The Evolving Story of Aphakic and Pseudophakic Glaucoma after Cataract Surgery in Children: What’s New?

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Glaucoma in the aphakic and pseudophakic eye is the third most common cause of glaucoma in children, coming after congenital and traumatic glaucoma. Our knowledge regarding its incidence, pathogenesis, risk factors associated with its development and best management options is still evolving. We present here a review of the literature that forms the bulk of knowledge of this currently inevitable complication to pediatric cataract surgery.

Incidence of glaucoma in aphakic and pseudophakic eye of children:

The incidence of glaucoma following pediatric cataract removal has been reported to be as low as 5 % to as high as 41 %2-7. Comparing incidence from different studies is unreasonable, since studies use a variety of definitions to glaucoma and different instruments to measure the intraocular pressure (IOP). The incidence is further affected by the age, surgical technique, the length of follow up and the presence of risk factors for subsequent glaucoma development.

Francois2 reviewed 13 studies from the international literature on congenital cataract surgery in the 1940’s to 1950’s when the linear aspiration technique was used. Delayed glaucoma occurred in 0-14 % of the cases.

In 1984, Chrousos, Parks, and O’Neill3 reported their 15 year experience with pediatric cataract surgery using both the Scheie’s manual aspiration technique and the Ocute technique developed glaucoma. However, the follow up of the eyes operated using the aspiration technique was for a mean of 6.3 years versus 2 years for the eyes operated with Ocute.

Simon et al.4, using an IOP of 26 mmHg to define glaucoma, reported an incidence of 7 % for eyes with < 5 years of follow up after lensectomy and an incidence of 41 % for eyes followed up for > 5 years. This further exemplifies how the incidence is affected by the period of follow up.

Rabiah5 reported glaucoma in 118 of 570 eyes (21 %) at a mean age of 5.4 years (range 2 weeks- 15.6 years); average total follow up for eyes with and without glaucoma was 8.5 years and 10.9 years, respectively.

With 71 out of 76 eyes with at least 5 years of follow up, Michaelides et al.6 calculated a 5 year risk for developing aphakic glaucoma after lensectomy of 15.5 %, and a 5 year risk for a patient to develop aphakic glaucoma in at least one eye after surgery of 21.6 %. The onset of glaucoma ranged from one month after

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surgery to 7 years with an average yearly incidence of 5.3%.

Findings from the British congenital cataract study of patients with at least 6 years of follow up showed an overall annual incidence of postoperative glaucoma of 5.25%. The median time to development of glaucoma was 1.34 years with a range of 0.39 months to 6.73 years. Closed angle glaucoma was excluded from their analysis.

In the Denmark population based cohort study, ten years after cataract surgery 31.9% of the children who underwent cataract surgery before 9 months of age developed aphakic glaucoma. They note that glaucoma cases continued to occur even after 10 years from surgery.

We reported that after pediatric cataract surgery, 10/266 (3.8%) eyes with primary IOL were diagnosed with glaucoma, whereas 8/47 (17.0%) aphakic eyes were diagnosed with glaucoma. However, when focused on children operated before 4.5 months of age, the glaucoma incidence was 10/41 (24.4%) in children with pseudophakic eyes and 8/42 (19.0%) in age-matched children with aphakic eyes (risk ratio = 1.1, CI = 0.7-1.9; \( P = .555 \)).

Wong and colleagues reported the incidence of glaucoma, with onset within 1 year after cataract surgery (early onset) performed in the first year of life, with or without IOL implantation. At a mean follow-up of 2.51 years, 15.3% (12.2% within 1 year) of all eyes, 9.8% of eyes (6.6% within 1 year) in the planned aphakic group, all four eyes with failed implantation and 13.5% of the pseudophakic eyes (10.8% within 1 year) developed glaucoma.

Kirwan and colleagues reported the incidence and risk factors for glaucoma in pseudophakic and aphakic eyes following surgery for congenital cataract within the first year of life. The incidence of glaucoma was significantly greater (\( P = 0.02 \)) in the aphakic (15 eyes, 33%) compared to the pseudophakic (seven eyes, 13%) group. However, duration of follow-up was significantly longer (\( P < 0.001 \)) in the aphakic (113 ± 69 months) compared to the pseudophakic group (56 ± 44 months) and age at surgery was significantly less (\( P = 0.01 \)) in the aphakic group.

