Risk factors for strabismus following glaucoma drainage device implantation for refractory childhood glaucoma

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BACKGROUND Strabismus is common in children after glaucoma drainage device (GDD) implantation, but the risk factors for postoperative strabismus remain speculative. The purpose of this study was to investigate possible risk factors for strabismus following GDD implantation for refractory childhood glaucoma.

METHODS The medical records of consecutive patients who underwent GDD implantation for refractory childhood glaucoma at Duke Eye Center from 2005 to 2016 were reviewed retrospectively. Pre- and postoperative motility and alignment, best-corrected visual acuity, and demographic and surgical data were extracted from the record for analysis.

RESULTS A total of 81 patients (mean age, 7.9 ± 4.8 years) met inclusion criteria. The most common glaucoma type was glaucoma following cataract surgery (GFCS), and the most common GDD was a Baerveldt 250 mm^2 device. Before GDD surgery, 38 patients (47%) had documented strabismus. After GDD implantation, 25 (31%) had new or worsened strabismus, with vertical (16% of new/worsened), horizontal strabismus (exotropia, 48% of new/worsened; esotropia, 12% of new/worsened) and vertical and horizontal (24% of new/worsened) noted. New motility limitation occurred in 32 of 81 (40%) patients. Risk factors including age, type/location/number of GDD, revision, motility limitation, glaucoma type, asymmetric visual acuity, and visual impairment were not significantly associated with new or worsened post-GDD strabismus.

CONCLUSIONS Children with refractory childhood glaucoma are at high risk for strabismus, which increases after GDD implantation; this study identified no clear risk factors for new or worsened post-GDD strabismus. (J AAPOS 2019;23:145.e1-6)

Strabismus following glaucoma drainage device (GDD) implantation is a known complication in adults, with incidence ranging from 2% to 77%.[1,2] Strabismus has been documented following implantation of valved and nonvalved implants, including Baerveldt, Molteno, and Ahmed devices, although Baerveldt devices have been reported to have a higher incidence of postoperative diplopia than other implants.[2,3] GDDs in adults have been reported to be more likely to cause diplopia than trabeculectomy or medical treatment.[2] Several etiologies for post-GDD strabismus have been suggested, including scarring of the extraocular muscle to the GDD plate, compromise of muscle function due to surgical trauma, and displacement of the muscle or eye due to large bleb formation.[4] In adults, increased age has been found to be a risk factor for postoperative motility disturbance.[1]

Few reports have considered postoperative strabismus in children receiving GDDs.[5,6] Children with refractory glaucoma who undergo GDD implantation have several factors that increase the risk for postoperative strabismus, including anatomic abnormalities, decreased visual potential, and higher risk of GDD failure, sometimes requiring implantation of multiple GDDs. The incidence of postoperative strabismus in children after GDD surgery has been reported to be as high as 57% and 47% in subgroups with primary congenital glaucoma (PCG) and glaucoma following cataract surgery (GFCS), respectively.[5] No specific factors have been reported to be associated with postoperative strabismus after GDD implantation in children with refractory glaucoma. The purpose of this study was to investigate the frequency of new or worsened strabismus after GDD implantation in a large

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series of patients with refractory childhood glaucoma and to identify risk factors for strabismus following GDD implantation in this population.

Subjects and Methods

The medical records of consecutive patients who had at least one GDD implanted for refractory childhood glaucoma at Duke Eye Center from December 2005 to June 2016 under a single attending surgeon (SFF) were reviewed retrospectively. Approval from the Duke University Health System Institutional Review Board was obtained, and data was collected in compliance with the US Health Insurance Portability and Accountability Act of 1996. Data was collected from a preoperative visit (within 12 months of surgery) and an early (3 months to <6 months) postoperative and/or a late (6 months to <19 months) postoperative visit for single GDD implantation in one eye that met inclusion criteria. Only cases with motility and alignment data recorded at a preoperative visit and either an early and/or late postoperative visit were included in the analysis. If concomitant strabismus surgery was performed at the time of GDD implantation, that episode was excluded. If a second GDD was placed within the early postoperative period of a previous GDD, the first GDD implanted was excluded, ensuring that no postoperative data overlapped for GDD implantation events. Patients ≤18 years of age at GDD implantation were included in the analysis, provided they had refractory childhood-onset glaucoma. The data for each patient was analyzed for development of strabismus. If a patient had more than one GDD implanted during the study period, only the first GDD implanted with data meeting inclusion criteria was included.

