Int Ophthalmol (2019) 39:2335–2340
https://doi.org/10.1007/s10792-019-01072-1

ORIGINAL PAPER

One-month IOP in mitomycin C-augmented trabeculectomy can predict long-term IOP control in chronic primary angle-closure glaucoma

Chengguo Zuo · Shufen Lin · Keling Wu · Ruowen Gong · Yafen Liu · Mingkai Lin · Jian Ge

Received: 1 May 2018 / Accepted: 6 January 2019 / Published online: 24 January 2019
© Springer Nature B.V. 2019

Abstract

Purpose To investigate the predictors of long-term intraocular pressure (IOP) in chronic primary angle-closure glaucoma (CPACG) treated with primary trabeculectomy.

Methods This study systematically reviewed cases of CPACG treated with primary trabeculectomy. The scleral flaps in all cases were sutured with two stitches in situ and two releasable sutures to ensure watertight under normal IOP conditions during surgery. Mitomycin C was used in all eyes. All patients were followed for 2 years. Digital massage of the bulbus and removal of the releasable suture were performed according to the IOP and shape of the filtering bleb. Demographic data and clinical outcomes were recorded. Factors predicting long-term IOP were identified.

Results A total of 72 patients (88 eyes) with a mean age of 58.51 ± 10.60 years were included in this study. The complete success rate was 89.77% after 2 years. The IOP began to stabilize after 7 days and reached its lowest point at the 1-month follow-up. The preoperative and early postoperative high or low IOP does not affect long-term effects ($P > 0.05$). There was a positive correlation between postoperative IOP at the 1-month and 2-year follow-ups ($r = 0.64$, $P < 0.001$).

Conclusion In CPACG patients undergoing primary trabeculectomy, scleral flaps sutured watertightly with two stitches in situ and two releasable sutures under normal IOP conditions can ensure controllable, effective and safe treatment of CPACG. The preoperative and early postoperative high or low IOP does not affect long-term effects. One-month postoperative IOP can be used as a predictor of long-term IOP control.

Keywords Trabeculectomy · Intraocular pressure · Chronic primary angle-closure glaucoma · Predictor

Introduction

Trabeculectomy is a classic and widely used surgical procedure for the treatment of glaucoma [1]. However, the controllability of trabeculectomy can be unstable and unclear. Excessively low or high filtration will inevitably lead to scarring, shallow anterior chamber and other complications [2]. In chronic angle-closure glaucoma (CPACG), characterized by a shallower anterior chamber and shorter axial length, the possibility of complications is high and the success rate of the procedure is low [3, 4]. Clinicians often struggle to find a balance between low IOP-related complications

C. Zuo · S. Lin · K. Wu · R. Gong · Y. Liu · M. Lin (✉) · J. Ge
State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, 54 South Xianlie Road, Guangzhou 510060, China
e-mail: linmk@mail.sysu.edu.cn

in the early postoperative period and high IOP in the long-term follow-up. It is therefore important to find an early postoperative detection index to predict the long-term outcome of surgery, and to perform timely bleb maintenance, reduce postoperative complications and improve the surgical success rate.

Previous studies have shown that the perioperative IOP in trabeculectomy was closely related to the curative potential of the surgery [5]. However, because the surgical controllability is not enough, the effect of prediction is difficult to replicate [6]. The aim of this study was to identify the predictors of long-term IOP control by using a controllable trabeculectomy.

Methods

This study was approved by the Institutional Review Board of the Zhongshan Ophthalmic Center at the Sun Yat-sen University, and the study adhered to the tenets of the Declaration of Helsinki. All methods were performed in accordance with the relevant guidelines and regulations.

Study population

This study retrospectively collected data on CPACG patients undergoing trabeculectomy performed by the same professor in the Zhongshan Ophthalmic Center glaucoma ward.

