Original Article

# Outcomes of trabeculectomy in juvenile open angle glaucoma

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**Purpose:** This study was aimed at reporting the outcomes of trabeculectomy in primary juvenile open angle glaucoma (JOAG). **Design:** This study was a retrospective noncomparative case series. **Materials and Methods:** We included 60 eyes of 41 JOAG patients who underwent primary trabeculectomy without mitomycin-C (MMC) between 1995 and 2007. The primary outcome was success, defined as complete, if intraocular pressure (IOP) was >5 and ≤21 mmHg without medications or qualified if IOP was >5 and ≤21 mmHg with or without antiglaucoma medications. Secondary outcome measures were mean and percentage IOP reduction, complications, and risk factors for the failure of trabeculectomy. **Results:** The mean (±standard deviation) age at presentation was 24.1 ± 6.8 years (range, 12–35). Mean follow-up was 67 ± 41 months (range, 12–156). At 1 year, the probability of complete success was 92% ($n$ = 56, 95% CI: 81–96%), at 3 years it was 89% ($n$ = 47, 95% CI: 78–95%), and at the end of 5 years, it was 80% ($n$ = 34, 95% CI: 65–89%). The probability of qualified success was 100% ($n$ = 60) at 1 year, 98% ($n$ = 51, 95% CI: 87–100%) at 3 years, and 96% ($n$ = 36, 95% CI: 84–99%) at the end of 5 years. The mean IOP reduced from 35 ± 10 to 13 ± 2.5 mmHg ($P$ < 0.001) after trabeculectomy. There was no serious postoperative complication. Young age was the only significant risk factor associated with the failure (odds ratio = 0.89, $P$ = 0.03). **Conclusion:** Primary trabeculectomy without MMC has good success rates in JOAG.

**Key words:** Juvenile open angle glaucoma, juvenile glaucoma, primary trabeculectomy, trabeculectomy in young

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Primary juvenile-onset open angle glaucoma (JOAG) is a rare subset of open angle glaucoma characterized by an early age of onset, high intraocular pressure (IOP), and an autosomal dominant pattern of inheritance.[1,2] JOAG is differentiated from late congenital glaucoma and other childhood glaucoma by the absence of buphthalmos, megalocornea, Descemet's breaks (Haab's striae), or anterior segment dysgenesis.[2]

Although the treatment of JOAG is similar to POAG, management of JOAG poses a few challenges. It has been shown that medical therapy is not as efficient in JOAG compared to POAG and often (83%) requires filtering surgery for IOP control.[1,2]

Studies evaluating the outcomes of trabeculectomy in JOAG have reported success rates ranging from 50% to 87% at 3 year follow-up.[2-9] Most of these studies have included heterogeneous groups with primary and various types of secondary glaucomas, some studies with intraoperative mitomycin-C (MMC) use and these studies are reported from various ethnic groups; all these can influence the success rates of filtering surgery. Success of filtering surgery in JOAG has shown to be inferior to that in POAG because of exaggerated healing response in these young eyes, and use of antimetabolites during surgery is often recommended.[10-16] However, the use of antimetabolites at young age predisposes them to prolonged risk of postoperative bleb-related complications. Comparative studies with and without use of MMC in JOAG have either shown no statistical difference in the success of trabeculectomy between the groups (Yalvac *et al*.) or have shown better IOP control with MMC use but with increased sight threatening complications, ultimately decreasing the outcome of success (Tsai *et al*.). To the best of our knowledge, there are no reports on the outcomes of trabeculectomy in primary JOAG subjects with Indian ethnicity, hence the purpose of this study was to analyze the outcomes of trabeculectomy without MMC in Indian eyes with primary JOAG.

## Materials and Methods

We retrospectively reviewed the charts of patients with JOAG who underwent trabeculectomy without MMC at our centre between 1995 and 2007. JOAG was diagnosed in subjects between 10 and 35 years of age at the time of presentation, in the presence of an IOP > 21 mmHg, open anterior chamber angle on gonioscopy, glaucomatous optic disc damage on clinical examination (focal or diffuse neuroretinal rim thinning, localized notching or nerve fiber layer defects), and the corresponding visual field (VF) defects. During the study period, 364 subjects were diagnosed with primary JOAG. We excluded eyes with steroid-induced glaucoma and other types of secondary open angle glaucoma and JOAG eyes that underwent trabeculectomy with MMC or had a previous filtering surgery. The eyes with only ocular hypertension with no secondary causes were also excluded from the study. A total of 202 eyes of 139 subjects with JOAG underwent primary trabeculectomy. Glaucoma filtering surgery was required in about 40% of our JOAG patients (139/364), with uncontrolled glaucoma on maximum medical therapy. Of these, 159 eyes underwent simple trabeculectomy and 43 eyes underwent MMC augmented trabeculectomy. Eighty-eight of 159 eyes with follow-up less than 12 months following trabeculectomy

