• Clinical Research •

Ex-PRESS implantation with phacoemulsification in POAG versus CPACG

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Abstract

• AIM: To compare the long-term outcomes of the Ex-PRESS miniature glaucoma device implanted under a scleral flap in combination of phacoemulsification with intraocular lens implantation in primary open angle glaucoma (POAG) and chronic primary angle-closure glaucoma (CPACG).

• METHODS: Retrospective, comparative study. A total of 60 eyes (60 patients) receiving the Ex-PRESS miniature glaucoma device implantation combined with phacoemulsification were reviewed. Thirty eyes (30 patients) had the combined procedures for POAG, and the other 30 eyes (30 patients) for CPACG.

• RESULTS: The follow-up was 39.37±7.09mo (range 3 to 49mo) in patients with POAG and 37.10±9.26mo (range 9 to 49mo) in patients with CPACG (*P*=0.29). The mean change in best corrected visual acuity was 0.41 logMAR for POAG and 0.38 logMAR for CPACG at the last follow-up (*P*=0.22). The postoperative intraocular pressure (IOP) of the POAG group was significantly lower than the CPACG group at 1, 3, 12, and 18mo after surgery (*P*=0.02, 0.00, 0.04, 0.01) with similar glaucoma medications after surgery (*P*>0.16). At 3y after surgery, the cumulative complete and qualified success rates were 63.3% (POAG) and 53.3% (CPACG), 83.3% (POAG) and 73.3% (CPACG) (*P*=0.41, 0.49), respectively. The POAG group had more hypotony than the CPACG group (*P*=0.04).

• CONCLUSION: The long-term outcomes show the Ex-PRESS implantation combined with phacoemulcification can effectively lower the IOP in both the POAG and CPACG groups. The POAG group seems to have lower postoperative IOP and a higher risk of hypotony.

• KEYWORDS: glaucoma; Ex-PRESS miniature glaucoma device; cataract surgery; phacoemulsification

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INTRODUCTION

Glaucoma is the second leading cause of blindness worldwide. There will be 79.6 million people with open angle glaucoma and angle-closure glaucoma (ACG) in 2020. Asians will represent 47% of those with glaucoma and 87% of those with ACG[1]. Trabeculectomy is commonly performed as a filtering surgery in patients with glaucoma who experience degradation of visual acuity and visual filed despite maximum medication intervention, laser therapy, or both. Prognosis factors include patient age[2], preoperative topical medication use[2], glaucoma type[2-3], glaucoma severity[2], previous glaucoma surgery[4], pseudophakic status[5], titration of mitomycin C[6], and postoperative flat anterior chamber[7]. Combined surgery with phacoemulsification may also be a risk factor for the success of surgery[8]. Ex-PRESS miniature glaucoma device (Alcon, Fort Worth, TX, USA) has been used to shunt aqueous from the anterior chamber into a subconjunctival reservoir, with equivalent efficacy to trabeculectomy in controlling intraocular pressure (IOP) and better tolerance[9]. According to the Meta-analyses, Ex-PRESS is more likely to achieve complete success, with fewer postoperative interventions and a lower frequency of hyphema[10-11].

At the beginning, this miniature glaucoma device was implanted under the conjunctiva, but some complications were caused at the fixed position, like bleb failure due to subconjunctival scar tissue formation, conjunctival erosion, shunt rim exposure[12], and extrusion[13]. To improve the safety and efficacy, the implantation site was changed into under a scleral flap[14]. Compared to the conventional trabeculectomy, the stainless steel shunt instead of iridectomy also resulted in the change of aqueous humor dynamic[15]. In recent years, the risk factors for surgery failure were reported, and some factors like race[16], diabetes, and previous glaucoma surgery were confirmed[17]. Ex-PRESS implantation was initially observed to be appropriate in primary open angle glaucoma (POAG). Then narrow angle glaucoma surgery combined with cataract

extraction and secondary glaucoma surgery in pseudophakic/aphakic eyes were found to be safe and effective[18-20]. Since there are so many Asian patients with ACG, we attempted to investigate whether patients with ACG, especially chronic primary angle-closure glaucoma (CPACG), treated with combined phacoemulsification cataract surgery could achieve favorable results in the IOP control like those with POAG.