Childhood glaucoma type was recorded and grouped as PCG, GFCS, Sturge-Weber-associated glaucoma (SWG) and other (including glaucoma associated with Peters anomaly/anterior segment dysgenesis, uveitis, trauma, and angle closure). GDD type, size, and quadrant of device implantation were recorded. For patients with more than one GDD, the GDD was numbered by implant per patient and implant per eye. A GDD was designated a revision if the capsule surrounding a previous GDD was opened and a new GDD was placed in the original GDD capsule and was included in analysis. GDD implantation for all patients included occurred under a single attending surgeon with consistent surgical technique applied in each case.[7] We consistently sized the GDD reservoir to the eye, using a "home-grown" formula prior to the publication of the Freedman-Margeta small-eye formula and thereafter using the online calculator.[8] Additionally, we began using a limbus-based rather than fornix-based incision from approximately 2010. All GDD plates were meticulously placed with respect to the adjacent rectus muscles in the chosen quadrant, with the anterior GDD plate edge usually 8 mm from the limbus (ranging from 6–9 mm in special cases).

Sensorimotor examination was performed by trainees or orthoptists and the attending surgeon. Motility limitation (−1 or worse on a scale of −1 to −4) was recorded for each eye as either present or absent in horizontal and vertical versions or ductions. If a limitation was present, it was classified by the direction of limitation (superior, superotemporal, temporal, superonasal, nasal, inferonasal, inferotemporal, or inferior). Alignment was recorded for near and distance measurements where present and was evaluated by cover/uncover testing to determine whether a deviation was a phoria or tropia. Quantification of strabismus was then performed by alternate prism cover testing except where precluded by lack of fixation or cooperation. For those patients, measurements were done by Krimsky testing or Hirschberg estimation. Alignment was categorized by horizontal and vertical deviations. Phorias were not considered strabismic deviation and dissociated vertical deviations were considered the equivalent of a vertical tropia if recorded consistently at different office visits. New strabismus was defined as a tropia occurring in patients who were orthotropic in primary gaze at distance and near at the preoperative visit. Worsening strabismus was defined as $>10^{\Delta}$ increase in deviation measured in primary gaze by either distance or near measurement compared to the corresponding distance measurement preoperatively.

Visual acuity was measured by Snellen, HOTV, or Allen pictures in verbal children, and by fix and follow, preferential looking testing, or central/steady/maintained in preverbal children. A difference of >2 lines (optotype vision only) was defined as asymmetric visual acuity and assumed to be related to amblyopia and/or organic causes such as media opacity and optic nerve

Table 1. Baseline patient and GDD characteristics

Characteristic[a]	Result[b]
Age, years, at GDD implantation, mean ± SD	7.9 ± 4.8
Sex, no. (%)	
Female	41 (51)
Race, no. (%)	
White	53 (65)
Black	17 (21)
Hispanic	2 (2)
Other/unknown	9 (11)
Glaucoma diagnosis, no. (%)	
Glaucoma following cataract surgery	33 (41)
Primary congenital glaucoma	16 (20)
Sturge-Weber-associated	11 (14)
Other	21 (26)
GDD type, no. (%)	
BVT250	38 (47)
BVT350	13 (16)
Ahmed FP7 or S2	30 (37)
GDD plate location, no. (%)	
Superotemporal	68 (84)
Inferonasal	8 (10)
Inferotemporal	5 (6)
First GDD for eye, no. (%)	69 (85)
First GDD for patient, no. (%)	60 (74)
Pre-op strabismus, no. (%)	
Horizontal only	32 (40)
Exotropia	20 (25)
Esotropia	12 (15)
Vertical only	3 (4)
Horizontal and vertical	3 (4)
Total with any pre-op strabismus	38 (47)

BVT250, Baerveldt 250 mm^2; *BVT350*, Baerveldt 350 mm^2; *GDD*, glaucoma drainage device.
[a]Total number of patients = 81.
[b]Percentages are rounded.