\textbf{Proposed mechanisms for the development of glaucoma after pediatric cataract surgery}

Several theories have been proposed to explain the pathogenesis of glaucoma after pediatric cataract surgery and it is still not clear why glaucoma develops in these eyes; however it appears to be a consequence of surgery rather than cataract itself. Children with unoperated isolated congenital cataract do not tend to develop glaucoma\(^\text{15}\) and patients with bilateral congenital cataracts who have cataract surgery in one eye only, tend to develop glaucoma in the operated eye only\(^\text{4,16,17}\). In the predisposed eye, surgery to remove the cataract appears to trigger a cascade of events that can lead to glaucoma.

In 1986, Walton discussed pupillary block and chronic angle closure from peripheral anterior synechiae as the typical mechanism following cataract removal by the ‘aspiration’ mechanism\(^\text{18}\). A decade later, David Walton’s American Ophthalmological Society thesis\(^\text{19}\) concluded
that the asymptomatic, postoperative glaucoma in aphakic patients was actually an open-angle mechanism and that those that underwent surgery in the first year of life were at highest risk for this complication, but the etiology of the glaucoma was still speculative. Walton 19 studied the angle structure of 65 aphakic children with postoperative glaucoma from modern methods of pediatric cataract removal. Vitrectomy techniques were utilized in the majority (80 %) of cases. Preoperatively, the majority of patients with available gonioscopy (19/29 eyes) had no angle abnormalities, while 10 patients did have “anomalous attachments from the iris root to Schwalbe’s line and the trabecular meshwork. Postoperatively, the angles were open in 79 of 80 eyes, but in 76 of 79 (96 %) of eyes, “circumferential repositioning of the iris insertion anteriorly at the level of the posterior or mid-trabecular meshwork with resultant loss to view of the ciliary body band and scleral spur” occurred. Windows of visible scleral spur or ciliary body were visible in these eyes, confirming open angles. Walton 19 observed scattered pigment deposits in the exposed anterior trabecular meshwork, and less frequently, white crystalline deposits suggestive of lens protein. Phelps 16 observing similar gonioscopic findings in patients after surgery, implied that the uniformity of the angle findings “throughout its circumference” instead suggested that these findings were congenital and not related to the cataract surgery. There is no way to prove, however, that those angle findings were not indicative of subclinical dysfunction 20.

It is possible that cataract extraction may indeed damage a growing, vulnerable anterior chamber angle in an eye with a subclinically imperfect trabecular outflow in a way that creates high IOP years later. 17. This may be why patients with a preexisting ocular abnormality (such as trauma, dislocated lens, chronic uveitis, or anterior segment dysgenesis) may be at higher risk for post-operative glaucoma 21. Many studies 7,8,9 have shown age at surgery to be the major risk for the subsequent development of glaucoma. This would support the theory of cataract extraction damaging a growing, vulnerable anterior chamber, but what factors could be implicated in this damage? Recently, Michael et al. 22 studied the interactions between the trabecular meshwork cells (TMC) and the lens epithelial cells (LEC). They cocultured primary and transformed TMC’s with LEC’s and studied the structural changes, and differential protein and gene expression in the cocultured TMC’s, using TMC’s grown in a low serum medium for the same period as a control. They found the cocultured cells to be larger in size and volume with fewer cell to cell contacts. They also accumulated granules and had fewer vesicles. They had an increase in cytoskeletal protein expression and a differential gene expression with upregulation of 400 genes and downregulation of 566 genes. The most affected genes were the ones regulating cellular processes related to the extracellular space, vesicle and actin cytoskeleton. The changes were similar to changes seen in the ocular tissue of patients with primary open angle glaucoma. They aim in the future to further study the effect of young and adult LEC’s on the TMC’s and suggest examining the difference in the response of infant TMC’s to the presence of LEC’s.

Risk factors associated with aphakic and pseudophakic glaucoma

A number of reports have discussed the following risk factors associated with post-operative glaucoma in children with cataracts: age at surgery, age at cataract diagnosis, microcornea, poorly dilating pupils, the presence of other ocular disease (e.g., congenital rubella syndrome), nuclear cataract, persistent fetal vasculature (PFV), and performance of a posterior capsulorhexis. Mills 17 reported several risk factors for childhood glaucoma: cataract surgery at an age of < one year (relative risk (RR) = 9.9; P d” 0.001), microcornea (RR=4.4; P d”0.001), poor pupillary dilation (RR=5.2; P d” 0.001, and congenital rubella syndrome (RR= 5.8; P d” 0.001). The relative risk (RR) was notably high for patients undergoing surgery before the age of 6 months (RR= 5.4; P d” 0.001) and 1 year (9.9; P d” 0.001). No patient who had surgery after 1.25 years of age developed chronic open or closed angle glaucoma. The authors state, “the time at surgery may not be independent of other pathologic factors as a disproportionate share of those patients who had early cataract surgery had other ocular abnormalities (congenital rubella syndrome (10.1 % of 79 eyes operated on before 1 year of age), poorly dilating pupils (22.0 %), microcornea (10.1 %), or persistent fetal
vasculature (6.3 %))...or more complete lens opacity.” Congenital rubella syndrome, poor pupillary dilation, and microcornea were also determined to be independent risk factors in this report.

