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Early Phacoemulsification After Acute Angle Closure in Patients With Coexisting Cataract

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Purpose: The purpose of this study is to evaluate the effect of early phacoemulsification on the management of acute angle closure glaucoma in patients with coexisting cataract after initial treatment with medical therapy and laser peripheral iridotomy.

Patients and Methods: This study involved a retrospective analysis of patients presenting to the Maastricht University Medical Center+ with acute angle closure and coexisting cataract between 2005 and 2015. Patients were included after initial treatment with a standard protocol comprising topical and systemic medical therapy and laser peripheral iridotomy. Patients underwent small-incision phacoemulsification with intraocular lens implantation into the capsular bag by experienced surgeons within 3 months of the acute angle closure episode. The effect on intraocular pressure, number of glaucoma medications, visual acuity, and complications was assessed.

Results: A total 35 patients were included in the study (mean age, 71 ± 10 y; 20% male; mean refractive error, $+1.6 \pm 1.8$ diopters). The mean duration between acute angle closure episode and phacoemulsification was 37 ± 22 days. There were no complications. Intraocular pressure decreased in all patients from 17.0 ± 8.2 mm Hg to 13.2 ± 3.9 mm Hg after 3 months ($P=0.008$), whereas the mean number of glaucoma medications decreased from 2.9 ± 1.1 to 0.7 ± 0.9 ($P<0.001$), with 56% of patients discontinuing all medications. Visual acuity improved from 0.9 ± 0.9 logMAR to 0.2 ± 0.3 logMAR ($P<0.001$).

Conclusions: Early phacoemulsification with intraocular lens implantation results in a reduced intraocular pressure and number of glaucoma medications after an acute angle closure glaucoma crisis in patients with coexisting cataract. Although surgery may be challenging, the results are promising, with significant improvement in visual acuity in most patients.

Key Words: acute angle closure, glaucoma, cataract

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Primary angle closure glaucoma [PAC(G)] causes approximately 50% of cases of blindness related to glaucoma, although it accounts only for approximately 10% to 25% of all glaucoma cases.¹ Acute angle closure (AAC), a special form within the PAC(G) spectrum, is an ophthalmic emergency characterized by sudden closure of the anterior chamber angle followed by a sharp rise in intraocular pressure (IOP).²

Laser peripheral iridotomy (LPI) is recommended as the initial therapy for PAC(G) and AAC, as it eliminates the pupillary block, which is thought to be the main underlying mechanism of angle closure.² However, it is reported that LPI alone does not open all narrow angles^{3,4} and after LPI, some eyes develop peripheral anterior synechiae (PAS) and/or a rise in IOP.^{5–7} In patients with AAC long-term IOP control after LPI is not optimal, with an IOP rise in 58% of patients within 5 years after the initial attack.⁵ Although treatment in the acute phase of AAC is extensively described in major textbooks,² LPI alone may not always suffice and there is no consensus on treatment in the long term.

The development of and ongoing improvements in anterior segment optical coherence tomography (AS-OCT) have made it possible to obtain very detailed images of structures of the anterior chamber. These images demonstrate that the lens plays an important role in the development of angle closure. These new imaging techniques may provide important additional information in cases where LPI does not suffice to open the angle after an AAC glaucoma episode; however, evidence about the role of cataract extraction as a treatment in AAC is needed. Recently, the EAGLE study, published by Azuaro-Blanco and colleagues, reported the results of a multicenter randomized trial in which clear lens extraction was performed in patients with PAC and raised IOP or PACG. They concluded that clear lens extraction should be considered as an alternative treatment to conventional LPI in patients with chronic PAC (G).⁸ The EAGLE study supports the notion that early or clear lens extraction is an acceptable therapeutic approach in general to prevent AAC glaucoma.

The aim of the present study was to evaluate the efficacy of early phacoemulsification (within 3 months of the acute attack) in the management of patients after an AAC attack and coexisting cataract, by determining its effect on IOP, number of glaucoma medications, visual acuity (VA), and complications in a Caucasian (Dutch) population.

MATERIALS AND METHODS

This retrospective study was conducted in accordance with the tenets of the Declaration of Helsinki and was

approved by the Maastricht University Medical Center+ (Maastricht, the Netherlands) institutional review board.

