Details of the research work signed by applicant

Dr. Mandal published the largest series of patients with primary congenital glaucoma operated and followed-up by him over the last 3 decades.

Dr. Mandal evaluated the long-term visual and surgical outcomes, and associated risk factors for poor outcomes in patients with primary congenital glaucoma (PCG) over a 21-year period. The medical records of children who underwent combined trabeculotomy-trabeculectomy (CTT) as the first surgical procedure by Dr. Mandal between January 1990 and December 2010 were reviewed. Data on diagnosis and surgical procedures were extracted. Primary outcome measure was complete success defined as intraocular pressure (IOP) <16mmHg in patients examined under general anesthesia or <21mmHg in patients who were old enough to be examined with the slit-lamp and when there was no progression of disc cupping or enlargement of corneal diameter at last follow-up. Qualified success occurred if one ocular antihypotensive agent was required to maintain these criteria. The WHO criteria of vision loss was used to categorize the visual outcomes. The cohort included 653 consecutive PCG patients (1128 eyes; mean age, 26.34 months) of whom 475 (73%) underwent simultaneous bilateral CTT. Kaplan-Meier survival analysis revealed 1, 5, 10, 15, and 19-year complete success rates of 92.6%, 75.5%, 55.9%, 44.7% and 21.6% respectively. Multivariate analysis revealed independent associations between failure, preoperative corneal clarity, and prior glaucoma surgery. Of the VA data obtained at last follow-up (n=333, 51%), 92 (28%) had no visual impairment, 145 (43%) had low vision, and 96 (29%) were blind. It was concluded that primary CTT may be safely employed to control IOP and may provide long-term benefits in PCG patients.

Patients who presented with corneal scar from PCG performed significantly worse than those with corneal edema. The failure rate was higher among those who underwent prior glaucoma surgery than those who underwent primary CTT at our centre. There were no significant associations with age at surgery, gender, and preoperative horizontal corneal diameter. After multivariate analysis, independent associations were maintained between rate of failure, and preoperative corneal clarity, and history of prior glaucoma surgery.

In summary, three decades of our experience and the results of our published studies add to the body of the literature that early diagnosis and prompt surgical intervention in PCG is required to control the IOP. Primary CTT is safe and effective in Indian patients with PCG. Furthermore, long-term follow-up is essential to ensure that IOP control is maintained, so as to maximize the visual outcomes. Patients presenting with corneal scar and history of prior glaucoma surgery are the risk factors identified in our study for poor outcomes. Caregivers of patients with these risk factors should be counseled about the need for additional glaucoma medications or repeat glaucoma surgery along the course of the follow-up. Simultaneous bilateral surgery for bilateral PCG is a viable option for young children, but the pros and cons must be discussed with the caregivers of the child.

Table 1. Participant and Clinical Characteristics of 653 patients (1128 eyes) with Primary Congenital Glaucoma

Characteristic	Result
Age at surgery (months)	
Mean ± SD	26.34 ± 49.3
Range	0.03 to 353.13
Median	5
Gender, n (%)	
Male	370 (57)
Female	283 (43)
Laterality, n (%)	
Unilateral	178 (27)
Bilateral	475 (73)
Type of glaucoma[†], n (%)	
Neonatal (0-1 month)	104 (16)
Infantile (>1-24 months)	274 (42)
Late-onset (>24 months)	270 (42)
Horizontal corneal diameter at presentation, mm	
Mean ± SD	13.05 ±1.27
Range	10.50 – 18.00
Corneal clarity at presentation[§], n (%)	
Clear	113 (18)
Edema	485 (76)
Scar	42 (7)
Corneal clarity at last visit[Ψ], n (%)	
Clear	316 (51)
Edema	203 (32)
Scar	106 (17)
Intraocular pressure (mmHg), mean ± SD	
Preoperative	28.57 ± 6.94
Postoperative	15.51 ± 6.33
% Reduction in intraocular pressure (mean ± SD)	43.53 ± 26.89
Duration of follow-up, months	
Mean ± SD	40.81 ± 50.82
Range	6-228
Median	12
Number of antiglaucoma medications preoperatively	
Mean ± SD	0.63 ± 0.70
Range	0-3
Number of antiglaucoma medications at last visit	
Mean ± SD	0.23 ± 0.48
Range	0-2
Level of vision impairment (VI) at last visit[δ], n (%)	
No VI	92 (28)
Low vision	145 (43)
Blind	96 (29)
Refractive error, n (%)	
Emmetropia	43 (12)