Magnusson\textsuperscript{23} prospectively followed a cohort of 137 patients in Sweden for an average of 9 years and concluded that cataract extraction in children younger than 10 days of life is associated with double the frequency of glaucoma. Twenty-nine percent (4/14) of patients operated on before the age of 10 days developed glaucoma; operations performed after 10 days of life had half the frequency of glaucoma. The immature trabecular meshwork of patients undergoing cataract surgery at a very young age were exposed to inflammation or direct surgical trauma and led to glaucoma.

Rabiah\textsuperscript{5} concluded in a retrospective study of childhood aphakes that age at time of surgery is an important determinant of chronic glaucoma. Potential predictors of risk were entered into a univariate and multivariate model. The vast majority (86 %) of the glaucoma was diagnosed in patients who underwent surgery at or before 9 months of age. Of patients with cataracts in one or both eyes, no unoperated fellow eye developed glaucoma. The significant predictors of glaucoma in the multivariable analysis included: microcornea; primary posterior capsulotomy/anterior vitrectomy; secondary membrane surgery; and surgery at 9 months of age. The risk appeared substantially lower in children operated on after three years of age.

Watts et al.\textsuperscript{24} studied the complications after cataract extraction in the first 12 weeks of life. Their CART analysis showed an increased incidence of glaucoma when surgery is performed between 13.5 and 43 days of life. Vishwanath\textsuperscript{25} and colleagues found that after bilateral lensectomies the 5 year risk of glaucoma decreases from 50 % if cataract surgery was performed in the first months of life to 14 % if surgery was performed later in life. There was no statistical difference between the risk for eyes operated in the first half of the first month and eyes operated in the second half of the first month. There was no difference in the five year visual outcomes for eyes operated before and after the first month. This led them to conclude that it may be prudent in bilateral cases to postpone surgery to after the first month of life to decrease the subsequent risk of glaucoma without compromising the visual outcome.

In their study of the risk factors for the development of glaucoma after congenital cataract surgery, Chen and associates\textsuperscript{26} aimed to study if there is a time period during the first year when the risk for glaucoma after performing lensectomy becomes lower. By a multivariate analysis of 216 eyes that developed aphakic glaucoma and 152 eyes that did not develop glaucoma they found that having lensectomy in the first year and the development of postoperative complications were the risk factors of highest significance to the development of glaucoma. They did not find any time during the first year when the risk of glaucoma decreased significantly. After the ninth month fewer eyes had lensectomy which decreases the power for conclusions made after this period. Other risk factors found to be significantly associated with the development with glaucoma were postoperative cycloplegic use, a corneal diameter < 10mm and having a nuclear or total cataract. Would these factor still be significant after adjusting for age at cataract extraction? The British congenital cataract study\textsuperscript{7} showed that age at detection of cataract was the only factor significantly associated with the development of glaucoma. They found that a ten fold increase in the age at detection decreases the hazard ratio for the development of glaucoma by 64 %. Microphthalmia, insertion of an IOL, type of cataract surgery, and significant postoperative uveitis were not significantly associated with the development of glaucoma after univariate and multivariate analysis.

In the Denmark population-based cohort study\textsuperscript{8} of 946 eyes undergoing cataract surgery, age at surgery < 9 months was associated with a 7.2 fold increased risk for the development of glaucoma. All the other risk factors (type of surgery, posterior capsulotomy, surgery for secondary cataract, nystagmus, microcornea, etiology, laterality, insertion of an IOL, and morphology of the cataract) were not significantly associated with glaucoma when adjusted for age at surgery. In our recent study of 266 pseudophakic eyes and 47 aphakic eyes\textsuperscript{9}, we found that all of the eyes that developed glaucoma were operated before the age of 4.5 months. Wong and colleagues\textsuperscript{10} reported that excessive surgical trauma influences incidence of glaucoma. Microcornea,
PFV and age 4 weeks at surgery were not significant predictors of early-onset glaucoma in this series.

