Acta Ophthalmologica

Circumferential (360°) trabeculotomy in primary congenital glaucoma: 19–245 months of follow-up

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ABSTRACT.

Purpose: **To evaluate the long-term efficacy and safety of circumferential trabeculotomy (CT) in the treatment of primary congenital glaucoma (PCG).**

Methods: **Retrospective, single-institutional case series of CT performed for PCG in years 1997–2016. The surgery could be completed in 42 out of 65 eyes (65%) intended for CT, and 39 of them were included in the study. A follow-up examination was performed in 2017. Success was defined as intraocular pressure ≤ 16 mmHg without (complete) or with (qualified) glaucoma medication.**

Results: **Complete success was obtained in 33/39 eyes (85%), qualified success in 34/39 eyes (87%). Of the 39 eyes with CT, 4 eyes (10%) needed additional surgery. Median follow-up time was 120 months (range, 19–245 months). Median pre- and postoperative IOP were 26.0 mmHg (range, 10–41 mmHg) and 11.0 mmHg (range, 8–19 mmHg), respectively ($p < 0.001$). Cup-disc ratio was ≥0.5 in 82% at baseline, at follow-up in 9%. The median distance corrected visual acuity at follow-up was logMAR 0.06 (range, −0.2 to 1.1). Median number of glaucoma medication at follow-up was 0 (range, 0–2), at baseline 1.0 (range, 0–2). No serious complications were noted.**

Conclusion: **Circumferential trabeculotomy is an efficacious, safe and medication saving surgical treatment for PCG in the long term. After a median follow-up of 10 years (120 months), the morphological status of the optic nerve was either normalized or stabilized, and the visual acuity overall well preserved.**

Key words: 360° trabeculotomy – circumferential trabeculotomy – intraocular pressure – long-term outcomes – primary congenital glaucoma

A preliminary abstract of the study was presented at the Nordic Congress of Ophthalmology in Oslo on 24 of August, 2018.

Acta Ophthalmol. 2021: 99: e1449–e1457

doi: 10.1111/aos.14846

Introduction

Primary congenital glaucoma (PCG) is a rare, but potentially blinding childhood disease. It accounts for 5% of all childhood blindness (Gilbert et al., 2003). The condition has varying prevalence globally, depending largely on ethnicity and frequency of consanguinity (Badawi et al., 2019). The incidence in Western populations is about 1 in 10-22.000 live-born babies (Francois, 1980; Gencik, 1989; Papadopoulos et al., 2007). About 70% of the patients have both eyes affected. Sporadic cases have higher male prevalence, while familial cases show more equal gender distribution (Sarfarazi & Stoilov, 2000; Suri et al., 2009).

The main pathology in PCG seems to be maldevelopment of the trabecular meshwork (TM) and anterior chamber (AC) angle (Anderson, 1981). The dysgenesis results in a reduction or blockage of aqueous humour outflow and a secondary rise in the intraocular pressure (IOP) causing optic nerve head (ONH) damage. Primary congenital glaucoma (PCG) has to be treated surgically, preferably by angle surgery procedures, aiming directly at the site of pathology. The ab interno goniotomy technique described by Otto Barkan in 1942 (Barkan, 1942) was strongly contributing to change the belief that the treatment of PCG was a lost battle. Goniotomy became the treatment of choice for many decades. The ab externo trabeculotomy technique as described by Burian and Smith (Burian, 1960; Smith, 1960) followed goniotomy, being a method bypassing the need for a clear cornea, but still treating only a third to a half of the angle. Both procedures often need to be repeated in order to maintain adequate IOP control (Russell-Eggitt et al., 1992; Dietlein et al., 1999).

The further development of standard trabeculotomy into 360° trabeculotomy or circumferential trabeculotomy (CT), almost initiated a new era (Smith, 1962). The procedure was performed by rupturing the entire circumference of the TM and the inner wall of Schlemm's canal, using a polypropylene suture. This seemed to establish a near to normal aqueous outflow that gained at least as low IOP as standard trabeculotomy and goniotomy (Lynn et al., 1988). In their retrospective study, Beck and Lynch reported on 12 months results which were promising as 85% of the eyes met the criteria of success (Beck & Lynch, 1995). Later reports suggested that the IOP appeared to be better controlled than after goniotomy or standard trabeculotomy, and the visual acuity somewhat better (Mendicino et al., 2000; Neustein & Beck, 2017). However, there were reports on complications such as misdirection of the suture into the suprachoroidal or subretinal spaces as well as lasting hypotony (Gloor, 1998; Neely, 2005; Verner-Cole et al., 2006). In 2010, Sarkisian described the use of an illuminated microcatheter (Sarkisian, 2010). This technical advancement seems to have reduced the adverse events.

Since 1997, the Department of Ophthalmology at Oslo University Hospital (OUH) has been the national referral centre for congenital glaucoma. Concurrently, the CT procedure was introduced to our clinic and became the preferred surgical treatment for PCG. The CT surgery has gained much attention among paediatric glaucoma surgeons over the last years, and multiple papers have been published addressing the subject. However, most reports have a short- or medium-term follow-up. The aim of the present study was to present long-term data on the efficacy and safety of CT-surgeries in Norway.

Materials and Methods

The study covers the period from January 1997 to December 2016. Our main intention was to evaluate the therapeutic persistence of the CT procedure in patients with PCG. The definition of a completed CT procedure was when 360° of Schlemm's canal was tunnelled and ruptured. In some patients, only segments of the canal were possible to tunnel. To assure sufficient reduction of IOP in these eyes, the treatment was changed to procedures like trabeculectomy with Mitomycin C (MMC), Ahmed glaucoma valve implantation or partial trabeculotomy with rigid probe (Harms trabeculotome; Geuder, Heidelberg, Germany). These patients (n = 23 eyes) were not included in the study.

