

Outcomes of trabeculectomy in eyes with refractory acute primary angle-closure in Indian eyes

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Purpose: To report the outcomes of trabeculectomy in eyes with refractory acute primary angle-closure attack. **Methods:** Patients with acute primary angle-closure attack and who underwent trabeculectomy for medically uncontrolled intraocular pressure within 2 months of presentation were retrospectively analyzed. Primary outcome was intraocular pressure (IOP). Secondary outcome measures were visual acuity, number of antiglaucoma medication (AGM), complications, and risk factors for failure of trabeculectomy. **Results:** Thirty-five eyes of 31 patients with median (interquartile range) follow-up of 3 (0.5, 9) years were included in the study. Median age at presentation was 55 (47, 60) years. Median duration of symptoms at presentation was 10 (4, 16) days and median time from presentation to surgery was 13 (6, 25) days. Median IOP reduced from 42 (36, 46) to 13 (12, 16) mmHg ($P < 0.001$) and median number of AGM reduced from 3 (1, 3) to 0 (0, 0) after trabeculectomy at the end of 1 year. The probability of complete and qualified success was 88% (95% confidence interval [CI]: 72%–95%) and was 97% (95% CI: 81%–99%) at 1 year, respectively. Failure was noted in six eyes. Subsequent cataract surgery was needed in 13 eyes (37%) with a median duration from trabeculectomy being 6.75 (1, 11) years. None of the preoperative, intraoperative, or postoperative factors tested were associated with failure ($P > 0.10$ for all associations on Cox proportional hazard regression analysis). **Conclusion:** In medically unresponsive cases of acute primary angle-closure attack, primary trabeculectomy seems safe and effective in Indian eyes.

Key words: Acute primary angle closure, refractory glaucoma, trabeculectomy

Acute primary angle-closure (APAC) attack is an ophthalmic emergency. Incidence of acute attack in Indian eyes is between 20% and 30% of the primary angle-closure disease.^[1] With timely and appropriate treatment, serious vision-threatening complications can be prevented without further glaucomatous damage. The conventional management of APAC attacks is to reduce the intraocular pressure medically, followed by laser peripheral iridotomy (LPI) to relieve pupillary block.^[2] Laser PI alone may be effective in the early stages in many eyes, and hence prompt intraocular pressure (IOP) reduction could be achieved with medical and laser treatment in the majority of cases.^[3,4] However, surgery is needed in few refractory cases. Over the years, various surgical treatment modalities have been described for refractory APAC, most common being trabeculectomy^[5,6] and lens extraction.^[4,7-9]

Recent studies have shown that early lens extraction in eyes with medically uncontrolled APAC attack resulted in significant IOP reduction, improved visual acuity, thus halting progression to chronic glaucoma.^[7,8] However, it has been documented that lens extraction in these eyes is technically demanding due to multiple preoperative, intraoperative, and postoperative challenges.^[10]

Trabeculectomy outcomes in APAC were studied earlier in Chinese eyes.^[11] The reported complete success probability was 33.3%–56.2%.^[5,11] Although it is a common practice in India to perform trabeculectomy in eyes with refractory acute

angle-closure attack, to our knowledge, there are no reports on long-term outcomes of the same in Indian eyes.^[12] In this study, we have reported the outcomes of trabeculectomy in refractory APAC performed at a tertiary eye care center.

Methods

We conducted a retrospective review of the charts of newly presented patients with acute primary angle-closure attacks who underwent trabeculectomy at our center between 1990 and 2017. Our study was approved by the institutional review board. All the patients who underwent trabeculectomy within 2 months from the date of APAC attack and with a minimum of 3 months of follow-up were included in the study. Trabeculectomy in eyes with chronic angle-closure or those with acute angle-closure later than 2 months of the attack were excluded. Cases of secondary acute angle-closure such as phacomorphic glaucoma, traumatic lens subluxation, and drug-induced uveal effusion were excluded.