SUBJECTS AND METHODS

Subjects This retrospective, comparative study was approved by the ethics committee of Shandong Eye Institute and conformed to the tenets of the Helsinki Declaration. Patients with POAG or CPACG treated with the Ex-PRESS miniature glaucoma device (model P-50) at our institution between May 2012 and April 2013 were included. Informed consent was obtained from each patient. The criteria for Ex-PRESS implantation combined with phacoemulsification and intraocular lens (IOL) implantation in patients were same with those for trabeculectomy combined with cataract extraction. Patients had the presence of glaucomatous optic nerve damage with IOP greater than 21 mm Hg without medications. Gonioscopy was performed to distinguish the presence and range of peripheral anterior synechia before surgery. All patients had observed lens opancity with the visual acuity less than 20/40. The surgical procedure lasted between 10 and 20min with topical anesthesia. After a sulcus-based sclera flap was made, a cotton piece about 2×2-mm^2 with mitomycin C (0.4 mg/mL) was put under the sclera flap and conjunctiva for 1 to 2min according to the patient age and conjunctiva status. Then balanced salt solution was irrigated. After phacoemulsification and IOL (Akreos Adapt; Bausch and Lomb, Rochester, NY, USA) implantation in the capsule were completed through a 3.2-mm clear cornea incision, the Ex-PRESS device was inserted in the anterior chamber under the sclera flap when the viscoelastic agent was remained in the anterior chamber, then the viscoelastic agent was irrigated by balanced salt solution. Patient age, sex, baseline IOP measured by Goldmann applanation tonometry, best corrected visual acuity (BCVA), antiglaucoma medications, and surgical complications were collected. The patients were examined and followed up on day 1, weeks 1, 2, 3, months 1, 3, and 6 after surgery, and thereafter every 3mo. Complete success was determined as IOP between 5 and 18 mm Hg without glaucoma medication, no further glaucoma surgery, no loss of vision. Qualified success was determined by the same criteria with and without less than two kinds of antiglaucoma medications. Laser or needling suture lysis and needling of the bleb with 5-fluouracil injection (5 mg in 0.1 mL) were not considered as failures of the treatment. Early hypotony[21] was defined as IOP<5 mm Hg in the first week after surgery.

Table 1 Preoperative characteristics of patients with POAG/CPACG receiving Ex-PRESS implantation combined with phacoemulsification cataract surgery $\bar{x} \pm s$

Parameters	POAG	CPACG	*P*
Age (a)	58.63±9.96	57.27±9.94	0.60
Sex (M/F)	19/11	12/18	0.07
Baseline IOP (mm Hg)	30.43±9.044	29.67±10.04	0.76
Baseline BCVA (logMAR)	0.79±0.45	0.72±0.53	0.40
Glaucoma medications	1.90±1.06	1.17±0.95	0.01

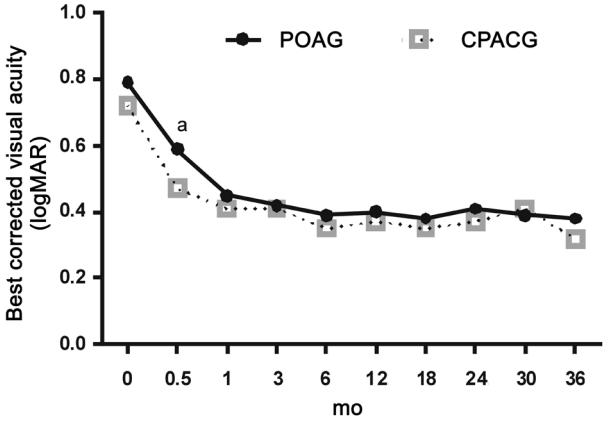

Figure 1 BCVA progression as a function of time in the two groups [a]*P*<0.05 comparing the two groups. Time 0 means the baseline BCVA.

Statistical Analysis Statistical analysis was performed using SPSS statistical package (version 17.0). Continuous variables were compared using the independent sample *t* test or Mann-Whitney *U* test. Categorical variables were analyzed with the Chi-square analysis. Kaplan-Meier and log-rank tests were used to compare the rates of surgery success. Data were expressed as means±standard deviation (SD), and a *P* value less than 0.05 was considered statistically significant. The data obtained from the first operated eye of each patient was used for statistical analysis.