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were excluded from the analysis for success. Hence our study included 60 eyes of 41 JOAG subjects who underwent primary trabeculectomy without MMC with at least 12 months of follow-up. The institutional review board approved the study. Preoperative examinations included detailed medical history, corrected visual acuity (CVA), slit-lamp examination, IOP measurement with Goldmann applanation tonometer, gonioscopy, dilated fundus examination, VF examination on Humphrey VF analyzer (Carl Zeiss Meditec, Inc. Dublin, CA) either with full threshold or Swedish Interactive Threshold Algorithm-standard; either 24-2 or 30-2 program. VF defects were considered glaucomatous if at least two of the three Anderson's criteria (three or more nonedged points in a cluster depressed to $P < 5\%$ and one of which is depressed to $P < 1\%$, the Glaucoma Hemifield Test outside normal limits and Pattern Standard Deviation depressed to $P < 5\%$) were fulfilled.

Trabeculectomy was performed in eyes with IOP ≥ 21 mmHg with maximum tolerated antiglaucoma medications. Trabeculectomy was performed either by a fornix-based or limbus-based conjunctival approach. A 4 × 4 mm triangular scleral flap was dissected up to clear cornea, a 2 × 2 mm deep scleral block was excised and peripheral iridectomy was performed. The scleral flap was closed with 1 apical or 3 10-0 nylon sutures and conjunctiva was closed with 8-0 vicryl suture. Postoperative follow-up visits were scheduled on the first day, first week, first month, and at 4-month intervals thereafter. CVA, IOP, and slit lamp biomicroscopy were performed during all visits and dilated fundus examination along with VF examination was performed once a year.

### Statistical analysis

Descriptive statistics included mean and standard deviation for normally distributed variables and median, first quartile, and third quartile values for nonnormally distributed variables. As both eyes of few patients were included for the analysis, generalized estimating equations were used to adjust the standard errors.

Kaplan–Meier survival curves were used to assess the cumulative probability of success. The primary outcome measure was success which was defined as complete success if IOP was between 5 and 21 mmHg without any antiglaucoma medication and qualified success if IOP was between 5 and 21 mmHg with or without antiglaucoma medications. Eyes not falling into complete success criteria or eyes that required re-surgery or eyes that had sight-threatening complications in the postoperative period were labelled as failure. Associations between failure and baseline factors such as age, gender, refractive error, preoperative IOP, number of preoperative medications, mean deviation on VF, duration of follow-up, and duration of medical treatment before surgery were assessed using the multivariate logistic regression model. A *P*-value of ≤0.05 was considered statistically significant. Statistical analysis was performed using commercial software (Stata ver. 10.0; StataCorp, College Station, TX).

## Results

Our study included 60 eyes of 41 primary JOAG patients who underwent primary trabeculectomy with at least 12 months of postoperative follow-up. The demographics and clinical features are given in Table 1. The mean age at presentation was 24.1 ± 6.8 years (range, 12–35). The majority of the JOAG patients were male (79%) and all eyes had severe VF loss at the time of presentation with median mean deviation (MD) of −23 dB. There was positive family history of glaucoma in only 3 patients (7%).

**Table 1: Demographic and clinical features of the patients before surgery**

| | Mean ± SD | Range |
|---|---|---|
| Age (years) | 24.1 ± 6.8 | 12–35 |
| Male:female (number) | 33:9 | |
| Family history of glaucoma (*n*, %) | 3 (7.14%) | |
| IOP before surgery (mmHg) | 35 ± 10 | 12–55 |
| Number of antiglaucoma medications | 1.75 ± 0.97 | 0–3 |
| LogMAR visual acuity[a] | 0.1 (0, 0.5) | 0–2 |
| Spherical equivalent manifest refraction (diopters)[a] | 0 (−2, 0) | −12.5–0 |
| Mean deviation (dB)[a] | −23.01 (-31.29, −8.63) | −35.75 to −0.83 |
| Pattern standard deviation (dB)[a] | 6.27 (2.83, 9.55) | 0.8–13.81 |
| Total follow-up duration (months) | 69 ± 40 | 12–156 |

IOP: Intraocular pressure, LogMAR: Logarithm of minimum angle of resolution, dB: decibel, [a]Values are median with first and third quartiles

The mean (±standard deviation) IOP reduced significantly ($P < 0.001$) from 35 ± 10 mmHg before surgery to 13 ± 2.5 mmHg at the last follow-up after the surgery. The mean percentage reduction in IOP after surgery was 55 ± 22%. The median CVA after surgery (0.1 log MAR units) was similar ($P < 0.45$) to that before surgery (0.1 log MAR units). The parameters were compared before surgery and at the last follow-up after surgery.