The following criteria were used to define cases of APAC in addition to the symptoms of eye pain, redness, visual disturbance with or without nausea or vomiting. a) 360 degrees closed angles not opening on indentation gonioscopy, b) intraocular pressure (IOP measured by Goldmann applanation

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tonometry) of >21 mmHg or <21 mmHg on antiglaucoma medications (started elsewhere for the present episode), c) presence of two or more of the following signs at presentation: mid-dilated fixed pupil with or without sphincter atrophy, glaucomflecken, corneal edema (epithelial \pm stromal) with ciliary congestion, d) optic disc changes such as hyperemic rims, pallor, or glaucomatous damage, in cases with reasonable fundus view.

Management of acute attack involved initial medical treatment with topical antiglaucoma medications including pilocarpine hydrochloride 2% (Pilocar 2%, FDC) eye drops, oral acetazolamide (Tablet Diamox 250 mg, Pfizer), and topical steroid (Pred Forte, Allergan) eye drops followed by Nd: YAG (neodymium-doped yttrium aluminum garnet) LPI. If the initial presenting IOP was more than 40 mmHg or in the presence of severe corneal edema precluding iris visualization, intravenous mannitol 20% was administered before performing PI. In a few eyes, patent iridotomy was not achieved due to thick, edematous, and inflamed irides. They were continued on medical treatment and repeat PI was attempted at a later date when inflammation decreased. Post iridotomy, topical and oral glaucoma medications were continued based on the IOP and the status of the optic disc and were followed up weekly. When the IOP was uncontrolled despite medical and laser treatment, trabeculectomy was performed. Prophylactic laser iridotomy was routinely performed in the fellow eye of all patients who presented with APAC.

Surgical technique

Trabeculectomy was performed by experienced glaucoma specialists (SS, AKM, GCS, RKM), either with a limbus-based or fornix-based conjunctival flap. The need for MMC was decided by the operating surgeon, when used, multiple sponges soaked in 0.04% mitomycin C (MMC) were applied over a wide area subconjunctivally for 2 min. A partial-thickness scleral flap (triangular) was dissected up to the clear cornea, a 2×2 mm deep block was made with a number 11 blade or 20G micro vitreoretinal blade (MVR) blade and was excised using Vannas scissors and basal iridectomy was completed. The preplaced apical scleral flap sutures with 10-0 nylon were quickly closed and watertight conjunctival closure was achieved with continuous suture in case of limbus-based flaps and three-wing sutures for fornix-based flaps with 8-0 vicryl suture (on round-bodied needle). At the conclusion of the surgery, topical cyclopentolate hydrochloride 1% eye drops and 5% povidone-iodine eye drops were instilled.

Postoperatively, topical steroids for 6 weeks in tapering doses, topical antibiotic eye drops four times a day for 1 week, and topical cycloplegic eye drops three times a day for 2 weeks were prescribed. Follow-up visits were noted at 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, and 6 monthly thereafter. Additional visits were based on the postoperative course for each patient. Antiglaucoma medication was restarted based on the IOP during the follow-up visits.

Primary outcome measure was the IOP control. Secondary outcome measures were the visual acuity, number of antiglaucoma medication, complications, and risk factors for failure.

Visual fields were not possible during the acute attack due to symptoms (pain, redness, vomiting) and signs (corneal edema or high IOP). Preoperative HVF was possible in a few eyes and was performed in the postoperative period in few eyes with reasonable visual acuity and cooperative patients and hence was not included in the analysis. Complete success was defined as IOP ≤ 21 mmHg and >5 mmHg without any antiglaucoma medication. Qualified success was defined

as IOP ≤ 21 mmHg and >5 mmHg with or without topical antiglaucoma medications. Percentage of eyes with IOP levels <12 mmHg, <15 mmHg, <18 mmHg, and <21 mmHg at different time points were separately analyzed. Eyes not falling into qualified success criteria, complications resulting in loss of light perception or phthisis bulbi, or eyes requiring additional surgical procedures for IOP control were considered failures.

