 (8) |
| Laser iridotomy, n (%) | 1 (2.1) | 4 (11.7) | 1 (5) | 6 (6) |
| CPC, n (%) | 0 (0) | 1 (2.9) | 0 (0) | 1 (1) |
| Viscocanalostomy, n (%) | 1 (2.1) | 0 (0) | 0 (0) | 1 (1) |

* ph: phakic, ps: pseudophakic, CPC: Cyclophotocoagulation, n: number

Eighty eyes (80%) had the classic canaloplasty with suture surgery, of which 46 (46%) were on phakic eyes and 34 (34%) on pseudophakic eyes (Group 1). Otherwise, twenty eyes (20%) had canaloplasty surgery combined with phacoemulsification and IOL implantation (phacocanaloplasty) (Group 2).

There were only 2 eyes with 3 types of previous ocular surgery, one eye with cataract surgery and two antiglaucoma laser therapies (Argon laser trabeculoplasty (ALTP) and laser iridotomy (LI)) and one eye with ALTP and cyclophotocoagulation (CPC); both eyes had advanced glaucoma with papillary excavation 0.8 and 1.0, respectively. LI was done by POAG with narrow but not occludable angles.

Only one eye had canaloplasty in previous viscocanalostomy operation which was done 3 years before this operation. In the other eyes, the previous ocular surgery was distributed between antiglaucoma laser therapy and cataract surgery with only one antiglaucoma laser therapy.

There were also other previous ocular surgeries such as retinal laser coagulation in four eyes, of which one eye was affected by ischemic ophthalmopathy and one eye by branch retinal vein occlusion. Other previous ocular surgeries include YAG laser posterior capsulotomy in three eyes and vitrectomy surgery by epiretinal membrane in one case.

## 6.2 Intraocular pressure results

### 6.2.1 Intraocular pressure in relation to surgical groups

Table 3 shows the efficacy results of the intraocular pressure (IOP) over time for the canaloplasty groups and the phacocanaloplasty group. Group 1A consisting of canaloplasty on phakic eyes had a mean ± standard deviation baseline IOP of 22.5 ± 5.1 mmHg, which decreased at 24 months to 14.4 ± 4.3 mmHg in 41.3% from the baseline of the represented eyes, this represents a 36% reduction. Group 1B consisting of canaloplasty on pseudophakic eyes had a mean ± standard deviation baseline IOP of 25.2 ± 7.4 mmHg, which decreased at 24 months to 14.7 ± 3.9 mmHg in 23.5% from the baseline of the represented eyes, this represents a 42% reduction. Group 2 consisting of eyes having canaloplasty with phacoemulsification had a mean ± standard deviation baseline IOP of 24.6 ± 8.8 mmHg, which decreased at 24 months to 12.0 ± 0.0 mmHg in 10% from the baseline of the represented eyes, this represents a 51% reduction.

**Table 3. IOP in relation to surgical groups**

| Exam | Group 1 Canaloplasty (80) | | | | Group 2 Phacocanaloplasty (20) | |
|---|---|---|---|---|---|---|
| | A) ph* eyes (46) | | B) ps eyes (34) | | | |
| | Mean IOP ± SD | n | Mean IOP ± SD | n | Mean IOP ± SD | n |
| **Baseline** | 22.5 ± 5.1 | 46 | 25.2 ± 7.4 | 34 | 24.6 ± 8.8 | 20 |
| **Postoperative** | | | | | | |
| 1 day | 8.9 ± 6.6 | 40 | 9.9 ± 5.9 | 31 | 12.7 ± 7.4 | 20 |
| 1 months | 15.5 ± 6.5 | 40 | 14.9 ± 5.8 | 28 | 14.6 ± 2.7 | 19 |
| 3 months | 13.8 ± 3.7 | 40 | 12.8 ± 3.3 | 25 | 12.7 ± 3.6 | 19 |
| 6 months | 14.7 ± 4.3 | 38 | 13.2 ± 3.4 | 24 | 13.7 ± 4.3 | 20 |
| 12 months | 14.8 ± 2.9 | 35 | 13.0 ± 2.4 | 24 | 14.2 ± 5.6 | 18 |
| 18 months | 15.3 ± 2.8 | 16 | 14.7 ± 3.3 | 12 | 13.5 ± 3.0 | 8 |
| 24 months | 14.4 ± 4.3 | 19 | 14.7 ± 3.9 | 8 | 12.0 ± 0.0 | 2 |

* ph: phakic, ps: pseudophakic, n: number

A paired sample t-test for significance confirmed that the difference between preoperative data and postoperative data at all time periods was statistically significant for all groups ($P \leq 0.05$) with the exception of Group 2 at 18 and 24 months, where the amount of data was too small for a meaningful statistical comparison. Since clinical statistical significance was demonstrated across the board, it should also be assumed at 18 and 24 months postoperatively for Group 2.

In Figure 18, which illustrates the decrease in IOP from preoperatively > 21 mmHg mostly to < 15 mmHg without medications at 24 months in all groups, there was a temporarily significance decrease of IOP to ≤10 mmHg on the first day after the surgery in all groups, which is considered as a positive sign. Otherwise, there was then a gradual increase in IOP to 15 mmHg in one month. While there were small differences in the changes of IOP between canaloplasty on phakic and pseudophakic eyes in 1 and 24 months, the differences in changes between phacocanaloplasty compared to canaloplasty is very notable.

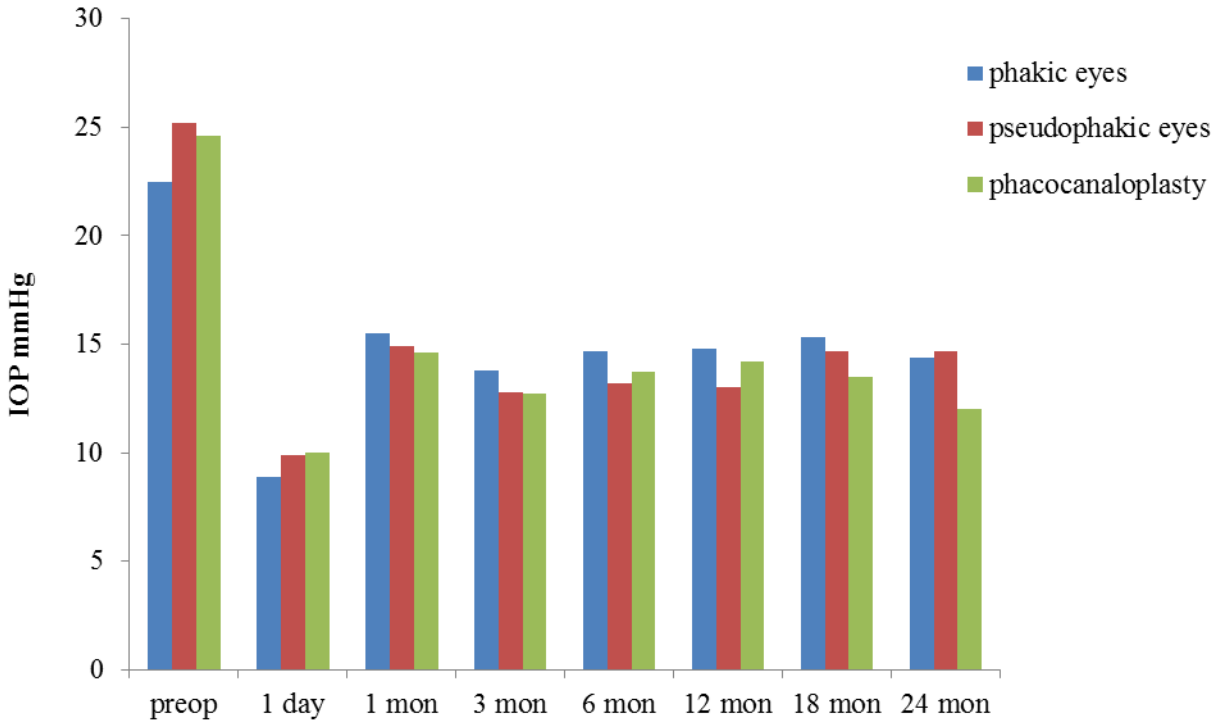
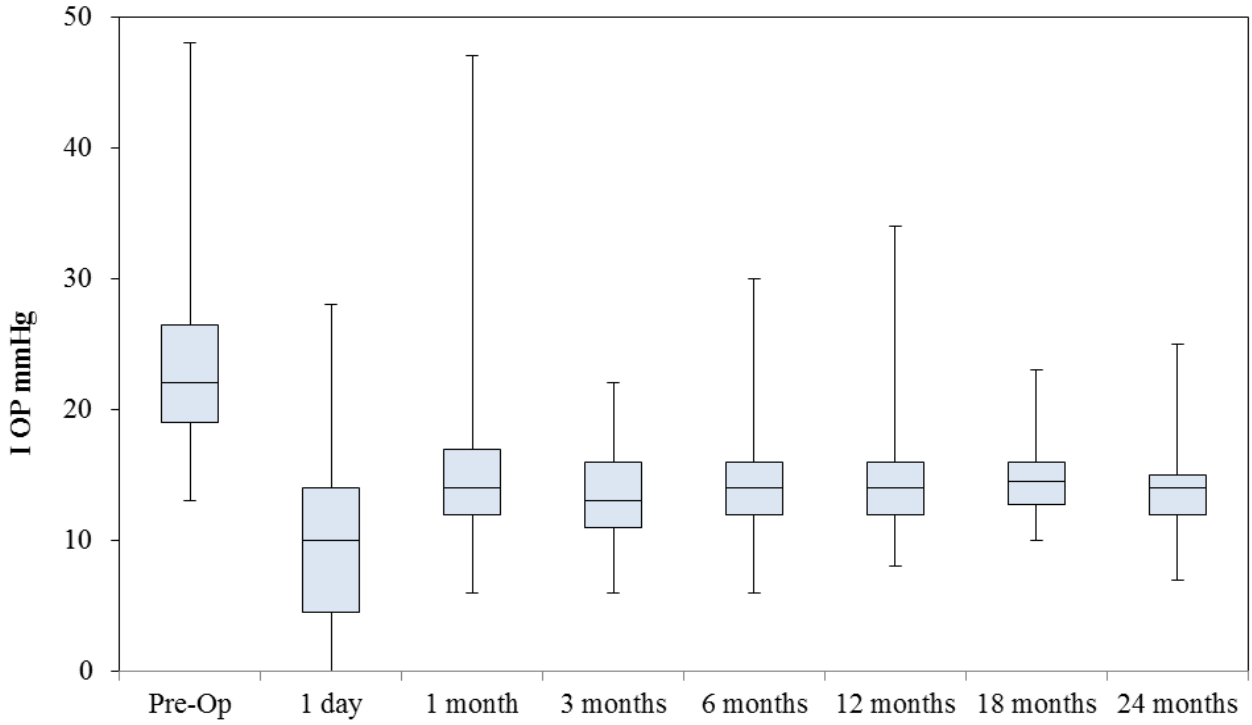



**Fig. 18.** Postoperative intraocular pressure results in canaloplasty and phacocanaloplasty.

Of the total, the mean ± standard deviation IOP of 23.8 ± 6.8 mmHg at the baseline is decreased at 24 months to 14.3 ± 4.0 mmHg, this represent a 40% reduction.

The box-and-whisker diagram is plotted to show the IOP values over time.




*At 1 month, the high standard deviation is influenced postoperatively by steroid response

**Fig. 19.** Box-and-whisker diagram shows the IOP values over time in total eyes.

### 6.2.2 Intraocular pressure in relation to previous glaucoma surgeries

This study was conducted to determine whether previous glaucoma surgeries played a significant role in the IOP reduction after canaloplasty surgery. 14% of all eyes already had one previous glaucoma surgery; these surgeries, included Argon laser trabeculoplasty (ALTP) in 8% of all eyes, laser iridotomy in 6% of all eyes, cyclophotocoagulation (CPC) in 1 % of all eyes and viscocanaloplasty also in 1% of all eyes. Out of the total, two eyes had two previous antiglaucoma surgeries, one eye with ALTP and laser iridotomy and the other with ALTP and CPC. For the group of eyes with previous glaucoma surgeries, the IOP decreased from a mean ± standard deviation baseline IOP of 24.5 ± 7.4 mmHg to 16.0 ± 4.4 mmHg at 24 months postoperatively, this represents a 35% reduction; otherwise, for the group of eyes without previous glaucoma surgeries, the IOP decreased from a mean ± standard deviation baseline IOP of 23.7 ± to 14.0 ± 4.0 mmHg at 24 months postoperatively, representing a 41% reduction. A paired sample t-test significance test

confirmed the statistically significant IOP decrease from the baseline at all-time points (*P ≤0.05*) in both groups.

**Table 4. IOP in relation to previous glaucoma surgeries**

| | **Eyes with previous surgery** | | | **Eyes without previous surgery** | | |
|---|---|---|---|---|---|---|
| | Mean IOP ± SD | n | *P-value* | Mean IOP ± SD | n | *P-value* |
| **Baseline** | 24.5 ± 7.4 | 14 | - | 23.7 ± 6.8 | 86 | - |
| **Postoperative** | | | | | | |
| 12 months | 13.6 ± 2.0 | 12 | *<0.05* | 14.2 ± 3.8 | 65 | *<0.05* |
| 18 months | 14.5 ± 4.3 | 7 | *<0.05* | 14.7 ± 2.7 | 29 | *<0.05* |
| 24 months | 16.0 ± 4.4 | 5 | *<0.05* | 14.0 ± 4.0 | 24 | *<0.05* |

### 6.2.3 Intraocular pressure in relation to postoperative use of medication and/or surgery

The Scatter diagram (Fig. 20) shows the IOP distribution in relation to postoperative use of medication and/or surgery. Out of the total, 29 eyes had data for both preoperative IOP and 24 months postoperative IOP with and without medication or surgery. The figure shows the IOP distribution in two groups of eyes; one group includes 18 eyes (62%), which had preoperatively a mean ± standard deviation IOP of 21.7 ± 7.3 mmHg with medications and postoperatively of 13.5 ± 3.8 mmHg without medications and/or surgery at 24 months. This represents 37.8% reduction. Complete success rate was defined as reaching the specified IOP, in this study defined as ≤ 21 mmHg, without medication and/or surgery. Out of the total of 18 eyes, the number of eyes with complete success was 17 eyes with a percentage of 94% at 24 months. Only one eye recorded an IOP of 25 mmHg, this eye was myopic and did not tolerate medication. The other group of eyes includes 11 eyes (38%), which had preoperatively a mean ± standard deviation IOP of 23.2 ± 4.3 mmHg with medication and postoperatively of 15.7 ± 4.2 mmHg with medication and/or surgery at 24 months representing a 32.4% reduction. Seven eyes from this group had postoperative antiglaucoma eye drops, 3 eyes with postoperative interventions (canaloplasty revision, cyclophotocoagulation, trabeculectomy with mitomycin, iris reposition and cataract surgery) and one eye with both antiglaucoma eye drops and postoperative intervention.