The complete and qualified success probabilities of trabeculectomy in JOAG are shown in Figs. 1 and 2. At 1 year, the probability of complete success was 92% (*n* = 56, 95% CI: 81–96%), at 3 years, it was 89% (*n* = 47, 95% CI: 78–95%) and at the end of 5 years, it was 80% (*n* = 34, 95% CI: 65–89%). The probability of qualified success was 100% (*n* = 60) at 1 year, 98% (*n* = 51, 95% CI: 87–100%) at 3 years, and 96% (*n* = 36, 95% CI: 84–99%) at 5 years. Fifty-five percent of the eyes (33/60) had IOP ≤ 18 mmHg without antiglaucoma medications during the entire follow-up.

Early postoperative complications (within 3 months) included hyphema (*n* = 2, 3.3%), encapsulated bleb (*n* = 2, 3.2%), shallow anterior chamber (*n* = 1, 1.6%), and hypotony with choroidal detachment (*n* = 1, 1.6%). All of these resolved with conservative management except in one patient where an anterior chamber (AC) reformation with air was done for persistent shallow AC, which resolved completely within 10 days. In the late postoperative period, 2 eyes (3.2%) developed visually significant cataracts at 5 and 10 years after trabeculectomy, which needed surgery.

Table 2 shows the results of the logistic regression model evaluating the associations between failure and the baseline factors. The age was the only factor significantly associated with failure (odds ratio: 0.89, $P = 0.03$). Fig. 3 represents the results of the logistic regression model showing the predicted probability

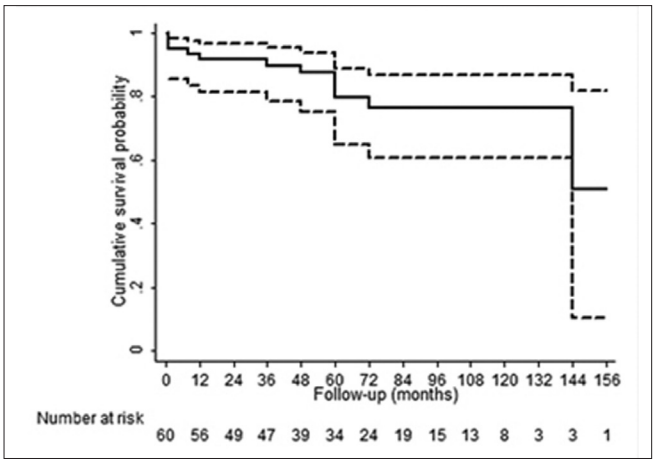


**Figure 1:** Kaplan–Meier survival curve showing the cumulative probability of complete success after trabeculectomy in juvenile open angle glaucoma (dotted lines represent 95% confidence limits)

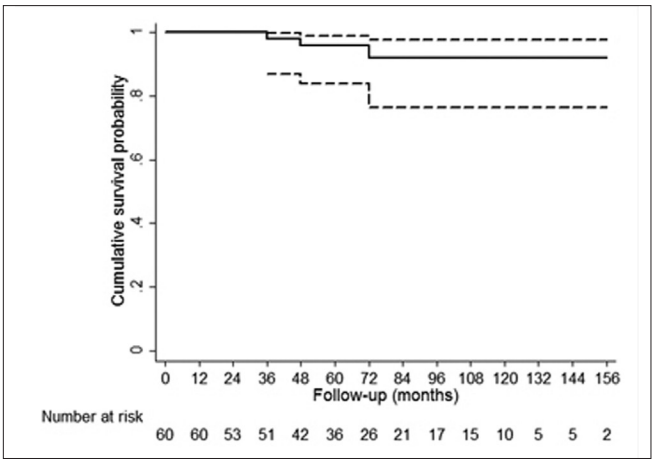


**Figure 2:** Kaplan–Meier survival curve showing the cumulative probability of qualified success after trabeculectomy in juvenile open angle glaucoma (dotted lines represent 95% confidence limits)