Statistical analysis

Descriptive statistics included mean and standard deviation (SD) for normally distributed variables and median and interquartile range (IQR) for non-normally distributed variables. Kaplan–Meier survival curves were used to assess the cumulative probability of success. Associations between failure and the preoperative factors (age at surgery, duration of symptoms, preoperative IOP, number of preoperative medications, presence of patent iridotomy, presence of disc damage at presentation), intraoperative factors (use of mitomycin C, conjunctival opening, fornix, or limbal based) as well as the postoperative factors (development of cataract, cataract surgery, duration between trabeculectomy and cataract surgery) were assessed using Cox proportional hazard regression model.

A $P \leq 0.05$ was considered statistically significant. Statistical analysis was performed using commercial software (Stata ver. 11.0; StataCorp, College Station, TX).

Results

During the study period of 27 years (1990–2017), 4,561 eyes of 4,550 patients had presented with acute primary angle-closure attack. Of the 4,561 eyes, 45 eyes (about 1%) needed surgical intervention for IOP control within 2 months of the acute attack. We excluded 10 eyes that underwent combined cataract and trabeculectomy surgery. Hence, our study included 35 eyes of 31 subjects (4 eyes had simultaneous bilateral primary acute angle-closure attack) that underwent trabeculectomy for IOP control. Of the 35 eyes that underwent trabeculectomy, 15 eyes had trabeculectomy with MMC and 20 eyes underwent trabeculectomy without MMC. The decision to use MMC was based on the surgeon's practice and preference. The demographic and clinical features of these patients are summarized in Table 1.

At presentation, seven eyes had best-corrected visual acuity (BCVA) better than 20/200, 10 eyes had very poor vision, ranging from counting fingers (CF) close-to-face to perception of light and projection of rays and remaining eyes with vision between CF 1 m to 20/200. Median (IQR) IOP at presentation was 42 (36, 46) ranging from 26 mmHg to 62 mmHg. Three patients directly presented to us for the first time, whereas 28 patients were referred from other hospitals and were on topical AGM (21/29 eyes on additional oral acetazolamide).

Detailed examination of anterior and posterior segment at presentation could be done only in 29/35 eyes that had relatively clear media (due to no/minimal corneal edema). Gonioscopically, all 29 eyes had closed angles and could not be opened on indentation. Seventeen eyes had clear lens and 12 eyes had early nuclear sclerosis. Glaucomatous disc damage (cup-disc ratio [CDR] >0.7) was noted in 13 eyes. Preoperative Humphrey visual field was/could be performed in seven eyes with a mean MD (mean deviation) of -18.9 ± 9 . YAG PI could be performed in 27 eyes and in eight eyes laser could not be performed due to thick, edematous iris.

Surgical details: The shape of the superficial scleral flap was triangular in 33 eyes and rectangular in two eyes. MMC for 2 min was applied in 15 eyes. Of the 35 eyes, 30 eyes underwent surgery within 1 month of presentation with a majority (11 eyes) in the 1st week.

Table 1: Demographic and clinical details of patients (35 eyes of 31 subjects)

Characteristics	Preoperative data (n=35)
Age in years (means±standard deviation)	51.2±11.33 55 (47,60)*
Gender (male:female)	10:21 (n=31)
Duration of symptoms in days	10 (4, 16)*
Follow-up in years	3 (0.5, 9)*
Median time to surgery from presentation in days	13 (6, 25)* (Range: 1-57)
Preoperative Vision (logMAR)	1.3 (0.6, 2.2)*
Preoperative IOP (mmHg)	42 (36, 46)* (Range: 26-62 mmHg)
Number of topical AGM at presentation	3 (1, 3)*

*Median (interquartile range); IOP: Intraocular pressure, AGM: Antiglaucoma medications; logMAR: Logarithm of minimum angle of resolution

Complete success was noted in 25 eyes. Kaplan-Meier survival plot for complete success probability after trabeculectomy is shown in Fig. 1.

The probability of complete success was 88% (95% confidence interval [CI]: 72%–95%) at 1 year, which was maintained till 7 years. It reduced to 81% (95%CI: 56%–92%) at 7.5 years and was maintained until 10 years. The probability of qualified success was 97% (95% CI: 81%–99%) at 1 year, which was maintained till 10 years.