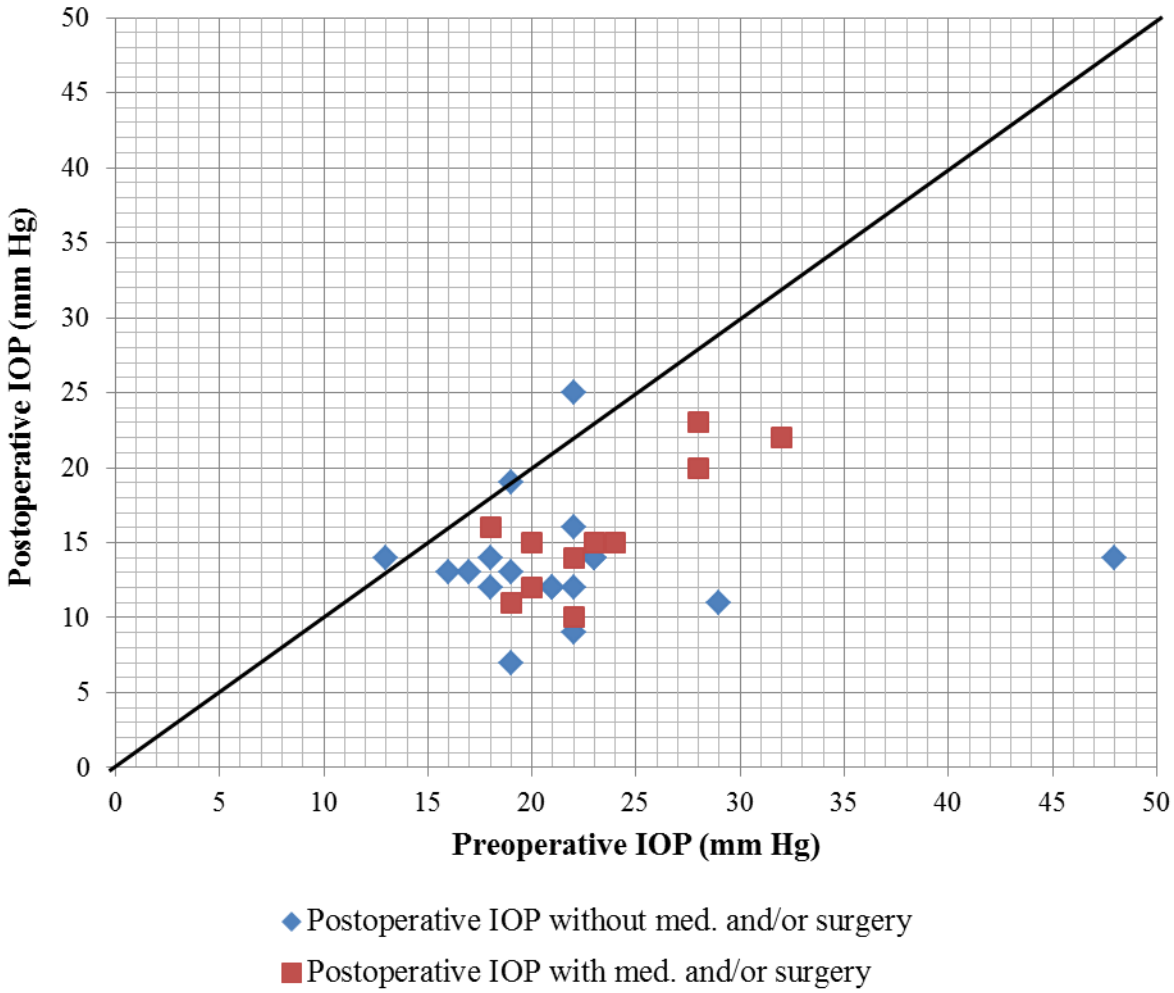



**Fig. 20.** Scatter diagram shows intraocular pressure results, preoperative with medications and 24 months postoperative with and without medications and/or surgery.

### 6.2.4 Intraocular pressure in relation to postoperative hyphema

**Table 5. IOP in relation to hyphema**

| | **Group 1 (with hyphema)** | | **Group 2 (without hyphema)** | | |
|---|---|---|---|---|---|
| **Postop. IOP** | Mean IOP ± SD | n | Mean IOP ± SD | n | *P-value* |
| 1 day | 9.0 ± 6.3 | 69 | 13.5 ± 6.5 | 22 | *0.011* |
| 24 months | 14.5 ± 4.1 | 21 | 14.0 ± 4.2 | 8 | *0.783* |

To test for significant differences in postoperative intraocular pressure results for patients with hyphema compared to those without, we followed a simple procedure. Firstly, all 100 patients were

divided into two groups; Group 1 included the 74 patients with reported hyphema, and Group 2 included the remaining 26 patients without hyphema. Then, the IOP measured both 1 day and 24 months after the operation were recorded for each group. Finally, a significance test was conducted to determine whether the different groups had significantly different IOP results both 1 day and 24 months post-operation. Table 5 shows the relation of IOP to hyphema. Through the paired sample t-test, it is clear that there is a clinically significant difference (*P =0.011*) between the IOP of the different groups at 1 day after the operation. However, as the table shows, there is no significant clinical difference (*P =0.783*) between the IOP of the different groups at 24 months after the operation.

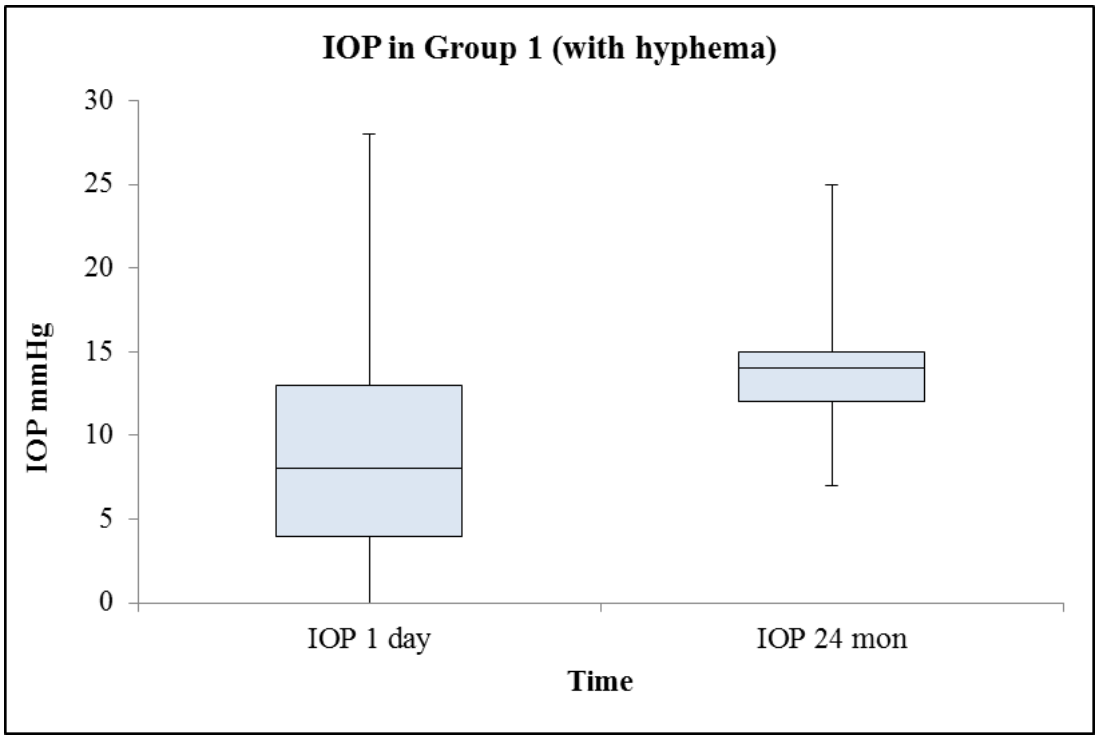



**Fig. 21.** Box-and-whisker diagram shows IOP in relation to hyphema in Group 1 (with hyphema).

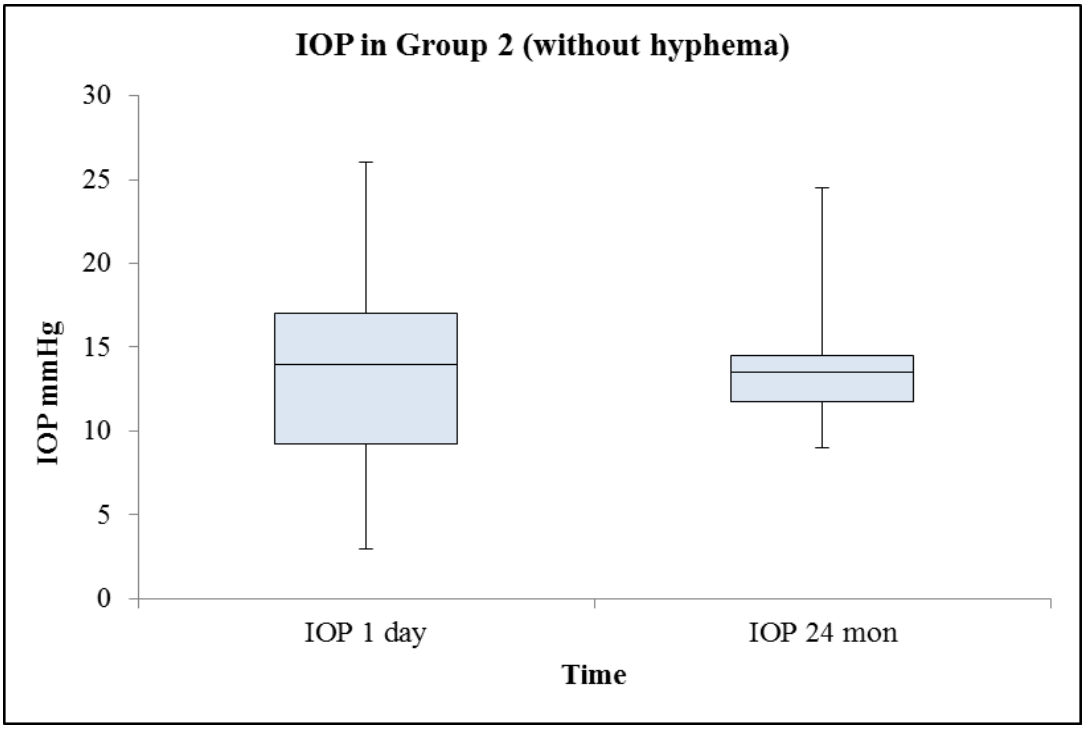



**Fig. 22.** Box-and-whisker diagram shows IOP in relation to hyphema in Group 2 (without hyphema).

### 6.2.5 Intraocular pressure in relation to primary and secondary glaucoma

The secondary glaucoma in this study includes pseudoexfoliation glaucoma (12%); pigmentary glaucoma (3%) and mixed glaucoma (2%), there were no other contraindicated types of glaucoma such as neovascular glaucoma. The primary glaucoma includes open angle glaucoma (82%) and normal pressure glaucoma (1%).

All eyes in this study were divided in to two groups, "Group 1: canaloplasty on eyes with primary glaucoma" and "Group 2: canaloplasty on eyes with secondary glaucoma". In both groups, there were significant decreases in the IOP at the first postoperative day with a mean ± standard deviation IOP of 10.2 ± 6.8 mmHg and 9.5 ± 5.6 mmHg, respectively. At 24 months, the average and standard deviation of the available IOP of 21 eyes from Group 1 was 14.9 ± 4.0 mmHg, this represented a 36% reduction. Of the 21 eyes in Group 1, 13% took medications. Also at 24 months, the available IOP of 8 eyes in Group 2 recorded an average and standard deviation of 13 ± 4.0 mmHg, representing a 50% reduction. Of these 8 eyes, 18% took medication. The results of a paired sample t-test, testing for clinical significance difference between preoperative IOP and that of all

postoperative periods, showed that at all time-points there was indeed a statistical significance (*P ≤0.05*) for both primary and secondary groups.

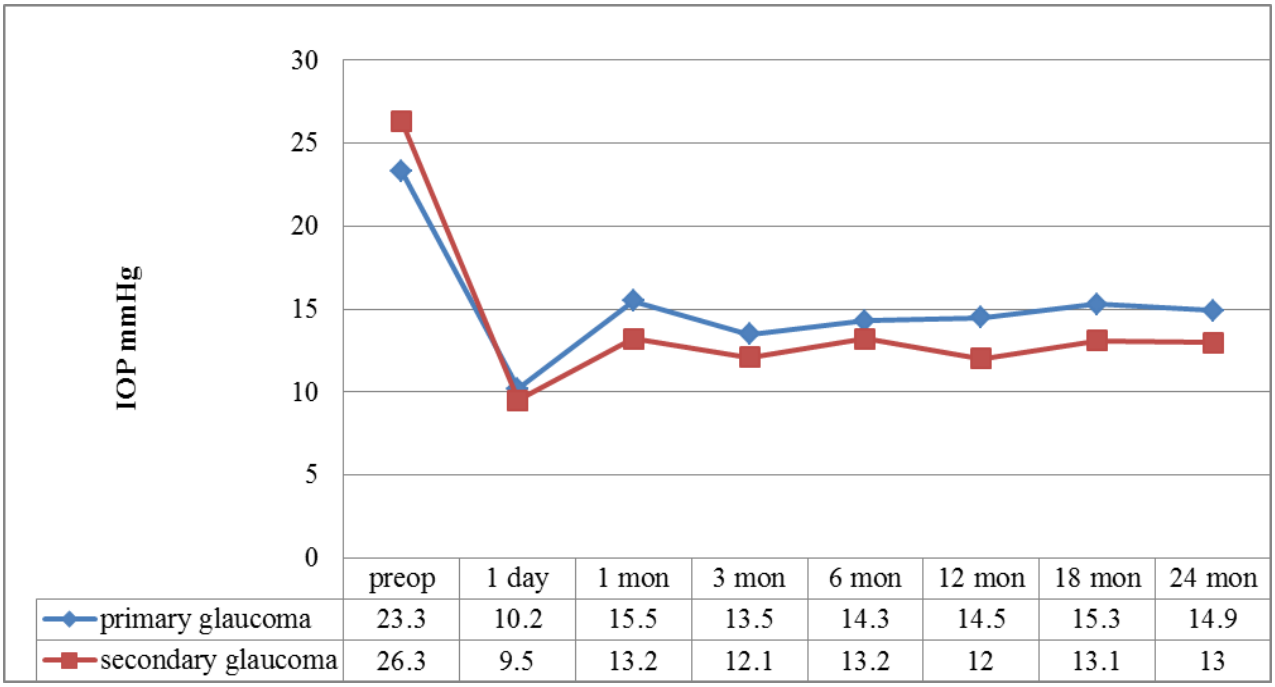



**Fig. 23.** IOP results over time in eyes with primary and secondary glaucoma.

### 6.2.6 Intraocular pressure in relation to age, gender and right and left eye

**Table 6. IOP in relation to age, gender and eye at 24 months**

| Mean IOP ± SD | n | Mean IOP ± SD | n | *P-value* |
|---|---|---|---|---|
| ≤ 60 years old | | > 60 years old | | |
| 14.1 ± 3.6 | 16 | 15.1 ± 4.9 | 11 | *0.52* |
| male | | female | | |
| 14.2 ± 4.3 | 10 | 14.7 ± 4.1 | 17 | *0.74* |
| right eye | | left eye | | |
| 14.2 ± 3.8 | 12 | 14.4 ± 4.3 | 17 | *0.88* |

There were 75 patients, 25 of them had the canaloplasty surgery in both eyes. There were 2 groups, Group 1 included patients 60 years old or younger with a mean ± standard deviation at the baseline IOP of 22.0 ± 6.3 mmHg, which decreased by 24 months to 14.1 ± 3.6 mmHg, and representing a 36% reduction. Group 2 included patients older than 60 years with a mean ± standard deviation

baseline IOP of 24.0 ± 7.4 mmHg, which decreased at 24 months to 15.1 ± 4.9 mmHg, representing a 37% reduction. A non-paired comparison of the mean IOP by t-test revealed that the mean IOP in patients of ≤ 60 years old was statistically insignificant compared to that of > 60 years old patients over time postoperatively (*P =0.52* at 24 months).