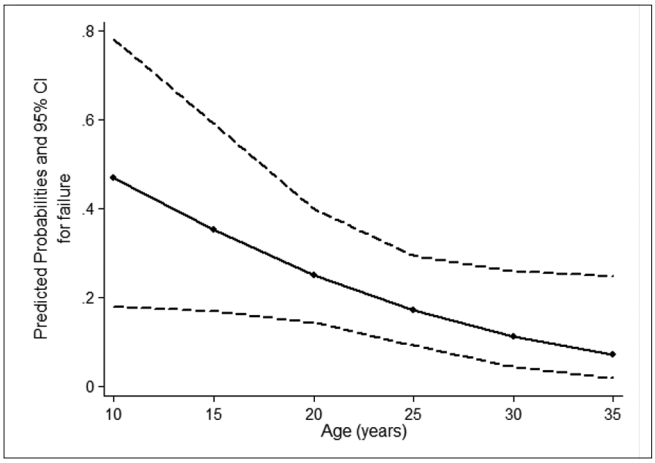


**Figure 3:** Relation between age and the predicted probability of failure, showing predicted probability of failure decreasing with increasing age

**Table 2: Results of the multivariate logistic regression model showing the associations between risk factors and failure of trabeculectomy**

| Risk factors | Odds ratio | 95% CI | *P* value |
|---|---|---|---|
| Age | 0.89 | 0.80–0.98 | 0.02 |
| Spherical equivalent | 0.98 | 0.69–1.38 | 0.89 |
| Preoperative IOP | 1.04 | 0.97–1.11 | 0.23 |
| Number of antiglaucoma medications before surgery | 1.10 | 0.44–2.75 | 0.85 |
| MD | 0.99 | 0.93–1.05 | 0.76 |
| Duration of follow-up | 1.01 | 0.99–1.03 | 0.48 |
| Duration of medical treatment before surgery | 1.00 | 0.99–1.01 | 0.37 |

IOP: Intraocular pressure, MD: Mean deviation, CI: Confidence interval

of failure decreasing with increasing age. When we looked at the success rate of trabeculectomy with age, the success rates increased with increasing age (decade wise). The success rate increased from 63.2% (12/19 eyes) in the second decade (12–20 years) to 83.3% (25/30 eyes) in the third decade (21–30 years) and 100% (11/11 eyes) in the fourth decade (31–35 years).

## Discussion

To the best of our knowledge, this is the first case series on the outcomes of trabeculectomy in JOAG patients of Indian origin. Glaucoma filtering surgery was required in about 40% of our JOAG patients who presented to our institute between 1995 and 2007. In our study, in primary trabeculectomy without MMC in JOAG, the complete success probability was 89% at 3 years and 79% at 5 years.

The success rates reported after trabeculectomy in JOAG have ranged from 38% to 100% in different studies.[2-9] Most of these studies have included heterogeneous group of patients (patients with primary and secondary causes of glaucoma). Studies also have shown different success rates of trabeculectomy in different ethnicities.

The long-term success rates of JOAG in our study are similar to the success rates reported in the literature.[4-8] Koraszewska *et al*. have reported a complete success rate of 79% ($n$ = 19) at 5.1 years and 66.7% ($n$ = 18) with a mean follow-up of 11.1 years.[8] However, their study predominantly included JOAG patients of Caucasian origin and in the age group of 6–18 years. The overall success rate by Jacobi *et al*.[7] (15–45 years) was 87% ($n$ = 23, in the JOAG subset) at 5 years and Costa *et al*.[6] (15–40 years) have reported an overall success rate of 84% ($n$ = 9) at 3 years in eyes that underwent trabeculectomy without MMC.

We found that younger age was significantly associated with the failure of trabeculectomy. Success rates which were 100% in patients presenting in the fourth decade decreased to 63% in those presenting in the second decade,[3-6] and previous studies have attributed this to vigorous healing response in young age compared to later life.[17–19] Gressel *et al*.[9] also reported that the success of trabeculectomy was only 44% in patients less than 30 years of age as compared to 83% in the age group of 30–49 years. The authors have suggested the use of antifibrotics or tube implants in younger patients for better success.[9] However, their study included heterogenous

glaucomas and there were more secondary glaucomas in the younger age group as compared to the older age group, which could have confounded their results.