Subjects

Patients visiting the University Eye Clinic Maastricht on an outpatient basis with AAC and coexisting cataract between 2005 and 2015 were eligible for inclusion. AAC was defined (according to the recent consensus reading) as an abrupt onset of symptomatic elevation of IOP resulting from total closure of the anterior chamber angle, which is typically not self-limiting.²

Patients were included in the study if they met the following inclusion criteria: (a) abrupt onset of symptomatic elevation of IOP (measured by the Goldmann applanation tonometry) caused by AAC (total closure of the angle), (b) coexisting cataract, and (c) age 18 years or older. Exclusion criteria included a previous history of intraocular surgery, trauma, or any other ophthalmic condition that may have affected the anterior chamber angle.

A standard protocol was used to initially treat the AAC attack with topical and systemic medical therapy to lower IOP, after which LPI was performed in the superior nasal or superior temporal quadrant in all patients, as soon as the cornea permitted good visualization (settings Nd: YAG laser, 1 to 3 pulses/burst, 5 to 6 mJ pulses, until a patent iridotomy was created). A topical steroid (dexamethasone 3 times daily) was prescribed and subsequently slowly tapered until the inflammation of the anterior eye segment had fully subsided, and phacoemulsification was scheduled within a maximum of 3 months after the AAC glaucoma crisis.

Phacoemulsification was performed (by experienced surgeons only) through a 2.2-mm corneal incision using a soft-shell technique,⁹ with implantation of a foldable monofocal intraocular lens (IOL) (AcrySof, Alcon Laboratories Inc.) into the capsular bag. Postoperative treatment consisted of a topical steroid and antibiotic fixed combination (Tobradex, Alcon Laboratories Inc.), a nonsteroidal antiinflammatory drug (nepafenac 0.3%, Alcon Laboratories Inc.), and glaucoma medications if necessary to control IOP.

After phacoemulsification, patients followed up at the outpatient clinic. After 1 and 3 months, best corrected visual acuity (BCVA), IOP, number of glaucoma medications, and postoperative complications were recorded and analyzed.

Analysis

All data were analyzed using a statistical software package (SPSS 23; SPSS Inc., Chicago, IL). First, histograms

and frequency analysis were performed to obtain information about the distribution of the data. Descriptive statistical results were described as the mean \pm SD. Analysis was also performed for both PAC and PACG patients separately. A *P*-value ≤ 0.05 was considered statistically significant.

For the continuous variables, the *t* test was used to compare differences between PAC and PACG. The paired sample *t* test was used to compare preoperative and postoperative differences. For the categorical variables, the χ^2 and McNemar tests were used.

RESULTS

We retrospectively collected all records of patients who were hospitalized and diagnosed either for glaucoma surgery (ie, trabeculectomy, glaucoma drainage device implantation), or because of an intraocular pressure-related emergency between 2005 and 2015. All charts were assessed for eligibility (ie “classic” AAC and cataract as described in the inclusion criteria previously). Reasons for noneligibility and thus exclusion in this study are presented and described in Table 1 (ie, patients with previous history of intraocular surgery, trauma, or any other ophthalmic condition that may have affected the anterior chamber angle).

In total, 1196 patients were hospitalized for the diagnosis or treatment of glaucoma. From these cases, 35 patients met the inclusion criteria (AAC, cataract and age of 18 years or older) and presented with an AAC crisis and coexisting cataract. These 35 patients were enrolled in this analysis; 1161 individuals were excluded for not meeting the inclusion criteria (Table 1). The maximum 3-month time window for phacoemulsification after the AAC episode was chosen in order to exclude patients with the development of cataract as the result of the acute episode or LPI from the analysis. The mean age at presentation was 70.6 ± 10.0 years, and the majority of the participants were female [*n* = 28 (80%)]. The demographic data are summarized in Table 2.

Data regarding initial IOP and number of topical medications are summarized in Table 2. Mean IOP at presentation was 54 ± 10 mm Hg. All patients underwent LPI within 7 days of presentation. In all eyes, the acute episode resolved after a combination of LPI and medical therapy and the IOP decreased to 17.0 ± 8.2 mm Hg. LPI was unsuccessful in 1 patient who had persistent corneal edema after the procedure and argon laser peripheral iridoplasty could not be performed as an alternative because of poor visualization. The patient with the unsuccessful LPI