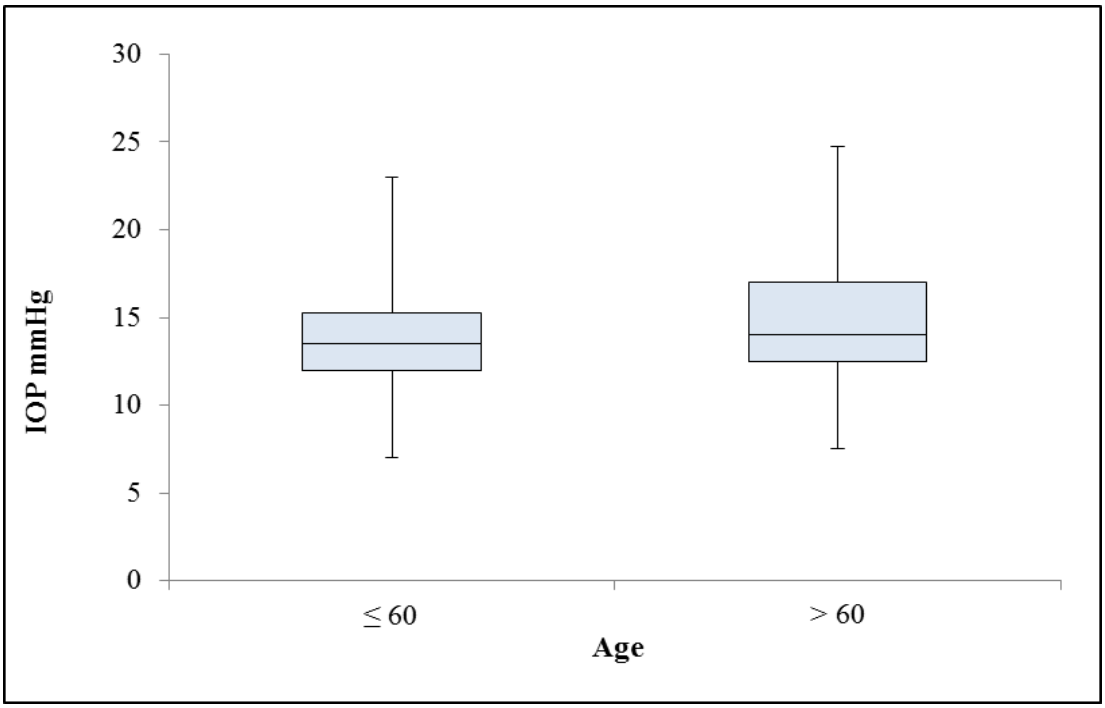



**Fig. 24.** Box-and-whisker diagram shows IOP in relation to age at 24 months.

The mean ± standard deviation baseline IOP of male group was 23.0 ± 6.8 mmHg, which decreased at 24 months to 14.2 ± 4.3 mmHg representing a 40% reduction. In the female group the mean ± standard deviation baseline IOP was 24.2 ± 6.9 mmHg, which decreased at 24 months to 14.7 ± 4.1 mmHg representing a 39% reduction. A non-paired comparisons of the mean IOP by t-test revealed that the mean IOP in the male group was statistically not significant compared to that of the female group over time postoperatively (*P =0.74* at 24 months).

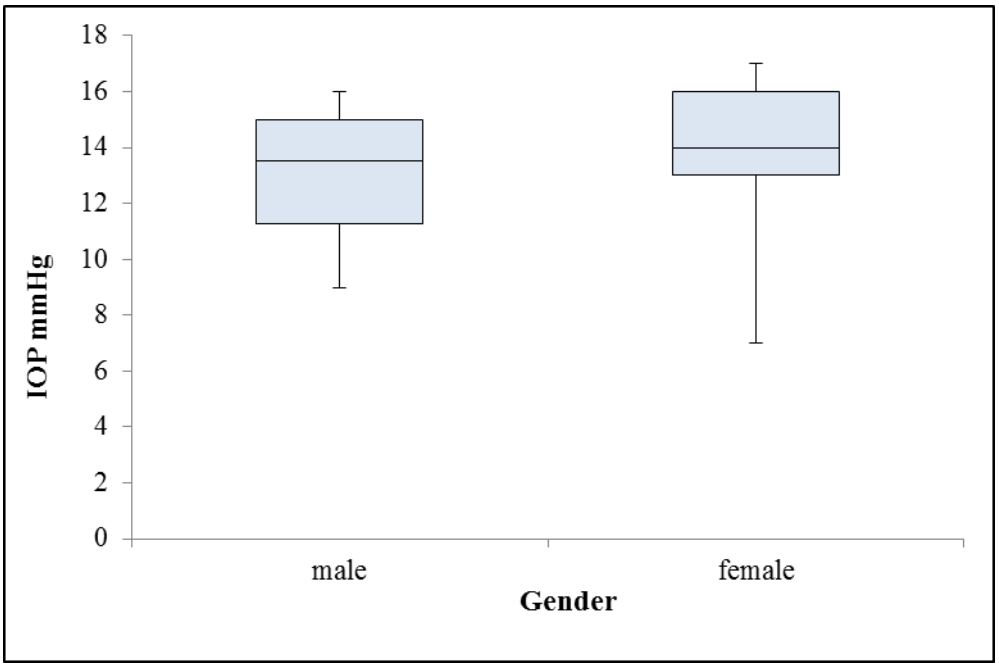



**Fig. 25.** Box-and-whisker diagram shows IOP in relation to gender at 24 months.

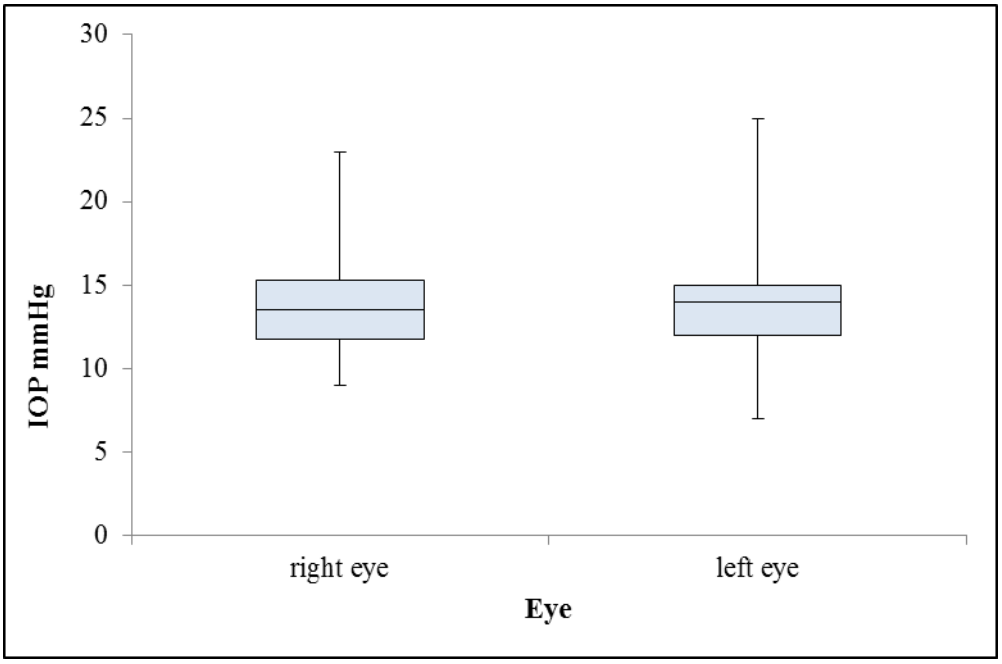



**Fig. 26.** Box-and-whisker diagram shows IOP in relation to right and left eyes at 24 months.

In the right eye, the mean ± standard deviation of the baseline IOP was at 24.1 ± 6.6 mmHg, which decreased at 24 months to 14.2 ± 3.8 mmHg representing a 41% reduction. In the left eye, the mean ± standard deviation baseline IOP of 23.6 ± 7.1 mmHg, which decreased at 24 months to 14.4 ± 4.3

mmHg, representing a 39% reduction. Non-paired comparisons of the mean IOP by t-test revealed that the mean IOP in the right eye was statistically insignificant compared to that of left eye over time postoperatively (*P =0.88* at 24 months).

### 6.2.7 Dependency of postoperative IOP on preoperative intraocular pressure level

To assess if the postoperative IOP at 24 months depend on preoperative IOP level, IOP at baseline was divided in to 2 groups (Figure 27):

Group 1: Preoperative IOP < 21 mmHg.

Group 2: Preoperative IOP ≥ 21 mmHg.

From the total of 29 eyes at 24 months, there were 12 eyes represented in Group 1 with a mean ± standard deviation IOP preoperatively of 18 ± 1.9 mmHg, which decreased postoperatively to a mean ± standard deviation IOP of 13.2 ± 2.8 mmHg.

In Group 2, there were 17 eyes represented with a mean ± standard deviation IOP preoperatively of 25.4 ± 6.6 mmHg, which decreased postoperatively to a mean ± standard deviation IOP of 15.1 ± 4.6 mmHg.

In the higher preoperative level group, the decrease in the mean IOP from the baseline was 40.5%, while in the lower preoperative level group, the decrease was 26.6%.

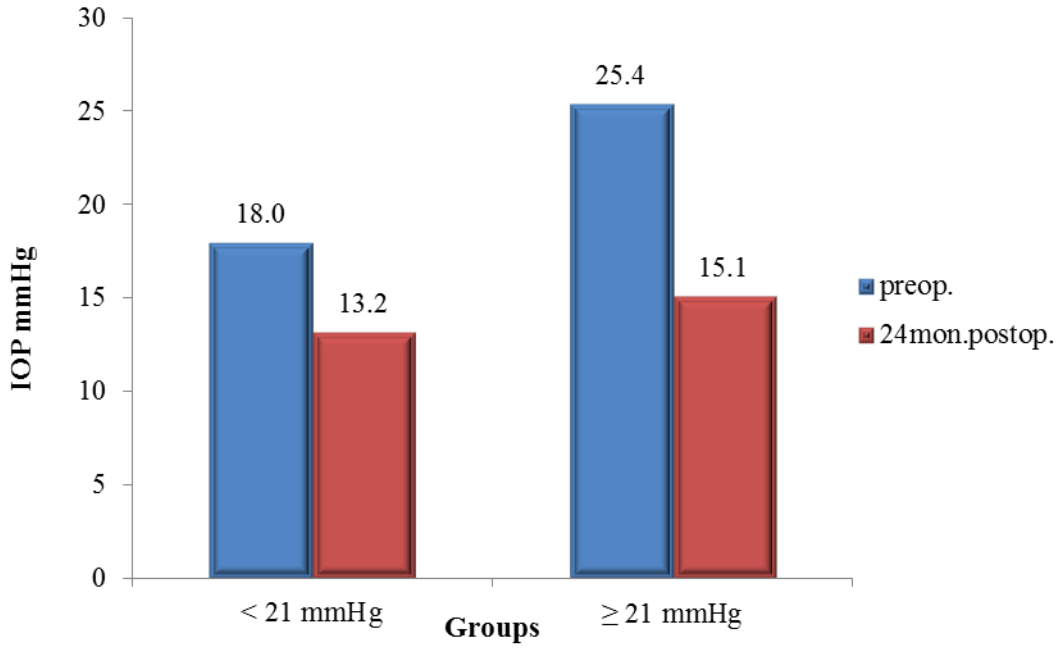



**Fig. 27.** Postoperative IOP in dependency of preoperative IOP level.

### 6.2.8 Success

The surgical outcome is shown in Table 7. The IOP qualified success was evaluated as the percentage of eyes at or below target values with or without medication. In this study the target values of IOP were at or below 21, 18, and 15 mm Hg. The table summarizes the qualified IOP success results at 6, 12 and 18 months and the corresponding number of patients in Group 1 canaloplasty and Group 2 phacocanaloplasty. 89% and 50% of Group 1 eyes attained an IOP of 18, 15 mmHg or lower respectively at 18 months. In Group 2 phacocanaloplasty, 100% and 75% of the eyes attained an IOP of 18, 15 mmHg or lower respectively. We observe that the success rate over time for eyes at or below 15 mmHg is more favorable in phacocanaloplasty group than in the canaloplasty group.