Table 2. Preoperative best-corrected visual acuity, fusion, and stereopsis

Characteristic[a]	Result
Visual acuity asymmetry, no. (%)	
>2 line difference between eyes	38 (47)
≤2 line difference between eyes	23 (28)
Unable to assess,[b] no. (%)	20 (25)
VI,[c] no. (%)	
None to mild (BCVA ≥20/60)	53 (65)
Moderate (BCVA 20/70 to 20/200)	6 (7)
Severe (BCVA ≤20/200)	3 (4)
Unable to assess,[b] no. (%)	19 (23)
BCVA operative eye, no. (%)	
Median optotype BCVA (range)	20/60 (20/20 to LP)
None to mild VI	25 (31)
Moderate VI	15 (19)
Severe VI	21 (26)
Unable to assess	20 (25)
Fusion, no. (%)	
Present	4 (5)
Absent	22 (27)
Not recorded	55 (68)
Stereopsis, no. (%)	
Present	8 (10)
Absent	14 (17)
Not recorded	59 (73)

BCVA, best-corrected visual acuity; *LP*, light perception; *VA*, visual acuity; *VI*, visual impairment.
[a]Total number of patients = 81.
[b]VA could not documented by HOTV, Snellen, or Allen. Of these, 9 were documented as "fix and follow," 3 were documented by Teller cards, 3 by other methods, and 4 had no visual assessment recorded.
[c]BCVA in better eye or both eyes together.

damage. Categories of visual impairment were defined as follows: none/mild (best-corrected visual acuity of ≥20/60), moderate (best-corrected visual acuity between 20/70-20/200), and severe (best-corrected visual acuity of <20/200). Stereopsis (Titmus testing) and fusion were recorded when documented. Fusion was documented by Worth four dot testing at both distance and near, and recorded as present if documented as present at either distance or near testing. Any mention of diplopia in the medical record was recorded.

Statistical analysis was performed using Matlab (The MathWorks Inc, Natick, MA) and Graphpad Prism (Graphpad Prism Software Inc., La Jolla, CA). Testing for factors associated with development of new or worsening postoperative alignment and subgroup analysis was performed using the Fisher exact test for binary variables and χ^2 test for categorical values. A P value of <0.05 was considered statistically significant. The Holm-Bonferroni method was used to control for family-wise error rate due to multiple comparisons.

Results

A total of 214 GDDs were implanted during the study period; 81 patients who had GDDs implanted met inclusion criteria. Table 1 outlines the baseline preoperative characteristics of the patients, including demographic information, motility, GDD type, and location. The mean

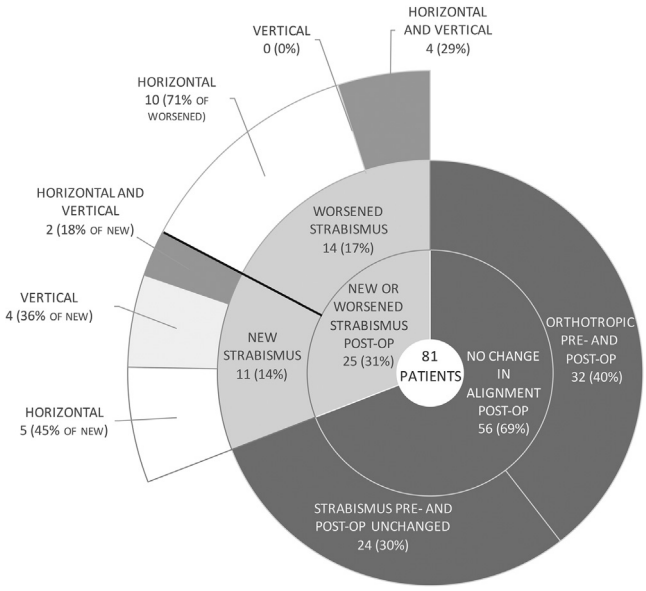

FIG 1. Presence of strabismus both pre- and post-glaucoma drainage device (GDD) implantation with strabismus type post-implantation. N = 81 patients (percentages rounded).

age at study-eligible GDD implantation was 7.9 ± 4.8 years. The most common indication for GDD was refractory GFCS (33/81 [41%]), and the most commonly placed GDD (38/81 [47%]) was a Baerveldt 250 mm^2 implant (Johnson & Johnson Vision, Santa Ana, CA), positioned in the superotemporal quadrant (68/81 [84%]). Preoperatively, of the 81 patients, 38 (47%) patients had strabismus, including 32 (40%) with horizontal misalignment only and 3 (4%) with vertical misalignment only. Of the subset of 21 patients with a prior GDD, 14 (67%) had strabismus preoperatively compared to 24 of 60 (40%) with no previous GDD.