Myopia	265 (76)
Hyperopia	40 (12)
Spherical equivalent at last visit, Diopters	
Mean ± SD	-3.86 ± 5.05
Range	12.50 to -32.00

[†] using CGRN classification and data missing for 5 cases;[§]data missing for 13 patients; [Ψ]data missing for 15 patients; [δ] using World Health Organization categories of vision loss (based on best-corrected visual acuity in better eye for bilateral cases and affected eye for unilateral cases)

Table 2. Success rate of patients with primary congenital glaucoma at 5-year intervals.

		Success rate % (95% CI)	
Visit duration (years)	No. patients	Complete	Complete + Qualified
1	372	92.6 (89.8, 94.6)	96.6 (94.6, 97.9)
5	173	75.5 (69.9, 80.1)	85.4 (80.5, 89.2)
10	72	55.9 (48.2, 62.9)	69.8 (61.4, 76.7)
15	19	44.7 (34.6, 54.2)	60.3 (48.7, 70.1)
19	3	21.6 (6.2, 42.9)	29.2 (7.7, 55.3)

CI = confidence interval.

Table 3. Summary table of clinical characteristics of patients with primary congenital glaucoma followed-up at different time intervals (5, 10, 15, and 19 years).

	Follow-up duration (years)			
Parameter	5 (n = 173)	10 (n = 72)	15 (n = 19)	19 (n = 3)
Visual acuity (logMAR) Mean ± SD (Snellen equivalent)	0.87 ± 0.69 (20/125)	0.91 ± 0.80 (20/160)	0.70 ± 0.81 (20/100)	1.09 ± 0.95 (20/200)
Median (IQR)	0.66 (0.37 to 1.53)	0.69 (0.18 to 1.48)	0.35 (0.15 to 1.15)	1.18 (0.64 to 1.59)
Snellen equivalent (median)	$20/100^{-3}$	20/100	$20/40^{-3}$	20/300
Intraocular pressure, mmHg				
Mean ± SD	19 ± 8	19 ± 6	14 ± 3	16 ± 2
Range	9-42	10-30	10-18	14-18
Number of antiglaucoma medications				
0	131	40	8	1
1	22	18	7	0
2	10	8	2	0
3	10	6	2	2

IQR = interquartile range; LogMAR = logarithm of minimum angle of resolution (higher values represent worse visual acuity); SD = standard deviation.

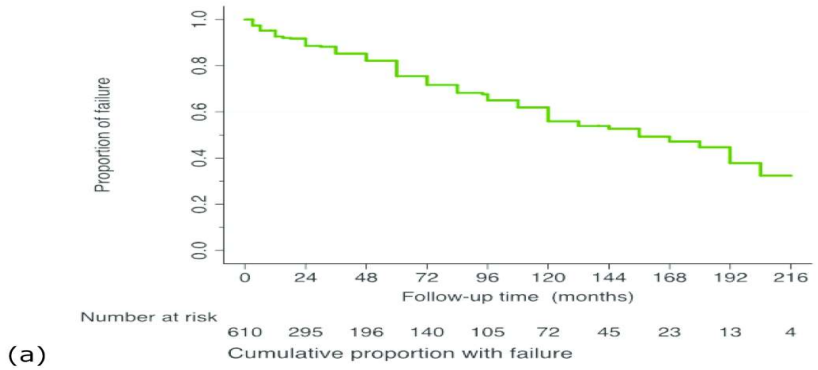
Table 4. Association of sociodemographic and clinical variables with outcome of treatment in Primary Congenital Glaucoma