RESULTS

The Ex-PRESS device was implanted under a scleral flap combined with cataract surgery in 30 patients (30 eyes) with POAG and 30 patients (30 eyes) with CPACG. The mean follow-up was 39.37±7.09mo (range 3 to 49mo) in patients treated for POAG and 37.10±9.26mo (range 9 to 49mo) in patients treated for CPACG (*P*=0.29). All of the patients were Han people. Except preoperative glaucoma medication numbers, there was no significant difference between the two groups in age, sex, baseline IOP, and baseline BCVA (Table 1). The postoperative changes in BCVA are shown in Figure 1. The mean change in BCVA was 0.41 logMAR for POAG and 0.38 logMAR for CPACG at the last follow-up (*P*=0.22), while only at 2wk after surgery, the CPACG group had better BCVA than the POAG group (*P*=0.03).

The IOP and number of antiglaucoma medications used preoperatively and postoperatively are shown in Figures 2 and 3.

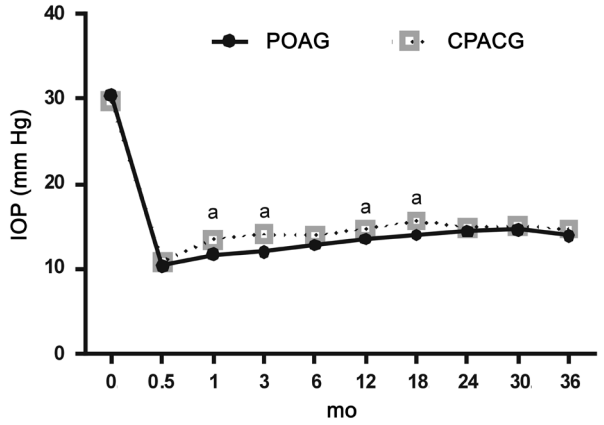

Figure 2 Mean IOP progression as a function of time in the two groups [a]*P*<0.05 comparing the two groups. Time 0 means the baseline IOP.

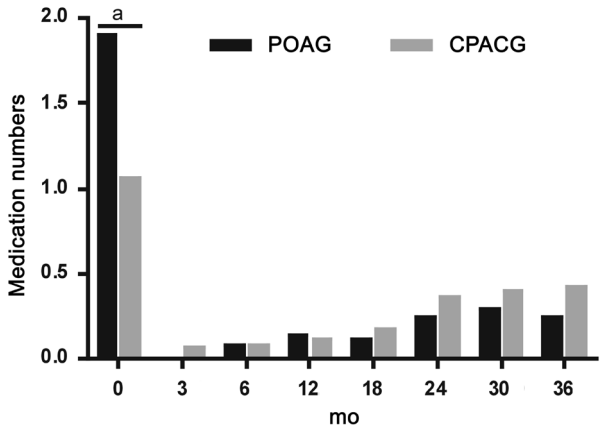

Figure 3 Mean number of glaucoma medications in two groups [a]*P*<0.05 comparing the two groups. Time 0 means the baseline number of medicines.

The time points of lowest IOP in both groups were found at 2wk after surgery, which was 10.43±2.86 mm Hg in the POAG group and 10.87±2.33 mm Hg in the CPACG group (*P*=0.47). The IOP was significantly lower in the POAG group than the CPACG group at 1, 3, 12 and 18mo after surgery (*P*=0.02, 0.00, 0.04, 0.01; Figure 2).

Both groups had a significant decrease in the number of glaucoma medications required postoperatively compared with preoperatively. There was no significant difference in the number of medications during the postoperative period (*P*> 0.16). At 36mo, the POAG group and CPACG group required 0.23±0.51 and 0.41±0.67 medications, respectively (*P*=0.30).

The postoperative complications are listed in Table 2. The major complications were hypotony (13.33% in the POAG group *vs* 0 in the CPACG group, *P*=0.04) and choroidal detachment (10% *vs* 0, *P*=0.08); these patients recovered with conventional treatment, and no further operation was required. In the POAG group, one patient had macular edema at 3mo and was treated by dexamethasone intravitreal injection; one patient had bleb leak at 32mo and received repair surgery. In the CPACG group, one patient with the Ex-PRESS shunt exposed for trauma had to have the implant removed at 9mo after surgery.

