

Retrospective analysis of the risk factors for developing phacomorphic glaucoma

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Aim: To determine the risk factors for developing phacomorphic glaucoma in eyes with mature cataracts. **Materials and Methods:** This is a case-control study comprising of 90 eyes with phacomorphic glaucoma and 90 age- and sex-matched control eyes with mature cataracts without phacomorphic glaucoma. Patients with pre-existing glaucoma, previous intraocular surgery and /or absence of documented axial lengths were excluded from this study. Binary logistic regression analysis of the variables, axial length and anterior chamber depth, was performed. Anterior chamber depth of the contralateral eye was used as a proxy measure of the pre-phacomorphic state in the eye with phacomorphic glaucoma as majority of them first presented to our center during the phacomorphic attack without prior measurements of the pre-phacomorphic ACD or lens thickness; therefore, their anterior chamber depth would not be representative of their pre-phacomorphic state. Axial length of 23.7 mm was selected as a cut-off for dichotomized logistic regression based on the local population mean from published demographic data. **Results:** The mean age was 73.1 ± 10.2 years. All phacomorphic and control eyes were ethnic Chinese. The mean presenting intraocular pressures were 49.5 ± 11.8 mmHg and 16.7 ± 1.7 mmHg in the phacomorphic and control eyes respectively ($P < 0.0001$), whilst the median Snellen best corrected visual acuity were light perception and hand movement in the phacomorphic and control eyes respectively. Eyes with phacomorphic glaucoma had shorter axial length of 23.1 ± 0.9 mm median when compared with that of control eyes, 23.7 ± 1.5 mm ($P = 0.0006$). Eyes with AL ≤ 23.7 mm were 4.3 times as likely to develop phacomorphic glaucoma when compared with AL > 23.7 mm ($P = 0.003$). **Conclusion:** Axial length less than ≤ 23.7 mm was a risk factor for developing phacomorphic glaucoma. Eyes with AL shorter than the population mean were 4.3 times as likely to develop phacomorphic glaucoma compared with eyes with longer than average AL. In an area where phacomorphic glaucoma is prevalent and medical resources are limited, patients with AL shorter than their population mean may be considered for earlier elective cataract extraction as a preventive measure.

Key words: Anterior chamber depth, axial length, lens thickness, phacomorphic glaucoma, risk factor.

Cataract and glaucoma are leading causes of visual impairment in Asia. In Mongolia, cataract and glaucoma contribute to 36 and 35% of blindness respectively.^[1] As both are diseases of advancing age, they can co-exist and under certain circumstances, one disease may even lead to the other. Delay in the extraction of mature cataracts can result in phacomorphic glaucoma, a type of secondary angle closure caused by the forward displacement of an intumescent (swollen and white) cataract giving rise to pupillary block or iridocorneal angle closure. In India, phacomorphic glaucoma accounts for 3.9% of all cataract extractions.^[2] Though phacomorphic glaucoma develops in the presence of a mature cataract, not all patients with mature cataract necessarily go on to develop phacomorphic glaucoma.

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Various population studies have established advancing age, female gender, shallow anterior chamber depth (ACD), short axial length (AL) and Chinese ethnicity as risk factors for primary angle-closure suspects, primary angle closures and primary angle closure glaucomas.^[3-9]

Cataract extraction is usually indicated if visual gain is expected after the surgery. However not all patients with mature cataracts can afford the surgery, especially in developing countries, and for those in the lower social economic class where they usually seek medical attention from public institutions where they are likely to be put on a long waiting list. In Hong Kong, the current waiting list for elective cataract extraction ranges from 20.1 to 82.0 months.^[10] During this period, cataracts may progress from an immature state to a mature cataract and subsequently develop phacomorphic glaucoma. It is important to identify which of these patients with mature cataracts are at an increased risk of phacomorphic glaucoma; so priority may be given to them to prevent such complication [Table 1].