Variable	Total N=653	HR[ŧ] (95% CI)	P value	HR[§] (95% CI)	P value
Age at surgery (months)[Ψ]	648	1.00 (0.99 -1.01)	0.498	-	
Gender					
Female	283	1.00	0.486	-	
Male	370	1.18 (0.73-1.91)			
Prior glaucoma surgery					
No	621	1.00	**<0.0001***	2.82 (1.24-6.45)	**0.014***
Yes	32	4.04 (2.24-7.28)			
Preoperative IOP (mmHg)	653	1.03 (1.00-1.06)	**0.035***	1.04 (0.99-1.08)	0.060
Horizontal corneal diameter[§] (mm)					
≤14	391	1.00	0.121	-	
>14	165	1.52 (0.89-2.59)			
Preoperative corneal clarity					
Edema	203	1.00	0.058[ζ]	5.09 (1.29-19.95)	**0.020***
Scar	106	2.35 (0.97-5.69)			

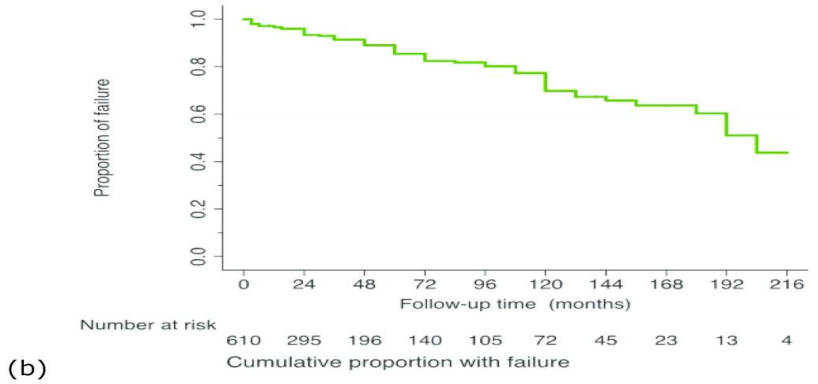
IOP- intraocular pressure; CI- confidence interval; HR- Hazards ratio

[§]Data not available for 97 cases

[ŧ] Univariate analysis; [§]Multivariate analysis;[Ψ] Data not available for 5 cases; [*]Bold - P<0.05; [ζ]P<0.1



(a)



(b)

Figure 1. Kaplan–Meier survival curves show the success probabilities [(a) complete success and (b) complete plus qualified success] of CTT for patients with primary congenital glaucoma (n=653).