**Table 7. IOP Success**

| **IOP mmHg** | **Qualified success rate, n* (%)** | | | | | |
|---|---|---|---|---|---|---|
| | **Group 1 canaloplasty** | | | **Group 2 phacocanaloplasty** | | |
| | 6 months | 12 months | 18 months | 6 months | 12 months | 18 months |
| | n = 62 | n = 59 | n = 28 | n = 20 | n = 18 | n = 8 |
| ≤ 21 | 59 (95) | 59 (100) | 27 (96) | 19 (95) | 17 (94) | 8 (100) |
| ≤ 18 | 55 (89) | 56 (95) | 25 (89) | 17 (85) | 17 (94) | 8 (100) |
| ≤ 15 | 41 (66) | 39 (66) | 14 (50) | 16 (80) | 13 (72) | 6 (75) |

* n: number of eyes present at follow up

### 6.2.9 Kaplan-Meier

Figure 28 shows a Kaplan-Meier survival model for cumulative failure rates in Group 1A (canaloplasty on phakic eyes), Group 1B (canaloplasty on pseudophakic eyes) and Group 2 (phacocanaloplasty) using the failure criterion of an IOP over 21 mm Hg over time. Of the 46 eyes Group 1A, 34 eyes Group 1B and 20 eyes Group 2; nine, five and two eyes, respectively, failed to achieve qualified success criteria in a period of time from 1 month to 24 months after surgery and were considered failures.

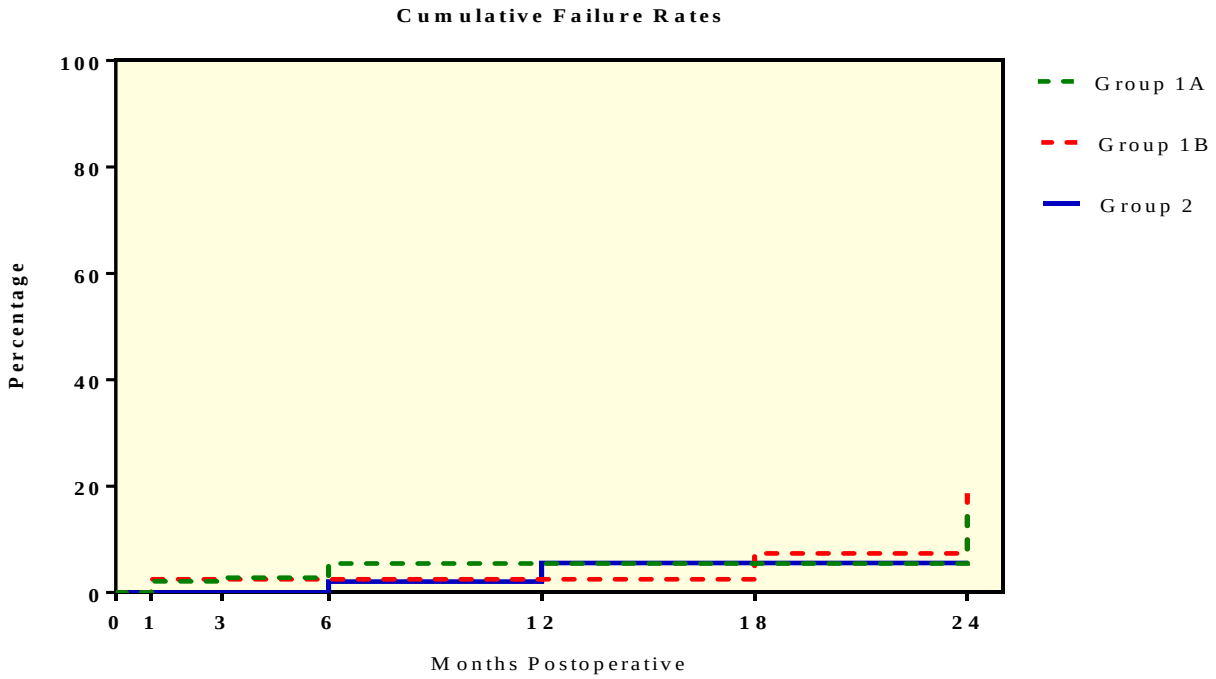



**Fig. 28.** Kaplan–Meier plot of the cumulative probability of failure for Group 1A (canaloplasty in phakic eyes), Group 1B (canaloplasty in pseudophakic eyes) and Group 2 (phacocanaloplasty). Failure was defined as an IOP > 21 mmHg.

The chi-square approximations for log-rank and Wilcoxon tests comparing the failure proportions in Group 1A, Group 1B and Group 2 show insignificant difference in the cumulative failure rate (*P =0 .491*).

**Table 8. Total comparison**

| | Chi-square | Degree of Freedom | Significance |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 1.421 | 2 | *0.491* |
| Test of comparison of the survival distribution between the different groups | | | |

## 6.3 Vision

Decimal BCVA was converted to LogMAR values for analysis. Table 9 shows the LogMAR best corrected visual acuity (BCVA) results of Group 1 canaloplasty (on both phakic and pseudophakic eyes), Group 2 phacocanaloplasty and the total eyes. Initially, there was a temporary significant decline in LogMAR BCVA with statistically significant *P-value of ≤0.05* in all groups in the first postoperative day, where the vision dropped to a Mean LogMAR BCVA 1.03 in 91% of total eyes. Visual acuity returned to just below preoperative level in a few weeks after surgery. The mean LogMAR BCVA ± SD was 0.13 ± 0.2 before surgery and 0.26 ± 0.5 at 24 months after surgery in canaloplasty alone, while it increased significantly from 0.20 ± 0.1 at the baseline to 0.06 ± 0.1 at 24 months in phacocanaloplasty eyes. There were 7 (9%) eyes from Group 1 with a history of other ocular disease that may affect visual acuity, of which two eyes had a history of macular epiretinal membrane, two eyes had age-related macular degeneration, one eye had branch retinal vein occlusion, one eye was affected by suspected ischemic ophthalmopathy and one eye was amblyopic. A paired sample t-test for significance confirmed that the difference between preoperative data and 24 months after surgery was statistically insignificant for all groups.

**Table 9. Visual acuity**

| Exam | Group 1 Canaloplasty | | | Group 2 Phacocanaloplasty | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean LogMAR BCVA* ± SD | n | *P-value* | Mean LogMAR BCVA ± SD | n | *P-value* | Mean LogMAR BCVA ± SD | n | *P-value* |
| **Baseline** | 0.13 ± 0.2 | 78 | - | 0.20 ± 0.1 | 19 | - | 0.14 ± 0.2 | 97 | - |
| **Postop.** | | | | | | | | | |
| 1 day | 1.00 ± 0.6 | 69 | *<0.05* | 1.00 ± 0.7 | 19 | *<0.05* | 1.03 ± 0.6 | 88 | *<0.05* |
| 1 mon | 0.27 ± 0.3 | 55 | *<0.05* | 0.15 ± 0.1 | 17 | *0.35* | 0.24 ± 0.3 | 72 | *0.05* |
| 3 mon | 0.20 ± 0.4 | 53 | *0.13* | 0.09 ± 0.1 | 16 | *<0.05* | 0.18 ± 0.3 | 69 | *0.88* |
| 6 mon | 0.22 ± 0.4 | 50 | *0.12* | 0.16 ± 0.2 | 18 | *0.67* | 0.20 ± 0.4 | 68 | *0.44* |
| 12 mon | 0.21 ± 0.4 | 48 | *0.12* | 0.31 ± 0.6 | 16 | *0.54* | 0.24 ± 0.4 | 64 | *0.16* |
| 18 mon | 0.24 ± 0.4 | 24 | *0.60* | 0.18 ± 0.3 | 8 | *0.93* | 0.23 ± 0.4 | 32 | *0.62* |
| 24 mon | 0.26 ± 0.5 | 24 | *0.37* | 0.06 ± 0.1 | 5 | *0.18* | 0.23 ± 0.5 | 29 | *0.53* |

* BCVA: best corrected visual acuity, n: number, mon: months

### 6.3.1 Astigmatism

Table 10 shows the change in the corneal astigmatism. There was a significantly increased corneal astigmatism in the first 2 weeks after surgery, from a baseline mean cylinder ± SD 0.9 ± 0.6 D increased to 3.3 ± 1.9 D at 1-2 weeks post-surgery in 81.0% of the eyes in Group 1 canaloplasty, and from a baseline mean cylinder ± SD 1.2 ± 0.7 D increased to 3.2 ± 1.3 D at 1-2 weeks postoperative in 83.3% of the eyes in Group 2, phacocanaloplasty, thereafter decreased to its previous preoperative level without intervention, then remains stable over time. Pair-wise comparisons of the mean cylinder by *t*-test revealed that the mean cylinder in the first 1-2 weeks in both groups was statistically significantly increased from that of the baseline ($P \leq 0.05$) and it was statistically insignificant at 5-12 weeks in both groups; canaloplasty group ($P = 0.06$) and phacocanaloplasty ($P = 0.10$).

**Table 10. Astigmatism, magnitude in diopters (D) of cylinder**

| | **Group 1 Canaloplasty** | | | **Group 2 Phacocanaloplasty** | | |
|---|---|---|---|---|---|---|
| **Exam** | Mean cyl * ± SD | n | *P-value* | Mean cyl ± SD | n | *P-value* |
| **Baseline** | 0.9 ± 0.6 | 75 | - | 1.2 ± 0.7 | 19 | - |
| **Postoperative** | | | | | | |
| 1 - 2 weeks | 3.3 ± 1.9 | 62 | *≤ 0.05* | 3.2 ± 1.3 | 19 | *≤ 0.05* |
| 5 - 12 weeks | 1.1 ± 0.8 | 57 | *0.06* | 0.8 ± 0.2 | 16 | *0.10* |

* cyl: cylinder, n: number

## 6.4 Medications

All groups required fewer medications postoperatively than preoperatively. 9% of the eyes were on no antiglaucoma medications while 91% were on between 1 to 4 medications at the baseline. At 24 months after surgery, 65% of the total eyes, 62%, 64% and 75% of the Group 1A, 1B and Group 2 respectively, were on no medications. Pair-wise comparisons of the mean medication by *t*-test revealed that the mean antiglaucoma medications at 24 months were statistically significantly lower than preoperatively in all groups ($P \leq 0.05$) as illustrated in Tables 11 and 12.

**Table 11. Medications Group 1**

| Exam | Group 1 Canaloplasty | | | | | |
|---|---|---|---|---|---|---|
| | A) phakic eyes | | | B) pseudophakic eyes | | |
| | Mean med* ± SD | n | *P-value* | Mean med ± SD | n | *P-value* |
| Baseline | 2.1 ± 0.8 | 45 | - | 1.8 ± 0.9 | 27 | - |
| 24 months | 0.5 ± 0.8 | 21 | $\leq 0.05$ | 0.4 ± 0.6 | 11 | $\leq 0.05$ |

* med: medication, n: number

**Table 12. Medications Group 2 and the Total**

| Exam | Group 2 Phacocanaloplasty | | | Total | | |
|---|---|---|---|---|---|---|
| | Mean med* ± SD | n | *P-value* | Mean med ± SD | n | *P-value* |
| Baseline | 2.5 ± 0.6 | 19 | - | 2.1 ± 0.8 | 91 | - |
| 24 months | 0.5 ± 0.9 | 8 | $\leq 0.05$ | 0.5 ± 0.7 | 40 | $\leq 0.05$ |

* med: medication, n: number

The number of antiglaucoma medications administered per day preoperatively ranged between a minimum of no substance to a maximum of 4 substances, 9% of eyes were provided with no medication, 29.6% with 1 medication, 28.5% with 2 medications, 38.4% with 3 medications and 3.2% with 4 medications. The number of antiglaucoma medications administered per day at 24 months postoperatively ranged from 0 to 2 medications, of which 65% of eyes received no medication, 17.5% one medication, and 17.5% two medications.

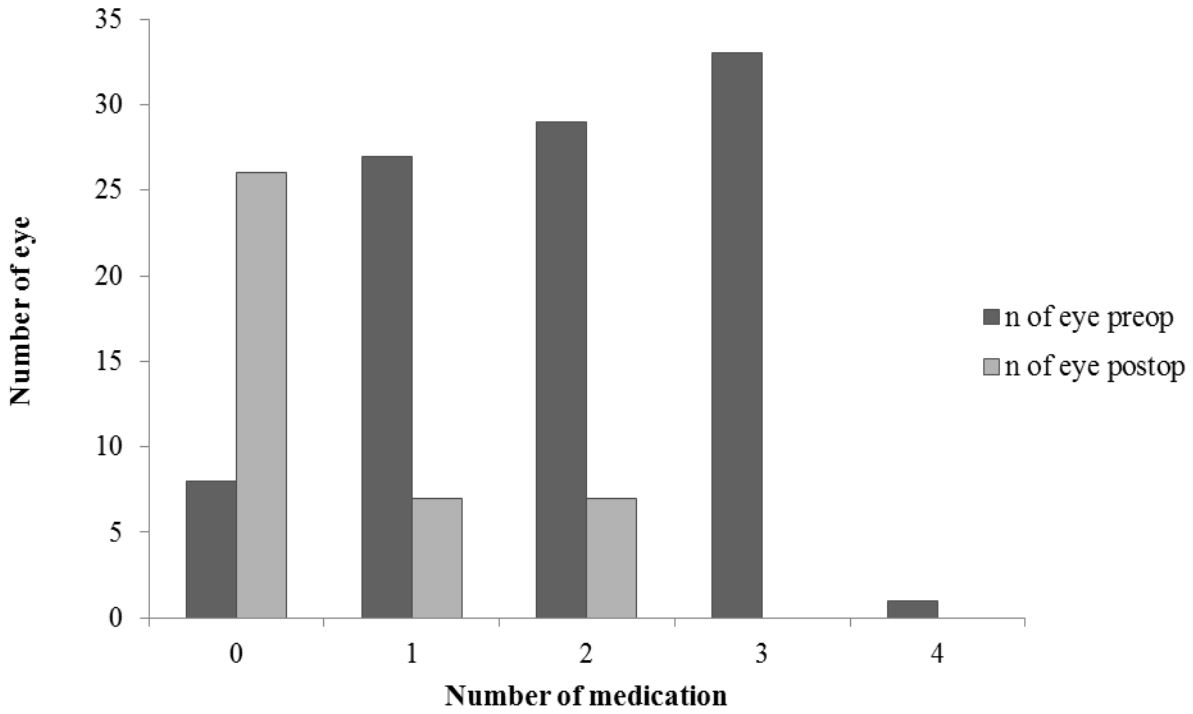



**Fig. 29.** Comparison of number of preoperative to postoperative medications.

## 6.5 Morphological manifestations after canaloplasty

Postoperative slit lamp evaluations of the eyes revealed a positive Seidel sign in 4 (4%) eyes. The cornea was transparent in 96 % of the eyes. Only 4 eyes (4%) had temporary descemet folds which were treated with eye drops, of these 4 eyes, 2 eyes were from Group 1A (canaloplasty on phakic eye), 1 eye in Group 1B (canaloplasty on pseudophakic eye), and 1 eye in Group 2, (phacocanaloplasty). There was no intracorneal hematoma, but one eye had a small corneal delle. All eyes had anterior chambers with normal depth; however, hyphema was found in 74% of eyes. Fortunately, this hyphema gradually resolved itself within a few days without further intervention and no recurrence. There were no suture extrusion, and 6 eyes had harmless fibrin exudate, most of which were from the phacocanaloplasty group.