Phacomorphic glaucoma can occur in both eyes with shallow or deep anterior chambers^[11] as the pathology is the intumescent cataract rather than the angle configuration like in primary angle closures. This study investigated the roles of axial length and anterior chamber depth as risk factors for the

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Table 1: Risk factors for developing phacomorphic glaucoma

	Odds ratio	P value
Axial length (ipsilateral) \leq 23.7 mm	4.3	0.003
Anterior chamber depth (contralateral)	0.4	0.6

development of phacomorphic glaucoma in eyes with mature cataract.

Materials and Methods

This was a case-control study involving 90 eyes with phacomorphic glaucoma and 90 control eyes. Cases were eyes with phacomorphic glaucoma who presented to the Caritas Medical Centre, Hong Kong Special Administrative Region, China, from January 2000 to April 2009. The diagnosis of phacomorphic glaucoma was based on an intraocular pressure (IOP) above 21 mmHg^[12] in the presence of an intumescent cataract in conjunction with signs consistent with phacomorphic glaucoma such as corneal edema, mid-dilated pupil, and conjunctival injection, and a shallow central anterior chamber from slit lamp examination. Gonioscopy was not required for the diagnosis of phacomorphic glaucoma as it was often not feasible in the presence of corneal edema from the acute IOP elevation.^[13] Cases were excluded if there were any documented suspicion of acute primary angle closure from the medical records.

Controls were eyes with mature cataracts without phacomorphic glaucoma. A mature cataract was defined as a crystalline lens that was completely opaque. Control eyes were randomly selected from a pool of patients on the waiting list for elective cataract operations during the same time interval. Control eyes were matched in terms of age and sex with a 1:1 ratio to the eyes with phacomorphic glaucoma. The laterality of the control eyes was matched with that of the eye with phacomorphic glaucoma. Patients with pre-existing glaucoma, previous intraocular surgery, and absence of documented axial length from the medical records were excluded.

Axial length and lens thickness were measured from the control eyes. Seventy cases of phacomorphic glaucoma presented for the first time to our center during the phacomorphic attack without prior measurements of the pre-phacomorphic ACD or lens thickness. During the phacomorphic attack, the anterior chamber depth of the involved eye would be shallower and the lens thickness would be thicker than the pre-phacomorphic state making these parameters unreliable as risk factors for the development of phacomorphic glaucoma. To overcome this problem, we measured the contralateral anterior chamber depth as proxy measures of the pre-phacomorphic state of the eye with phacomorphic glaucoma. However, the contralateral lens thickness was not implemented as a proxy measure of the eye with phacomorphic glaucoma because we cannot rule out the possibility that the lens may be originally thicker in the phacomorphic eye prior to the attack since the primary pathology of the secondary angle closure is in the thickened opaque lens. As for the axial length which should be constant before or during a phacomorphic attack, we were able to directly use the ipsilateral axial length in our calculations.

Age, gender, presenting IOP and Snellen best corrected

visual acuity (BCVA) and AL were recorded. Axial lengths and anterior chamber depths were measured using contact A-scan ultrasonography (Compact II, Quantel Medical, Clermont-Ferrand -CEDEX 2, France). All A-scans were performed by two optometrists and the average of ten readings was taken for the axial length and anterior chamber depth. Intraocular pressure was measured by Goldman applanation tonometry.

The institutional review board of the Hospital Authority of Hong Kong approved this study. The study protocol followed the principles in the Declaration of Helsinki. Informed consent was obtained from all patients prior to cataract extraction.

Definitions

A study by Lam *et al*, involving 220 Hong Kong Chinese adults aged 40 and over showed a mean axial length of 23.4 ± 1.1 and 23.9 ± 1.2 in females and males respectively.^[14] We adopted the mean value, 23.7 mm, as the mean axial length for our population.