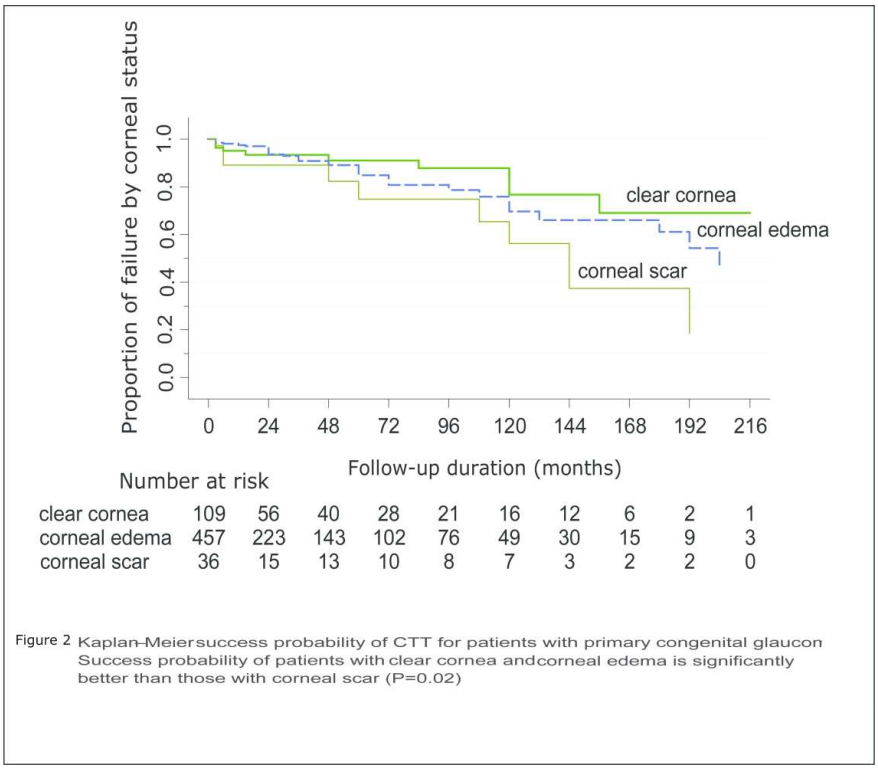


Figure 2 Kaplan–Meier success probability of CTT for patients with primary congenital glaucon Success probability of patients with clear cornea and corneal edema is significantly better than those with corneal scar (P=0.02)

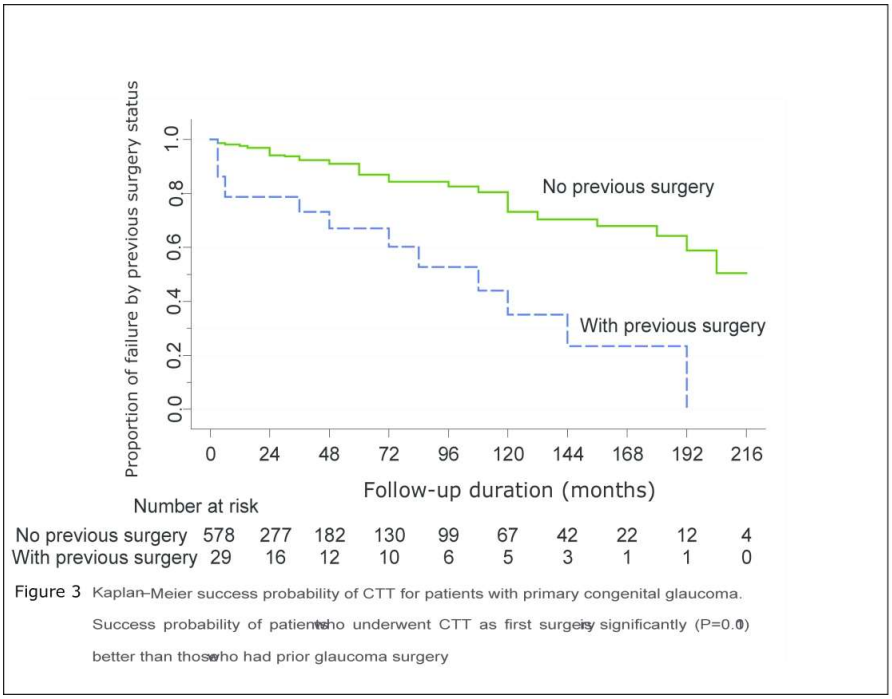


Figure 3 Kaplan–Meier success probability of CTT for patients with primary congenital glaucoma. Success probability of patients who underwent CTT as first surgery is significantly (P=0.0) better than those who had prior glaucoma surgery