TABLE 1. Flowchart of Exclusion Criteria for the Study Group

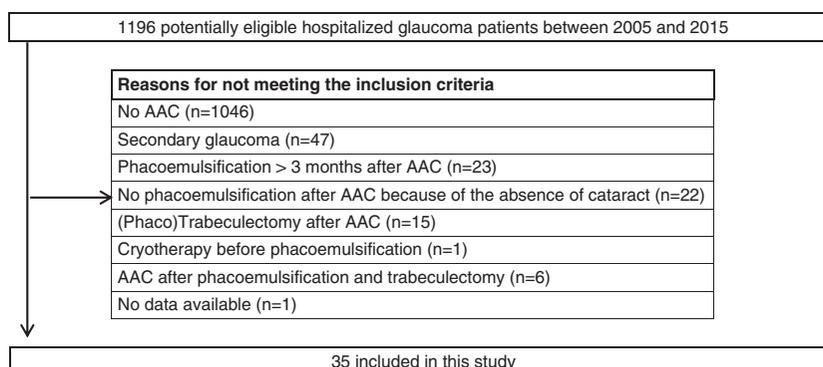


TABLE 2. Demographic Data of the Study Group and for PAC and PACG Patients

	All		PAC		PACG		P
	N	Mean ± SD (Range)	N	Mean ± SD (Range)	N	Mean ± SD (Range)	
Sex (female/male)	28/7		18/5		10/2		0.7
Age (y)	35	70.6 ± 10.0 (36.7, 86.8)	23	70.3 ± 11.4 (36.7, 86.8)	12	71.2 ± 6.8 (60.0, 80.3)	0.8
Maximum IOP at presentation (mm Hg)	35	53.7 ± 10.2 (31.0, 78.0)	23	53.5 ± 10.5 (31.0, 78.0)	12	54.0 ± 10.3 (34.0, 70.0)	0.9
Refractive error (D)	32	1.6 ± 1.8 (-2.0, 5.9)	21	1.3 ± 1.8 (-2.0, 4.4)	11	2.2 ± 1.8 (-0.6, 5.9)	0.2
Refractive error ≥ +2D	17		9		8		0.1
Axial length (mm)	35	22.3 ± 1.0 (20.5, 24.7)	23	22.5 ± 1.0 (20.5, 24.7)	12	21.9 ± 0.8 (20.7, 23.0)	0.1
ACD (mm) (IOLMaster)	26	2.3 ± 0.2 (1.7, 2.7)	17	2.3 ± 0.2 (1.7, 2.7)	9	2.2 ± 0.1 (2.0, 2.4)	0.8
ACD (mm) (anterior segment OCT)	14	1.6 ± 0.3 (0.9, 2.0)	9	1.6 ± 0.4 (0.9, 2.0)	5	1.6 ± 0.2 (1.4, 1.8)	0.9
ACD (mm)* [anterior segment OCT (n = 14), IOLMaster (n = 13)]	27	1.6 ± 0.2 (0.9, 2.0)	18	1.6 ± 0.3 (0.9, 2.0)	9	1.7 ± 0.2 (1.4, 1.8)	0.5
Days between attack and phacoemulsification (d)	35	36.9 ± 22.5 (1.0, 84.0)	23	37.2 ± 21.3 (2.0, 67.0)	12	36.7 ± 27.1 (1.0, 84.0)	1.0

*ACD calculated from anterior segment OCT or from IOLMaster. IOLMaster defines ACD as follows: “Anterior chamber depth on the IOLMaster is understood as the distance between the anterior vertex of the cornea and the anterior vertex of the eye lens.”¹⁰ As a result in our calculations, in ACD values from the IOLMaster, 540 μm was abstracted from the total ACD to exclude the cornea.¹¹

ACD indicates anterior chamber depth; IOL, intraocular lens; IOP, intraocular pressure; OCT, optical coherence tomography; PAC, primary angle closure (N = 23); PACG, primary angle closure glaucoma (N = 12).

remained included in the study because the characteristics and results for this patient fell within the value range of all others and therefore did not influence the results. The mean time between AAC episode and phacoemulsification was 37 ± 23 days (range, 1 to 84 days).