In the iris, there was 1 eye with iris prolapse which occurred within 2 weeks postoperative and there were 6 eyes with previous laser peripheral iridotomy. No eye showed signs of endophthalmitis.

54 eyes had a posterior chamber intraocular lens (IOL), 20 of which had undergone phacocanaloplasty surgery (Group 2) and 34 eyes had already undergone a cataract operation before the canaloplasty operation (Group 1B). Additionally, of the latter group of 34 eyes previously mentioned, 3 eyes had an opening posterior capsule from a previous YAG capsulotomy. 46 eyes were with normal lens (Group 1A).

In the posterior part of the eyes, only one eye had a temporary choroidal peripheral effusion as postoperative complication, which subsided with topical treatment, otherwise there were retinal manifestations attributed to pre-existing/concomitant conditions, including preoperative diabetic retinopathy, retinal vein occlusion and age-related macular degeneration in some eyes.

The vast majority of patients tended to have a perfectly normal looking eye after a few weeks, without any ocular discomfort.

### 6.5.1 Bleb morphology

Postoperatively, the eye almost always had a slightly elevated diffuse filtering bleb which flattened within a week or two. From collected data of 56 eyes between 12-24 months postoperatively, there were 48 (85.7%) eyes with blebless, two eyes with relatively high filtering blebs, four eyes with relatively flat blebs and two with microcystic bleb. Figure 30 shows the postoperative blebless appearance.

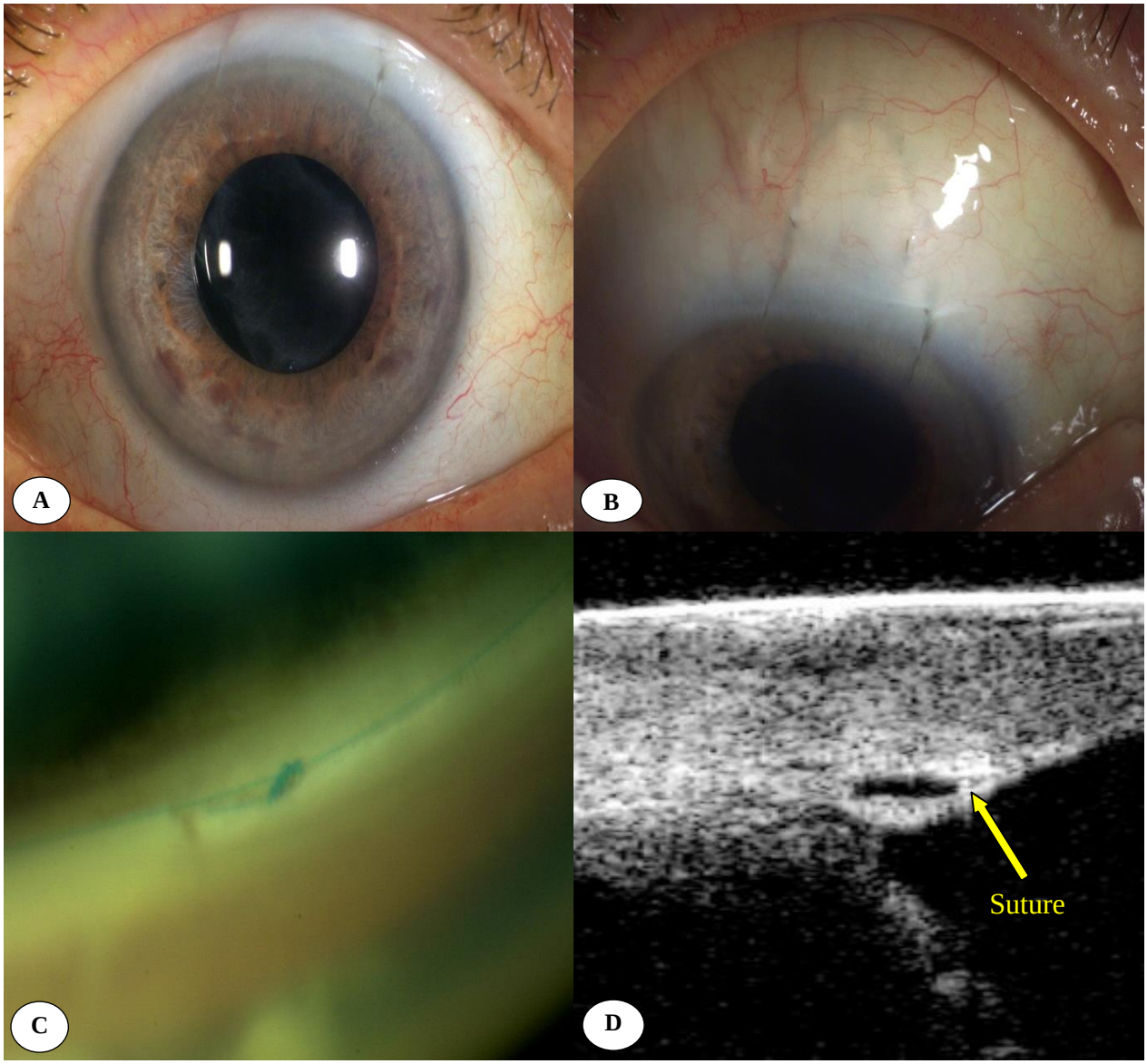



**Fig. 30.** Postoperative blebless appearance. **(A)** Eye postoperative, **(B)** Blebless appearance **(C)** Gonioscopy: suture in Schlemm´s canal, **(D)** Ultrasound biomicroscopic image of anterior chamber angle showing the enlarged Schlemm's canal and the prolene suture within the canal.

## 6.6 Ocular-related postsurgical complications

Overall, the frequency of postsurgical complications was low as illustrated in Table 13, most of them occurred in the early postoperative phase (≤ 90 days postoperatively) with few complications during the late phase (> 90 days post-operatively).

During the early postoperative period, microhyphema was observed in 52 eyes (52%), while gross hyphema only in 22 eyes (22%), no additional therapy to the standard postoperative therapy or anterior chamber lavage was necessary in these cases, as they all resolved in a few days. There was no hypotony-related flat anterior chamber. Six eyes (6%) had fibrin reaction in the anterior chamber, most of them in phacocanaloplasty group. This resulted in a transient IOP rises ≥ 21 mmHg; which resolved by a short course of glaucoma medical therapy in addition to anti-inflammatory medications. Two eyes (2%) had a spike elevation IOP ≥ 30 mmHg, one of these eyes with IOP 34 mmHg, treated with YAG iridotomy at 1 month postoperatively and one eye with IOP 47 mmHg, treated with iris reposition intervention in 2 weeks postoperatively. 17% of the eyes were considered as steroid responders, treated with non-steroid anti-inflammatory medications and not included as a complication of the surgery. One case (1%) of choroidal effusion was transient with no associated maculopathy and treated with steroid eye drops.

During the late postoperative period, 6% of the eyes had IOP elevation ≥ 21 mmHg. Of these eyes, only 2 eyes had a spiked elevation IOP ≥ 30 mmHg, one eye registered an IOP of 30 mmHg which was effectively treated by canaloplasty revision with mitomycin interventions and another eye with an IOP of 34 mmHg which was treated with neodymium:yttrium aluminum garnet (Nd:YAG) goniopuncture, after which the IOP immediately dropped to 10 mmHg. From 56 eyes, there were eight eyes (14%) with bleb, 2 of them with microcysts. There was no endophthalmitis, hypotony or related complications.

**Table 13. Adverse events postoperative**

| Complications | Group 1 Canaloplasty | | Group 2 Phacocanaloplasty | Total |
|---|---|---|---|---|
| | A) ph* eyes n (%) | B) ps eyes n (%) | n (%) | n (%) |
| **Early postoperative complications ( ≤ 90 days post-operative)** | | | | |
| Microhyphema (<1mm) | 20 (43) | 19 (56) | 13 (65) | 52 (52) |
| Macrohyphema (>1mm) | 12 (26) | 10 (29) | 0 (0) | 22 (22) |
| Fibrin reaction | 1 (2.1) | 1 (2.9) | 4 (20) | 6 (6) |
| Early elevated IOP (Not include steroid response IOP increase) | 1 (2.1) | 1 (2.9) | 0 (0) | 2 (2) |
| Choroidal effusion | 0 (0) | 1 (2.9) | 0 (0) | 1 (1) |
| Descemet membrane detachment with iris prolapse | 1 (2.1) | 0 (0) | 0 (0) | 1 (1) |
| **Late postoperative complications ( > 90 days post-operative)** | | | | |
| Blebs | 5 (10.8) | 2 (5.8) | 1 (5) | 8 (8) |
| Late elevated IOP | 2 (4.3) | 2 (5.8) | 2 (10) | 6 (6) |
| Cataracts | 4 (8.7) | 0 (0) | 0 (0) | 4 (4) |
| Endophthalmitis | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Hypotony (IOP ≤ 5 mmHg with shallow anterior chamber) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

* ph: phakic, ps: pseudophakic, n: number

## 6.7 Postoperative interventions

Table 14 shows 8 types of postoperative interventions in all groups. The most commonly performed procedures included cataract extraction on 8.7 % of eyes in Group 1A, canaloplasty revision on 3% of total eyes, one of them with MMC one year postoperatively, and cyclophotocoagulation on 2% of total eyes. Each of the other interventions was performed only on 1% of total eyes. YAG-goniopuncture was performed 1 year post surgery as a filtration through the TDM was insufficient at IOP >30 mmHg and directly thereafter the IOP dropped to 10 mmHg. One eye with uncontrolled IOP had received cyclophotocoagulation in 1 year and TE with MMC in >1 year by another surgeon in another hospital. Iris repositioning was performed after 2 weeks and after that revision and cataract surgery were performed in the same eye.

**Table 14. Postoperative interventions**

| **Type of surgery** | **Group 1 Canaloplasty** | | **Group 2 Phacocanaloplasty** | **Total** |
|---|---|---|---|---|
| | **A) phakic eyes** | **B) pseudophakic eyes** | | |
| | n* (%) | n (%) | n (%) | n (%) |
| Cataract surgery | 4 (8.7) | 0 (0) | 0 (0) | 4 (4) |
| Canaloplasty revision | 2 (4.3) | 0 (0) | 1 (5) | 3 (3) |
| Cyclophotocoagulation | 0 (0) | 1 (2.9) | 1 (5) | 2 (2) |
| YAG-Goniopuncture | 0 (0) | 0 (0) | 1 (5) | 1 (1) |
| YAG-Iridotomy | 0 (0) | 1 (2.9) | 0 (0) | 1 (1) |
| TE with MMC | 0 (0) | 1 (2.9) | 0 (0) | 1 (1) |
| Needling with 5 FU | 1 (2.1) | 0 (0) | 0 (0) | 1 (1) |
| Iris reposition | 1 (2.1) | 0 (0) | 0 (0) | 1 (1) |

* n: number, TE: trabeculectomy, MMC: mitomycin, FU: fluorouracil

# 7. **Discussion**

Although non-penetrating filtering surgery (NPFS) has a reported history of 40 years in the ophthalmic literature, the techniques only achieved popularity in recent years after the publication of studies demonstrating their safety and efficacy [81]. Canaloplasty is a non-penetrating surgical procedure that attempts to lower IOP with few surgical complications by restoring natural aqueous outflow pathways through a permanent enlargement of Schlemm's canal. In a previous study, a microcatheter was used to viscodilate discrete regions of Schlemm's canal distal from a surgical access site during non-penetrating glaucoma surgery. The results indicated a decrease of IOP and a trend toward increased IOP control with progressively greater lengths achieved in canal treated. In canaloplasty, a microcatheter was used to viscodilate the entire canal length and installs a trabecular tensioning suture [61]. Potentially, the suture tension may increase trabecular meshwork permeability, similar to the action of pilocarpine [82], helping to reduce the IOP postoperatively.

Combined surgery to treat both glaucoma and cataract is a good option and has historically been of interest; as the reduction in surgical trauma from two separate surgical procedures and the high incidence of cataract development after glaucoma surgery are factors supporting the application of a combined procedure in appropriate cases [83]. Typically, non-penetrating glaucoma surgical methods have a lower rate of postsurgical complications and this may complement the minimal complications and rapid visual recovery after clear corneal phacoemulsification and posterior chamber intraocular lens (IOL) implantation.

Of 100 eyes with canaloplasty operation in this study, nine eyes were without medications at the baseline and the other 91 eyes with mean medications of $2.1 \pm 0.8$. All patients with medications ceased using topical antiglaucoma medications two weeks before canaloplasty operation in order to reversal its effect on the conjunctiva and instead they were instructed to take oral medication. This preoperative regimen may be of clinical benefit in improving the success rate of the surgery as proved by Broadway et al. in their trabeculectomy study [84].

Because of the significant scarring ALTP causes to the trabecular meshwork, which prevents the full circumference dilation and suturing of Schlemm's channel, none of the 8 previously treated ALTP eyes had more than two ALTP.

## 7.1 Intraocular pressure

An achievement of target intraocular pressure, which is associated with a minimal likelihood of visual field or optic nerve lesion, is the goal of every efficient antiglaucoma therapy.

The preoperative intraocular pressure was almost always high and not safe for the eye, and the target intraocular pressure was not achieved despite maximal use of antiglaucoma medications and antiglaucoma laser and surgery therapy. The preoperative mean ± standard deviation IOP in Group 1A (canaloplasty on phakic eyes), Group 1B (canaloplasty on pseudophakic eyes), Group 2 (phacocanaloplasty) and the total eyes were 22.5 ± 5.1, 25.2 ± 7.4, 24.6 ± 8.8 and 23.8 ± 6.9 mmHg respectively, which are comparable with Lewis study (n=157) were 23.5 ± 4.5, 23.5 ± 5.2, 23.8 ± 5.0 mmHg in canaloplasty alone with suture placement, phacocanaloplasty with suture placement and all eyes, respectively [71].