To be eligible for inclusion, CPACG patients were aged 18–80 years and undergoing trabeculectomy for the first time. The diagnostic criterion of CPACG and the indication to surgery were: (1) An asymptomatic history of creeping angle closure. (2) Ultrasound biomicroscopy and gonioscopy examination confirmed the presence of angle closure. (3) Glaucomatous optic neuropathy was defined as a vertical cup/disc (C/D) ratio > 0.7 and/or C/D asymmetry > 0.2 and/or focal notching. (4) Compatible visual field loss on static automated perimetry and the corresponding retinal nerve fibre layer defect on optical coherence tomography.

Patients were excluded if they had a history of another serious ocular disease, obvious conjunctival scarring or an ocular surgical history. Those with a history or signs of acute angle closure were also excluded.

Surgical procedure

The surgical procedure was performed following the standard previously documented process with minor changes to keep the controllability of the surgery. A fornix-based or corneal limbus-based conjunctival and Tenon's capsule flap was created in the superior quadrant. The scleral flap was corneal limbus-based, at 12 o'clock, rectangular, 4×3 mm and 1/2 scleral thickness. Mitomycin C (MMC) was routinely used to pre-treat the sclera bed. The surgical area was then rinsed with 100 ml of balanced salt solution. The anterior chamber puncture was performed in the 10 o'clock clear corneal area, and a 2×1 mm section of corneal trabecular tissue in the deep sclera bed was removed. Following resection of the peripheral iris at 12 o'clock, the scleral flap was sutured with 10–0 nylon thread. The two upper corners of the scleral flap were stitched in situ to maintain slow outflow of the aqueous humour while reforming the anterior chamber to maintain normal IOP. The two longitudinal edges of the scleral flap were secured with releasable watertight sutures using 10–0 nylon thread (Alcon, USA) under normal ocular tension. The conjunctiva was sutured in a watertight fashion with 8–0 Vicryl thread (Johnson & Johnson, USA).

Postoperative maintenance

In cases of postoperative IOP less than or equal to 21 mmHg with a flat bleb, or with IOP more than 21 mmHg, digital massage was performed. The releasable suture could be removed when the shape of the filtering bubble exhibited little change after digital massage.

Surgical success criteria

Based on the IOP at the 2-year follow-up, patient outcome was classified into one of three categories. Complete success was defined as an IOP less than or equal to 21 mmHg and more than or equal to 6 mmHg, without the need for additional pharmacologic or surgical intervention for IOP control with functional filtering bleb formation and no serious complications. Qualified success was reported if an anti-glaucoma drug was required to maintain an IOP of less than or equal to 21 mmHg. Operation failure was defined as an IOP of higher than 21 mmHg, with the IOP unable

to be controlled by medication and requiring additional anti-glaucoma surgery.

Statistical analysis

Statistical analysis was performed using SPSS software, version 20.0 (SPSS, Inc., Chicago, IL, USA). Student's paired *t* test with Bonferroni correction was used to compare preoperative and postoperative IOP data. The Chi-square test was used to compare frequencies; Spearman correlation analysis was used to analyse the relationship between IOP at 2-year follow-up and the other time points. Statistical significance was defined as $P < 0.05$.

Results

Demographic and clinical features of the participants

A total of 72 patients (88 eyes) with CPACG were enrolled in this study, including 30 males and 42 females. The mean age of the patients was 58.51 ± 10.60 (19–78) years. The mean axial length and anterior chamber depth were 22.43 ± 0.76 and 2.00 ± 0.22 mm, respectively. The mean retinal nerve fibre layer thickness and subfoveal choroidal thickness were 53.6 ± 18.10 and 414 ± 168.66 μm, respectively. The mean visual field defect was − 21.59 ± 9.32 dB. The duration of angle-closure glaucoma prior to surgery was 1.61 ± 2.02 year. The demographic and clinical features of study participants were listed in Table 1.