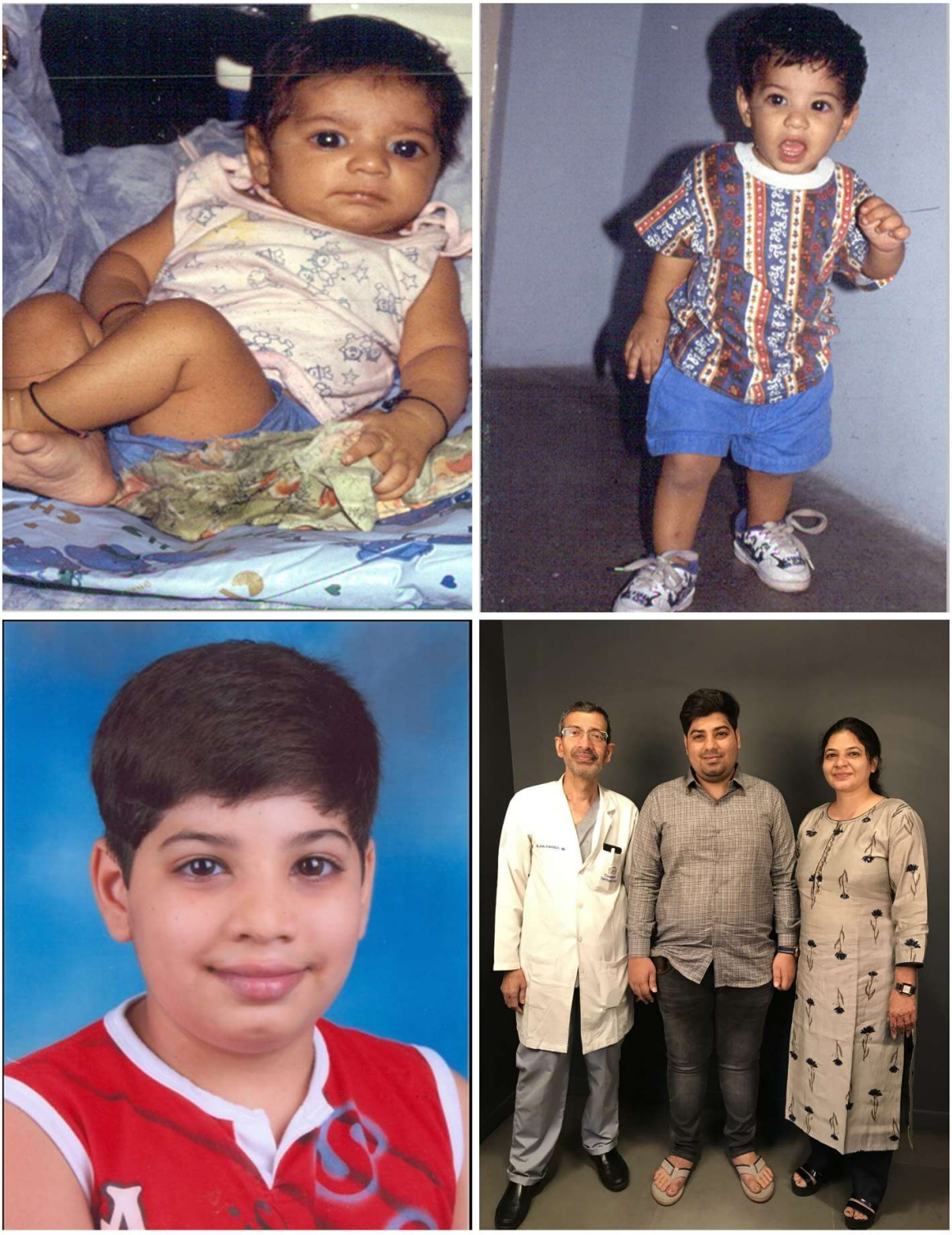


Fig.1: Collage showing a child who was operated for primary congenital glaucoma in both eyes at 1 month of age and has been followed up by me for 30 years. He is self-employed and managing his business independently.

In 2013, Dr. Mandal was invited by the World Glaucoma Association as one of the section leaders for consensus building for ‘Glaucoma surgery in children”.