In this study, the percentage of pressure reduction is influenced by the preoperative pressure level; patients with higher preoperative IOPs demonstrated the greatest reductions of 40.5% IOP postoperatively compared with a 26.6% reduction in eyes with lower preoperative IOPs. Schlemm's canal, which may be much narrowed in eyes with an increased IOP [85] would be restored and kept open by the suture stent. Furthermore, the pathological site of outflow resistance is directly targeted by canaloplasty [86].

In all groups and subgroups, the mean IOP on the first postoperative day in the study was significantly reduced to 0-10 mmHg.12 eyes with IOP ranging between 0 and 3 mmHg. There were no late hypotony or hypotonic maculopathy. Shaarawy et al. postulate that early hypotony without any perforation during the first postoperative days is an excellent indicator of good surgical dissection and a positive prognostic factor for long-term IOP reduction [87]. A progressive increase in IOP occurs in all patients in the next few days to reach up to 15 mmHg in 1 month. At 24 months, there is no difference in the mean IOP between the canaloplasty subgroups (i.e. between Group 1A canaloplasty on phakic and Group 1B canaloplasty on pseudophakic eyes which reported 14.4 and 14.7 mmHg, respectively); however, there is a difference to Group 2 phacocanaloplasty that scored an IOP of 12 mmHg. It is well established that cataract surgery alone produces a postoperative reduction in IOP that ranges from approximately 1 to 5 mmHg [69,88]. The mechanism of IOP reduction has been postulated to be associated with increased outflow facility due to tensioning of the trabecular meshwork, reduced aqueous production due to increased traction

on the ciliary body by the zonular fibers, or alterations in the blood-aqueous barrier [89]. Except for phacocanaloplasty group at 18 and 24 months due to the small number of eyes, the IOP was significantly decreased at all time intervals compared to baseline in all groups ($P \leq 0.05$). This is consistent with the other canaloplasty studies. The IOP reduction is significantly higher after canaloplasty combined with cataract surgery compared to IOP reduction after cataract surgery combined with other forms of glaucoma surgery [68]. Arthur et al. confirmed that combining canaloplasty with phacoemulsification achieves IOP lowering with fewer medications and increasing the complete success rate for IOP-lowering effect without medication compared with phacoemulsification alone [90]. However, it is important to note here that the small number of eyes examined after 12 months restricted the evaluation. The mean IOP decreased from baseline by 51% in the combined group, 36% in canaloplasty on phakic and 42% in canaloplasty on pseudophakic eyes and 40% of the total eyes at 24 months. Bull et al. reported a prospective three-year canaloplasty outcome in which 109 eyes of consecutive 109 patients were enrolled, the mean IOP dropped by 43% in phacocanaloplasty group, and by 34% in canaloplasty group at 3 years [91]. Lewis et al. reported the mean decreased of IOP from baseline at 12, 24 and 36 months in 3 different studies, the mean IOP decreased by 46% from baseline in the combined group and by 33% in the canaloplasty group at 12 months in the 1-year study [62], 42% from baseline in the combined group and by 30% in the canaloplasty group and 32% from total eyes at 24 months in 2-year study [63] and 42.1% from baseline in the combined group and 34% in the canaloplasty group and 36% from total eyes at 36 months in the 3-year study [71]. Vold S.D. reported the mean IOP decreased by 22% in the combined group, 26% in the canaloplasty group and 23.3% from total eyes at 24 months in the 2-year study [92]. Shingleton et al. reported the mean IOP decreased by 44% from baseline in phacocanaloplasty at 12 months [68].

There is no doubt that the previous (before canaloplasty) glaucoma surgeries were done in eyes with relatively long history of glaucoma. In this study, there were 14 (16 previous glaucoma surgery) eyes. Although in both groups (the group of canaloplasty with previous glaucoma surgery and the group without), there was a statistically significant clinical postoperative IOP decrease in the mean IOP over time in relation to preoperative ($P \leq 0.05$), the mean IOP at the baseline and 24 months in eyes with previous glaucoma surgeries was higher than in those eyes without. Moreover, the IOP reduction postoperatively of 35% was lower than the postoperative reduction of 41% in eyes without previous glaucoma surgeries. The reasons for that could be a scarring in the trabecular

meshwork caused by ALTP (8%), relatively narrow anterior chamber angle in eyes with previous laser iridotomy (6%), re-collapse of the canal and the closures of the ostia of the collector channels in eye with CPC (1%) and viscocanalostomy (1%), which have been found to be among the main causes for failure in viscocanalostomy [8]. Additionally, success of canaloplasty may be limited if aqueous outflow channels distal to the canal are collapsed or scarred [93].

Early and transient hyphema is a common finding after canaloplasty. In the present study, 74% of total eyes with hyphema (Group 1) and 26% without hyphema (Group 2) at 1 day postoperatively. There was a statistically clinical significant IOP reduction (*P =0.011)* between both groups at 1-day postoperatively, where a mean ± standard deviation IOP was 9.0 ± 6.3 mmHg in 69 eyes with hyphema and a mean ± standard deviation IOP was 13.5 ± 6.5 mmHg in 22 eyes without. There were no clinical statistically significant difference between patients with versus without hyphema (*P =0.783* ) in regard to IOP at 24 months, where a mean ± standard deviation IOP was 14.5 ± 4.1 mmHg in eyes with hyphema and a mean ± standard deviation IOP was 14.0 ± 4.2 mmHg in eyes without. In contradiction the study by Grieshaber M.C et al., where the mean IOP was not significantly lower in eyes with 8.1 mmHg than without 9.4 mmHg hyphema 1-day postoperative IOP. The reason for this difference could be due to different study population and different surgeon. It is currently understood that hyphema is produced by early postoperative hypotony with inherent reversal of the pressure gradient between episcleral venous pressure and IOP. However, hyphema is not merely a sign of low IOP after canaloplasty [94]. In this study there were 5 eyes with a low IOP < 8 mmHg that did not have hyphema. Finally, hyphema may indicate an adequate tension and viscodilation of the inner wall of Schlemm's canal.

The preoperative IOP in primary glaucoma was 23.3 mmHg; decreased to 14.9 mmHg, which represents a 36% reduction from the baseline IOP, secondary glaucoma was 26.3 mmHg, decreased to 13 mmHg, which represents a 50% reduction from the baseline IOP at 24 months. This difference may be related to more medications being used postoperatively of secondary glaucoma 18% than of primary glaucoma 13%.

In the present study there were 50 right eyes and 50 left eyes, we found there was no statistically significant clinical difference in the mean IOP over time between them (*P =0.88)***;** we concluded that the canaloplasty surgery had the same efficacy in both right and left eyes.

We also studied the effect of age and gender on IOP reduction postoperatively in canaloplasty surgery, there were no statistically clinical significant effect of the patient age (*P =0.52*) or gender,

(*P =0.74*) on IOP reduction postoperatively. Similar results were reported by Grieshaber et al. study [86].

For defining the success, the European Glaucoma Society in their "Terminology & Guidelines for Glaucoma, 2nd Ed 2003" state: "There is no single IOP level that is safe for every patient. However, it is generally assumed in glaucoma that aiming to achieve at least a 20% reduction from the initial pressure at which damage occurred, or in advanced glaucoma to lower the IOP to a level below 18 mm Hg at all visits is a useful way to achieve the initial target IOP [95].″ Using the criteria of success as ≤ 21 mmHg with or without medications in the present study, canaloplasty achieved a success rate of 96% and phacocanaloplasty 100% at 18 months. The success rate is the same as that reported by the Bull et al. study, where the qualified success rate of ≤ 21 mmHg with one or two medications was 98.6% in canaloplasty and 100% in phacocanaloplasty at 36 months [91] and higher than that reported by the Lewis et al. study, where the qualified success rate was 77.5% in canaloplasty, 88.9% in phacocanaloplasty at 36 months [71] and the Grieshaber et al. study where the qualified success rate was 81.6% at 36 months in a prospective study of 60 consecutive black African patients with POAG who underwent canaloplasty [86].

One of 28 eyes of canaloplasty groups at 18 months failed to achieve the success criteria and was considered a failure; this may be due to a previous ALTP that the patient had received. Canaloplasty is ideal for patients with uncontrollable IOP that have not undergone other procedures.

In this study, there was no significant difference in the cumulative failure rate between all surgical groups of canaloplasty as found by chi-square approximations for log-rank and Wilcoxon tests (*P =0.491)*. This was comparable with the findings of the Bull et al. study, where *P <0.27* [91] and not comparable with those reported in the study by Lewis et al., where *P <0.03* [71].

The postoperative IOP may be determined by the limitation of canaloplasty in its ability to lower IOP by the resistance of the distal outflow system and by the pressure of the episcleral vasculature. This may explain why IOP levels below 12 mmHg are less likely to be attained even after successful canaloplasty, in contrast to penetrating glaucoma surgery with external filtration [62,68,86].

Tables 15 and 16 show the comparisons of this study with other canaloplasty studies. Although it is difficult to compare absolute postoperative IOP levels in different studies that may have different

patient populations and study methods, it is important to note that the IOP reduction is ≥ 30% and it is relatively favorably after combined canaloplasty and cataract surgery rather than canaloplasty alone in all represented studies.

**Table 15. Canaloplasty alone**

| Autor | Year | N* of eyes | Follow up (month) | Main preop. IOP mmHg | Main postop. IOP mmHg | Red % |
|---|---|---|---|---|---|---|
| This study | - | 80 | 24 | 23.7 | 14.5 | 39 |
| Lews et al. [62] | 2007 | 74 | 12 | 24.1 | 16.2 | 33 |
| Lews et al. [63] | 2009 | 84 | 24 | 23.2 | 16.3 | 30 |
| Lews et al. [71] | 2011 | 103 | 36 | 23.5 | 15.5 | 34 |
| Grieshaber et al. [86] | 2010 | 60 | 36 | 45.0 | 13.3 | - |
| Grieshaber et al. [96] | 2011 | 32 | 18 | 27.3 | 13.1 | - |
| Bull et al. [91] | 2011 | 82 | 36 | 23.0 | 15.1 | 34 |
| Matthaei et al. [97] | 2011 | 33 | 12 | 18.5 | 12.4 | 33 |
| Ayyala, et al. [98] | 2011 | 33 | 12 | 19.3 | 13.3 | 32 |
| Koerber et al. [99] | 2012 | 15 | 18 | 26.5 | 14.5 | 44 |
| Klink, et al. [100] | 2012 | 20 | 9 | 22.1 | 13.3 | 40 |
| Brüggemann et al. [101] | 2013 | 15 | 12 | 26.7 | 13.2 | 50 |
| Brusini [102] | 2014 | 214 | 42 | 29.4 | 17.0 | 42 |

* N: Number, Red: Reduction

**Table 16. Combined canaloplasty with phacoemulsification**

| Autor | Year | N* of eyes | Follow up (month) | Main preop. IOP mmHg | Main postop. IOP mmHg | Red % |
|---|---|---|---|---|---|---|
| This study | - | 20 | 24 | 24.6 | 12.0 | 51 |
| Lews et al. [62] | 2007 | 13 | 12 | 23.5 | 12.8 | 46 |
| Lews et al. [71] | 2011 | 54 | 36 | 23.5 | 13.6 | 42 |
| Shingleton et al. [68] | 2008 | 54 | 12 | 24.4 | 13.7 | 44 |
| Bull et al. [91] | 2011 | 16 | 36 | 24.3 | 13.8 | 43 |
| Matthaei et al. [97] | 2011 | 13 | 12 | 17.5 | 12.8 | 27 |

* N: Number, Red: Reduction

## 7.2 Vision

Visual acuity was temporally decreased postoperatively. First, due to an IOP decrease, this was increase progressively in the first few days. Second cause of generally temporary fluctuations in vision is surgically induced astigmatism from the suture used to close the surgical incision, this almost always resolved in a few weeks. In the present study, the mean cylinder ± SD corneal astigmatism in canaloplasty and phacocanaloplasty at the base line was 0.9 ± 0.6 D and 1.2 ± 0.7 D, respectively, which increased to 3.3 ± 1.9 D and 3.2 ± 1.3 D in the first 1-2 weeks postoperatively, respectively, and gradually decreased to its preoperative value of 1.1 ± 0.8 D and 0.8 ± 0.2 D in the 5-12 weeks, respectively, once the eye is fully healed, then it remained stable over time. Similar results were reported in a study by Moelle et al., who studied the time course of induced astigmatism after canaloplasty, where the mean astigmatism preoperatively was 0.77 ± 0.5 D, which increased to 3.3 ± 1.7 D at 2 weeks postoperatively. Thereafter, the astigmatism underwent a spontaneous decline, reaching 1.9 ± 0.8 D at 4 weeks and 1.2 ± 0.74 D at 12 weeks postoperatively [103]. A transient decrease in visual acuity due to an induce with-the-rule astigmatism in the first 2 weeks was reported also in Brusini study [64].

The outcome of visual acuity in this study was not affected by canaloplasty surgery, similar results were reported by Lewis et al. in a 1, 2, 3 year canaloplasty studies [62,63,71], and by Bull and co-authors in a three year canaloplasty study [91]. This phenomenon may be explained by avoiding perforation in to the anterior chamber, which does not lead to inflammation, use of mydriatics, or hypotony-related complications. Furthermore, because no surgery-related cataracts developed after canaloplasty, visual acuity remained stable. The visual acuity of 7 (9%) eyes in Group 1 were with a history of other ocular disease that may affect the visual acuity, from them two eyes with history of macular epiretinal membrane, two eyes with age-related macular degeneration, one eye had branch retinal vein occlusion, one eye with suspected ischemic ophthalmopathy and one eye amblyopic.

In this study, the mean LogMAR BCVA ± SD in phacocanaloplasty group improved from a baseline of 0.20 ± 0.1 to 0.06 ± 0.1 at 24 months, this is similar to study by Shingleton et al. who reported in their one-year prospective investigation of canaloplasty combined with cataract surgery results of 54 eyes of 54 patients a mean improvement in BCVA at 12 months [68]. This is also

consistent with a study by Vold S D. that reported an improvement in visual acuity after phacocanaloplasty in compare to canaloplasty alone surgery at 24 months postoperatively [92].

## 7.3 Medication

The most common approach to treat glaucoma is to begin with medical treatment, taking into account the patient's risk factors, medical history, allergies, drug efficacy and experience with previous glaucoma medications. The antiglaucoma medications were used as topical eye drops in single use or combination. In this study, the most commonly used drugs were prostaglandin analogs, which are the most potent currently available medical treatment. They were administered topically once daily in the evening (46 eyes as single eye drop and 19 eyes combined with other medications). The international glaucoma society has widely supported the use of prostaglandin analogs as the most effective first-line IOP-lowering class of drugs in developed countries [104]. The second most commonly used medications was β blocker (10 eyes as single medication and 40 in combination with other medications), less common carbonic anhydrase inhibitors (26 eyes as single medication and 15 in combination with other medications), alpha-selective agonists (17 eyes as single medication and 6 as combined with other medications) and cholinergic drugs (3 eyes as single medication). Medications containing a combination of drugs were used in 40% of the eyes.

