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Intra-ocular pressure fluctuation after cataract surgery in primary angle-closure glaucoma eyes medically controlled after laser iridotomy

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ABSTRACT.

Purpose: **To analyse the effect of cataract surgery on diurnal intra-ocular pressure (IOP) fluctuation in primary angle-closure glaucoma (PACG) eyes.**

Methods: **Thirty-nine eyes of 24 patients with PACG scheduled for cataract surgery were enrolled to this prospective study. A record was made which included mean IOP measurement, anterior chamber depth (ACD), anterior chamber angle (ACA), number of antiglaucomatous medications, visual field analysis (mean deviation – MD and pattern standard deviation – PSD) and responses to the Glaucoma Quality of Life-15 (GQL-15) questionnaires. The eyes were re-evaluated at 2 and 3 months of cataract surgery.**

Results: **IOP fluctuation was decreased from 4.58 ± 2.07 mmHg to 2.84 ± 1.5 mmHg ($p < 0.001$). The decrease in mean IOP, the number of glaucoma eye drops required ($p < 0.001$, $p = 0.012$, respectively) and the increase in mean ACD, ACA grading and SITA-standard MD ($p < 0.001$, $p < 0.001$, and $p = 0.01$, respectively) were statistically significant. The mean GQL-15 score was also improved ($p < 0.001$). The change in IOP fluctuation correlated positively with the preoperative IOP fluctuation ($r = 0.56$ $p = 0.00$), the change in ACD ($r = 0.703$, $p < 0.001$) and the change in ACA ($r = 0.664$, $p < 0.001$). In multivariate analysis, preoperative IOP fluctuation and postoperative increase in ACD were significantly associated with a reduction in IOP fluctuation of an average of 1.1 mmHg per unit change ($p = 0.00$ and $p = 0.019$, respectively).**

Conclusions: **Cataract surgery in PACG provides the opportunity to address many pathologies with one intervention; improving vision, diminishing IOP, blunting IOP fluctuation, reducing need for medications, eliminating a narrow angle and improving GQL-15 scores.**

Key words: cataract surgery – intra-ocular pressure – intra-ocular pressure fluctuation – primary angle-closure glaucoma

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Introduction

Primary angle-closure glaucoma (PACG) may account for half of the cases with primary glaucoma worldwide by 2020 (Quigley & Broman 2006). A crowded anterior segment is a predisposing factor for PACG (Quigley et al. 2003), and laser iridotomy effectively relieves pupillary block, which is the mechanism responsible for angle closure in most eyes (Wright et al. 2015). Despite a patent laser iridotomy, accumulating evidence indicates that a large and anteriorly positioned lens is responsible for residual angle closure and elevated intraocular pressure (IOP) in those eyes (Nonaka et al. 2005). Meanwhile, researchers have shown that there is substantial reduction of the average IOP in PACG after cataract surgery (Gunning & Greve 1998; Kubota et al. 2003; Lai et al. 2006; Shams & Foster 2012; Tham et al. 2013; Brown et al. 2014).

It has been speculated that the visual field loss may be related, at least in part, to the larger fluctuations in circadian IOP in PACG patients (Baskaran et al. 2009). Large fluctuations in circadian IOP are also a significant risk factor for progression of visual field loss in primary open-angle glaucoma patients (Asrani et al. 2000; Baskaran et al. 2009).

Thus, treatment for PACG, that is laser iridotomy, medical therapy or surgical treatment, should provide the reduction of IOP as well as the reduction of the risks of pressure peaks and elevated IOP fluctuation. Although PACG is a common form of glaucoma worldwide (Quigley & Broman 2006; Wright et al. 2015), data on the change in IOP fluctuations in eyes with PACG after cataract surgery are limited.

The purpose of this study was to analyse the effect of cataract surgery on IOP fluctuation in PACG eyes with visually significant cataract and to evaluate factors associated with postoperative changes in IOP fluctuation.

Patients and Methods

This prospective study was performed according to the tenets of Declaration of Helsinki. All patients signed a written informed consent agreement approved by an institutional review board before any procedure was performed.