In the study period, a total of 42 eyes of 32 PCG patients underwent CT surgery. Informed consent was obtained from 29 of these 32 patients (39 eyes). The medical records of the included 29 patients were reviewed for relevant information from their first referral to our clinic until the last thorough follow-up study examination in 2017. A study flow-chart is presented in Fig. 1.

Eyes (n = 4) that underwent additional glaucoma surgery after CT was left out from further analysis subsequent to the intervention. Main study endpoint was postoperative reduction in IOP. Surgical success was defined as IOP $\leq$ 16 mmHg without (complete) or with (qualified) medication. Surgical failure was defined as IOP > 16 mmHg or need for further glaucoma surgery.

The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Regional Ethic Committee and Institutional Review Board (REC ref.no: 2107/174). The study patients were recruited after due informed consent. Parents or legal guardian was giving the informed consent in cases of children under 16 years of age.

Study parameters

The first preoperative, diagnostic (baseline) examination under anaesthesia (EUA) was performed using ketamine with spontaneous ventilation, and a full eye inspection was completed as far as possible. Some of the eyes were treated with topical glaucoma medication at baseline. The IOP was measured. In some patients, there was no information in the medical record of the IOP at baseline before glaucoma medication was initiated. In these

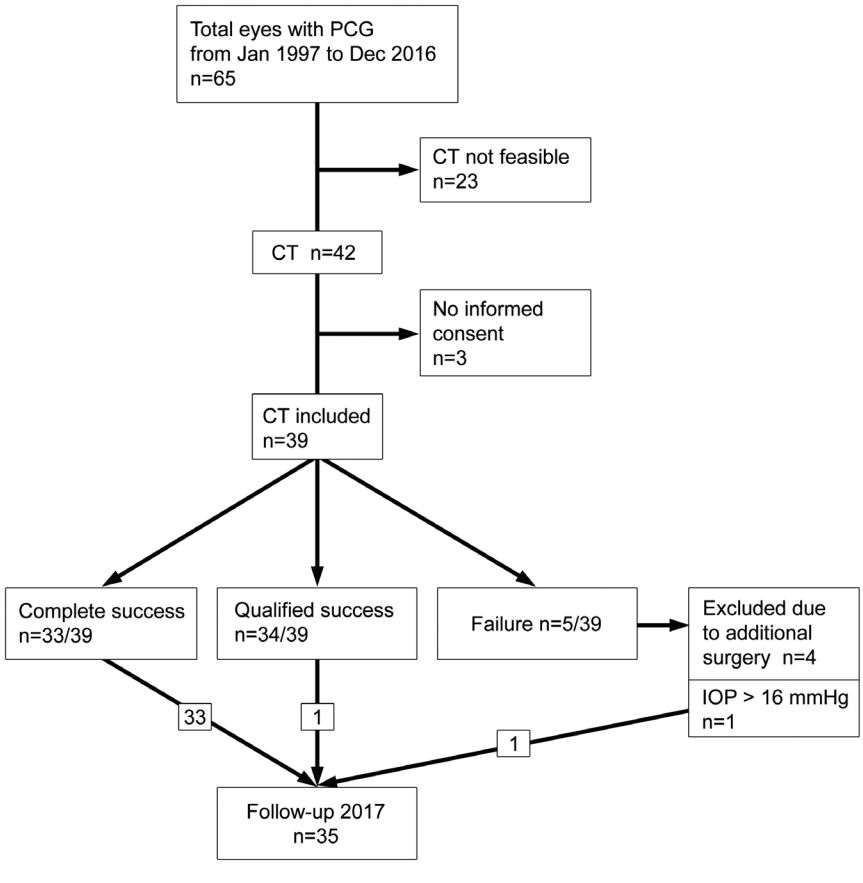

Fig. 1. Study flow chart. CT = circumferential trabeculotomy; IOP = intraocular pressure; N = number of eyes; PCG = primary congenital glaucoma.

cases, the IOP with medication was recorded. The cup-disc ratio (CDR) of the ONH was estimated in all cases by the surgeon. As the majority of the children were younger than 7 months, and the diagnosis was rapidly followed by surgery, baseline visual acuity and refraction data were unavailable. The final follow-up examination was carried out after a fixed protocol to ensure complete information of the ophthalmic status of all included patients. These examinations were performed by an experienced ophthalmologist, optometrists and orthoptists. The follow-up examinations were carried out from March to October 2017. The two youngest patients (8%) needed a EUA (ketamine) for the purpose of the study examination. Three patients (12%) were unable to attend the follow-up examination in Oslo. Instead, data were gathered from their local ophthalmologist according to the study protocol.

The final examinations included the following parameters: IOP, visual acuity [distance corrected visual acuity (DCVA)], axial length (AL), central corneal thickness (CCT), keratometry (*K*-values in diopters), corneal diameter, orthoptic evaluation with information including strabismus, amblyopia treatment and involuntary eye movements. Depending on the child's age and cooperation, the examination primarily aimed at including slit lamp biomicroscopy, corneal endothelial cell density (ECD), automated perimetry or visual field testing by Donders' method and performing optical coherence tomography (OCT) of the ONH; secondarily clinical estimation of the CDR.

A detailed history of the child's general health and the need for glaucoma medication postoperatively were collected.