Preoperatively, 38% of the eyes on three medications, while at 24 months postoperatively 65% of the eyes with no medication and the remaining 35% were used one or two medications, no patient remained on glaucoma medical therapy of more than 2 medications.

This study provides further evidence that the use of medications significantly decreased in glaucoma patients after canaloplasty surgery. At 24 months, the mean reduction in medication from the baseline was 80% in phacocanaloplasty group, 77.7% in canaloplasty on pseudophakic eyes, 76.1% in canaloplasty on phakic eyes and 76.1% in total eyes. In Lewis canaloplasty studies, the mean reduction in medication at 24 months from the baseline was 88% in phacocanaloplasty group, 70% in canaloplasty alone group in one study [63] and 80% in phacocanaloplasty group, 52.6% in canaloplasty alone group and 55.5% in total eyes in another study [71]. In the Bull et al. study, the mean reduction in medications at 36 months from the baseline was 66.6% in phacocanaloplasty eyes and 52.6% in canaloplasty alone [91]. This study, with those studies by Bull and Lewis confirm that the combined surgery decreased the use of medication postoperatively more than canaloplasty surgery alone.

## 7.4 Morphological manifestations after canaloplasty and complications

There is agreement among published reports that non-penetrating glaucoma surgery (NPGS) offers a lower rate of complications compared with conventional trabeculectomy.

Most of the eyes were with favorable morphological findings postoperatively. Seidel sign was positive only in 4 (4%) eyes directly postoperatively, these were transient and disappeared with reduction of steroid eye drops; this was less than reported by Matthaei et al., were Seidel sign was positive in 26.1% [97].

It is worth noting that with trabeculectomy, the formation of a stable bleb is necessary for success, while with canaloplasty, it is considered to be an undesirable outcome, or "risk". A "high bleb" can cause (or may exacerbate) tear dysfunctional syndrome resulting in chronic irritation, tearing, and blurred vision. Because the wall of the bleb is so thin, any trauma to the eye can rupture it. With canaloplasty, no fistulas are created and without a bleb, there is no worsening of tear dysfunctional syndrome or risk of blebitis. Late complications in the present study were infrequent, because success in controlling IOP in canaloplasty is not dependent on bleb formation, in most cases (85.7%); no bleb was found postoperatively, only two eyes with relatively high filtering blebs, four eyes with relatively flat and two eyes with microcystic blebs. One relatively high filtering bleb occurred after a canaloplasty revision with mitomycin, one after trabeculectomy with mitomycin. Importantly, no filtering bleb-associated problems like blebitis or dysesthesia were observed. Grieshaber et al. reported a very shallow diffuse bleb without microcysts in four eyes from a total of 32 eyes in a prospective study over 18 months [96]. Bull et al. reported no blebs were present at 3 years, and there were no reports of postoperative complications related to blebs [91].

In one case, the lid cannot spread tears over the adjacent cornea due to an encapsulated bleb resulting in a self-limited delle, which was treated with ointment, frequent tear replacement eye drop and non-steroidal anti-inflammatory drop applications.

In the present study, there was no postoperative intracorneal hematoma, while it was reported as a very rare complication by the Gismondi and Rosseti studies, where it affected individual patients who were 45 and 71 years old respectively, as a result of excessive amount of high-molecular weight viscoelastic injection that may have resulted in a limited and temporary hemorrhagic detachment of Descemet's membrane and could be removed by partial thickness paracentesis [105,106].

As a result of IOP decrease to less than episcleral venous pressure, it is not uncommon following canaloplasty to observe a small amount of blood in the anterior chamber due to blood reflux into Schlemm's canal which filters through the surgically enlarged canal and trabeculo-descemetic window [94]; this blood reflux indicates that the outflow pathway distal to the Schlemm's canal was patent and that the trabecular meshwork was permeable to red blood cells [96]. Microhyphema is defined as a small hyphema characterized by suspended red blood cells in the anterior chamber without the formation of a layered clot. In present study, microhyphema, decreased visual acuity and hypotony were the most common early transient complications, gross hyphema was less common. Of the total eyes, which underwent canaloplasty, the incidence of hyphema (including microhyphema 52% and macrohyphema 22%) was 74%, higher than that reported by other canaloplasty studies; Bull et al. reported 12.8% [91]. Lewis et al. reported a 3.2%, 7.9%, and 12.1% in 3 different studies [62,63,71]. Shingleton reported 28% [68], while Koch et al. reported that anterior chamber hemorrhage with hyphema was found in 15 of 21 eyes (71.4%) on day 1 after canaloplasty, and the eyes without hyphema showed higher IOP than those with hyphema [107]. Furthermore, the microhyphema was 85.1% of the eyes in Grieshaber's prospective non-randomized study that was carried out to assess the risk factors for failure in canaloplasty. Grieshaber also reported that the absence of microhyphema after uneventful canaloplasty seems to be a poor prognostic factor in relation to IOP reduction and these eyes required more frequent and earlier Nd: YAG laser goniopuncture after surgery [94].

In the present study, there was anterior chamber inflammation of short duration and mild intensity after phacocanaloplasty compared to canaloplasty, which results in fibrin exudate. From the total of 100 eyes, 6% were with fibrin exudate postoperatively, 4 of these eyes underwent canaloplasty combined with cataract surgery and were treated with short course of steroid eye drops; this may be due to irrigation-aspiration and penetration of anterior chamber.

Two eyes (2%) had an early postoperative (≤ 90 days) spiked elevation IOP ≥30 mmHg. In one eye, this was due to a relatively narrowed angle with an IOP of 34 mmHg and treated with YAG iridotomy at 1 month postoperatively and the other eye with an IOP of 47 mmHg due to iris prolapse (1%), which could be a result of a descemet membrane tear by suddenly increased body's pressure postoperatively, this case was treated with iris repositioning after 2 weeks, as a conversion to a fully penetrating procedure was not required. The incidence of Descemet's membrane perforations was suggested to be an indicator of an individual surgeon's experience in non-

penetrating techniques [108]. In this study, Descemet's membrane perforations did not appear to be related to a learning curve effect, as the surgeon was experienced in non-penetrating glaucoma surgery and the perforation occurred 2 weeks postoperatively. In this study, this complication is less than that reported in other studies such as that by Bull et al. 3.4% [91], Grieshaber et al. 3.3% [94], Shingleton et al. 1.9% [68] and Lewis et al. 1.1%, 1.6%, 3.2% in years 2007, 2009, and 2011 respectively [62,63,71].

Intraocular lens (IOL) in posterior chamber in 54 eyes, 20 of them in phacocanaloplasty operation and 34 eyes were already pseudophakic before the canaloplasty operation and 46 eyes with normal lens. Removal of the crystalline lens could potentially improve outflow by further increasing trabecular meshwork tensioning in conjunction with canaloplasty. Other studies investigating non-penetrating glaucoma surgery in combination with phacoemulsification cataract surgery are supportive of this combined beneficial effect [91].

One case (1%) of the eyes with choroidal effusion was transient and associated with normal depth anterior chamber. Matthaei et al. reported that 7.7% of the eyes had Fibrin reaction and choroidal effusion in 4.3% [97].

Other late complications include elevated IOP of ≥ 21 mmHg (6% of eyes), of them only 2 eyes with IOP spike ≥ 30 mmHg, one eye due to insufficient infiltration through trabeculo-descemtic window and treated with neodymium:yttrium aluminum garnet (Nd:YAG) goniopuncture, the IOP was immediately reduced from 34 to 10 mmHg. Studies reporting a high rate of goniopuncture achieved lower mean IOP than studies that had a low rate of goniopuncture [109]. The other eye was treated with canaloplasty revision with mitomycin.

Compared to a 3 year-study by Lewis et al. [71], where 12.7% of patients had cataract progression, in this study, only 4% of phakic eyes developed cataract after more than 1 year postoperatively, this was not related to canaloplasty, it occurred as age-related progression.

In this study, there were no visually serious complications such as chronic hypotony (leading to hypotony maculopathy), malignant glaucoma, retinal detachment, corneal complications (corneal decompensation, corneal graft failure), endophthalmitis or phthisis bulbi. In general, this study confirms the findings of other canaloplasty studies [62,63,68,71,91] and studies of non-penetrating glaucoma surgery of deep sclerectomy and viscocanalostomy [110-112] in that the canaloplasty procedure appears to present with a low rate of surgical complication.

## 7.5 Postoperative intervention

Postoperative intervention is defined as any procedure or process undertaken following surgery with the goal of enhancing the success of the surgical outcome [113]. Because canaloplasty is a blebless procedure, the immediate postoperative care does not necessitate bleb manipulation such as massage or suture release to enhance flow, which is often required after trabeculectomy [114].

The most common postoperative intervention was cataract surgery (8.7% of phakic eye). All eyes in our sample underwent cataract extraction during the 3-year postoperative period. The study found that cataract was due to age progression and not related to canaloplasty surgery. This is less than the 19.1% of the phakic eyes reported in the 3-year study by Bull et al. [91].

Mitomycin C with its powerful antiproliferative properties, improves the success of ocular surgeries, it was administered only in 3 cases of canaloplasty revision surgery to manage refractory increased IOP due to conjunctival or subconjunctival fibrosis postoperatively.

In comparing with other studies such as Matthaei et al. [97] and Vold S.D. [92] where neodymium:yttrium aluminum garnet (Nd:YAG) goniopuncture was done in 21.7% and 3.6% respectively, in present study, only one case (1%) was treated with YAG-goniopuncture for scarring of the trabeculo-descemtic window (TDW). Goniopuncture was performed using the free running Q-switch mode with energy of 5.6 mJ. Laser shots were aimed at the TDM to create a small hole in the TDM, thereby achieving adequate pressure lowering and allowing a direct passage of aqueous humor from the anterior chamber to the intrascleral space at an average time of 12 months after surgery. Intraocular pressure was decreased immediately after goniopuncture from 34 to 10 mmHg. By opening the trabeculo-descemet membrane, goniopuncture converts a non-perforating filtration procedure into a microperforating one. Laser goniopuncture in the postoperative course was not considered a failure, as it is so integral to success in up to 60% of the cases in non-penetrating glaucoma surgery (NPGS) [109].

An encapsulated bleb through a fibroblastic overgrowth as a continuation of the acute wound-healing process was formed in one eye in the first 4 weeks postoperatively; it was managed with 2 administrations of sub-conjunctival 5-Fluorouracil (5-FU) as antifibrotic factor with 4 weeks between them, the bleb was relatively flat after that.

Only one case of cyclophotocoagulation (CPC) was done postoperatively due to increased IOP as a result of ischemic changes by ischemic neuropathy diseases, the other CPC with trabeculectomy surgery was done by another surgeon.

Fortunately, the rate of postoperative surgical intervention remained low following canaloplasty procedure.

## 7.6 Comparison with other nonpenetrating glaucoma surgical procedures

### 7.6.1 Viscocanalostomy

Viscocanalostomy, according to Stegmann and co-authors, relies on creating a scleral reservoir, where the inner deep scleral lamella has been resected. From there, drainage may occur in to the canal, in which cut ostia are created to maintain their patency after dilation and plugged with a high-molecular-weight viscoelastic substance [58].

The mean preoperative IOP level in most viscocanalostomy studies ranged between 24 and 36 mmHg, this difference may be due to differing patient populations and groups, in the Stegmann study, none of their patients was on topical medication before surgery; this resulted in a higher mean preoperative IOP. In the present study, a hypotony during the first postoperative week are similar to those found in viscocanalostomy studies [58,115,116]. The percentage of pressure reduction is influenced by the preoperative pressure; the same finding was reported in the viscocanalostomy study by Drüsedau and co-authors [117]. The late IOP spikes in this study were found in 2 eyes are similar to results of Jonescu-Cuypers and co-authors [118] that found IOP spikes with viscocanalostomy, where 3 eyes required repeat surgery (two trabeculectomies with mitomycin and one sclerectomy with basal iridectomy) to control the IOP spikes. Steroid response IOP spiked in this study to 17%, which was comparable with that reported by Wishart and coauthors [81] 18% of a steroid response IOP spikes and treated by reducing the steroid regimen.

In the present study, the IOP reduction and success rate of canaloplasty surgery is higher than that reported in viscocanalostomy study by Sunaric-Megevand and co-authors, but with similarly low complication rates. Furthermore in the present study, the mean IOP reduction of the total eyes was 40% at 24 months and the success rate was 96% in canaloplasty (target IOP $\leq$ 21 mmHg) at 18 months, where in the study by Sunaric-Megevand and co-authors [116], the mean IOP dropped by 39.3% and the overall success rate was 88% at 1 year, 90% at 2 years, and 88% at 3 years. This comparison is similar to other studies, which reported a higher efficacy of canaloplasty surgery in

reducing the IOP, but with similar complication rates as those of viscocanalostomy surgery. In 3-year study of canaloplasty, a critical evaluation of and comparison with viscocanalostomy were performed, in which 97 eyes underwent canaloplasty, showing a mean lowering of IOP from 27 to 14 mmHg (a mean reduction of 48%), 120 eyes underwent viscocanalostomy, showing a mean lowering of IOP from 25 to 16 mmHg (a mean reduction of 36%). The study concluded that canaloplasty produced significantly better results than viscocanalostomy, but was associated with similar low complication rates [119]. Koerber found in a comparative study of 30 eyes of 15 adult patients with bilateral primary open-angle glaucoma who had undergone a canaloplasty on one eye and a viscocanalostomy on the contralateral eye that canaloplasty procedures showed superior efficacy to viscocanalostomy in the reduction of IOP and both procedures demonstrated excellent safety profiles [99].

Studies of combination phacoemulsification and PC IOL implantation with viscocanalostomy show IOP results similar to those with viscocanalostomy alone [81]. This was not consistent with the present study, where phacocanaloplasty surgery proves to be more effective than canaloplasty alone.

Most published data suggest that viscocanalostomy is effective but tends to yield final IOPs in the mid or high teens [112].