Glaucoma Characteristics and Postoperative Outcome

Table 3 displays the preoperative and postoperative characteristics. Because of multiple tests carried out on the

TABLE 3. Patient Glaucoma Characteristics

Patient Glaucoma Characteristics	Preoperative	Postoperative	P
IOP (mm Hg)	17.0 ± 8.2	13.2 ± 3.9	0.008
PAC	15.4 ± 6.4	13.4 ± 3.9	0.11
PACG	19.9 ± 10.5	12.8 ± 4.1	0.038
P	0.13	0.63	
Number topical medications	2.9 ± 1.1	0.7 ± 0.9	< 0.001
PAC	2.7 ± 1.1	0.4 ± 0.7	< 0.001
PACG	3.1 ± 1.2	1.2 ± 1.0	0.002
P	0.41	0.009	
Carbonic anhydrase systemic	25/35 (71%)	1/34 (3%)	< 0.001
PAC	14/23 (61%)	0/23 (0%)	< 0.001
PACG	11/12 (92%)	1/11 (9%)	0.004
P	0.056	0.14	
No medications	0/35 (0%)	19/34 (56%)	< 0.001
PAC	0/23 (0%)	16/23 (70%)	0.016
PACG	0/12 (0%)	3/11 (27%)	0.008
P	NA	0.020	
Visual acuity (logMAR)	0.9 ± 0.9	0.2 ± 0.3	< 0.001
PAC	1.0 ± 0.9	0.1 ± 0.2	< 0.001
PACG	0.6 ± 0.7	0.4 ± 0.4	0.22
P	0.24	0.04	

Because of multiple testing only P-values < 0.05/25 = 0.002 (Bonferroni) should be considered significant.

IOP indicates intraocular pressure; NA, not applicable; NS, not significant; PAC, primary angle closure (N = 23); PACG, primary angle closure glaucoma (N = 12).

data presented in Table 3, only P-values < 0.05/25 = 0.002 (Bonferroni) should be considered significant. After phacoemulsification, there was a decrease in IOP (P = 0.008), number of topical glaucoma medications (P < 0.001) and use of systemic carbonic anhydrase inhibitors (P < 0.001). IOP decreased from 17.0 ± 8.2 mm Hg preoperatively to 13.2 ± 3.9 mm Hg at 3 months after the AAC event. However, there were no statistical differences between PACG patients (P = 0.038) and PAC patients (P = 0.11). In addition, there was no statistically significant difference in the final IOP between PAC or PACG patients at 3 months (P = 0.63). The mean number of glaucoma medications decreased significantly, from 2.9 ± 1.1 preoperatively to 0.7 ± 0.9 at 3 months postoperatively, with 56% of patients totally off medication. The IOP ranged from 8 to 24 mm Hg in patients with PACG who were typically using more topical glaucoma medications than patients with PAC (P = 0.009), although this difference was not statistically significant. Before surgery, PACG patients used more systemic carbonic anhydrase inhibitors than PAC patients; however, this result was not statistically significant. Only 1 patient (with PACG) remained on systemic carbonic anhydrase inhibitors, and the use only continued for the first 3 postoperative months.

AAC did not recur in any patient. Figure 1 shows the IOP change in both groups during follow-up visits. VA improved from 0.9 ± 0.9 logMAR preoperatively to 0.2 ± 0.3 logMAR after 3 months. Table 3 demonstrates the change in VA (logMAR) for both PAC and PACG patients. There was a difference in VA between PAC and PACG patients, with PAC patients achieving a significant improvement in level of VA; whereas, PACG patients showed only moderate improvement, although this result was not statistically significant.

Details of Surgery and Complications

In 14 patients with very shallow anterior chambers, intravenous mannitol (500 mL of a 15% solution, Baxter B. V.) was administered preoperatively over 45 minutes to lower IOP before phacoemulsification. In 6 eyes, a capsular tension ring was inserted because of zonular weakness. In 4 patients with very short axial lengths (mean 21.1 mm vs. 22.4 mm in the total group), phacoemulsification was