Surgical procedure

The surgical procedures were performed under general anaesthesia by three experienced glaucoma surgeons (JEJ; 21 cases, JHT; nine cases, and TST; five cases). The external access to Schlemm's canal was located nasally on the globe. Conjunctiva was opened fornix-based. Schlemm's canal was located by vertical dissection with a 15° stab knife under a partial thickness, rectangular scleral flap. Since 2014, the technique was changed to both a superficial and a deep scleral flap, similar to the procedure of deep sclerectomy (Mermoud, 1999). The 360° tunnelling of the canal was from 1997 carried out by using a blunted polypropylene 6-0 suture ($n = 28$ eyes). From 2012, the suture was replaced by an illuminated microcatheter ($n = 11$ eyes; DORC Glaucolight Canaloplasty Device, Zuidland, Netherlands). The suture/fibre was aligned with the opening of Schlemm's canal and gently introduced into the canal in one direction with tying forceps. The probe was tunnelled all the way back to the primary insertion site. After having made a small corneal paracentesis with 15° stab knife, acetylcholine was injected into the AC to achieve miosis for stretching of the iris and lens protection. A cohesive ophthalmic viscosurgical device (OVD) was subsequently installed to stabilize the AC and to ensure sufficient firmness of the eye before rupturing the canal. The rupturing procedure was done in a 'purse-string' manoeuver, tearing the entire TM and the inner wall of Schlemm's canal into the AC. The OVD was not removed from the AC after rupturing. The scleral flap(s) and conjunctiva were adapted watertight.

At the end of the procedure, cefuroxime 1 mg was injected into the AC and a steroid (dexamethasone 2–3 mg or methylprednisolone 15–25 mg) was injected subconjunctivally inferiorly. Chloramphenicol ointment was administered on the eye at the end of surgery, and the eye was patched and given a transparent shield with attempted continuous wear the first 2 weeks after surgery.

Standard postoperative treatment was topical miotics (Pilokarpine® 2%) bid for 2 weeks. A combination of steroid and antibiotics [Tobrasone® (tobramycin 3 mg/ml, dexamethasone 1 mg/ml)] was used topically five times a day for 4 weeks, then switching to only steroid drops (Spersadex®/Monopex® [dexamethasone 1 mg/ml)] in tapering doses for the next 6 weeks. Steroid ointment [Ultracortenol® (prednisolone pivalate 5 mg)] was used at night for 2 weeks.

Equipment

Intraocular pressure was measured at baseline either with Tono-Pen (XL, Reichert Technologies, Depew, USA) or Perkins handheld tonometer(Clement Clarke, Harlow, UK), and at follow-up by Goldman applanation tonometer (GAT 900; Haag-Streit Diagnostics, Köniz, Switzerland), iCare tonometer (iCare, Helsinki, Finland) or Perkins handheld tonometer.

Automated perimetry was performed with the Octopus 900 perimeter (Haag-Streit Diagnostics, Köniz, Switzerland), using 30-degree G-TOP test.

The OCT of the ONH was obtained by the Optovue Avanti (Optovue Inc, Fremont, CA, USA). We used a non-contact confocal microscope (ConfoScan 4; Nidek Technologies Srl, Padova, Italy) for measuring ECD. Corneal diameter, AL and CCT were measured with Nidek A-scan Optical Biometer (Nidek Co., Ltd., Tokyo, Japan). In the EAU cases, AL and CCT were obtained by Nidek US-500 A-scan/pachymeter (Nidek Co., Ltd., Tokyo, Japan) and a manual calliper for measuring the corneal diameter.

Statistical analyses

Due to real-life study with patients examined at different time after surgery, we adjusted for time in our statistical analysis. To model age-dependence, we also included measurements from examinations between surgery and the study follow-up examination for IOP, AL, corneal diameter and spherical equivalent (SE). For these variables, we used generalized additive mixed models to explore the relationship with time. To account for the correlation induced by multiple measurements on each eye and measurements on both eyes for each patient, we used random effects in the regression models. A survival analysis (Kaplan–Meier) was used to calculate the cumulative complete and qualified success rates. Histograms and Q-Q plots were visually inspected and most variables were not normally distributed; thus, non-parametric analyses were used for all variables. Comparisons between baseline and the follow-up examination were performed with the Wilcoxon signed-rank test. Fisher's exact test was used to compare categorical data. Two-sided significance testing and a significance level of 5% were applied. All continuous data are presented as medians (range) and

categorical data as number (%). The statistical analysis was performed in R (R Core Team 2020) and in SPSS (version 26, IBM Corp., Armonk, NY, USA).

Results

Success rates

Our overall rate in completing CT in PCG eyes in the period 1997 to 2016 was 42/65 eyes (65%). Twenty-nine patients (39 eyes) were included after informed consent, and median follow-up time was 120 months (range, 19–245 months). The complete and qualified success rates were 85% (33/39 eyes) and 87% (34/39 eyes), respectively (Fig. 1). In four eyes (three patients), the IOP was not rated sufficiently reduced after CT and additional filtering surgery (trabeculectomy with Mitomycin C and implantation of Ahmed valve glaucoma device) was performed during the first 10 weeks after CT. One of these patients with unilateral glaucoma had a trabeculectomy with MMC 12 days after CT. The second patient had bilateral glaucoma and a trabeculectomy with MMC in both eyes; after 19 and 70 days following CT. The third patient (unilateral glaucoma) received an Ahmed glaucoma valve was implanted 35 days after CT. These four eyes (failures) were consequently excluded from further follow-up analysis according to the study protocol.