**How should a clinician use these data?** It may be reasonable to require more frequent anesthetized exams for children operated on at three months of age than those at three years. In our opinion, the data are not of sufficient strength to postpone surgery of a seven month old with a visually significant cataract to lower the presumed risk of future glaucoma. A few authors have discussed the critical period for binocular development beginning at about the 5th or 6th week of life. At our current level of knowledge, we feel it is reasonable to postpone surgeries in neonates with unilateral or bilateral cataracts until about the 5th week of life, which allows one to operate on a firmer, more developed eye.

**Does microcornea appear to be a risk factor for glaucoma?** Parks and colleagues found a 32% incidence of aphakic glaucoma among those eyes with corneal diameters of 10 mm at surgery. By contrast, eyes with corneal diameters >10 mm at surgery had only a 2.9% incidence of glaucoma during the follow-up period. Simon and coworkers found no association between microcornea and the development of glaucoma in their patients. Wallace and Plager noted microcornea to be a significant risk factor for aphakic glaucoma. During our initial analysis, we also observed that eyes that developed glaucoma had a significantly smaller corneal diameter than eyes that did not develop glaucoma. However, when we focused our analysis on eyes in children who underwent surgery at an early age (4.5 months of age), we did not find a significant difference in corneal diameter between those that developed glaucoma and those that did not (pseudophakic eyes, \( P = .860 \); aphakic eyes, \( P = .254 \)).

Different approaches when comparing corneal diameter could have resulted in different conclusions between our and other studies. Wallace and Plager defined microcornea as any corneal diameter smaller than that established by the authors’ age-related curve. They compared corneal diameter in aphakic eyes that developed glaucoma with that of normal corneal diameter. It may be possible that all or most of the aphakic eyes had microcornea (even those eyes that did not develop glaucoma). These authors did not have a control group of aphakic eyes that did not develop glaucoma. In contrast to the most eyes with postoperative corneal diameter in the Wallace and Plager series, we compared preoperative corneal diameter of eyes that developed glaucoma with those eyes that did not develop glaucoma and treated corneal diameter as a continuous variable. In addition, our analysis included only eyes of children who underwent surgery in the first 4.5 months of life. Unfortunately, we do not have comparative age-related data. Ideally, we should compare 3 groups (children with normal, aphakic, and pseudophakic eyes) that developed glaucoma with those that did not. Comparing these 3 groups in age-matched data may help us to give a definitive answer. However, for now, on the basis of the results of our study, we fail to find corneal diameter as a significant and independent risk factor for the development of glaucoma. Eyes operated early in life more often are associated with having microcornea, and age at surgery rather than corneal diameter itself may play a role in the development of glaucoma after cataract surgery.

**Does primary IOL implantation prevent “aphakic” glaucoma in children?**

A growing number of surgeons are using intraocular lens (IOL) implantation as the preferred mode of optical rehabilitation in patients after pediatric cataract surgery. However, the effect of IOL implantation on the incidence of glaucoma after cataract surgery is unclear. Several authors have noted a low incidence of glaucoma in children with pseudophakic eyes, and the implication being that pseudophakia in children somehow protects against glaucoma. The reported decreased incidence of pseudophakic glaucoma after pediatric cataract surgery in some studies may be related to a protective effect of the synthetic lens from a vitreous component, alteration of the lens-iris-drainage angle relationship by the synthetic lens, or selection bias (patients most at risk for developing glaucoma simply may be selected not to receive IOLs).

Like other clinicians, during the initial years of our IOL implant practice, we also observed a lower incidence of glaucoma in these children. However, during those years of practice, children who underwent eye surgery in the first year of life and who had microcornea, coexisting ocular anomalies, or PFV often were left aphakic. These conditions are reported risk factors for the development of aphakic glaucoma.
In a multicenter retrospective review, Asrani and coworkers\(^2\) reported a lower incidence (0.3 %, or 1 in 377 cases) of open-angle glaucoma in eyes receiving a primary IOL implant compared with those that remained aphakic (11.3 %, or 14 in 124 cases) after cataract surgery. In our series, we\(^9\) noted that glaucoma developed in 10 (3.8 % of 266) pseudophakic eyes and 8 (17.0 % of 47) aphakic eyes. However, when focused on eyes operated before 4.5 months of age, in an age-matched cohort, we note no significant difference between the rate of development of glaucoma between the aphakic and pseudophakic eyes\(^9\). We found that among the patients who underwent surgery before 4.5 months, the corneal diameter, keratometry and axial length were significantly different among the aphakic and pseudophakic groups reflecting a tendency to leave the smaller eyes aphakic which may underestimate the incidence of glaucoma in the pseudophakic group. The incidence of aphakic glaucoma has been reported as higher when children are followed for longer period after cataract surgery. We might expect the same trend with pseudophakic eyes and the incidence reported in our series (or any other series) may be higher as we have longer-term follow-up. Different methods of patient selection may help explain the difference in our results compared with the Asrani's multicenter study. Asrani and colleagues\(^2\) reported eyes with open-angle glaucoma and excluded eyes with microcornea.