In this study, 24 consecutive patients diagnosed with PACG were enrolled. The diagnosis of PACG was based on elevated IOP (IOP $\geq$ 21 mmHg without antiglaucoma medication), an occludable anterior chamber angle in which the trabecular meshwork was visible for a circumference of <90°, and glaucomatous optic disc changes with or without visual field defects. The optic disc changes included asymmetric cupping between the eyes of >0.2 or cup elongation with excavation of the neuroretinal rim. Thirty-nine eyes with previous laser peripheral iridotomy of 24 patients scheduled to undergo cataract surgery due to visually significant cataract were evaluated for statistical analysis. Primary angle-closure glaucoma (PACG) eyes with IOP $\geq$ 30 mmHg under antiglaucomatous medication, or with peripheral anterior synechiae (PAS) of 6 clock hours or more, primary open-angle glaucoma, any secondary glaucoma, uveitis, retinal disease, corneal abnormalities that might influence IOP measurements, and history of previous ocular surgery were excluded.

All eyes were underwent cataract surgery and implantation of a foldable acrylic IOL through a 2.2-mm superotemporal corneal tunnel incision under topical anaesthesia by same surgeon.

Postoperatively, a 4-week course of tapering topical steroid and antibiotic was routinely prescribed. Preoperative antiglaucomatous medications were continued 2 months postoperatively and adjusted gradually to keep IOP $\leq$ 18 mmHg, when 20% or more reduction in IOP was detected.

Best-corrected visual acuity (BCVA), IOP measurements, anterior chamber depth (ACD), angle of anterior chamber, number of antiglaucomatous medications, visual field analysis and the Glaucoma Quality of Life-15 (GQL-15) questionnaire were recorded 1 week before cataract surgery. At 3 months of surgery BCVA, ACD, anterior chamber angle, the number of requiring glaucomatous medication, visual field analysis and the GQL-15 questionnaire were evaluated while the mean IOP and IOP fluctuation were analysed at 2 months of cataract surgery before adjusting antiglaucomatous medication to assess the true effect of the surgery.

Best-corrected visual acuity (BCVA) was measured using a Snellen chart, and the Snellen fraction was then converted to LogMAR (logarithm of the minimum angle of resolution) equivalents to calculate the geometric mean BCVA, standard deviation for statistical analysis. Intraocular pressure (IOP) measurements were taken at 8 AM, 12 AM and 4 PM. At each measurement time-point, three assessments were performed for each eye, and the IOP for a given time-point was defined as the average of three measurements. For each patient, the IOP assessments were performed by the same examiner using the same calibrated Goldmann applanation tonometer at each visit. Intraocular pressure (IOP) fluctuation was calculated as 'the highest IOP measurement – lowest IOP measurement'. The mean IOP was calculated as the average measurements of IOPs at 8 AM, 12 AM and 4 PM. The observer was masked to the results of the preoperative IOP values.

Anterior chamber depth (ACD) was measured with A-scan ultrasonography (Compact Touch Ultrasound System, Cedex, France). Anterior chamber angle was graded via gonioscopy with Goldmann three-mirror lens. The anterior chamber angle was graded as: 4, a wide open angle with visible ciliary body band; 3, an angle with visible scleral spur; 2, an angle with visible posterior trabecular meshwork; 1, an angle in which only the Schwalbe line is visible; and 0, an angle with no visible angle structure. The anterior chamber angle was recorded as the mean angle degree of 4 quadrants.

Mean deviation and pattern standard deviation obtained from visual field analysis – Swedish Interactive Threshold Algorithm (SITA)-Standard 24-2 program of the Humphrey perimeter (Carl Zeiss Meditec Inc. Dublin, CA, USA) were recorded. The patients were interviewed using the GQL-15 questionnaire to determine the impact of visual impairment on their quality of life. The GQL-15 questionnaire is a glaucoma-specific, written questionnaire that assesses patients' perceived visual disability in 15 daily tasks. The tasks are categorized in four areas of visual disability: (i) central and near vision, (ii) peripheral vision, (iii) dark adaptation and glare and (iv) outdoor mobility. A 5-point rating scale for the level of difficulty of each task totals a score from 0 to 75. A higher score signifies a poorer GQL. The GQL-15 was translated to Turkish using a forward and backward translation protocol, with attention paid to maintain the actual meaning of each question. The Turkish version of the GQL-15 was self-administered by the patients in the clinic 1 week before and 3 months after surgery.