Preoperative fusion, stereopsis, and optotype visual acuity data are detailed in Table 2. Optotype visual acuity was documented in 62 of 81 patients (77%). Asymmetric visual acuity was found in 38 patients (47%), whereas 53 (65%) had best-corrected visual acuity of ≥20/60. Preoperatively, 26 patients had documented fusion testing; 4 demonstrated fusion. Of 22 patients with stereoacuity testing recorded preoperatively, gross stereopsis (positive response to Titmus stereo fly) was noted in 8 patients.

New or worsened postoperative misalignment was documented in 25 of 81 patients (31%) after GDD implantation (Figure 1). Of these 25, 11 represented new strabismus and 14 had worsening of pre-GDD strabismus. Of 47 patients with both early and late postoperative alignment recorded, 9 of the 47 patients (19%) had no change in alignment at the early postoperative visit but were noted to have new or worsened strabismus at the late postoperative visit. Postoperative motility limitation is detailed in Table 3. Of those with postoperative motility limitation (32/81 [40%]), 13 had new or worsened primary gaze strabismus. Exotropia was the most common deviation both

Table 3. Post–glaucoma drainage device implantation motility limitation

	n (%)
New post-op motility limitation[a]	32 (40)
Horizontal[b]	18 (22)
Vertical[c]	24 (30)
Alignment change with motility limitation	13 (16)

[a]Subjects may have had both horizontal and vertical limitations.
[b]Nasal or temporal gaze.
[c]Superotemporal/superior/superonasal/inferonasal/inferior/inferotemporal field of gaze.

preoperatively (20/38 [53%]) and among those with new or worsened postoperative strabismus (12 of 25 [48%]) (Figure 2). Of 38 patients with preoperative strabismus, 6 (16%) had a vertical misalignment; of 25 patients with new or worsened strabismus post-GDD implantation, 10 (40%) had vertical strabismus.

Table 4 shows analysis of possible factors associated with development of new or worsening strabismus post-GDD implantation. The following factors were not found to be associated with worsened postoperative alignment: patient age at GDD implantation, type of GDD, location of GDD, GDD number per eye or patient, revision, motility limitation, asymmetric visual acuity, and visual impairment category. Only glaucoma type (GFCS vs other childhood glaucoma types) had an association ($P = 0.04$) with risk of postoperative strabismus, which was not significant when stricter criteria ($P < 0.004$) were applied using the Holm-Bonferroni method.

Discussion

Strabismus following GDD implantation has been reported in both pediatric and adult populations.[1,5,9,10] Numerous etiologies have been proposed for postoperative strabismus, including restriction due to the effect of the GDD plate on adjacent muscles, dislocation of the eye due to the presence of the GDD and surrounding capsule, and a posterior fixation suturelike effect on adjacent muscles due to the presence of the GDD plate and scarring.[5,9,10] In this large, retrospective study of strabismus following GDD implantation for refractory childhood glaucoma, 31% of patients showed new or worsened strabismus after GDD implantation. Only GFCS (versus other glaucoma types) showed a weak statistical association with new or worsened strabismus post-GDD implantation; all other potential risk factors examined failed to demonstrate a statistically significant association.

Strabismus in the setting of refractory childhood glaucoma is likely multifactorial, and those risk factors for new or worsened strabismus following GDD implantation are unknown. The rate of strabismus in childhood glaucoma was high (47%) in this study, both among patients with no prior GDD (40%) and among those in whom a prior GDD was in place in one or both eyes (67%).