Adding challenge and better understanding to the diagnosis of aphakic and pseudophakic glaucoma: Central corneal thickness (CCT)

Central corneal thickness can affect the accuracy of measuring IOP. A thicker cornea can overestimate the IOP\(^3\). Moreover, in recent studies in adults, a lower CCT predicted the progression to primary open angle glaucoma\(^32,33\). Simon et al.\(^34\) in a prospective masked study measured the corneal thickness of 36 aphakic and 6 pseudophakic eyes and used the CCT measurements from the phakic fellow eyes in unilateral cases (14 eyes) as controls. The mean CCT in the operated eyes was 660 microns, significantly higher than the mean of 576 microns in the phakic fellow eyes. They suggest refining the definition of glaucoma based on this finding to include eyes with an IOP above 22mmHg with documented optic disc or visual field changes and use the IOP measurement on its own if it was above 35mmHg. Based on this definition, glaucoma would be diagnosed in 21 % of the eyes in their study group and ocular hypertension in 60 %. If only an IOP of more than 26 mmHg was used as a criterion for the diagnosis, then glaucoma would be diagnosed in 50 % of the eyes.

Is this increased CCT present in all pediatric Glaucomas? Tai et al.\(^35\) found the mean CCT in eyes with aphakic glaucoma (651 microns) to be significantly higher than that in primary infantile glaucoma and glaucoma associated with Axenfeld-Reiger anomaly, even after adjusting for age. Simsek et al.\(^36\), in a randomized masked prospective study used healthy volunteers matched for age and sex as controls. Unlike Simon et al., they included only one eye, randomly chosen, in bilateral cases to further increase the power of their study. They found the median CCT (662microns) in the aphakic and pseudophakic group to be significantly higher than the median CCT (556microns) in the control group. They also found a negative correlation between the age at lensectomy and the CCT. They found a significant difference between the CCT in aphakic eyes and the CCT in the pseudophakic eyes with primary IOL implantation. However, they only had 5 eyes in the pseudophakic group, none of which had glaucoma, which decreases the power of such a result. Further studies are needed to explore the effect of IOL implantation on the CCT measurements.
Is this increase in corneal thickness caused by the cataract extraction or is it that the eyes with congenital cataract start off with developmentally thicker corneas?

Muir et al. in their study of the CCT in 369 eyes found that the mean CCT of eyes with cataract was not different from the mean CCT of the controls. Further, the mean CCT of eyes with pseudophakia was significantly higher than that of eyes with cataract and eyes of controls. The mean CCT of eyes with aphakia was significantly greater than the mean CCT of eyes with pseudophakia, cataract and controls. They found a positive correlation between the time since cataract surgery and CCT, while there was no correlation between increasing age and CCT in controls. When comparing the mean CCT of aphakic eyes with glaucoma with the mean CCT of aphakic eyes without glaucoma, they found the mean CCT to be higher in the eyes with glaucoma (they used a cup to disc ration of >0.4, or an asymmetry of >0.2 to diagnose glaucoma, so this increase in CCT in eyes with glaucoma probably is not related to a diagnostic selection bias of eyes with thicker corneas into the glaucoma category). They acknowledge that there might be a selection bias with the eyes with aphakic glaucoma having thicker corneas because they are eyes with microcornea or other structural corneal abnormalities not represented in the study. They discuss that a study that compares the CCT in the same eye before and after cataract surgery may be better able to answer this question.

What causes this increase in CCT after cataract surgery is still unknown. Is it related to endothelial injury at the time of cataract surgery?