Statistical analysis

SPSS v 20.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continous variables were compared using parametric (paired *t*-test) and nonparametric (Wilcoxon's signed-ranks test) tests according to Shapiro–Wilk test. Pearson's correlation analysis was performed to assess the correlation between the change in IOP fluctuation and other variables. Multivariate linear regression analysis with the change in IOP fluctuation as a dependent parameter and preoperative mean IOP, preoperative mean IOP fluctuation, the change in ACD and the change in anterior chamber angle grading parameters as independent parameters was performed to assess the predictors of the IOP fluctuation change among PACG patients after cataract surgery. p values of 0.05 or less were considered to be statistically significant.

Power analysis was performed using GPOWER 3.1 program (G*Power, Franz Faul, Universitat Kiel, Kiel, Germany). Assuming a standard deviation of 1.44 mmHg and an α-level of 0.05 for a 2-sided test, this study provided an 86% power to detect a difference IOP fluctuation of 2.0 mmHg between baseline and after 2 months of cataract surgery.

Results

The mean age was 73.3 ± 8.95 years (range, 67–81 years). There were 15 female patients and nine male patients. All patients had prior laser iridotomy. The mean BCVA was 0.72 ± 0.6 LogMAR before surgery and 0.22 ± 0.2 LogMAR at 3 months ($p < 0.001$). BCVA improved in 94.9% of eyes with a mean of 0.14 ± 0.1 LogMAR and remained unchanged in 5.1% of eyes with a mean of 0.74 ± 0.2 LogMAR, and there was no patient with a worse vision postoperatively.

The mean IOP and IOP fluctuation of PACG eyes under antiglaucomatous medication before and after cataract surgery were shown in Table 1. IOP was decreased from a mean preoperative level of 18.5 ± 4.2 mmHg to 14.0 ± 2.8 mmHg ($p < 0.001$). Intraocular pressure (IOP) fluctuation was decreased from 4.6 ± 2.1 mmHg to 2.8 ± 1.5 mmHg ($p < 0.001$). Figure 1 illustrates the proportion of eyes, subdivided into categories of absolute change in postoperative IOP. The IOP increased in three eyes (7.7%) and remained unchanged in four eyes (% 10.3). In all three eyes, the IOP was <18 mmHg, and they were using the same number of antiglaucomatous medication.

There was no intra-operative complication in any eyes; however, a postoperative rise in IOP up to 6 mmHg (>22 mmHg) developed within 24 hr in two eyes under prostaglandin monotherapy. Prostaglandin/β-blocker fixed combination was initiated in those eyes for controlling IOP elevations. The antiglaucomatous medication was changed to prostaglandin monotherapy again after a week. There were no major postoperative complications.

The number of requiring antiglaucomatous eye drops was decreased from 1.9 ± 0.7 to 0.8 ± 0.4 ($p = 0.012$) after antiglaucomatous medication was adjusted at 2 months of cataract surgery. No eyes required more glaucomatous medication postoperatively. Three eyes had IOP ≤ 17 mmHg with a prostaglandin/β-blocker fixed combination, 21 eyes had IOP ≤ 15 mmHg with prostaglandin monotherapy, and 15 eyes had IOP ≤ 17 mmHg without any medications.

While the mean ACD was increased from 1.7 ± 0.1 mm to 3.25 ± 0.3 mm ($p < 0.001$), average angle width increased significantly from grade 0.46 ± 0.48 preoperatively to grade 2.5 ± 0.5 at 3 months postoperatively ($p < 0.001$). After cataract surgery, SITA-standard mean MD improved from -9.9 ± 0.8 dB to -8.7 ± 0.6 dB ($p = 0.01$), whereas the change in mean PSD was statistically non-significant (from 5.9 ± 1.2 dB to 5.88 ± 1.2 dB; $p = 0.659$). The GQL-15 score was also improved from a mean preoperative level 35.3 ± 4.7–28.0 ± 4.1 at 3 months ($p < 0.001$). No patient provided a worse quality life score after cataract surgery.

Pearson's correlation analysis showed that the change in IOP fluctuation correlated positively with the preoperative IOP fluctuation ($r = 0.56$ $p = 0.00$), the change in ACD ($r = 0.703$, $p < 0.001$) and the change in anterior chamber angle ($r = 0.664$, $p < 0.001$).