On subgroup analysis, complete success probability in eyes without glaucomatous optic neuropathy (CDR < 0.7) was 93% (95% CI 63%–99%) at 3 years, which was maintained till 7 years. In eyes with CDR > 0.7, complete success was 84% (95% CI 51%–95%) from 1 month and was maintained till 10 years.

IOP

There was significant reduction in IOP 1 year after surgery ($P = 0.0001$) from 42 (36, 46) mmHg to 13 (12, 16) mmHg. Postoperative IOP at different time points is summarized in Table 2. Median duration of follow-up was 3 years (IQR 6 months, 9 years). At last follow-up, eight eyes were on topical antiglaucoma medication (5 eyes on 1 AGM; 3 eyes on 2 AGM). Percentage of eyes (qualified success) with IOP <12 mmHg, <15 mmHg, <18 mmHg, and <21 mmHg were separately analyzed and is shown in Table 3.

Visual acuity

There was significant ($P = 0.0009$) improvement in median logMAR visual acuity from 1.3 (0.6, 2.2) at presentation to 0.4 (0.1, 0.8) at the final follow-up. Overall, >2-line improvement was noted in 24 eyes (68.5%), of which 15 eyes (42.8%) had logMAR visual acuity better than 0.3 at last follow-up. However, no change (or <2-line improvement) in final visual acuity was found in five eyes (14.2%), loss of 1-line was found in one eye (2.8%), and loss of two or more lines was found in five patients (14.2%). Of the five patients who lost >2 lines, three patients developed total glaucomatous optic neuropathy (no perception of light), one patient had cataract (logMAR vision 0 to 1.3) but did not undergo surgery and one patient had developed cystoid macular edema (logMAR vision 0 to 0.8) due to macular branch vein occlusion.

All patients had 360 degrees synechially closed angles at presentation and at last follow-up. Median (IQR) mean deviation on Humphrey visual field at last follow-up ($n = 20$) was -9.36 ($-6.9, -26.5$). None of the preoperative factors (age at surgery, duration of symptoms, preoperative IOP, number of preoperative medications, presence of patent iridotomy, presence of disc damage at presentation), intraoperative

Table 2: Postoperative IOP in eyes with qualified success at various time points

	Median IOP	Interquartile range
IOP at 1 month (n=33)	15	12, 18
IOP at 3 months (n=30)	13.5	10, 18
IOP at 6 months (n=23)	14	12, 16
IOP at 1 year (n=21)	13	12, 16
IOP at 2 years (n=13)	14	8, 16
IOP at 3 years (n=12)	12	10, 16.5
IOP at last follow-up (n=35)	12	10, 16

factors (use of mitomycin C, conjunctival opening, fornix or limbal based) as well as the postoperative factors (development of cataract, cataract surgery, duration between trabeculectomy, and cataract surgery) were significantly associated with failure of trabeculectomy ($P > 0.10$ for all associations on Cox proportional hazard regression analysis).

Complications and failure

Early complications were seen in eight eyes and late complications in 16 eyes. Visually significant cataract, which needed cataract surgery, was noted in 13 eyes (37%). Median duration between trabeculectomy and cataract surgery was 6.7 (1, 11) years. Details of the complications are summarized in Table 4. Serious vision-threatening complications were seen in six eyes, which were deemed as a failure. Three of the eyes (9%) had corneal decompensation after cataract surgery during the follow-up period (1 year, 10 years, and 15 years).

Discussion

Acute primary angle closure is a potentially blinding disease and is an ophthalmological emergency. Hence, lowering of the IOP to physiological levels is a matter of urgency to minimize irreversible visual loss.^[3] In cases of medically refractory acute angle closure after iridotomy, surgical management is the only option. Surgical options of trabeculectomy^[5] and lens extraction^[10] have been described extensively in the literature. Corneal edema in the presence of high IOP would make the lens extraction difficult to perform.^[6] In the past 3 decades, surgery of choice in our institute was trabeculectomy when lens was clear. In this study, we retrospectively analyzed the long-term outcomes of trabeculectomy in our population. Previous studies have shown a surgical success rate of trabeculectomy at the end of 1 year to be as low as 33.3%^[6] and 56.2%^[5] in Asian eyes. A study by Aung *et al.*^[5] showed a qualified success rate of 56.2% ($n = 32$) and a complete success rate of 9.4% when trabeculectomy was