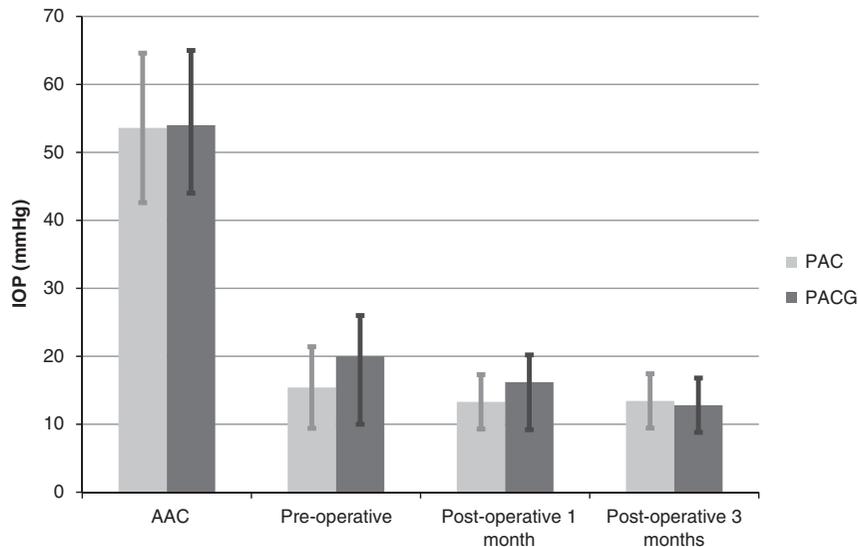


FIGURE 1. The change in IOP from presentation to 3 months postoperatively is shown for patients with PAC and PACG. AAC indicates acute angle closure; IOP, intraocular pressure; PAC, primary angle closure; PACG, primary angle closure glaucoma.

combined with vitrectomy (debulking). Posterior synechiolysis was performed in 9 patients. Rupture of the posterior capsule did not occur.

DISCUSSION

This study demonstrates that in Caucasian (Dutch) patients with AAC and coexisting cataract, after initial medical treatment and LPI, small-incision phacoemulsification with IOL implantation results in a reduction in IOP and a significant reduction of number of glaucoma medications. Although surgery is often challenging (eg, because of a shallow anterior chamber, synechiae, or weak zonules), the results are encouraging with significant improvement in VA; however, patients with PACG had a less favorable outcome in terms of VA improvement than patients with PAC.

AAC accounts for 6% of all glaucoma cases and occurs in up to 0.6% of the general population. Women have a 3 times higher risk of developing AAC than men.¹² This statistic correlates to our study, in which women made up 80% of the study population. There were 5 eyes with an axial length <21 mm (14%). In general, the refractive error in our study was only minimally hyperopic. This seems surprising, however, a myopic shift in many of our patients (mean age of 70 y with significant cataract) may account for this.

An important and treatable underlying mechanism of AAC and PAC(G) is the pupillary block. LPI is considered the initial therapy for AAC and PAC(G) as it eliminates the pupillary block.¹ However, it is reported that after LPI, eyes with PAC can develop PAS and/or a rise in IOP, indicating that LPI alone may not always suffice for the long-term treatment of angle closure.^{5,6} He et al³ concluded that 19.4% of eyes with PAC in a Chinese population had residual angle closure after LPI. Another study reported that 60% of their patient population had a positive dark-room provocative test after LPI.⁷ In addition, it is reported that LPI alone does not open all narrow angles.^{3,4} It is also reported that 58.1% of Asian eyes who were treated with the conventional treatment (IOP-lowering medications and LPI) eventually developed increased IOP.⁵

The lens is thought to play a major role in the development of AAC, although its exact role in the pathogenesis is not fully understood.¹² In recent years, there has been an increase in the number phacoemulsification procedures, likely because of an aging population, but also because cataract surgery techniques have improved, making surgery safer and more effective with a lower risk for complications. As a result, cataract surgery is performed at an earlier stage, resulting in a decrease in the number of AAC cases seen.¹³ This trend may provide some evidence regarding the role of the lens in the development of AAC, and thus underlines the importance of (early) lens extraction in these patients in the long-term treatment of angle closure to prevent progression of PACG. Compared with earlier extracapsular techniques, current small-incision phacoemulsification is much less hazardous (eg, improved stabilization of the anterior chamber during surgery and less risk of iris prolapse). Although concerns regarding damage to the corneal endothelium during phacoemulsification are documented, in this particular group of patients, it has been reported that there was no significant increased endothelial cell loss compared with open anterior chamber angles.¹⁴ In our group, no corneal decompensation occurred after surgery; however, surgery was solely performed by highly experienced surgeons using a soft-shell technique with dispersive viscoelastics to protect the endothelium.

The proposed mechanism for the reduction of IOP after phacoemulsification is the widening of the anterior chamber and angle.¹⁵ Moghimi et al¹⁶ found that eyes with AAC have a thicker lens and larger lens vault than other subtypes of glaucoma, and it seems that the lens plays a major role in the development of AAC.¹⁷ Therefore, by removing the lens through phacoemulsification and widening the anterior chamber angle, the effects of phacoemulsification result in greater decrease in IOP in patients with angle closure compared with open angles.^{18,19} Although the influence of the lens on the etiology of AAC is well-established, early phacoemulsification is still considered controversial. Jacobi et al²⁰ concluded that in patients with AAC, IOP control was achieved in 72% of eyes after phacoemulsification with IOL implantation, compared