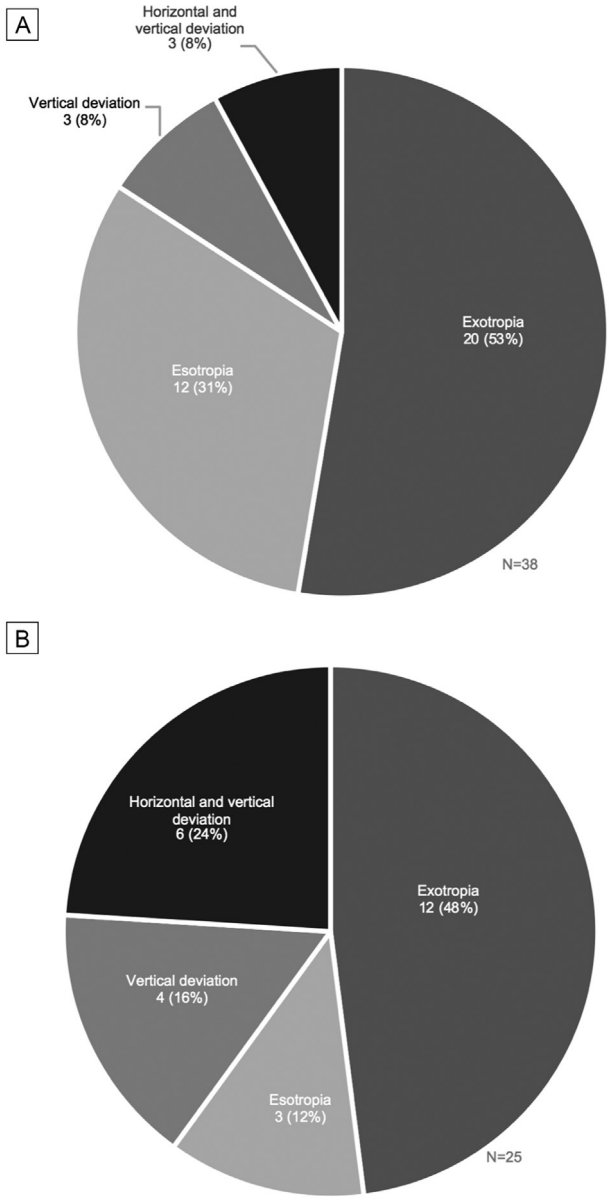

FIG 2. Comparison of type of strabismus pre-GDD implantation versus type of new or worsened strabismus post-GDD implantation. Preoperative strabismus (A) included 38 patients with documented primary gaze strabismus. Postoperative strabismus (B) included 25 patients with new or worsened primary gaze strabismus. Vertical strabismus in any form was noted in 6 of 38 (16%) preoperatively but increased to 10 of 25 (40%) postoperatively among those with new or worsened strabismus post-GDD implantation. This trend was not statistically significant ($P = 0.07$).

Though higher than reported by Schotthoefer and colleagues,[5] who noted pre-GDD strabismus in 28% of eyes with GFCS versus only 14% with PCG, our study included diverse glaucoma types. This population is already at high risk for strabismus even prior to GDD implantation because there is a risk of asymmetric visual acuity (from amblyopia and organic causes) and binocular visual impairment from anisometropia, ocular and orbital anatomic

Table 4. Analysis of possible risk factors for new or worsened after GDD implantation

Risk factor	*P* value
Age at GDD surgery	0.89
Diagnosis[a]	0.04
Type of GDD[b]	0.64
Location of GDD[c]	0.47
Revision[d]	0.75
GDD no. per patient[e]	1
GDD no. per eye[f]	0.58
New motility limitation	0.15
New horizontal motility limitation	0.25
New vertical motility limitation	0.20
VI category[g]	1.0
VA asymmetry (difference of >2 lines BCVA)	0.41

BCVA, best-corrected visual acuity; *GDD*, glaucoma drainage device; *VA*, visual acuity; *VI*, visual impairment.
[a]Primary congenital glaucoma, glaucoma following cataract surgery, Sturge-Weber associated glaucoma, other.
[b]Baerveldt 250 mm^2, Baerveldt 350 mm^2, Ahmed FP7, or S2.
[c]Location by quadrant: superotemporal, superonasal, inferonasal, inferotemporal.
[d]Revision: old capsule opened and new GDD placed in previous capsule.
[e]Total no. GDDs patient received: 1 vs > 1.
[f]GDD no. per eye: 1 vs > 1.
[g]VI categories: no/mild VI (BCVA of ≥20/60), moderate VI (BCVA of 20/70-20/200), severe VI (BCVA of <20/200).

changes, and glaucomatous optic neuropathy. A minority of cases demonstrated fusion or any stereopsis, although most patients lacked documentation of such testing, presumably because of age, cooperation, or poor vision; this poor binocular function has been previously reported.[5] The somewhat counterintuitive finding that a few more cases were documented to have gross stereopsis than fusion (8 vs 4, resp.) may be due to the relatively greater ease with which children identified the Titmus fly versus reliably performed Worth 4-Dot testing. In children with poor binocular function, the anatomical changes associated with GDD implantation may be sufficient to create a postsurgical manifest deviation or worsen previously stable misalignment.