Nilforushan and associates reported an increased CCT in children with aphakia compared with age-matched control eyes, but with similar endothelial cell counts and morphologic features in both groups. Simsek et al. postulate that surgical trauma to the cornea in the early months of life, when the cornea is undergoing a rapid decrease in its thickness may account for an arrest in the process and the development of thicker corneas in aphakic eyes. This would explain their finding of a negative correlation between the age at cataract surgery and CCT. They also postulate that the presence of an IOL would protect the cornea from exposure to vitreous factors affecting corneal development. Is the same mechanism that affects the trabecular meshwork and leads to aphakic glaucoma, the culprit affecting corneal development and leading to increased corneal thickness? Would corneal endothelial cells cocultured with LEC’s show similar changes found in cocultured TMC’s? Further studies are needed to better understand the changes cataract surgery introduces to the developing eye.

How would the emmerging data regarding CCT in aphakia modify our clinical practice?

We could probably follow Simon’s recommendations of reserving the diagnosis of glaucoma to eyes that show optic disc or visual field changes and the eyes with an IOP of >35mmHg. When the IOP is elevated it would be recommended to measure the CCT to aid in the interpretation. Lopes et al. showed that when a CCT correction formula was applied to the IOP, more than half of the eyes had a 3mmHg difference between measured and adjusted IOP. With a rate of progression from OHTN to glaucoma of 23%, all eyes with elevated IOP should be monitored closely for any changes in optic nerve function that would warrant aggressive medical and surgical management. Would the CCT help us predict which eyes would progress to glaucoma? Further studies are needed to explore this question.

Treatment:

The management of children with post-operative aphakic or pseudophakic glaucoma differs from that of congenital glaucoma. Medical management is often initiated after aphakic glaucoma is diagnosed. There is a paucity of the literature comparing different medical treatment modalities.

When medical management fails, realistic surgical options include seton implantation, trabeculectomy or cyclo-destructive procedures. Aphakia has been previously reported as a significant risk factor for failure of trabeculectomy with mitomycin-C (TMMC) in not only adult patients but also in patients under one year of age; the latter studies are discussed below. Freedman et al retrospectively evaluated results of
17 consecutive children (21 eyes) under 17 years of age (median age 2.6 years) who had failed maximum medical therapy, prior angle or filtration surgery (goniotomy, trabeculotomy, trabeculectomy), or both. TMMC with or without post-operative 5-Fluorouracil (5-FU) or laser suture lysis or both were performed. Aphakic patients performed worse than phakic patients whether TMMC was performed before or after one year of age. Success was poor in all patients less than a year of age, whether phakic (3/8 eyes, 38 %) or aphakic (0/2 eyes). Success rates were higher in patients one year of age, both for phakic (6/6 eyes) and aphakic (2/5, 40%) groups. The authors contend that laser-suture lysis or 5-FU augmentation of TMMC did not improve success in younger, aphakic children and may have increased complication rate. The study is limited by the small number of patients in each subgroup and limited (median 23 month) follow-up of successful cases. Mandal et al. also reported high success rates in older, phakic patients without identifying success in the subgroup of patients who were younger or aphakic.

Beck and colleagues provide another report of failure of TMMC in aphakic patients less than a year of age. Records of 49 patients (60 eyes) 17 years of age or younger (mean age 7.6 years) who had undergone TMMC for various etiologies were retrospectively reviewed. Success (IOP 22 without glaucoma progression or visually devastating complications) rates were 67% at one year and 59 % at two years. Young age (≥ 1 year) and aphakic status were statistically significant risk factors in multivariate analysis. Failure occurred in 60 % of aphakic eyes and in 24 % of phakic eyes. Failure occurred in 7 of 8 eyes of children < 1 year old and in 29 % of 41 eyes of patients one to 17 years of age. Late onset, bleb-related endophthalmitis occurred in 5 of 60 (8 %) eyes. Although TMMC demonstrated considerable efficacy in phakic patients greater than one year old in this and other reports, the authors express concern about the 'substantial' risk of infection with TMMC in aphakic infants.

Age less than one year and aphakia are risk factors for failure of TMMC in the two aforementioned retrospective studies. How do aqueous shunt devices compare? For children two years and younger, Beck, Freedman, and colleagues reported greater efficacy of aqueous shunt devices over TMMC. Only the minority of these patients studied were aphakic or pseudophakic. In this retrospective, age-matched comparison of aqueous shunt devices (ASD) and TMMC, Beck et al. determined the likelihood of maintaining an IOP of less than 23 mmHg in 46 eyes of 32 patients under two years of age. According to the authors, pressure below this level provides clinical stability in very young patients with glaucoma. For the 46 eyes receiving aqueous shunts, 16 eyes (34.8 %) were aphakic or pseudophakic compared to three of 24 eyes (12.5 %) in the TMMC group.