One eye had an IOP of 19 mmHg on glaucoma medication at follow-up (failure) and did not fulfil the criteria of success. In 28 of the study eyes, CT was performed using a prolene suture probe while a Glaucolight microcatheter probe was used in 11 eyes. The complete success rate in the prolene suture probe group and Glaucolight probe group was 82% and 91%, respectively. The qualified success rate in the prolene suture probe group and Glaucolight probe group was 82% and 100%, respectively. The failure eyes (n = 5) were all from the prolene suture group. Failure was seen in both eyes of only one patient with bilateral glaucoma (n = 2 eyes), the remaining failure eyes were from patients with unilateral disease (n = 3).

The Kaplan–Meier survival curves for the cumulative probability of complete and qualified success of the 39 eyes are shown in Fig. 2.

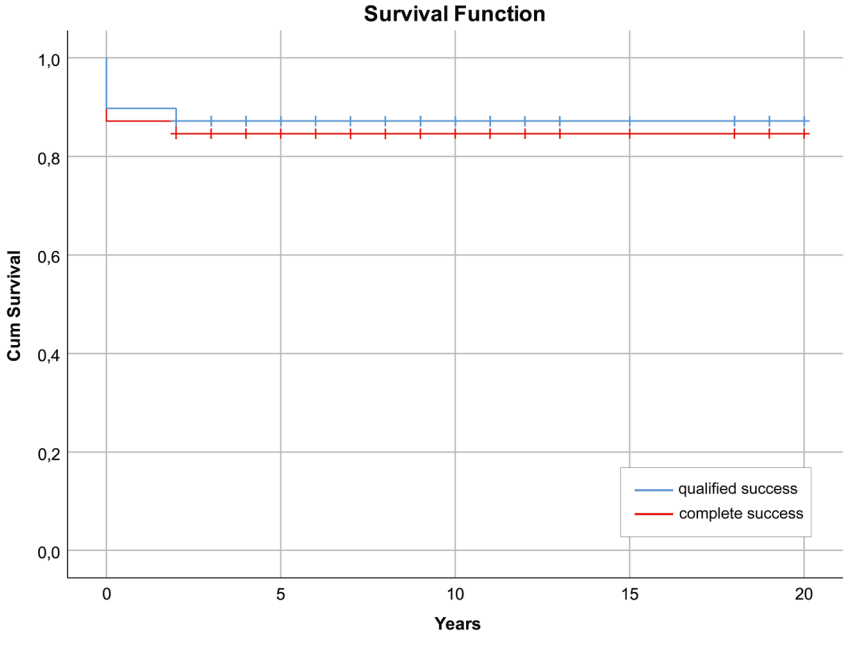

Fig. 2. Kaplan–Meier survival analysis of complete success (defined as eyes with intraocular pressure ≤ 16 mmHg without need for anti-glaucoma medication after circumferential trabeculotomy (CT), n = 33) and qualified success (defined as eyes with intraocular pressure ≤ 16 mmHg with or without need for anti-glaucoma medication after CT, n = 34) in primary congenital glaucoma. A total of 39 eyes are included in the analysis. Four of the eyes (three patients) needed additional filtering surgery shortly after CT (failures). Thirty-five eyes had no additional surgery during follow-up.

Patients characteristics

The demographics and characteristics of the included 29 patients (39 eyes) are listed in Table 1. The majority of the study participants were Caucasian (69%) and males (76%). Barely half of the patients (45%) had bilateral disease. In three out of 13 patients with bilateral disease (23%), CT was obtained in one eye only. Hence, only the CT eye was included in the study.

In one of the 39 eyes, the tunnelling of Schlemm's canal was completed through 320-degrees. A second scleral cut down was made to rupture the 320-degrees of TM. As nearly 90% of the channel circumference was ruptured, the eye was included in the study. One of the patients was not diagnosed with glaucoma until the age of 4.5 years, but we still consider the case being a bilateral PCG, and the patient was included in the study. Prematurity was seen in two patients (7%); 9 and 14 days, respectively. One patient (3%) was treated with antibiotics for a period of 7 days after birth due to infection.

We did not have specific information registered regarding consanguinity. None of the patients had familiar glaucoma and there were no known coexisting syndromes or systemic diseases.

Incidence

For the time span 1997 to 2016, we diagnosed 44 new PCG patients nationwide. The birth rates in this period were 1.176 232 live-born babies (Statistics Norway S. 2020). From these numbers, we estimated an annual incidence of PCG in Norway during the study period of 3.7:100 000 (95% confidence interval: 3.74–4.97), corresponding to approximately 2 PCG patients per year.

Findings at baseline and follow-up in 2017

As shown in Table 2 and Fig. 3A, the median IOP reduction was 15.0 mmHg (range, 0–32 mmHg) or 58% ($p < 0.001$). As mentioned, in some cases there was no information at baseline about the IOP before starting glaucoma medication. This explains minimal reduction in some of the eyes. The corneal diameter did not change significantly during follow-up (Table 2, Fig. 3C). Breaks in Descemets membrane (Haab's striae) were apparent in

Table 1. Demographics and characteristics of 29 patients (39 eyes) with primary congenital glaucoma treated with circumferential trabeculotomy (CT). In 10 of the 13 patients with bilateral disease, both eyes were included in the study after completed CT. The remaining three patients had one CT eye included.

Parameter	Demographics	Number (%)/median (range)*
Sex	Male	22 (75.9)
	Female	7 (24.1)
PCG	Unilateral	16 (55.2)
	Bilateral	13 (44.8)
Ethnicity	Caucasian	20 (69.0)
	African	4 (13.8)
	Asian	1 (3.4)
	Arabian	2 (6.9)
	Caucasian/Arabian	1 (3.4)
	African/Asian	1 (3.4)
Other	Hereditary glaucoma	0 (0.0)
	Systemic disease/syndrome	0 (0.0)
	Prematurity	2 (6.9)
	Age at diagnosis, months	5 (1–55)*
	Age at surgery, months	5 (3–56)*

Table 2. Ocular characteristics of the 39 eyes of 29 patients at baseline, and of the 35 eyes of 26 patients at follow-up in 2017, after circumferential trabeculotomy (CT) for primary congenital glaucoma.