with 35% after surgical peripheral iridectomy ($P=0.03$). Phacoemulsification after LPI in Asian patients with AAC resulted in lower IOP failure compared with LPI alone.¹⁴ Husain and colleagues compared treatment with LPI alone versus treatment with phacoemulsification with IOL implantation in patients with AAC and coexisting cataract. Phacoemulsification with IOL implantation was performed within 1 week of a medically controlled AAC event. It was concluded that phacoemulsification resulted in a lower rate of IOP failure after 2 years compared with LPI, prevents PAS formation, and eliminates lens-induced angle narrowing.¹⁴ This evidence suggests that phacoemulsification may be considered as the superior option compared with LPI in patients with AAC.

Lam and colleagues concluded that it is worthwhile to perform phacoemulsification with IOL implantation at an early stage after AAC in patients with coexisting cataract.²¹ This treatment plan was also suggested by our study; however, there is no evidence yet on the optimal timing to perform phacoemulsification after AAC, and more evidence is necessary to determine the most optimal time to perform phacoemulsification after AAC to prevent further glaucomatous damage. To assess potential differences between patients operated on within a few days or after a few weeks after AAC crisis, a regression analysis was performed to assess potential differences. There was no difference between these groups with either IOP decrease ($r < 0.001$; $P = 0.99$) or the IOP at 3 months ($r = -0.006$; $P = 0.97$). The degree of optic nerve damage after AAC is not well established and evidence is limited. AAC can lead to glaucomatous optic nerve damage and the development of primary angle closure glaucoma. Aung et al²² reported 50% of their study population developed glaucomatous damage over time, suggesting that timely diagnosis and treatment are crucial.

For the 8 AS-OCT images available for analysis of anterior segment parameters, we analyzed the anterior segment parameters to determine parameters predictive of the IOP-lowering effect in angle closure patients. All images showed iridotrabecular contact in the nasal and temporal angle and the lens vault measured at least 1 mm. Because of the small group of available images for further analysis and the homogeneity of the data, we were not able to perform regression analysis to detect differences to determine which factors would be predictive of the IOP-lowering effect in these patients.

Our study reports the effect of phacoemulsification on eyes with recent AAC episode after aborting the acute attack in a Caucasian (Dutch) population. However, there are some limitations that may affect the generalizability of our findings. The retrospective nature of the study resulted in some missing data. For example, the lack of pachymetry results made the calculation of the anterior chamber depth less accurate and therefore less comparable between the IOLMaster and the AS-OCT, making the generalizability of the data more difficult. The study population was small and may have limited the power of outcome comparisons. Also, in some patients with uncontrolled IOP, a combined treatment of phacoemulsification with trabeculectomy was performed, however these patients were not included in this study (Table 1). Finally, as this study was conducted in a Dutch population, its results may not be generalizable to other populations.

Previous studies reported that phacoemulsification in subjects with PACG shows greater efficacy in IOP reduction in the long term,^{8,23} and widening of the anterior chamber angle. It has been demonstrated that phacoemulsification

with implantation of an IOL results in long-term reduction of IOP in subjects without glaucoma but also in patients with glaucoma.^{24–28} Eyes with higher preoperative IOP showed the largest IOP decrease postoperatively.²⁴ This statistic is similar to our results, which showed that PACG patients with higher preoperative IOP gained a proportionally larger IOP decrease after phacoemulsification and reaffirms the fact that the eyes with highest IOP, most in need of IOP reduction, showed the greatest benefit from phacoemulsification. Recently, the EAGLE study, published by Azuara-Blanco and colleagues, reported the results of a multicenter randomized trial in which clear lens extraction was performed in patients with PAC with raised IOP or PACG. They concluded that clear lens extraction should be considered as a first-line treatment option for these patients.⁸ This study underscores the importance of phacoemulsification to prevent glaucomatous progression in our study.

Although the EAGLE study promotes early or clear lens extraction in general to prevent AAC, our study also encourages early cataract surgery in Caucasian patients after an AAC attack, to improve VA and control IOP, even if the cataract surgery may have risks. A recent study suggests that a larger lens vault may predict zonular instability, further highlighting the importance of imaging techniques in these patients.²⁹ Early intervention with phacoemulsification and IOL implantation should be considered as a reasonable alternative to the first-line treatment of AAC in patients with coexisting cataract. Further evidence is necessary to define the optimal time window to perform phacoemulsification.

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