Beck and colleagues employed Baerveldt implants for 32 eyes and Ahmed valves for 14 eyes. After the aforementioned procedures, success achieved at one and three years was 87 % and 53 % in the ASD group, respectively, compared to 36 % and 19 % with the TMMC group at the same intervals. Interestingly, although the seton implantation group was comprised of more high risk patients (16/46 (34.8 %) eyes aphakic or pseudophakic) than the TMMC group (3/24 (12.5 %) eyes), the seton group overall (no separate success rates were reported for aphakic and pseudophakic patients) fared better (72 % success versus 21 % success in TMMC group) and had no infections (versus 8.3 % in TMMC group). Infection is an even larger concern for contact-lens wearing aphakic patients.

The poor success rates and potential for infection with TMMC for young, aphakic patients in the retrospective studies previously discussed corroborate the results of Beck’s work discussed above. For the first surgical procedure for aphakic or pseudophakic patients on maximal medical therapy, seton implantation appears more likely to succeed in controlling IOP than TMMC, especially in infants.

Recently, Chen et al. report a success rate (defined as an IOP of ≥ 21 mmHg with or without medications and no need for further surgery) of 16 % for goniotomies or trabeculotomies, 24.6 % for trabeculectomy with mitomycin-C(MMC) or 5FU, and 44.1 % for seton implants. Pakravan and colleagues performed a randomized prospective clinical trial in which patients were allocated to either TMMC or Ahmed valve with MMC. They did not find a significant difference in the success rates between the two groups. They only had 15 eyes in each group which decreases the power of their study. There was no significant
difference in the rate of complications between the two groups. 6 eyes in the TMMC group had complications which included 4 eyes with choroidal effusions, one with vitreous hemorrhage and one with endophthalmitis. 4 eyes had complications in the Ahmed valve with MMC group with 2 eyes having a choroidal effusion and two eyes a suprachoroidal hemorrhage in the first day after surgery. Ghadhfan and Khan in their literature review of cases of suprachoroidal hemorrhage after pediatric glaucoma surgery conclude that MMC might increase the risk for delayed suprachoroidal hemorrhage and advice against its use with an Ahmed valve without evidence of improved valve function with its use. May be if MMC was not used when implanting an Ahmed valve in Pakravan’s clinical trial, the results would have been different.

Seton implantation size and type are additional surgical considerations. Higher success rates have been reported for Ahmed glaucoma valve implants, Baerveldt implants, and double-plate Molteno implants than single-plate Molteno implants. An attractive feature of Ahmed valve implants is the immediate pressure lowering effect delivered to the glaucomatous eye without a high risking of hypotony; the non-valved Baerveldt implants will not lower pressure until the temporary tube occluder is removed at least one month after the original surgery. Without this temporary tube occlusion the Baerveldt implant would produce marked early hypotony. Rapid IOP reduction may be less crucial in aphakic glaucoma than in patients with congenital glaucoma who fail angle surgery - these latter patients depend upon rapid clearing of the visual axis from lower pressure. Patients with aphakic glaucoma typically have clear corneas. It is easier to implant an Ahmed glaucoma valve than a Baerveldt in an infant due to eye and orbit size, but aphakic glaucoma is most commonly diagnosed four to five year after the cataract surgery is performed. The valve in the Ahmed implant may fail, and there is a greater probability of having a hypertensive phase in an Ahmed valve than in a Baerveldt in pediatric patients. The hypertensive phase tends to peak at a month and resolve by six months after Ahmed implantation in adults.

In children, success has been reported with Molteno implants, Ahmed valve glaucoma implants, and Baerveldt implants. Since all types of glaucoma implants will demonstrate a decline in success rates over time, the ideal seton implant for the aphakic or pseudophakic child with glaucoma is not currently agreed upon. In a recent report on the long term outcomes after aqueous drainage device surgery in refractory pediatric glaucoma, Schotthoefer and associates found that there was no significant difference between the success rates of Ahmed and Baerveldt implants in all of the patients with refractory glaucoma as a group. They did use Ahmed valve more commonly in aphakic glaucoma because in this group there is less of a need for a rapid lowering of IOP; it is possible that the success rates of the two implants would have been different if they stratified for the type of glaucoma. They also did not find a significant difference in the motility limitations or strabismus complications between the two implants.