	Baseline		Follow-up 2017		p-value
Clinical parameters	Median	range, *n*	Median	range, *n*	
IOP (mmHg)	26	10–41, *n* = 39	11.5	8–19, *n* = 35	<0.001
CCT (μm)	639	508–930, *n* = 27	486	432–570, *n* = 31	<0.001
Corneal diameter (mm)	13.3	11.5-15.0, *n* = 38	13.5	12.0–15.0, *n* = 33	0.378
Number of glaucoma eye drops	1	0–2, *n* = 39	0	0–2, *n* = 35	<0.001
	ratio [%] of the eyes		ratio [%] of the eyes		
Corneal oedema	31/39 [80%]		0*		
Cataract	3/39 [8%]		3/35 [9%]		0.890
Cup-disc ratio (CDR)					
CDR < 0.3	0		20/34 [59%]		< 0.001
Mild 0.3–0.4	19/37 [51%]		3/34 [9%]		
Moderate 0.5–0.7	12/37 [32%]		11/34 [32%]		
Severe ≥ 0.8	6/37 [16%]		0		

CCT = central corneal thickness; IOP = intraocular pressure; *n* = number of eyes.
* Two eyes had clear cornea at follow-up after successful endothelial keratoplasty.

26 eyes (67%) at baseline, persisting at follow-up in 24 eyes. One patient with bilateral glaucoma had corneal decompensation in both eyes due to extensive Haab's striae. The patient underwent a Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) procedure in both eyes, in the right and left eye 17 and 19 years after CT surgery, respectively. The corneas cleared after this surgery and the DCVA returned to the habitual level in both eyes after the transplantations. Corneal oedema was described in 31 eyes (79%) at baseline. Nine eyes (23%) demonstrated mild oedema (iris could be fully visualized), and 22 eyes (56%) demonstrated moderate oedema (iris could be visualized but without recognizable details). No eyes had severe oedema with white corneas. Corneal oedema was not present in any eye at follow-up.

There was a significant reduction in the use of glaucoma medication ($p < 0.001$). Pressure-lowering eye drops were used at baseline in 28 eyes (72%) and at last follow-up only in two eyes (6%); one eye from the qualified success group and one eye that did not meet the criteria of success (failure). Both eyes were treated with dual topical glaucoma medication (timolol 1 mg/ml and brinzolamide 10 mg/ml).

The median AL was 21.82 mm (range, 20.54–23.99 mm) at baseline and 23.33 mm (range, 21.40–29.53 mm) at follow-up. The estimated AL as a function of age is presented in Fig. 3B. The visual acuity was overall good with median refractive status near emmetropia at follow-up (Table 3). The objective SE as a function of age is presented in Fig. 3D. Astigmatism was corrected in 26 eyes (74%). None of the patients developed nystagmus. Automated perimetry could be accomplished satisfactorily (catch trials < 20%) in 14 eyes (40%). Thirteen eyes (37%) were tested ad modum Donders with normal visual field boundaries. We did not succeed in testing visual field in 8 eyes (23%).

Two patients (3 eyes, 8%) had slight signs of cataract at diagnosis, not needing surgical treatment and showing no obvious progression during follow-up. One eye (3%) had a small, off-axis localized cataract at final follow-up that was not registered at baseline. We are not sure if the subsequent DSAEK surgery could have contributed to the development of this lens opacity.

At the final examination, the appearance of the ONH was nearly normalized with horizontal CDR < 0.3 in 59% of the eyes (Table 2). None of the 35 eyes had evidence of progression of the ONH status.

Complications associated with surgery

Peroperative bleeding into the AC occurred in 30 eyes (77%). Two eyes (7%) had postoperative high IOP, necessitating a lavage of the AC. One eye was reoperated at day 1, the other eye had a rebleeding into the AC on the second postoperative day and the lavage was performed at day 5. In the remaining 28 eyes, the hyphema usually cleared within one week. A small iris prolapse occurred at the incision site in one eye (3%) during surgery, remedied by a basal iridectomy. Conjunctival suture adjustment in one eye (3%) the first day postoperatively was necessary due to discomfort.

There were no serious complications like choroidal or retinal detachment, vitreous haemorrhage or prolonged hypotony.