Statistical analysis:

All analyses were performed using statistical softwares (GraphPadPrism for Windows, ver. 5.0; GraphPad Software, Inc., La Jolla, CA 92037 USA and SPSS for Windows, ver. 13.0; SPSS Inc., Chicago, IL 60606-6307 USA). Differences of means were analyzed using the t-test and paired t-test where appropriate and forward stepwise binary logistic regression was implemented for analysis of the variables: axial length and anterior chamber depth in association with the development of phacomorphic glaucoma. Dichotomization was performed comparing eyes with a shorter than mean AL (\leq 23.7 mm) to those with a longer than mean AL ($>$ 23.7 mm). The critical value of significance was set at $P < 0.05$ for all tests. All means were expressed as mean \pm standard deviation.

Results

There were 100 consecutive cases of phacomorphic glaucoma during the specified study period. Ten cases with phacomorphic glaucoma were excluded due to the absence of axial length measurements. As these patients did not receive any intraocular lens insertion after their cataract extraction, there was no perception of light in the glaucomatous eye on presentation. Twenty of the cases with phacomorphic glaucoma were already on the waiting list for elective cataract extraction prior to the acute attack. The mean waiting time prior to the phacomorphic attack was 9.0 ± 8.4 months. The cataract operation waiting time for the control eyes was 8.3 ± 7.6 months. There was no statistical difference between the waiting time of the two groups ($P = 0.8$).

Ninety eyes with phacomorphic glaucoma and 90 age and sex matched control eyes were included in the analysis. The mean age was 73.1 ± 10.2 years (range 40 - 95 years). There were 48 left eyes and 42 right eyes amongst the phacomorphic and control eyes. All phacomorphic glaucoma and control eyes were from ethnic Chinese with a male to female ratio of 1:1.5. The mean presenting intraocular pressures were 49.5 ± 11.8 mmHg and 16.7 ± 1.7 mmHg in phacomorphic glaucoma and control eyes respectively ($P < 0.0001$). The median presenting BCVA were light perception and hand movement in the phacomorphic and control eyes respectively. The poorer visual acuity in the phacomorphic group is likely contributed by the corneal edema and ocular inflammation as a result of the secondary angle closure.

The mean axial lengths were 23.1 ± 0.9 mm (95% CI: 22.9 to 23.3 mm) and 23.7 ± 1.5 mm (95% CI: 23.4 to 24.0 mm) in eyes with phacomorphic glaucoma and control eyes respectively. This was statistically significant ($P = 0.0006$). A dichotomized binary logistic regression showed that eyes with $AL \leq 23.7$ mm were 4.3 times (odds ratio, 95% CI: 1.6 to 11.1) as likely to develop phacomorphic glaucoma than eyes with $AL > 23.7$ mm ($P = 0.003$).

There was no significant difference between the means of the contralateral ACD and that of the control eyes ($P=0.3$). Logistic regression of the contralateral ACD did not show any significant association with the development of phacomorphic glaucoma ($P = 0.2$).

Discussion

Dating back to the 1900's, Gifford had recommended early cataract extraction before cataracts becoming hypermature.^[15] Yet a century later, this simple concept is not always feasible given the rapidly aging population, poverty in developing countries, and healthcare resource constraints in both developing and developed countries. Phacomorphic glaucoma may develop if these mature cataracts are not removed. The purpose of this study is to identify ways to decipher which individuals with mature cataracts would be more at risk for phacomorphic glaucoma in the hope to offer to them earlier cataract extraction.

We found that eyes with phacomorphic glaucoma had statistically shorter axial lengths compared with their age and sex matched control eyes (23.1 ± 0.9 mm versus 23.7 ± 1.5 mm, $P = 0.0006$). Those with $AL \leq 23.2$ mm were 4.3 times as likely to develop phacomorphic glaucoma compared to eyes with $AL > 23.7$ mm ($P = 0.003$).