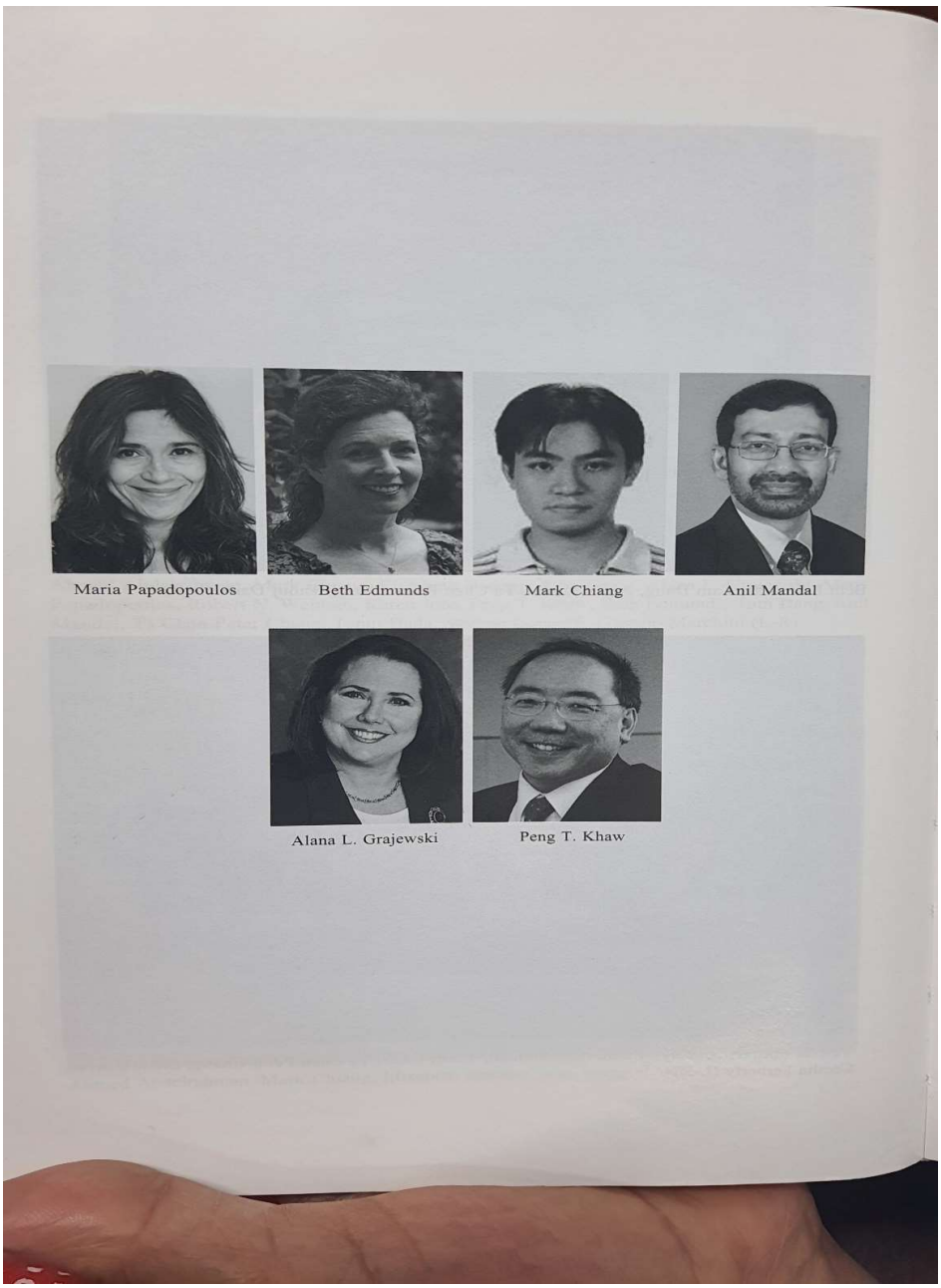


Fig: Section leaders (Includes Dr. Mandal) for the consensus building on ‘Glaucoma surgery in children” at the World Glaucoma Association in 2013