The corneal limbus-based conjunctival and Tenon's capsule flap was used in 81 eyes (92.05%), while the fornix-based conjunctival and Tenon's capsule flap was used in seven eyes (7.95%). The concentration of MMC used in surgery ranged from 0.25 to 0.33 mg/ml, with an average of 0.26 ± 0.03 mg/ml. The MMC standing time ranged from 1 to 5 min, with an average of 2.68 ± 1.10 min. The concentration and the duration of MMC application vary largely and were chosen intraoperatively at the discretion of the surgeon. The surgical parameters and comparisons of LogMAR visual acuity (VA) and IOPs from pre- and post-operation are summarized in Table 2. The LogMAR VA at the 2-year follow-up was lower than the pre-operation value. However, the difference was not significant ($P = 0.08$).

Control of IOP

The preoperative IOP was 36.44 ± 13.88 mmHg, and it obviously decreased after surgery (Fig. 1). The postoperative IOP reached 21.83 ± 9.80 mmHg, which was its peak at 3 days after surgery. Then, IOP tended to decline steadily and decreased to 12.04 ± 3.77 mmHg, which was its lowest point at 30 days after surgery. After that, the postoperative IOP achieved a basically stable state. Compared to the baseline values, IOP was significantly lower at all time points after surgery; the differences were all statistically significant ($P < 0.01$).

By the last follow-up visit, 79 of 88 (89.77%) eyes were considered a complete success; the qualified success and failure rates were 9.09% and 1.14%, respectively. The number of medications for qualified

Table 1 Demographic and clinical features of study participants

Variables	Minimum	Maximum	Mean ± SD/n
Frequency (*n*)			72
Male sex [*n* (%)]			30 (41.67%)
Unilateral lesions [*n* (%)]			56 (77.78%)
Mean age (years)	19	78	58.51 ± 10.60
LogMAR VA	0	3	1.11 ± 1.36
Mean defect (dB)	− 32.82	− 2.38	− 21.59 ± 9.32
Anterior chamber depth (mm)	1.58	2.71	2.00 ± 0.22
Retinal nerve fibre layer thickness (μm)	22	88	53.6 ± 18.10
Subfoveal choroidal thickness (μm)	167	845	414 ± 168.66
Axial length (mm)	20.57	24.09	22.43 ± 0.76
Years of angle-closure glaucoma prior to surgery	0.08	10	1.61 ± 2.02

VA visual acuity

Table 2 Surgical parameters and comparisons of pre- and 2 years post-operation

	Minimum	Maximum	Mean ± SD or interquartile range
IOP before operation (mmHg)	9.2	76	36.44 ± 13.88 mmHg
IOP after operation (mmHg)	8	30	14.35 ± 6.12 mmHg
LogMAR VA before operation	− 0.18	4	1.11 ± 1.36
LogMAR VA after operation	0	4	1.16 ± 1.31
Drug use before operation	1	5	3.07 ± 0.81
Drug use after operation	0	3	0.17 ± 0.55
Drug use after operation (qualified success)	1	3	1.67 ± 0.71
MMC concentration (mg/ml)	0.25	0.33	0.26 ± 0.03
MMC standing time (min)	1	5	2.68 ± 1.10
First Suture removing time (days)	1	66	3.5–21.5 (Median 6)
Second Suture removing time (days)	20	58	23–37.5 (Median 28)

IOP intraocular pressure, *VA* visual acuity, *MMC* mitomycin C

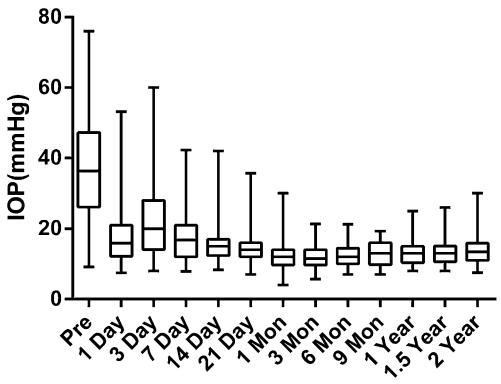

Fig. 1 IOPs before and after surgery. Boxes show the interquartile range. Bold lines in boxes represent the median and the whiskers represent extreme values. Compared with baseline, IOP was significantly decreased at all time points after operation

success group was 1.67 ± 0.71. The relationship between IOP at the 2-year follow-up and other perioperative time points is presented in Fig. 2, and a significant positive correlation with IOP at 1 and 3 months after surgery was observed ($r = 0.64$, $P = 0.00$ and $r = 0.79$, $P = 0.00$).