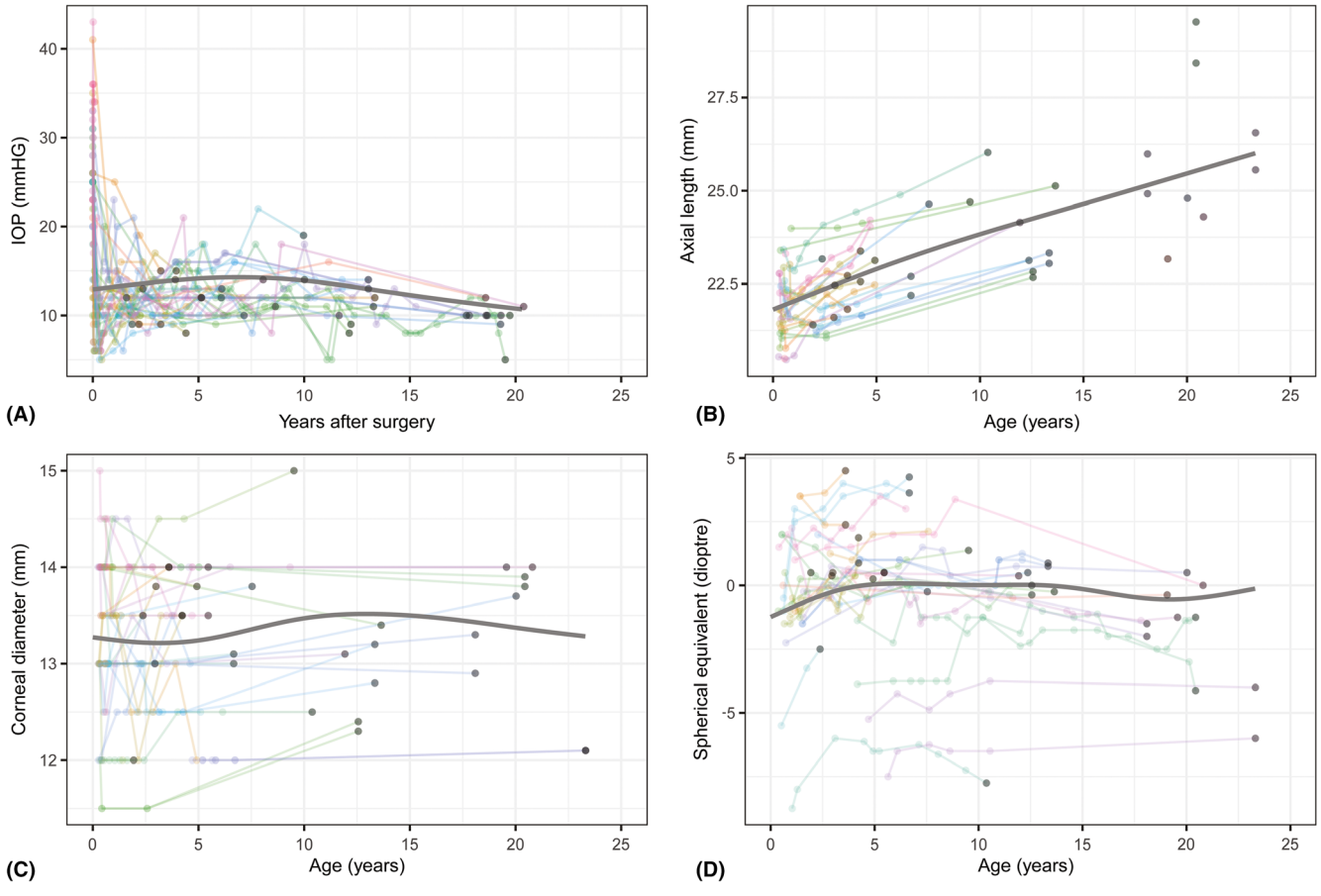

Fig. 3. Intraocular pressure (IOP) versus years after surgery (A). For the estimated trend line, the observations at surgery are excluded. Axial length (B), corneal diameter (C) and spherical equivalent (D) versus age (years) with estimated trend lines (black). The black dots represent the values measured at follow-up examination, the other dots represent other examinations, and the lines connect measurements from the same eye.

Table 3. Variables at last follow-up after circumferential trabeculotomy in 26 children (35 eyes) with primary congenital glaucoma.

Parameter	Median	range, *n*
DCVA LogMAR	0.06	−0.2 to 1.1, *n* = 33
Objective SE (diopters)	+0.5	−7.88 to 4.50, *n* = 33
Cylinder (diopters)	−1.25	−3.75 to −0.25, *n* = 32
Keratometry (diopters)	42.25	37.12–47.56, *n* = 27
Visual field defect (MD, dB)	3.30	0.30–5.20, *n* = 14
ECD (cells/mm^2)	1999	1369–3002, *n* = 16
	ratio [%] of the eyes	
Amblyopia	13/34 [38%]	
Patching	17/34 [50%]	
Strabismus	10/34 [29%]	
Exotropia	1/10 [10%]	
Interm.exo	1/10 [10%]	
Esotropia	4/10 [40%]	
Vert.deviation	4/10 [40%]	
Corneal decompensation	2/35[a] [6%]	

cells/mm^2 = cells per square millimetre; dB = decibel; DCVA = distance corrected visual acuity; ECD = endothelial cell density; Interm.exo = intermittent exotropia; MD = mean deviation; SE = spherical equivalent; Vert.deviation = vertical deviation.
[a] Two eyes underwent endothelial keratoplasty before follow-up examination.

DISCUSSION

As the procedures of angle surgery in PCG have evolved into removing the whole circumference of the dysfunctional TM, there has been concurrent publishing of data comparing the circumferential approach with goniotomy, standard trabeculotomy or the combination standard trabeculotomy and trabeculectomy. The different angle surgery procedures have a reported overall success rate of 63–93% (Chen et al., 2014), and the success rates are mainly in favour of CT. In contrast to filtering surgery like trabeculectomy, the CT procedure is performed without creating a filtering bleb. This helps protecting the child from a lifelong threat of blebitis and endophthalmitis (Zahid et al., 2013; Kim et al., 2015). The CT technique appears to be the most anatomically precise procedure as the tunnelling probe is introduced to the Schlemm's canal through an opening and returns after 360° tunnelling to the same site. In goniotomy, the surgeon is not guided by the tissue structures in the same way, and the cut through the angle structures may not be even throughout the treated area. An unwanted passage to the suprachoroidal space could accidentally be cut open. In standard trabeculotomy, it

might be difficult to recognize if the whole probe is in the right place before rupturing, or the lumen could be missed initially. There is also a risk of rupturing the rigid probe into the AC too early as the curvature of the probe does not necessarily align with all corneal curvatures. Goniotomy and standard trabeculotomy are often needed to be repeated in order to control the IOP. The CT procedure has the therapeutic advantage of being performed as a single procedure. Recent publications on CT report complete success in a frequency of 80%–92% (Mendicino et al., 2000; Neustein & Beck, 2017; Toshev et al., 2018). Our result is comparable to these reports.