5. GLAUCOMA SURGERY IN CHILDREN

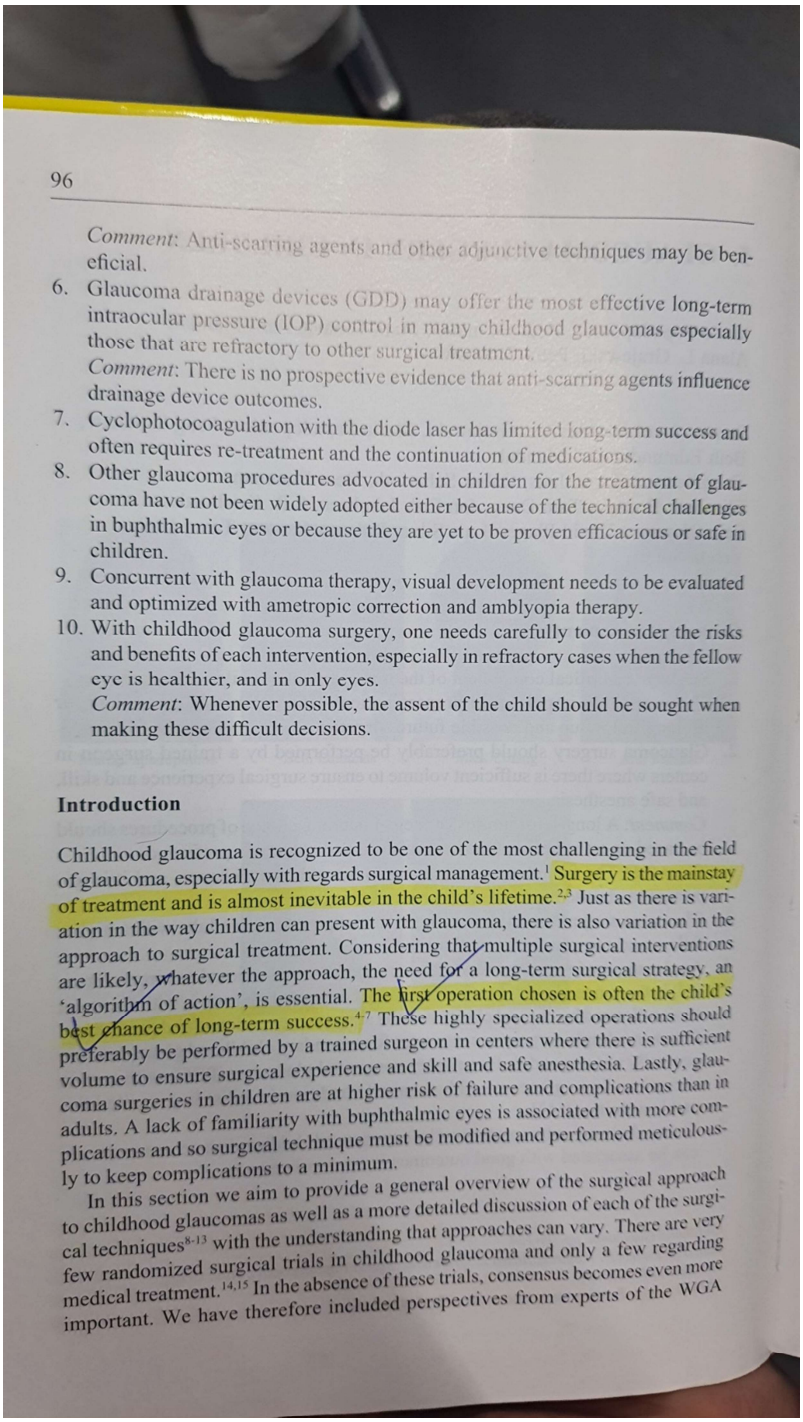
Maria Papadopoulos, Beth Edmunds, Mark Chiang, Anil Mandal, Alana L. Grajewski, Peng T. Khaw

Section Leaders: Alana L. Grajewski, Maria Papadopoulos, Peng T. Khaw, Beth Edmunds, Anil Mandal
Contributors: Karen Joos, Gabor Scharioth, Vera Essuman, Elizabeth Hodapp, Tam Dang, Jan Erik Jakobsen, S.R. Krishnadas, Sola Olawoye, David Plager, Luis Silva, Roberto Caputo, Tanuj Dada, Velota Sung