In multivariate regression analysis, preoperative IOP fluctuation and postoperative increase in ACD were significantly associated with a reduction in IOP fluctuation of an average of 1.1 mmHg per unit change ($p = 0.00$ and $p = 0.019$, respectively) (Figs 2 and 3). There was no correlation between the change in IOP fluctuation and the change in anterior chamber angle grading ($p = 0.22$) or preoperative mean IOP ($p = 0.086$) at $\alpha = 0.05$ significance level.

Discussion

This prospective study suggests that lens extraction by phacoemulsification leads to a significant reduction in diurnal IOP fluctuation as well as in IOP levels and the number of requiring antiglaucoma medication in PACG eyes with previous laser iridotomy. The change in IOP fluctuation values in PACG correlated positively with the change in ACD and preoperative IOP fluctuation. To the best of the authors' knowledge, there is no study that observes directly IOP fluctuation changes in mmHg and associated factors after cataract surgery in PACG eyes with previous laser iridotomy. Recently, the decrease in IOP fluctuations during nocturnal period after cataract surgery using a contact lens sensor (CLS) in PACG patients was reported (Tojo et al. 2014). However, only relative changes of millivolt equivalent can be evaluated with a CLS that does not directly show the values of mmHg. Also, the spikes in IOP monitoring with a CLS can be affected by eye movements, blinking or cardiac activity owing to ocular pulsation changes. Therefore, the different results between studies may be depend on different measurement methods.

The mechanism responsible for IOP decrease after cataract extraction is still unclear. It is generally accepted that relief of pupillary block, opening of the anterior chamber angle and reducing the extent of PAS are possible mechanisms for IOP decrease in these patients (Gunning & Greve 1998). It was shown production of endogenous interleukin-1 by cultured trabecular meshwork cells in response to phacoemulsification ultrasound (Wang et al. 2003). Therefore, phacoemulsification may reduce IOP by increasing facility of the aqueous outflow (Meyer et al. 1997; Wang et al. 2003).

Similarly with previous studies (Gunning & Greve 1998; Kubota et al. 2003; Lai et al. 2006), more recently studies also reported the decrease in mean IOP and the number of requiring glaucoma medication after cataract

Table 1. The mean IOP and IOP fluctuation under antiglaucomatous medication before and after cataract surgery.

		The mean IOP (mmHg)		IOP fluctuation (mmHg)	
Antiglaucomatous medication	Eyes (n)	Baseline	Postoperative	Baseline	Postoperative
Prostaglandin monotherapy	18	15.9 ± 2.8	12.3 ± 2.1*	4.1 ± 1.2	2.1 ± 1.1*
Prostaglandin/β-blocker fixed combination	16	18.2 ± 3.0	14.1 ± 1.9*	4.3 ± 2.5	3.0 ± 1.8*
Prostaglandin/β-blocker fixed combination and α-agonist	5	21.3 ± 4.1	15.7 ± 3.5*	5.4 ± 2.5	3.3 ± 1.5*

* The decrease is statistically significant (Wilcoxon's signed-ranks test, $p < 0.001$, for all comparisons).

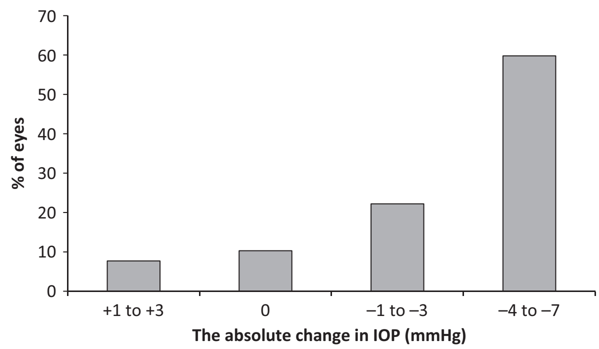

Fig. 1. The absolute change in intra-ocular pressure.