A shallow anterior chamber was observed in five cases (five eyes). Among them, the anterior chamber was steadily deepened with atropine in two cases, with a pressure bandage in one case and with adjustment of the loose suture line in one case. Phacoemulsification and intraocular lens implantation with anterior vitrectomy were performed in one case due to atropine dependence. The complications were primarily found in younger patients (19–39 years) with relatively high dose MMC, which was 0.28 ± 0.04% and 3.20 ± 0.76 min. The observed complications occurred a relatively long time (more than 2 months) after surgery.

Discussion

Trabeculectomy decreases IOP by creating an artificial "fistula". To reduce scarring and improve surgical success, modern compound trabeculectomy with antimetabolic drugs and releasable suture has been widely used [7]. Unfortunately, investigators have identified a number of risk factors as low IOP, shallow anterior chamber and thin-wall filtering bleb et al. [8, 9], but failed to find a suitable predictor of the effect of trabecular surgery. Whether the long-term prognosis can be predicted by means of preoperative and early postoperative indicators which remains a relevant clinical question yet to be answered [10].

To better investigate the prediction of long-term IOP, the controllability of the operation is crucial. The present study used standard previously documented trabeculectomy process with minor changes. The fixed sclera suture maintains microfiltration under normal IOP during surgery, which ensures the presence of the filtering channel and filtering bleb. The releasable suture achieves a watertight state under normal IOP,

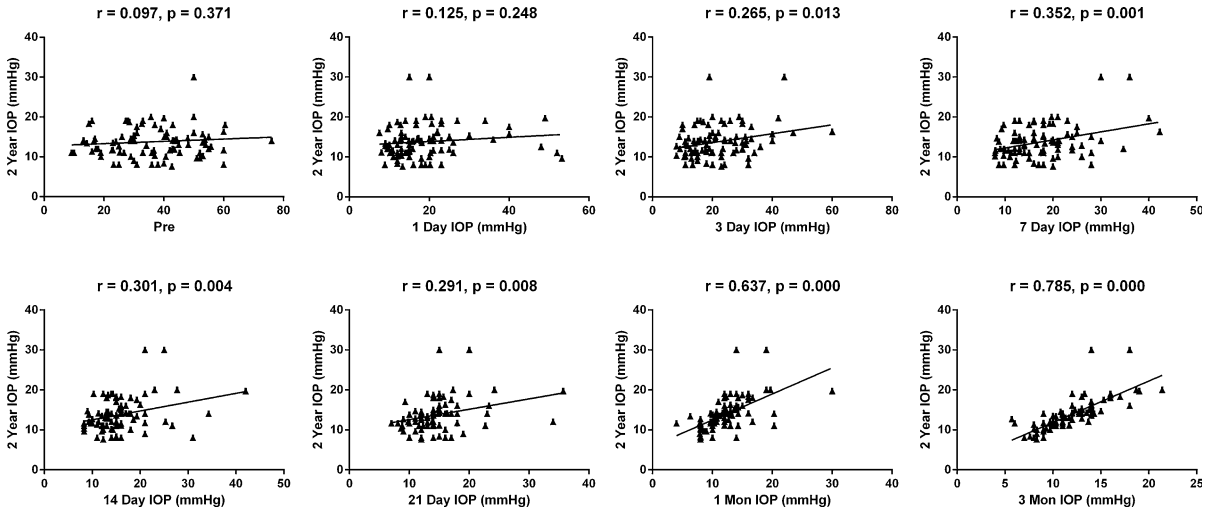

Fig. 2 Relationship between IOP at the 2-year follow-up and other perioperative time points