performed without mitomycin-C at 1 week of the acute attack. Contrary to this, we found that the success rates were better with complete success of 88% and qualified success of 97% at the end of 1 year. Our results in eyes with the acute angle-closure attack were comparable with chronic angle-closure glaucoma and primary open-angle glaucoma, which ranged from 70%^[6] to 95%.^[13] MMC did not have any additional benefit in success

in these eyes. The IOP control was not different in the eight eyes where YAG PI could not be performed preoperatively.

Aung *et al.*^[5] have described that surgery within 1 week of presentation on these hot and inflamed eyes with high IOP resulted in poor trabeculectomy outcomes. We agree that outcomes of trabeculectomy in inflamed eyes are poor, however, we found contrary results that could be possibly due to pretreatment with topical steroids and shorter duration of angle closure. Initial treatment protocols that were followed including intense topical steroids and antiglaucoma medications started in the acute stage, could have decreased the inflammation. The median (IQR) duration from the time of onset of symptoms to the date of surgery was 22.5 (14, 34) days. Furthermore, 85% of the eyes (30 eyes) underwent surgery within 1 month of presentation with majority in the 1st week (31%). Prompt and timely IOP reduction could have helped in better success rates in our study.

Only 1% of all acute attack patients (45 of 4,561 APAC eyes) needed filtration surgery after medical and laser treatment. A study by Buckley *et al.*^[14] showed that good IOP control was maintained in 80 eyes (58.4%) after peripheral iridotomy and required no further medications, whereas 21 eyes (15.3%) ultimately required trabeculectomy. However, in a study by Aung *et al.*^[5] in Chinese population, 32.5% of total patients with APAC underwent trabeculectomy. They suggested that the relatively high proportion required trabeculectomy reflecting the racial differences in the outcome of LPI after APAC in Asian populations. In an Indian

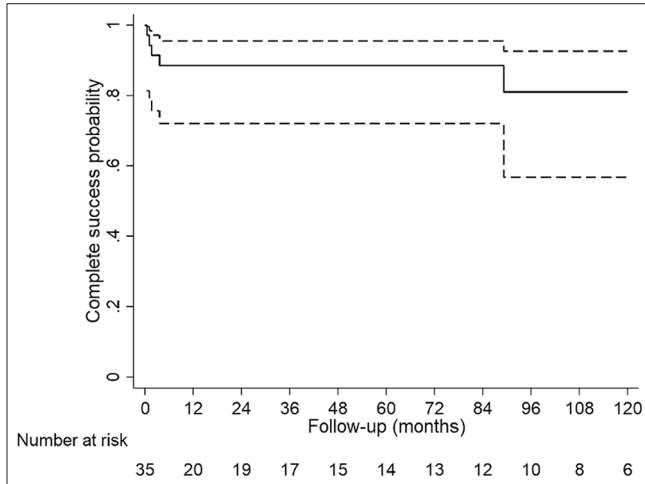


Figure 1: Kaplan–Meier survival plot of complete success probability after trabeculectomy in refractory acute angle closure

Table 3: Percentage of eyes with qualified success at various IOP levels

At the end of (n) years	Percentage of eyes with IOP <12 mmHg	Percentage of eyes with IOP <15 mmHg	Percentage of eyes with IOP <18 mmHg	Percentage of eyes with IOP <21 mmHg
1 year (n=16)	56	62	83	100
2 years (n=13)	46	61	92	100
3 years (n=12)	50	66	83	91
Last follow-up (n=35)	57	11	23	6