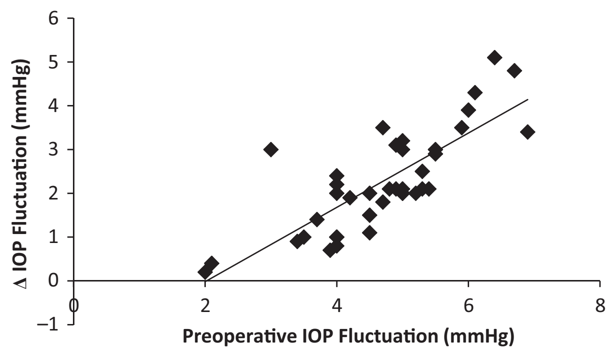

Fig. 2. Correlation between the change in mean intra-ocular pressure (IOP) fluctuation and the change in mean anterior chamber depth.

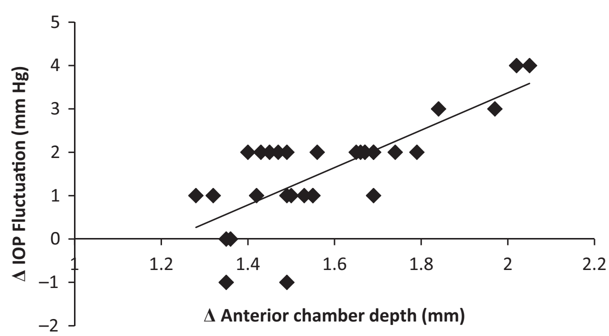

Fig. 3. Correlation between the change in mean intra-ocular pressure (IOP) fluctuation and the preoperative mean IOP fluctuation levels.

surgery in patients with primary angle closure and PACG. In a retrospective study, the authors reported that the mean IOP decreased from 18.7 to 14.1 mmHg in patients with primary angle closure or occludable angles and visually symptomatic cataract after phacoemulsification (Shams & Foster 2012). A randomized prospective study comparing outcomes with phacoemulsification versus trabeculectomy in patients without visually significant cataract was conducted on for treatment of medically uncontrolled PACG. The authors reported that the mean IOP decreased from 24.4 to 16.1 mmHg and the number of requiring glaucoma medication decreased from a mean 3.3–1.7 in phacoemulsification group (Tham et al. 2013). In a retrospective study in which preoperative IOP was strafied, it was reported that the magnitude of IOP decrease after cataract surgery was found highly positively correlated with preoperative IOP levels in patients with narrow angles and chronic angle-closure glaucoma (Brown et al. 2014). In the current study, a significant IOP decrease in medically controlled PACG eyes with laser iridotomy (4.7 ± 2.1 mmHg) also was found after cataract surgery and the number of requiring glaucoma medication was reduced in all eyes with a decrease from 1.9 to 0.8 and 38.4% of eyes had IOP ≤ 17 mmHg without any glaucoma medication.

After laser iridotomy, angle closure may develop in eyes with plateau iris syndrome, a thick and anteriorly positioned lens, or choroidal expansion (Quigley et al. 2003). Studies using ultrasound biomicroscopy and Scheimpflug videophotography have shown that the width and depth of the drainage angle in PACG increases and becomes similar to those of normal eyes after phacoemulsification (Liu et al. 2006; Huang et al. 2011). Consistent with previous studies, we have shown that phacoemulsification in eyes with PACG had significant alteration of the angle configuration and depth of anterior chamber.

Although higher IOP levels have been unquestionably demonstrated to be a risk factor for progression of glaucoma, larger IOP fluctuations could contribute to the progression of visual field deterioration (Kubota et al. 2003; Tan et al. 2015). In the current study, the visual field analysis showed that the improvement in MD was significant while changes in PSD were not. Although the improved MD is consisted with the removal of visually significant cataract, the effect of reduction in IOP fluctuation on progression of glaucoma after cataract surgery should be evaluated in long-term studies with a large sample size.

Patients with glaucoma and concomitant cataract suffer from impairment in quality of life due to vision decrement. In the current study, the GQL-15 questionnaire scores were improved after cataract surgery. The improvements seen in the GQL-15 questionnaire could be attributable to cataract surgery in those patients.