which ensures a relatively high postoperative IOP and stable anterior chamber. Then, the IOP decreased gradually through digital massage, which effectively avoids the complications related to low IOP as over-filtration and a shallow anterior chamber and improves the controllability of the operation. Many previous studies investigated the predictors of the surgery in primary open-angle glaucoma (POAG). In fact, the mechanism of trabecular meshwork cell apoptosis and endoplasmic reticulum stress in POAG and the inflammasome pathway in acute glaucoma made the prediction of prognosis in these patients more complicated [11, 12]. The present study chose CPACG patients because it is more dependent on pressure than other types of glaucoma so that the judgment of prognosis can be more accurate.

This study found that the postoperative IOP reached its peak at 3 days after surgery. It might be because the recovery of ciliary body low secretion, ciliary body shock and the washout of IOP-lowering drugs. By 7 days after surgery, IOP tended to decline steadily and decreased to its lowest point at 30 days after surgery. This is due to the role of digital massage and drainage. The correlation between postoperative IOP and IOP at year 2 increased gradually with time. At 1 month after surgery, the correlation began to be clinically significant. We observed a significant positive correlation between IOP at 1 month and at 2 years postoperatively ($r = 0.64$, $P < 0.001$). Previous studies have also shown that 2-week or 1-month postoperative IOP could be used to predict pressure control after trabeculectomy [5, 13]. The most likely reason was that, at 1 month after surgery, the repair of the filter channel was basically complete and the IOP achieved a relatively stable state. Because of this, the IOP at 1 month after surgery could be used as a predictor of long-term prognosis.

Traditionally, the early postoperative IOP of trabeculectomy should be low. Many investigators believed that if the IOP in the early postoperative stage was low, the IOP would have a greater natural ascending space, resulting in a better long-term prognosis [14–16]. However, these results mainly come from POAG. Generally, the initial IOP of CPACG is higher than that of POAG. Therefore, if the early postoperative IOP of CPACG is also controlled as low as possible, it will lead to a substantial decline in IOP in a short period of time. The low IOP immediately after surgery was associated with complications such as shallow anterior chamber, cyclodialysis and even choroidal detachment [17, 18]. The relatively high IOP at early stage of surgery is conducive to reduce the complications. Other investigators, however, believed that early postoperative IOP was not related to prognosis [6]. These differences may be related to different types of glaucoma and variations in intraoperative and postoperative processes surgical methods [5]. Our study suggests that using this controllable surgery to keep the early postoperative IOP at a relatively high position is conducive to long-term prognosis in CPACG.

In this and many other studies, medicine-controlled IOP before surgery was recorded as preoperative IOP, and the correlation between the preoperative IOP data and postoperative IOP was weak, which was similar to previous studies [10]. However, because the IOP data before surgery were influenced by medication or anterior chamber puncture, most of them obviously deviated from the baseline IOP. Therefore, there is a significant limitation in assessing the correlation between preoperative IOP and prognosis.

In summary, trabeculectomy with scleral flaps sutured watertightly with two stitches in situ and two releasable sutures under normal IOP conditions can be a controllable, effective and safe method for the treatment of CPACG. One month after surgery is the critical period of filtration bleb maintenance, within which the perioperative management of trabeculectomy should be emphasized. One-month postoperative IOP can be effectively used as a prognostic indicator for surgical success.

Compliance with ethical standards

Funding This study was funded by the National Natural Science Foundation of China (81570846).