Table 2 Postoperative complications in two groups

Complications	POAG	CPACG	*P*
Hypotony in first week	4	0	0.04
Choroidal detachment	3	0	0.08
Exposed implant	0	1	0.31
Macular edema	1	0	0.31
Bleb leak	1	0	0.31

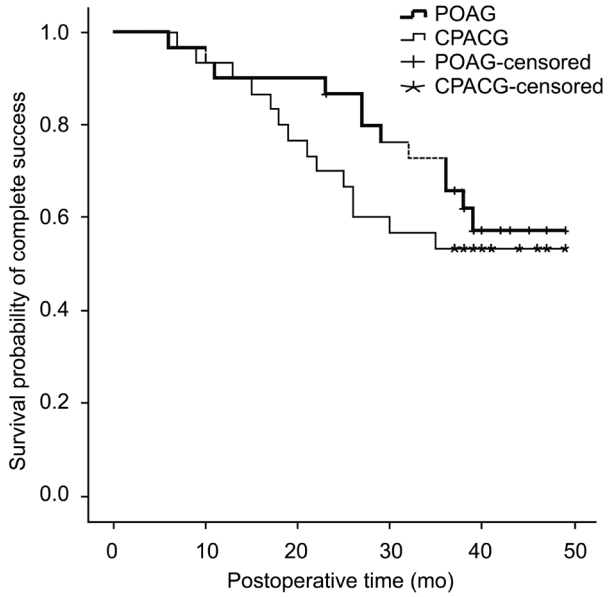

Figure 4 Complete survival probability curves as a function of time in two groups.

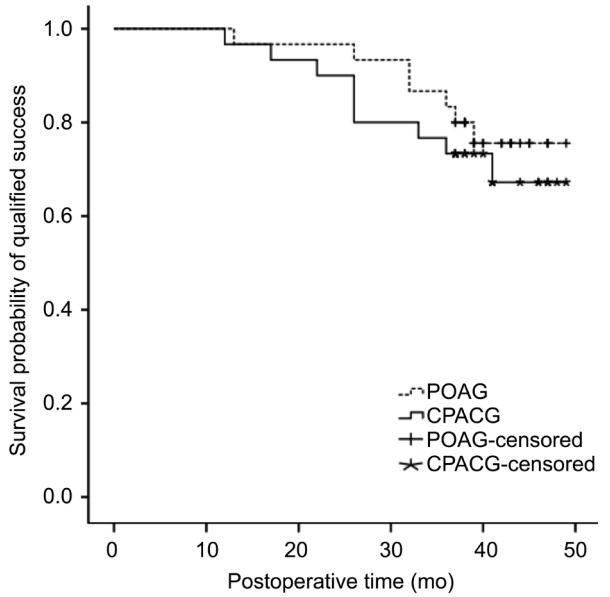

Figure 5 Qualified survival probability curves as a function of time in two groups.

The survival curves of eyes in the two groups are displayed in Figures 4 and 5. The cumulative complete and qualified success rates were 90% (POAG) and 93.3% (CPACG), 96.7% (POAG) and 96.7% (CPACG) at 1y after surgery. The rates were declined to 63.3% (POAG) and 53.3% (CPACG), 83.3% (POAG) and 73.3% (CPACG) at 3y after surgery (*P*=0.41, 0.49, respectively). Main reasons for surgical failure included increased IOP in 10% (3/30) of patients with POAG and

23.3% (7/30) of patients with CPACG. Other reasons included further surgery in 6.67% of patients in the POAG group (one eye with intravitreal injection for macular edema, and one eye with surgery for bleb leak) and 3.3% of patients in the CPACG group (one eye treated for exposed implant).

Laser or needling suture lysis was performed during the early stage of postoperative time. The POAG group had an average of 0.70±0.75 sutures cut, and the CPACG group had an average of 0.57±0.57 sutures cut (P=0.44). During the postoperative period, the times of needling of the bleb with 5-fluouracil injection were 1.83±1.51 times in the POAG group and 2.07±1.53 times in the CPACG group (P=0.56).