In our study, horizontal strabismus (and particularly exotropia) constituted the majority of cases of new or worsened strabismus, as has been reported in large adult series.[1] Possible explanations include a restrictive effect of the GDD plate (and/or the bleb over the plate) on the lateral rectus muscle from a superotemporal GDD, secondary scarring in this quadrant limiting adduction or poor binocularity in this patient population, predisposing them to sensory exodeviations. Concordant with O'Malley Schotthoefer and colleagues,[5] we found a trend toward increased vertical strabismus among those with new or worsened postoperative strabismus, but unlike the previous study, we did not find an association of vertical postoperative limitation with postoperative vertical strabismus.[5] Although limitation of motility was commonly noted after GDD placement for childhood glaucoma (40%), fewer than half of those patients had a corresponding worsening of strabismus in primary gaze. Since alignment was not documented in all gaze positions, it is possible that some patients with motility limitation may have had strabismus only in nonprimary gaze. Though cases of strabismus present only in nonprimary gaze would be of interest, lack of documentation of diplopia and consistent strabismus measurements in all fields of gaze at postoperative visits led us to include only the more clinically relevant primary gaze alignment.

Neither asymmetric visual acuity nor binocular visual impairment was associated with new or worsened strabismus. It may be that this study was underpowered to find a difference or that our asymmetric visual acuity criterion (difference of >2 lines) was too inclusive, because a majority of patients fell in that category. Because of the paucity of reliable fusion and stereopsis data, we were unable to analyze the association of those factors with new or worsened postoperative strabismus.

Our findings should be considered in light of several additional study limitations, most related to the retrospective nature of the study and the complexity of the pediatric glaucoma population receiving GDDs. Although it was standard in the Duke pediatric ophthalmology clinic to attempt complete sensorimotor testing on each patient at every visit, there was some unavoidable variability, because the sensorimotor examination was often performed by different examiners pre- and postoperatively, with varying experience with alignment measurements and with different levels of patient cooperation and fixation ability. The limited numbers of patients and our desire to examine numerous potential risk factors limited our power to find statistical associations. Axial length and refractive error could have provided a proxy for structural characteristics of the eye and orbit that might influence postoperative strabismus; however, we did not uniformly have access to that data in the cases reviewed.

Despite these limitations, this series is larger than previously published studies of strabismus post-GDD implantation for refractory childhood glaucoma, all GDDs were implanted under a single attending surgeon, and fairly rigorous inclusion criteria were applied for pre- and postoperative motility data. While there may be bleb-related and surgical technique–related features associated with an increased risk of postoperative strabismus, there were no cases of "giant" bleb in this series, which occurred infrequently in the authors' experience. Since we have a strict and fairly uniform surgical GDD implantation technique at Duke and calculate and execute plate trimming for short eyes, we suspect we would have no ability to identify these surgical features as risks for new or worsened strabismus in this series.[7,8] Nonetheless, the fact that we have documented new and worsened primary gaze strabismus in children who undergo GDD surgery, despite meticulous surgical technique, highlights the risk of this complication.

As previously documented, patients with refractory childhood glaucoma who undergo GDD implantation are at substantial risk for new or worsened strabismus, which can present even months after the GDD bleb has formed.

Though motility limitation does occur following GDD placement, the risk of primary-gaze strabismus may be heightened by baseline poor binocularity and anatomic features that remain to be well delineated. Though no specific risk factor was identified in this study, the families of patients undergoing GDD implantation should be counseled on the substantial risk of strabismus postoperatively. Additional study of strabismus and its relationship to GDDs in refractory childhood glaucoma is warranted.

Literature Search

PubMed was searched on December 30, 2018, without date or language restriction, using the search terms *glaucoma drainage device* OR *glaucoma drainage implant* AND *strabismus*. Of the 36 results, none involved identifying risk factors for strabismus in pediatric populations following GDD surgery.

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