Banitt and colleagues report on the insertion of a pars plana Baerveldt implant to decrease the risk of anterior rotation of an initially well positioned tube in the growing pediatric eye. The authors concluded that Baerveldt glaucoma implant surgery with pars plana tube insertion is a reasonable option for managing aphakic and pseudophakic children with uncontrolled glaucoma. Complications of Baerveldt glaucoma implant surgery related to anterior chamber tube placement, such as tube-cornea touch, are minimized with this approach. The incidence of posterior segment complications, although possibly higher compared with limbal tube insertion, was not excessive.

Cycloablative techniques have been generally reserved for refractory cases of glaucoma in children. Reported success rates have been low if these techniques are used as the initial surgical option. Cyclocryotherapy and laser cyclophotocoagulation in children may result in severe complications in some patients. Reported complications include retinal detachment, sympathetic ophthalmia, and phthisis. Surgical revision or addition of a second tube implant can also be associated with high rates of complications such as new corneal edema. Supplemental transcleral laser photocoagulation is a viable alternative for children suffering tube failure. Several laser treatments may be required to achieve long term control.
Endocyclophotocoagulation is a relatively recent technique which has demonstrated some promise in treating refractory glaucoma in children and adults. Would this be applicable to children with aphakic glaucoma? Neely and Plager \textsuperscript{72} reported on 51 endoscopic diode laser cyclophotocoagulation procedures performed on 36 eyes of 29 pediatric patients. Cumulative success rates after all procedures at a mean of 19 months of follow up was 43 %, which is similar to the 50% success rates achieved by Phelan et al \textsuperscript{76} and Bock et al \textsuperscript{75} with forms of transcleral Nd:YAG or diode laser. Severe visual complication rates were lowest with endocyclophotocoagulation (11 % with the endoscope versus 50 % or 19 % of patients with transcleral Nd:YAG or diode, respectively). In fact, the authors point out that when combining their study with other studies of this procedure \textsuperscript{79-82}, only 1/123 diode endolaser treated eyes progressed to phthisis. In contrast, cyclocyrotherapy is historically associated with more morbidity, as 12 % to 34 % of patients treated with cyclocyrotherapy progressed to phthisis in past reports \textsuperscript{83-89}. Nonetheless, for aphakic patients especially, Neely and Plager \textsuperscript{72} report that endocyclophotocoagulation is not undertaken without risk, as retinal detachment, hypotony, and decreased vision all have occurred. Long term results are not available, so this procedure should still be used with caution in children with refractory aphakic glaucoma.

Carter, Plager and associates \textsuperscript{90} recently reported a 53 % success rate with endoscopic diode laser photocoagulation after an average follow up of 44.4 months. They mention that they are increasingly using it as a primary procedure in aphakic glaucoma. 38 % of the eyes received only one treatment and were deemed a success. Retinal detachment did develop in two eyes out of 34 in the first month, however, hypotony was not encountered despite 8 eyes having 360\(^\circ\) of cycloablation.

**Outcome: how well are we doing in the management of aphakic and pseudophakic glaucoma**

Chen et al. \textsuperscript{47} report a median and mean final VA on the last follow up visit of 20/400 and 20/515 respectively. In their long term outcome study of pediatric aphakic glaucoma, Bhola and associates \textsuperscript{91} report a more promising visual outcome. At the time of the last follow up, 54.5 % of their patients had a VA of 20/40 or better, 34.5 % between 20/50 and 20/200 and 11 % less than 20/200. They included all patients with an IOP above 25mmHg, so their outcomes may represent a mixed group of OHTN and glaucoma, though 64 % of the eyes had an increase of 0.2 in the cup to disc ratio during the course of follow up and a similar percentage had visual field changes consistent with glaucoma. The percentage of eyes having 20/40 vision or better were equal in the unilateral and bilateral aphakic groups, however the percentage of eyes having less than 20/200 vision was greater in unilateral aphakia.

**Summary**

Ophthalmologists must be vigilant about assessing for post-operative glaucoma in children left aphakic or pseudophakic when cataract surgery is performed within 1\(^{st}\) year of life. We recommend regular follow-up (if needed, examination under anesthesia) for early diagnosis of glaucoma in children operated at early age.

**References**

33. Leske MC, Heijl A, Hyman L, Bengtsson B, Dong L, Yang Z. Predictors of long-term progression in the early manifest glaucoma trial. Ophthalmology 2007; 114:1965-72.