Consensus statements

1. Surgery is a critical component of the management of childhood glaucoma.
   Comment: It is important to prepare patients and parents or caregivers f lifelong follow-up and possible future surgeries.
2. Glaucoma surgery should preferably be performed by a trained surgeon centers where there is sufficient volume to ensure surgical experience and ski and safe anesthesia.
   Comment: A long-term surgical strategy including choice of procedures shou be based on training, experience, logistics, and surgeon's preference.
   Comment: The first chance for surgery is often the best chance, and it is im portant to choose the most appropriate operation.
3. Glaucoma surgery in children is more challenging than in adults with a highe failure and complication rate than in adults.
4. Angle surgery (goniotomy and trabeculotomy – conventional or circumferen tial) is the procedure of choice for primary congenital glaucoma with the exac choice dictated by corneal clarity and the surgeon's experience and preference
   Comment: Angle surgery success rates for secondary childhood glaucomas ar generally not as good as for primary congenital glaucoma (PCG) with certai exceptions [*e.g.*, glaucoma with acquired condition (uveitis) in juvenile idio pathic arthritis (JIA)].
5. Trabeculectomy, when performed by experienced childhood glaucoma surgeons can be associated with good outcomes in appropriate cases.

Childhood Glaucoma, pp. 95-134
Edited by Robert N. Weinreb, Alana L. Grajewski, Maria Papadopoulos, John Grigg, and Sharon Freedman



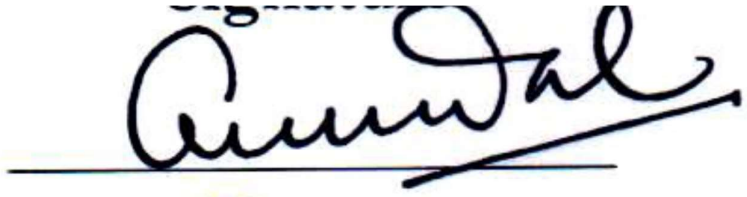
Comment: Anti-scarring agents and other adjunctive techniques may be beneficial.

6. Glaucoma drainage devices (GDD) may offer the most effective long-term intraocular pressure (IOP) control in many childhood glaucomas especially those that are refractory to other surgical treatment.
   Comment: There is no prospective evidence that anti-scarring agents influence drainage device outcomes.
7. Cyclophotocoagulation with the diode laser has limited long-term success and often requires re-treatment and the continuation of medications.
8. Other glaucoma procedures advocated in children for the treatment of glaucoma have not been widely adopted either because of the technical challenges in buphthalmic eyes or because they are yet to be proven efficacious or safe in children.
9. Concurrent with glaucoma therapy, visual development needs to be evaluated and optimized with ametropic correction and amblyopia therapy.
10. With childhood glaucoma surgery, one needs carefully to consider the risks and benefits of each intervention, especially in refractory cases when the fellow eye is healthier, and in only eyes.
    Comment: Whenever possible, the assent of the child should be sought when making these difficult decisions.

Introduction

Childhood glaucoma is recognized to be one of the most challenging in the field of glaucoma, especially with regards surgical management.[1] Surgery is the mainstay of treatment and is almost inevitable in the child's lifetime.[2,3] Just as there is variation in the way children can present with glaucoma, there is also variation in the approach to surgical treatment. Considering that multiple surgical interventions are likely, whatever the approach, the need for a long-term surgical strategy, an 'algorithm of action', is essential. The first operation chosen is often the child's best chance of long-term success.[4-7] These highly specialized operations should preferably be performed by a trained surgeon in centers where there is sufficient volume to ensure surgical experience and skill and safe anesthesia. Lastly, glaucoma surgeries in children are at higher risk of failure and complications than in adults. A lack of familiarity with buphthalmic eyes is associated with more complications and so surgical technique must be modified and performed meticulously to keep complications to a minimum.

In this section we aim to provide a general overview of the surgical approach to childhood glaucomas as well as a more detailed discussion of each of the surgical techniques[8-13] with the understanding that approaches can vary. There are very few randomized surgical trials in childhood glaucoma and only a few regarding medical treatment.[14,15] In the absence of these trials, consensus becomes even more important. We have therefore included perspectives from experts of the WGA



Dr. Anil K Mandal

29 August 2024