Table 4: Early and late complications after surgery

	Early (<3 months)	Late (3 months -1 year)	Remarks
Hypotony	1	0	Resolved with medical treatment
Shallow AC	2	0	Resolved with medical treatment
Hyphema	1	0	Resolved with medical treatment
Encapsulated bleb	2	2	1. Bleb needling done in one eye* had good IOP control with AGM. 2. Bleb needling with cataract surgery was done in one eye,* which had subsequent failure with high IOP and loss of perception of light
CD	1	0	Resolved with medical treatment
AC inflammation	0	1	One eye* had failure with loss of perception of light due to persistent inflammation with occlusio pupillae postcataract surgery (done after 1 year), but IOP was under control
Visually significant cataract that needed cataract surgery	1	12	Two eyes* had corneal decompensation after cataract surgery (after 10 years of trabeculectomy in one eye and 15 years in the other eye) and had failure with loss of perception of light. Between trabeculectomy and cataract surgery, both patients had moderate IOP control with intermittent IOP spikes with gradual glaucoma progression (from CDR 0.5-0.9)
Vision loss due to progression and total glaucomatous optic neuropathy	0	1	One patient* was lost for follow-up for 8 years and had disease progression
Total	8	16	* Eyes which had failure.

study by Sihota *et al.*^[12] published in 1998, the percentage of acute angle-closure eyes that required trabeculectomy was high (51.6%, $n = 124$) with a success probability of 64% at 3 months. However, the only AGM available at that time were timolol and pilocarpine. Thus, the percentage of eyes requiring surgeries has come down in recent times with the advent of newer AGM, and higher possibility of medical control. Glaucomatous optic disc damage at presentation was not found to be a risk factor for failure in our study, contrary to the study done by Sawada *et al.*^[15]

Lens extraction is another modality, which has been described extensively in the literature. In a pilot study done by Zhi *et al.*^[7] on nine eyes with high IOP with an acute attack, lens removal has been hypothesized to be useful in relieving acute attacks. There was a 10.2 mmHg drop in mean IOP between the preoperative and 7th postoperative days. However, long-term results were not reported. There are many randomized controlled trials, which have proven superiority or the same results between primary phacoemulsification and laser/surgical iridotomy in APAC eyes.^[8,10,16] Till date, no comparative studies have been done between trabeculectomy and lens extraction in these eyes.

The incidence of visually significant cataracts after trabeculectomy in acute angle-closure eyes was comparable with that seen in the advanced glaucoma intervention study.^[17] Cataract formation occurred in 34% (12 of 35) eyes. Other reported incidence of cataract formation varies from 6% to 56% post trabeculectomy.^[18] An increase in cataract formation/progression is attributed to hypotony, shallow anterior chamber, and inflammation, which commonly occur after trabeculectomy. In acute angle closure, this response may be little more than that seen in chronic glaucoma eyes undergoing trabeculectomy.

Failure was seen in six eyes. Two patients had high IOP. One patient lost vision due to increased inflammation with total occlusio pupillae, after complicated cataract surgery (done 1 year after trabeculectomy). Two patients had intermittent IOP spikes, were treated medically, had gradual glaucoma progression (from CDR 0.5 to 0.9). Both these patients developed corneal decompensation and eventually loss of light perception after cataract surgery was done 10 years and 15 years after trabeculectomy, respectively. According to a study done by Chen *et al.*,^[19] acute angle-closure attack is associated with a long-term significant decrease in corneal endothelial cell density compared with normal controls, which would probably predispose these eyes to corneal decompensation following any intraocular intervention. Post trabeculectomy, visual acuity had improved to 20/50 from hand movement's vision at presentation in these eyes.

The limitation of our study is its retrospective nature. In addition, visual field data were not available in all patients. Choosing the type of surgery was at the discretion of the surgeon, which could have contributed to bias in including the patients. Regrettably, the follow-up period was variable, ranging from 3 months to 21 years.

Conclusion

To conclude, primary trabeculectomy performed within 2 months of acute primary angle-closure attack seemed safe and effective in medically unresponsive patients. The possibility of corneal decompensation following cataract surgery in these eyes needs to be discussed and appropriate precautions need to be taken to document endothelial cell status and perform safe surgery. As there is an inherently greater risk of failure of trabeculectomy, a prospective randomized control study comparing trabeculectomy and primary phacoemulsification

might give us better insights in identifying treatment, which has a better visual outcome, better IOP control in long term with the least complications in these eyes.

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Conflicts of interest

There are no conflicts of interest.

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