To the best of our knowledge, no studies on CT have an equally long follow-up time as this study (median 10 years). Previous studies report a follow-up time of up to seven years (Neustein & Beck, 2017). In the present trial, 11 eyes (28%) were followed as long as 15–20 years and 19 eyes (49%) 10 years or more.

It may be difficult to compare different studies as inclusion and success criteria differ. So far, there is no international consensus on the definition of success regarding target IOP in childhood glaucoma eyes. Some reports on CT define the success criteria as IOP < 22 mmHg without/with medication or IOP ≤ 18 mmHg (Mendicino et al., 2000; Toshev et al., 2018). Others have success criteria in close proximity to ours; IOP ≤ 15 mmHg (Temkar et al., 2015). The measured IOP in a normal childhood population seems to be lower than in adult eyes (Sihota et al., 2006). In the present study, the IOP cut-off point for success (IOP ≤ 16 mmHg) reflects what we consider to be the upper limit for the primary target pressure when treating PCG. If the success criterion was set to IOP < 21 mmHg, we would have gained a qualified success of 100% in the 35 study eyes. On the other hand, if the IOP was set to ≤ 12 mmHg, the complete and qualified success would both have been 71%. Shakrawal et al. published a comparative randomized trial with 20 eyes undergoing illuminated microcatheter-assisted CT, and 20 eyes undergoing conventional partial trabeculotomy (Shakrawal et al., 2017). Success criteria were defined as IOP ≤ 12 mmHg without (absolute) or with (qualified) medication at 12 months of follow-up. Absolute success was 80% and 60% in the two groups, respectively. Absolute success in our study would be somewhat lower if the success criteria were set similarly. Our median follow-up time of 10 years is substantially longer and a higher number of eyes are included.

The population of our study is mainly of Caucasian origin (69%). The high success rate may indicate that this ethnicity is less affected than patients of, for example Arabian or Asian descent, where very high IOP (≥ 35 mmHg), pronounced buphthalmus (corneal diameter > 15 mm) and white, scarred corneas due to extensive oedema are frequent (Al-Hazmi et al., 2005; Mandal et al., 2007). The extent of consanguinity in the Norwegian Caucasian population is low, which may contribute to the low occurrence of the most severe cases (Surèn & Stoltenberg, 2007). Glaucoma onset in the neonatal period is likewise associated with serious disease. For the majority of our patients, the disease onset was after the initial 2 months of life. Less aggressive disease might also indicate that surgical treatment is beneficial regardless of type of procedure. Nevertheless, among the failure eyes (n = 5) in the present study, there were no patients of African, Arabian or Asian ethnicity.

On the other hand, our results may reflect that the eyes were treated in early stages of the disease. The Norwegian healthcare system is based on equal availability for all citizens. This implies the possibility of early confirmation of the diagnosis after the occurrence of symptoms followed by rapid treatment, in all likelihood leading to a brighter outcome.

The incidence of PGC in Norway derived from our data (3.7:100 000) (Statistics Norway S. 2020) is somewhat lower than the incidence of 4.8:100 000 in Denmark, recently reported in an epidemiologic study by Pedersen et al. (2020). According to national statistics on population composition in Scandinavia for 2012, Denmark has slightly higher immigration from countries in Asia (inclusive of Turkey), Africa and Latin America (Pettersen & Østby, 2013). This might be one factor influencing the difference in incidence between the two countries.

In the current study, 80% of the cases had an intraoperative AC-bleeding with a transient hyphema. This is almost a consistent finding and is not always considered a complication (deLuise & Anderson, 1983) nor does it seem to cause any lasting problems. In other reports, the occurrence of transient hyphema varies between 43.8 and 100% (Sarkisian, 2010; Toshev et al., 2018). In our trial, two eyes (6%) developed high IOP in the postoperative period due to intracameral hema and needed a lavage of the AC. This cleared the situation immediately.

Early recognition of glaucoma symptoms and rapid treatment after diagnosis is crucial to ensure the best visual development possible for the child. Treatment of amblyopia is highly important (Steffen, 2011). The median DCVA in the present study was 0.8 (converted to Snellen acuity). A DCVA ≥ 0.4 was found in 30 eyes (91%). This is slightly better than Mendicino et al who reported the best visual acuity (VA) ≥ 20/50 (≥ 0.4) in 79% after CT (Mendicino et al., 2000). Neustein and Beck reported a median VA in the CT group of 20/30 (0.67) (Neustein & Beck, 2017). The VA outcome seen in our and other trials, along with the good preservation of the visual field seen in our trial, is encouraging. Although these children are born with a serious eye disease, many of them are able to live a normal and active life, where skills like driving a car are attainable.

Optic nerve head status improved postoperatively in most patients and did not show evidence of progressive cupping in any of the eyes during the follow-up period. Lowering of the IOP seems to reverse the assumed preoperative backbowing of lamina cribrosa that was contributing to the enlarged CDR at baseline (Quigley, 1982). We observed an increase in the AL during follow-up. The normal AL of a 5 months child is around 20 mm (Bach et al., 2019), and in our study, the median AL before the CT procedure was nearly 2 mm above normal. We found that the estimated AL at 17 years of age was around 25 mmHg (Fig. 3B) as compared to the normal AL being reported to 23.41 at 15 years and 23.67 mm at adulthood (Tideman et al., 2018). Accordingly, our findings suggest that most of the pathological growth of the eyeball occurred prior to the CT surgery.