DISCUSSION

As a conduit for directing aqueous from the anterior chamber to the subconjunctival space, the advantage of the Ex-PRESS miniature device compared to conventional filtering surgeries is avoidance of removing scleral tissue and iris, but the insert position might cause many complications, mainly hypotony and erosion through the conjunctiva[20]. Dahan and Carmichael[14] first reported the Ex-PRESS device implanted under a scleral flap could be safe and effective with few complications, even in the high-risk patients. Maris *et al*[9] compared trabeculectomy with implantation of Ex-PRESS miniature glaucoma device under a scleral flap, finding similar reduction of IOP and number of postoperative glaucoma medications. Mariotti *et al*[17] conducted a long-term study on the Ex-PRESS shunt implanted under a scleral flap, suggesting that the complete (without drugs) and qualified success (with and without drugs) rates decreased gradually from 83% and 85% at 1y to 57% and 63% at 5y, respectively. Most patients were treated for POAG. Kanner *et al*[18] reported the comparison of Ex-PRESS miniature device implanted under a scleral flap alone and combined with phacoemulsification cataract surgery. At 3y after surgery, the surgical success rate was 94.8% and 95.6%, respectively, in the two groups. The change from baseline IOP was significantly greater after Ex-PRESS implantation alone compared with combined surgery. Several patients with CPACG were involved, but not compared to patients with POAG. Gindroz *et al*[21] performed modified deep sclerectomy using the Ex-PRESS in combined cataract and glaucoma surgery. At 24mo, the IOP decreased by 25.4%, the mean number of medications was 0.6±0.8, and the complete and qualified success rates were 45.6% and 85.2%. It was noticed that the pseudophakic status, specific surgical procedures, and glaucoma type might affect the outcomes. In our study, we focused on the question if the Ex-PRESS miniature device implanted combine with cataract surgery in patients with POAG achieved similar results to the patients with CPACG. Except the time point of two weeks after surgery, both groups had no significant difference in postoperative vision recovery, whereas the postsurgical IOP in the POAG group tended to be lower than the CPACG group (at 4 of 9 time points after surgery) with similar postoperative glaucoma medications used. Rao *et al*[22] compared phacotrabeculectomy in PACG and POAG in 2011. They found the two groups had insignificantly different postoperative IOP, but PACG group had higher percentage of IOP reduction, and suggested better IOP control in PACG patients might be due to angle widening after the removal of lens. In this study, the relatively tighter suture and less suture lysis to avoid hypotony in the CPACG group might make the difference compared with the article.

Similar to the previous reports[17,21], the complete and qualified success rates decreased with time elapse. However, they were not lower than the success rate of trabeculectomy combined with phacoemulsification cataract surgery[22-23]. To lessen the chance of bleb fibrosis, the surgeon usually used the mitomycin C under the scleral flap during the surgical procedures, and the suture lysis and 5-fluouracil injection were used in both groups. In this study, we found a low rate of device erosion and bleb leak, which might be related to the device implanted under a partial-thickness sclera flap and the suture to control the flow rate under the conjunctiva.

The most common device-related complications were hypotony and choroidal detachment early after surgery in the two groups. Both were resolved spontaneously, and flat anterior chamber angle (lens-cornea touch) was not formed. The flow study *in vitro* by Estermann *et al*[15] suggested that the tube diameter was the only parameter with a significant impact on flow and resistance. In the current study, all patients had the P-50 model implant, with an internal axial lumen of 50 μm and a vertical channel in the faceplate, so a relatively proportionate resistance to flow could be created. To avoid shallow anterior chamber, we recommend the suture of the scleral flap can be tighter than that in trabeculectomy. Other complications like device exposure, tube block, macular edema, and bleb leak were not common, with a similar rate with previous studies[12,21]. Limitation of this study included the lack of evaluation of the angle situation pre- and post-operatively in groups, so the role played by the lens removal in opening the angle needs further investigations.

In conclusion, Ex-PRESS miniature device implantation combined with phacoemulcification could achieve satisfied IOP control and a similar success rate in patients with POAG and CPACG. The POAG group seemed to have lower postoperative IOP and a higher risk of hypotony.

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Conflicts of Interest: Lan J, None; **Sun DP,** None; **Wu J,** None; **Wang YN,** None; **Xie LX,** None.

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