Conflict of interest The authors declare that there is no conflict of interest regarding the publication of this paper.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

References

1. Rulli E, Biagioli E, Riva I, Gambirasio G, De Simone I, Floriani I et al (2013) Efficacy and safety of trabeculectomy vs nonpenetrating surgical procedures: a systematic review and meta-analysis. JAMA Ophthalmol 131(12):1573–1582
2. Benson SE, Mandal K, BunceandS CV, Fraser G (2005) Is post-trabeculectomy hypotony a risk factor for subsequent failure? A case control study. BMC Ophthalmol 5:7
3. Tham CC, Kwong YY, Baig N, Leung DY, LiandD FC, Lam S (2013) Phacoemulsification versus trabeculectomy in medically uncontrolled chronic angle-closure glaucoma without cataract. Ophthalmology 120(1):62–67
4. Liang Y, Friedman DS, Zhou Q, Yang XH, Sun LP, Guo L et al (2011) Prevalence and characteristics of primary angle-closure diseases in a rural adult Chinese population: the Handan Eye Study. Invest Ophthalmol Vis Sci 52(12):8672–8679
5. Okimoto S, Kiuchi Y, Akitaand T, Tanaka J (2014) Using the early postoperative intraocular pressure to predict pressure control after a trabeculectomy. J Glaucoma 23(6):410–414
6. Polikoff LA, Taglienti A, Chanis RA, Ramos-Esteban JC, Donas N, Tsong J et al (2005) Is intraocular pressure in the early postoperative period predictive of antimetabolite-augmented filtration surgery success? J Glaucoma 14(6):497–503
7. Jones E, ClarkeandP J, Khaw T (2005) Recent advances in trabeculectomy technique. Curr Opin Ophthalmol 16(2):107–113
8. Landers J, Martin K, Sarkies N, Bourneand R, Watson P (2012) A twenty-year follow-up study of trabeculectomy: risk factors and outcomes. Ophthalmology 119(4):694–702
9. Saeedi OJ, Jefferys JL, Solus JF, JampelandH HD, Quigley A (2014) Risk factors for adverse consequences of low intraocular pressure after trabeculectomy. J Glaucoma 23(1):e60–e68
10. Nesaratnam N, Sarkies N, Martinand KR, Shahid H (2015) Pre-operative intraocular pressure does not influence outcome of trabeculectomy surgery: a retrospective cohort study. BMC Ophthalmol 15:17
11. Sacca SC, Pullieroand A, Izzotti A (2015) The dysfunction of the trabecular meshwork during glaucoma course. J Cell Physiol 230(3):510–525
12. Chi W, Chen H, Li F, Zhu Y, Yinand W, Zhuo Y (2015) HMGB1 promotes the activation of NLRP3 and caspase-8 inflammasomes via NF-kappaB pathway in acute glaucoma. J Neuroinflammation 12:137
13. Rong SS, Feng MY, Wang N, Meng H, Thomas R, Fan S et al (2013) Can early postoperative intraocular pressure predict success following mitomycin-C augmented trabeculectomy in primary angle-closure glaucoma. Eye (Lond) 27(3):403–409
14. Schwenn O, Kersten I, Dick HB, Mullerand H, Pfeiffer N (2001) Effects of early postfiltration ocular hypotony on visual acuity, long-term intraocular pressure control, and posterior segment morphology. J Glaucoma 10(2):85–88
15. Alwitry A, Moodie J, Rotchford A, Abedin A, PatelandA V, King J (2007) Predictive value of early IOP in mitomycin-C augmented trabeculectomy. J Glaucoma 16(7):616–621
16. Ehrnrooth P, Lehto I, Puskaand P, Laatikainen L (2003) Effects of early postoperative complications and the location of trephined block on long-term intraocular pressure control after trabeculectomy. Graefes Arch Clin Exp Ophthalmol 241(10):803–808
17. Akagi T, Nakano E, Nakanishi H, Ujiand A, Yoshimura N (2016) Transient ciliochoroidal detachment after ab interno trabeculotomy for open-angle glaucoma: a prospective anterior-segment optical coherence tomography study. JAMA Ophthalmol 134(3):304–311
18. Xinping Y, Weihua P, Meiand R, Jia Q (2011) Supraciliochoroidal fluid incidence at the early stage after trabeculectomy: study with anterior segment optical coherence tomography. Curr Eye Res 36(9):818–823