Axial length has been a significant predictor for various other forms of glaucoma. For primary angle closures, Casson *et al*, found that for each 1-mm decrease in axial length, the risk of primary angle closure gets doubled.^[16] Likewise, longer axial length is a known risk factor for primary open angle glaucoma as well as normal tension glaucoma.^[17] However, no such evidence currently exists for phacomorphic glaucoma, a condition that is seen in eyes with narrow angles and open angles.^[11] To the best of our knowledge, this is the first study demonstrating axial length as a risk factor for phacomorphic glaucoma. Axial length is easily accessible as most cataract extraction candidates would have had it measured in advance for calculation of intraocular lens power.

Phacomorphic glaucoma is often associated with a lower social economical class,^[2] possibly due to inadequate access to ophthalmic screening and surgery. But from the findings of Wong *et al*^[18] and from our study, an association may be present between a lower social economic class leading to a shorter axial length (because of less education and less near work) and subsequently a shorter axial length leading to a greater risk of phacomorphic glaucoma, offering an alternate explanation for the association between low social economical class and phacomorphic glaucoma.

We did not find any statistically significant association between the contralateral anterior chamber depths, most probably because of variations between the anterior chamber depths of the two eyes. Unfortunately, we were unable to

obtain the pre-phacomorphic anterior chamber depth and lens thickness measurements of all the eyes with phacomorphic glaucoma as the majority of them only presented to us during the acute attack and using the ACD and lens thickness measurements measured at the time of the phacomorphic attack would be meaningless as these parameters would surely be different than their pre-phacomorphic state rendering them inappropriate for use in risk factor calculations in the setting of a retrospective study. Population studies on ethnic Chinese in Singapore found that the biometric data including anterior chamber depth between the two eyes to be similar.^[19] Therefore, our best alternative was to use the contralateral ACD as a proxy measure of the pre-phacomorphic ACD in the eye with phacomorphic glaucoma but not the contralateral lens thickness, since the main pathology is in the intumescent cataract, the assumption of a similar lens thickness between the two eyes before the attack may not be the most sound for the purpose of this study. In future prospective studies, obtaining the pre-phacomorphic ACD and lens thickness of the eye with phacomorphic glaucoma may provide a better understanding of the role of ACD and lens thickness as risk factors of phacomorphic glaucoma. But unfortunately a prospective cohort study involving eyes with only mature cataracts without phacomorphic glaucoma would be unethical, as it would involve the deliberate delay of operations for these eyes. Having a large percentage of cataracts on the elective waitlist progress to phacomorphic glaucoma would also be unethical and would not be tolerated in most centers.

This study had some limitations. First, it was retrospective in nature. Although all efforts were made to retrieve patient information, inherent deficiencies of any retrospective studies such as incomplete records and inaccurate documentations still applied. In the diagnosis of phacomorphic glaucoma, every effort was made to differentiate any possible element of acute primary angle closure by excluding eyes with a documented occludable angle in the fellow eye. Second, we adopted the mean axial length of 23.7 mm based on a local study of 220 Hong Kong Chinese adults since large scale local population studies were lacking at the time of our study. Variations in mean axial length can exist even within the same ethnicity and different geographical region.^[19] Population studies in Singapore found the mean axial length of ethnic Chinese adults aged 40 years and above to be 23.2 ± 1.2 mm.^[19] Therefore, the axial length of 23.7 mm is the most representative of the Hong Kong adult population based on the available data in literature at present. Not only does AL varie between different populations and ethnicities, but also within a population based on differences in age, gender, refractive error, and corneal curvatures. Hence, the results from this small scale retrospective study may not be generalized to all population groups and that future prospective studies with pre-phacomorphic glaucoma ocular biometry data, categorized to each of the above variables, will offer a better understanding of the risk factors for phacomorphic glaucoma.

Conclusion

Eyes with axial lengths shorter than the population mean were 4.3 times as likely to develop phacomorphic glaucoma compared with eyes with longer than average axial length. In the setting of limited healthcare resources in an area where phacomorphic glaucoma is prevalent, patients with axial

length shorter than their population mean may be considered to receive earlier elective cataract extraction to prevent phacomorphic glaucoma.

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