In the literature, several management procedures have been examined for PACG. It has been reported that selective laser trabeculoplasty (SLT) may be an adjunctive treatment for selected patients with chronic angle-closure and some visible trabecular meshwork by Ho et al. (2009). The authors studied the use of SLT in eyes with PACG, a patent iridotomy and at least 90° of visible pigmented trabecular meshwork and reported a 24% reduction in mean IOP with no statistical change in medications at 6 months. If the patient has a visually significant cataract, phacoemulsification can be compared favourably to current standard treatments for PACG, functioning both alone and in combination with other therapies. Goniosynechialysis (GSL) and viscogonioplasty can be combined with phacoemulsification; however, there is little evidence that phaco-GSL or phacoviscogonioplasty is better that phacoemulsification alone in reducing IOP, especially in more chronic patients (Trikha et al. 2015). Endoscopic cyclophotocoagulation (ECP) also can be combined with phacoemulsification in patients with anteriorly positioned ciliary process to open angle and to reduce the production of aqueous humour (Wright et al. 2015). Morales et al. (2015) retrospectively evaluated the results of phacoemulsification combined with ECP for advanced glaucoma and cataract at least 1 year after surgery. Absolute success (≤15 mmHg without medicatons) and qualified success (≤15 mmHg with medications) were reported 13.6% and 42% for PACG patients. Narrow angles have previously been seen as a relative contraindication to ab interno trabeculectomy (AIT), whereas phaco-AIT has been performed in narrow angles with less concern because removal of the crystalline lens deepens the anterior chamber angle and may resolve angle closure. Bussel et al. (2015) reported that phacoemulsification-AIT with trabectome provided a 24% reduction in mean IOP with 0.8 fewer medications in eyes with narrow angles and visually significant cataract. Non-penetrating surgery is an another surgical procedure that is examined for combining with phacoemulsification. Yuen et al. (2007) retrospectively evaluated the results of 29 eyes of 26 patients who had undergone combined non-penetrating deep sclerectomy and phacoemulsification for cataract and PACG with a mean follow-up period of 33.8 months and reported the decrease in IOP (20.3 ± 3.9 versus 15.9 ± 3.1 mmHg) and in the number of antiglaucoma medications (2.9 ± 0.8 versus 1.0 ± 1.2). Phacotrabeculectomy seems to be more efficient in IOP control in PACG patients rapidly progressive and medically uncontrolled; however, the procedure is associated with more postoperative complications (Tham et al. 2009).

The timing of lens extraction in postiridotomy eyes with PACG may be critical because repeated appositional closure may allow to increase the extent of synechial closure and have an impact on the remaining trabecular outflow. This may result in moderate IOP reduction because of increased synechial closures when cataract surgery is performed at a later date. If the patient has a visually significant cataract it is a more widely accepted method of treatment. Despite evidence that lens extraction can improve IOP control in eyes with narrow angles, the use of clear lens extraction as a treatment option is still arguable. It is unclear whether or not early phacoemulsification and IOL implantation will be beneficial for PACG patients, but an ongoing study by the Effectiveness in Angle-closure Glaucoma of Lens Extraction (EAGLE) study group is currently investigating this question (Azuara-Blanco et al. 2011).

There are some limitations to this study. The use of antiglaucomatous medication might alter the IOP results; however, the standardize regimen pre- and postsurgery was administered for minimizing the medication effect on IOP changes. Moreover, most of the eyes were administered prostaglandin monotherapy or prostaglandin/β-blocker fixed combination that could compose a uniform sample in terms of antiglaucomatous medication. New imaging techniques such as anterior segment optical coherence tomography and ultrasound biomicroscopy might be useful in evaluating biometric changes in the anterior segment following cataract surgery; however, the devices were not available. Small sample size may not be a limitation factor because of adequate study power for statistical analysis. The lack of a control group is a limitation of this study; therefore, the results could not be compared with untreated group.

In the current study, we have reported clinical outcomes at 3 months after cataract surgery; however, these results may not reflect the long-term outcome of surgery in all eyes. Long-term follow-up is required in these patients, on account of the fact that the rise in IOP levels or requiring antiglaucomatous medication may occur over time.

In conclusion, cataract surgery in PACG provides the opportunity to address many pathologies with one intervention; improving vision, lowering IOP, reducing IOP fluctuation, reducing need for medications, improving GQL and eliminating a narrow angle. However, further studies should be conducted on long-term IOP fluctuation changes after cataract surgery and the effect of change in IOP fluctuation on PACG progression.

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