In our study, we excluded PCG patients in whom the CT procedure was not feasible. As earlier mentioned, from 1997 to 2016 we had an overall rate of 65% in performing complete CT. A successful CT procedure depends on an accessible Schlemm's canal. The younger the child, the larger the corneal diameter, and the higher the IOP, the more likely the Schlemm's canal is partly obliterated, or even absent, preventing complete tunnelling (Alkemade, 1969; Wright et al., 1983). In our study, concerning the 3 patients with bilateral disease and only one eye successfully treated with CT, the fellow eye was clearly the one with the most marked glaucoma stigmata.

The skills of the surgeon in localizing Schlemm's canal is another decisive aspect. Obviously, with an incidence of only 2–3 cases every year in Norway, time is needed to build sufficient experience. Our glaucoma surgeons do not routinely do viscocanaloplasty or deep sclerectomy in adult glaucoma patients. Mastering of these techniques naturally adds an advantage in pinpointing Schlemms canal. There were three surgeons trained at different times during the study follow-up period. In the period 1997–2011, mainly one surgeon was responsible for the CT surgery, and the failure rate was around 30%. From 2011 to 2016, two surgeons were in training and the failure rate was around 40%. The prolene suture was mainly used as tunnelling probe in the first time period and the Glaucolight probe at the end of the second. The failure rate in the prolene suture group and Glaucolight group was 18% and 0%, respectively. We consider the variation in skills of the surgeons during the long time period, being the main reason for the difference in failure rate, rather than the nature of the probe. Hence, we find that a statistical analysis comparing the different probes was not justified.

After the study period (late 2016), we have converted completely to the iTRACK™ Microcatheter (Ellex, Fremont, CA, USA). The catheter offers the possibility of injecting small amounts of OVD to gently dilate the canal in front of the probe while tunnelling. Preliminary observations with iTRACK™ microcatheter show further improvement of our success rate (complete CT in 7/7 eyes with PCG and 3/3 eyes with secondary glaucoma).

As mentioned, we excluded four CT eyes as failures as they underwent additional surgery during the study period. The etiology of these failures is not unambiguous. For two eyes (one patient), there was a suspicion of steroid-related IOP rise, bringing about the need for further glaucoma surgery rapidly. In one patient (one eye), the surgeon was slightly unsure of being in the correct place before rupturing the innerwall of Schlemms. For the fourth eye, there were no relevant comments in the medical record.

Regarding the cases with incomplete CTs, we did manage to tunnel Schlemm's canal for 3-8 clock hours in either or both directions. This allowed for a standard trabeculotomy to be carried out in some eyes. In the early days, we did not do additional scleral cut down to retrieve the suture and rupture as much as possible of the circumference. In retrospect, the eyes where the tunnelling was 270–340°, the procedure could likely have been successful if it had been completed for the probed area. In a prospective study by El Sayed and Gawdat comparing CT to standard trabeculotomy, a full 360° tunnelling of the Schlemm's canal was obtained in half (50%) of the CT eyes (El Sayed & Gawdat, 2017). The other half was tunnelled for 250–350° and a second scleral cut down was made. It is noteworthy that the success rate at 2 years was equal for the two groups.

The strength of our study is the long follow-up (median 10 years). The patients had a comprehensive follow-up examination with a stringent protocol. The vast majority of the examinations were performed by an experienced paediatric glaucoma ophthalmologist who ensured reliable follow-up results. Besides, all Norwegian PCG patients are treated at OUH, given our status as national referral centre. Hence, our results are not biased by non-randomly selected patient data. The study is limited by its retrospective, non-comparative design, and restricted number of included eyes. In Western countries, it is difficult to perform studies with high sample size due to the rarity of the disease. Moreover, the CT technique itself was modified during the study period (changing the scleral approach from one to two flaps and the tunnelling probe from a prolene suture to the illuminated Glaucolight fibre). However, we are not allowed to conclude on the significance of these changes as surgeons with different experience were involved during implementation of these different adjustments.

In conclusion, when CT is successfully performed in PCG infants, our study shows that nearly 90% of the patients were in no need of further surgery. Furthermore, if the IOP remains adequate and stable during the first 2–3 months after surgery, it is likely that the CT is the only procedure needed for decades. However, it is crucial to stress the importance of a lifelong monitoring of the glaucoma among these patients.

We did not observe any progression of the glaucoma in the long term. The CT procedure allows early visual rehabilitation, and the visual outcome is good. The therapeutic permanence of the procedure is favourable, as it enables the treatment of these children to consist of a single surgical procedure and consequently minimal exposure to anaesthesia. To ease the procedure and possibly minimize the risks of complications, the use of an illuminated microcatheter is recommended. The catheter though represents an extra economical cost. Nevertheless, concerns regarding cost should not be pivotal when considering CT, as the prolene suture indeed is a suitable choice.

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Received on August 7th, 2020.
Accepted on February 23rd, 2021.

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The Glaucoma Research Foundation of the Norwegian Association of Ophthalmology (Oslo, Norway), Norwegian Association of Blind People (Oslo, Norway) and Jon S. Larsen's Foundation (Tønsberg, Norway) have financially supported the study. The funding organizations had no role in the design or conduct of this research.

No conflicting relationship exists for any author.