Jacobi *et al*.[7] in their study including all types of primary and secondary glaucomas between the age of 15 and 45 years followed up for 5 years, reported the 100% success rate of primary trabeculectomy in subjects less than 30 years and the success rate of 63% and 64% in third and fourth decades, respectively. This could be because of a greater number of high-risk secondary glaucomas (Iridocorneal endothelial syndrome, uveitic glaucoma, Axenfeld Rieger syndrome) and higher percentage of laser trabeculoplasty in subjects more than 30 years in their study, which would significantly decrease the success of trabeculectomy. When the type of glaucoma was adjusted, age more than 30 years was not a risk factor for failure.

The overall success rate of trabeculectomy at the end of 5 years in our study was 79%. When we analyzed the success stratifying age at surgery (decade wise), it showed favorable surgical outcomes in older individuals. The complete success probability at the end of 5 years was 100% in those more than 30 years of age ($n = 12$); it was 82% (95% CI: 58.0–93.1) between 21 and 30 years of age ($n = 31$), and 66% (95% CI: 38.6–83.2) in those less than 20 years of age ($n = 19$). Increasing success in the older age group could be due to exaggerated healing response in the young eyes; and whether MMC use would reduce the failure in eyes less than 20 years of age can be answered only by a prospective comparative study, considering other risk factors like the duration of the disease, highest preoperative IOP, number and duration of antiglaucoma medications use which could affect the success of surgery.

Yalvac *et al*.[5] compared trabeculectomy and trabeculectomy with MMC in JOAG and reported no statistical difference in the success of trabeculectomy between the groups (73% in the MMC group *vs*. 68% in the trab group, $P = 0.89$). Tsai *et al*.[4] have shown better IOP control with MMC use but with increased sight threatening complications ultimately decreasing the outcome of success at 3 year follow-up. Tsai *et al*.[4] reported a 20% incidence of hypotonic maculopathy in the MMC group and none in the trabeculectomy group. They proposed that longer eyeballs and higher incidence of axial myopia in JOAG eyes in response to high IOP may be responsible for high incidence of hypotony maculopathy in these eyes.[4,20]

Bleb-related infection over long follow-up in these eyes is a serious problem. Sidoti *et al*.[15] have reported 17% incidence of bleb-related infection (three blebitis and two eyes with bleb-related endophthalmitis) with the use of MMC in pediatric glaucomas. Hence one should weigh the benefit and the risk before using MMC in young patients keeping in mind the long-term risk of bleb-related problems associated with MMC use in these eyes.

The postoperative complications noted in our series were few and all except one resolved with conservative medical management. Early postoperative complications included hyphema and encapsulated bleb (3.2% each), shallow anterior chamber, and hypotony with choroidal detachment (1.6% each). All of these resolved with conservative management except in one patient where an anterior chamber (AC) reformation was performed for persistent shallow AC. Our complication rates are comparable to other studies wherein shallow anterior chamber, choroidal detachment, and encapsulated bleb were seen in 4.2% ($n = 24$) of the study population by Yalvac *et al*.[5] Similarly, Tsai *et al*.[4] had one case (3%) each of conjunctival dehiscence and cataract and two cases of encapsulated bleb (7%) in their study. Adelman *et al*.[21] have shown the rate of cataract extraction to be 24% ($n = 8$) following trabeculectomy in young glaucoma patients. This was a significant complication, which was noted during the follow-up over 11–90 months. In our study, the cataract was noted in two eyes (3%), one at 5 years and one at 10 years of follow-up, which needed cataract surgery.

The surgical failures in our study were due to inadequate IOP control and none required re-surgery or had any sight threatening complication. All the eyes with IOP > 21 mmHg that did not qualify for the complete success in our study were controlled medically with one or two medications and none needed a second surgical intervention.

The limitations of our study are its retrospective design. Multiple surgeons were involved, and there was no standardized surgical procedure. Few surgeries were through the fornix-based conjunctival approach while others were through the limbal-based approach. However, this is unlikely to have influenced the results as studies comparing success rates of fornix- and limbal-based conjunctival approaches have shown similar results.[22-24]

Also in our study, close to half the patients were lost to follow-up by the end of 5 years. We evaluated our results considering the worst-case scenario in the eyes that were lost to follow-up. Even after considering all eyes lost to follow-up within 3 years after surgery as failed, the complete success probability remained good, being 74% at 3 years and 65% at the end of 5 years.

## Conclusion

In our study, trabeculectomy without MMC had good success rates in Indian eyes with primary JOAG.

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