### 7.6.2 Deep sclerectomy

#### 7.6.2.1 Deep sclerectomy without an implant

The surgical procedure of deep sclerectomy without the use of intrascleral implants has been studied by several authors. Although deep sclerectomy maintains good IOP control in the early postoperative phase, studies show that without adjunctive therapies a large number of deep sclerectomies fail in the long term. For example, in the study of Khairy et al., which looked at a prospective series of 43 patients undergoing deep sclerectomy without implant or antimetabolite, it was found that the success rate (determined when IOP is less than 22 mmHg without medication) at 12, 24 and 30 months was at 61.4, 36.6, and 18.9%, respectively [120]. Additionally, other prospective studies [110,121] did not find a significant difference between deep sclerectomy alone and phaco-deep sclerectomy with regard to the postoperative decreases in the mean IOP and in the mean number of glaucoma medications at the end of a two-year follow-up period. Rekas et al. [122] reported in a prospective, randomised study of phacocanaloplasty versus phaco-non-

penetrating deep sclerectomy a similar safety and efficacy profile for both procedures, but patients with phacocanaloplasty required no postoperative management, which means that a hypotensive effect was achieved solely with surgery, whereas in phaco-deep sclerectomy, the mean IOP was reached with the help of additional postoperative interventions in about half of the cases.

#### 7.6.2.2 Deep sclerectomy with an implant

Secondary collapse of scleral flap can be avoided by placing a space-maintaining implant in a surgically created scleral bed. This can be seen in studies such as the non-randomised prospective study of 100 eyes that found an IOP reduction of 53.2%. Furthermore, a total success rate of 44.6% (defined as IOP less than 21 mm Hg without medication) and the qualified success rate of 97.7% (defined as IOP less than 21 mm Hg with medication) were found at 36 months [123]. Other examples include the long-term results reported by Shaarawy et al. where the mean preoperative IOP was recorded at 26.8 mmHg and 12.24 mmHg at 48 months with a reduction of 55.4%. At 60 months, and the qualified success rate was recorded at 94.8%. All patients had a shallow diffuse subconjunctival bleb, and subconjunctival five-fluorouracil (5-FU) injections were required in 23.8% [74] Another study by Shaarawy and Mermoud comparing deep sclerectomy in one eye and deep sclerectomy with collagen implant in the other eye found complete success at 48 months in 38.5% of deep sclerectomy eyes and 69.2% of eyes after deep sclerectomy with implant [56]. Bissig et al. report 10-year postoperative outcomes after deep sclerectomy with implant in 105 eyes and found 44.6% complete success and 77.6% qualified success (defined as IOP $\leq$ 21 mmHg with glaucoma medications) with laser goniopuncture in 59.8% of patients. Here, subconjunctival five-fluorouracil (5-FU) injections were required in 24.5% of cases to treat bleb fibrosis or encapsulation [124].

## 7.7 Comparison with penetrating glaucoma surgery (Trabeculectomy)

For many decades, trabeculectomy was viewed as the gold standard glaucoma surgery and one of the most provocative questions regarding non-penetrating surgery is how well it fared compared to trabeculectomy, which all other glaucoma procedures are tested against.

The canaloplasty efficacy results are comparable to published reports of trabeculectomy 2 years postoperatively. Comparative studies of trabeculectomy [125-127] report a mean IOP after 2 years that is within the range of 10.1 to 16.9 mmHg and a mean medication usage in the range of 0.1-1.2 medications. The lowest IOP and medication results were usually associated with the use of adjunctive antimetabolites and careful postoperative management of the eye [128,114]. Additionally, in the study by Matlach et al., which consisted of a randomized clinical study that compared trabeculectomy and canaloplasty, the findings show that less medication were used and a higher IOP reduction in trabeculectomy was recorded 48% compared to canaloplasty 39% at 24 months at the cost of a higher rate of complications [129].

Combined trabeculectomy and cataract surgery has been extensively studied. Some comparative studies of phacotrabeculectomy and trabeculectomy found greater IOP reduction with the non-combined procedure [130,131]. In contrast, this study shows a trend toward greater IOP reduction when combined with phacoemulsification cataract surgery. In a comparison study between phacotrabeculectomy and phacocanaloplasty, Matlach et al. reported no statistically significant difference in IOP reduction between the two groups and they considered that phacocanaloplasty offers a new alternative to phacotrabeculectomy for the treatment of glaucoma concomitant with cataract [132].

The safety profile of canaloplasty continues to be preferable to trabeculectomy. In the present study, the earliest complication includes a 74% hyphema. In canaloplasty surgery, it is commonly to observe a hyphema in the anterior chamber, which is considered as a positive sign. In comparison, the incidence of hyphema following a trabeculectomy is reported in the range of 8% to 42% and hypotony in the range of 4% to 42% [112,127,133]. Choroidal detachment subsequent to a trabeculectomy has been reported in the range of 1% to 29% [112,127,128].

Although canaloplasty is designed as a blebless procedure, there were 8 eyes complicated with bleb formation as late complications, two of them were formed after postoperative intervention (canaloplasty revision with mitomycin, trabeculectomy with mitomycin), and however there was no

potential risk for postoperative infection and no bleb-related problems. In contrast, blebitis is a well-known and potentially dangerous infection after trabeculectomy that can lead to endophthalmitis [134]. Bleb formation after trabeculectomy frequently requires treatment or surgical revision to maintain or restore function. Taube et al. [114] reported that the average number of follow-up visits during the first postoperative year was 14.1 per patient (SD 3.1, range 8-19) with 93% of patients requiring bleb manipulations to enhance flow, such as massage, needling, laser suture lysis, subconjunctival injections of anti-metabolites. King et al. [113] examined the type and frequency of postoperative bleb manipulations after trabeculectomy with intraoperative MMC and found that 93 of 119 (78.2%) trabeculectomies were followed by some form of bleb manipulation, with the first intervention occurring after a median period of 5 days.

In the 2-year follow-up period of this canaloplasty study, 4% experienced cataract progression; which can be described as an age-related cataract. Cataract progression after canaloplasty is still less frequent than after trabeculectomy, which has been reported to increase the risk of cataract formation by 78% [95]. Daugeliene et al. [135] found that slight cataractous changes develop after trabeculectomy with mitomycin C as early as 1 month postoperatively and gradually increase in extent and intensity during the next 11 months. Bindlish et al. [128] reported that 55.3% of patients in their study underwent subsequent cataract surgery over 5 years of follow-up post trabeculectomy. Adelman et al. [136] reported a cataract extraction rate of 24% after initial trabeculectomy, with an average time to postoperative cataract of 26 months in a study comprised of patients with a mean age of 43.7 years.

In this study, visual acuity was not affected after canaloplasty alone and increased in canaloplasty combined with cataract. In contrast, loss of visual acuity is an important complication of trabeculectomy and is likely to increase with longer follow-up as reported by Edmunds et al. [137].

Traditionally, safety concerns have often posed a barrier to earlier incisional glaucoma surgery, particularly in regard to the potential vision-threatening complications associated with trabeculectomy. However, the distal collector system may have a better chance of survival if intervention is undertaken earlier in the disease process, before the outflow system collapses or before chronic topical medication negatively impacts the tissues [138].

The excellent safety profile of canaloplasty or other non-penetrating surgery may make such procedures an earlier option in many instances, such as in younger patients, where cataract formation is of concern, where medical therapy has proven insufficient, or the conjunctiva is not

prone to bleb formation. A non-filtering, bleb-independent procedure such as canaloplasty can also be offered to patients, where complications are unacceptable, such as single-eyed patients, patients with high myopia, and patients with tubular visual fields [78].

In a study by Brüggemann and Müller it was confirmed that trabeculectomy requires a longer hospitalisation, has higher re-admission rates and needs more frequent post-operative monitoring, which makes TE more costly and time-consuming than canaloplasty [101].

As glaucoma surgery is not only a method used to reduce intraocular pressure, but also specifically to maintain visual fields and visual acuity in order to preserve the patient's quality of life and independence. A study evaluating the quality of life after canaloplasty and trabeculectomy by Klink T. et al., reported that canaloplasty surgery indeed reaches its goals as patients had a higher quality of life, satisfaction with outcomes of surgery, and lower rates of visual and non-visual symptoms and stress caused by surgery. No difference between the two procedures was seen in terms of restriction from social contacts or loss of independence [139].

# 8. Conclusion

Glaucoma surgery is indicated when target pressures are not achieved, or when neural tissue or visual function is progressively lost despite maximally tolerated medical and laser therapies.

Non-penetrating glaucoma surgery (NPGS) was introduced as a new surgical approach that would be safer than the standard filtering operation. It is essentially extraocular surgery as opposed to other surgical modalities that necessitate eye penetration (trabeculectomy). The avoidance of penetration into the eye reduces the risk of hypotony and related complications. One type of non-penetrating glaucoma surgery introduced most recently is canaloplasty, which is considered a new and exciting development in the evolution of glaucoma surgery. This surgery is designed to re-establish outflow through Schlemm's canal and collector channels.

To review the postoperative results of a non-penetrating glaucoma surgery, including intraocular pressure, vision, medication, complications and postoperative interventions, in the present 100 eyes with various types of open angle glaucoma underwent a canaloplasty or canaloplasty combined with cataract surgery which was then followed for up to 24 months postoperatively.

The objective also was to determine if the postoperative effect is better after canaloplasty surgery alone or if it is better when canaloplasty surgery is combined with cataract surgery.

Canaloplasty on phakic eyes renders a 36% reduction of IOP, canaloplasty on pseudophakic renders a 42% reduction and phacocanaloplasty group renders a 51 % reduction of IOP. The qualified success rate was 96% and 100% (target IOP $\leq$ 21 mmHg with or without medication) at 18 months in canaloplasty and phacocanaloplasty groups, respectively.

The vision in phacocanaloplasty is improved from the mean LogMAR BCVA ± SD 0.20 ± 0.1 to 0.06 ± 0.1 at 24 months postoperatively, but statistically insignificant in all groups.

There were 62%, 64% and 75% of the eyes in canaloplasty on phakic, canaloplasty on pseudophakic and phacocanaloplasty groups, respectively, without medications at 24 months postoperatively.

This canaloplasty study did not find any serious permanent complications and needed a very low percentage of postoperative treatments. The vast majority of postoperative canaloplasty patients tended to have a perfectly normal looking eye without any ocular discomfort.

# Conclusion

The findings of this study show that combined surgery is better in terms of reducing the IOP, medication use postoperatively with higher success rate and better visual acuity, lower complications and postoperative interventions than canaloplasty surgery alone.

The advantage of canaloplasty over trabeculectomy include the following: (1) the physiological aqueous humor outflow is restored; (2) subconjunctival blebless; furthermore, even eyes with chronic conjunctivitis resulting from long use of antiglaucoma eyes drops or affected by severe conjunctival scarring, can be considered for canaloplasty surgery; (3) antimetabolites are not needed; (4) faster visual rehabilitation after surgery; (5) fewer and simplified postoperative follow-ups; (6) limited postoperative complications; and (7) postoperative results and IOP levels tend to be stable over time.

In conclusion, canaloplasty surgery as a minimally invasive, effective in reducing IOP with low complication rate can be offered as a first-line treatment in selected patients affected by various types of open-angle glaucoma.

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# 10. Affidavit

“I, Nahla Hasan Abdulla Al-Asbahi certify under penalty of perjury by my own signature that I have submitted the thesis on the topic [clinical and morphological findings after canaloplasty] I wrote this thesis independently and without assistance from third parties, I used no other aids than the listed sources and resources.

All points based literally or in spirit on publications or presentations of other authors are, as such, in proper citations (see ″ uniform requirements for manuscripts (URM) ″ the ICMJE www.icmje.org) indicated. The sections on methodology (in particular practical work, laboratory requirements, statistical processing) and results (in particular images, graphics and tables) correspond to the URM (s.o) and are answered by me. My interest in any publications to this dissertation correspond to those that are specified in the following joint declaration with the responsible person and supervisor. All publications resulting from this thesis and which I am author correspond to the URM (see above) and I am solely responsible.

The importance of this affidavit and the criminal consequences of a false affidavit (section 156, 161 of the Criminal Code) are known to me and I understand the rights and responsibilities stated therein.

Date Signature

# 11. Curriculum Vitae (CV)

To ensure data protection, my CV will not be published in the electronic version of my dissertation.

# 12. **Acknowledgments**

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At the end of my thesis I would like to thank all those people who made this thesis possible and an unforgettable experience for me. At the end of my thesis, it is a pleasant task to express my thanks to all those who contributed in many ways to the success of this study and made it an unforgettable experience for me.

# 13. Appendix

## 13.1 List of figures

## 13.2 List of tables

## 13.3 List of abbreviations

| | |
|---|---|
| AC | Anterior chamber |
| ALTP | Argon laser trabeculoplasty |
| BCVA | Best corrected visual acuity |
| CPC | Cyclophotocoagulation |
| CSTM | Corneoscleral trabecular meshwok |
| CSW | External corneoscleral wall |
| CYL | Cylinder |
| D | Diopter |
| ECM | Extracellular matrix |
| Fig | Figure |
| FU | Fluorouracil |
| GV | Giant Vacuole |
| HRT | Heidelberg Retinal Tomograp |
| IOL | Intraocular Lens |
| IOP | Intraocular Pressure |
| LI | Laser Iridotomy |
| Med | Medication |
| MMC | Mitomycin C |
| Nd:YAG | Neodymium:yttrium aluminum garnet |
| NPDS | Non-penetrating deep sclerectomy |
| NPGS | Non-penetrating glaucoma surgery |
| N | Nuclei |
| Nr | Number |
| OVD | Ophthalmic viscosurgical device |
| OCT | Optical coherence tomography |
| Pat | Patient |
| PC | Posterior chamber |
| PACG | Primary close angle glaucoma |
| POAG | Primary open angle glaucoma |

| | |
|---|---|
| Ph | Phakic |
| Ps | Pseudophakic |
| SC | Schlemm's canal |
| SD | Standard deviation |
| SPSS | Statistical Analysis in Social Science, a computer program used for statistical analysis |
| SCE | Stegmann canal expander |
| JCT | The Juxtacanalicular connective tissue |
| UBM | The Ultrasound Biomicroscopic imaging |
| TM | Trabecular meshwork |
| TE | Trabeculectomy |
| TDW | Trabeculo-Descemetic Window |
| TDM | Trabeculo-Descemet's membrane |
| Yr | Year |
| **Length** | |
| µ | Micron |
| µm | Micrometer. 1 micrometer (micron) = $10^{-6}$ m |
| mm | Millimeter. 1 millimeter = $10^{-3}$ m |
| **Other** | |
| mmHg | Millimetres of mercury – non-systemic pressure unit. 1mmHg = 133,22Pa |
| µl/min | Flow rate. 1 µl/min=1,67*$10^{-10}$ $m^3$/s |
| µl/min/mmHg | Rate of the outflow facility. 1 µl/min/mmHg=1,25*$10^{-12}$ $m^3$/s/Pa |
| MHz | Megahertz One million cycles per second |