The Malaysian Cataract Surgery Registry: Surgically induced astigmatism in phacoemulsification cataract surgery

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Abstract

Purpose: Surgically induced astigmatism is an often-neglected issue in phacoemulsification cataract surgery. It is a significant problem resulting in poor refractive outcome and patients' dissatisfaction. The objective of this study was to describe the preoperative astigmatism and the postoperative surgically induced astigmatism and its contributing factors. **Design:** Retrospective study on the Malaysian Cataract Surgery Registry between 2008 and 2011.

Method: Data on phacoemulsification cataract surgery from 37 ophthalmology units were studied and filtered. Patients > 50 year-old with complete refractive assessment results and with no ocular comorbidity were included. Contributing factors, namely patients' age, race, gender, laterality of the operated eyes, surgeon's status and intraoperative complications, were analyzed.

Results: The mean age of the 5350 patients was 68.0 years; the majority of patients were Chinese. The mean postoperative cylinder was 1.19 Diopter (D) (SD = 0.91) compared to the preoperative mean cylinder of 0.88 D (SD = 0.83D). Multivariate regression analysis on postoperative data revealed statistically significant high cylinder power (> 1.0 D) for older patients, Chinese race, operated left eyes (p < 0.001), surgery performed by trainee ophthalmologists (p < 0.001), and eyes with intraoperative complications (p < 0.001). The overall difference of cylinder power before and after phacoemulsification cataract surgery was high; signifying high degree of surgically induced astigmatism.

Conclusion: Surgically induced astigmatism could result in significant postoperative astigmatism with poor refractive outcome. The contributing factors are old age, Chinese race, operated left eyes, surgery by trainee ophthalmologists and eyes with intraoperative complications.

Introduction

The trend in cataract surgery today has moved from mere lens extraction towards achieving the best refractive outcome. Although the outcome of cataract surgery has improved significantly over the years with marked advances in surgical technique, surgical instruments and intraocular lens technology, there are still issues that need to be addressed. Pre-existing astigmatism and SIA are two often neglected but important factors that compromise the visual outcome after phaco-emulsification cataract surgery.

With cataract surgery and intraocular lens implantation, the most pronounced

Correspondence: Pik-Pin Goh, Clinical Research Centre, Ministry of Health, Kuala Lumpur, Malaysia. E-mail: <u>gohpp@crc.gov.my</u> effect is a change in spherocylindrical power. Spherical power is a single variable, which could be calculated and achieved quite accurately; whereas astigmatism power is a complex entity characterized by magnitude and meridian that could change significantly after cataract surgery. Surgical incision for cataract surgery induces a flattening effect on the cornea surface and this is termed surgically induced astigmatism (SIA).¹ SIA would alter and worsen the pre-existing astigmatism of a patient if it is not taken into consideration in the planning of cataract surgery.

Extracapsular cataract extraction (ECCE) and intracapsular cataract extraction (ICCE) commonly produce high SIA due to the size of the cornea or limbal wound.² Phacoemulsification cataract surgery had since gained popularity over the old technique mainly because of the most significant advantage it offers in the form of a small incision wound with less SIA. Nevertheless, the hidden problem that compromises the refractive outcome of phacoemulsification cataract surgery in many cataract centers today is still the failure to modulate the preexisting astigmatism and failure to recognize the issue of SIA.

The objective of this study was to describe pre-existing/preoperative astigmatism among patients who underwent phacoemulsification cataract surgery registered in the Cataract Surgery Registry (CSR) under Ministry of Health (MOH) from year 2008 to 2011, and to assess the magnitude of SIA postoperatively. Possible factors contributing to SIA were analyzed.

Material and method

This is a retrospective study on cataract surgery data derived from the Cataract Surgery Registry of the Ministry of Health Malaysia from year 2008 to 2011. It is a web-based registry hosted in (www.acrm.org.my/ned).³ All cataract surgery data entry was done by designated staff in 37 hospitals under the Ministry of Health Malaysia. It was performed under the supervision of on-site coordinators and optometrists to ensure a complete, updated and standardized method of data collection and entry. Data were entered consecutively for each cataract surgery performed into preoperative, operative and postoperative outcome forms. Data on postoperative complications and visual acuity were collected up to 12 weeks during follow-up visits.

The available data was then filtered to include only patients who had undergone phacoemulsification cataract surgery with successful intraocular lens implantation. Patients aged 50 year-old and above with no ocular co-morbidity at the time of surgery and had complete data entry on preoperative and postoperative refractive assessment results were included. This age group was chosen based on a population study where patients below that age limit shared a similar trend in their refractive pattern.²

The main outcome measures in this study were preoperative astigmatism and postoperative astigmatism in cylinder power. Preoperative and postoperative refractive assessment was performed by qualified optometrists in the respective participating ophthalmology units. Postoperative refractive assessment was done within 12 weeks postoperatively. SIA was calculated as cylinder power difference between preoperative and postoperative as recorded in the postoperative refractive assessment forms. Other possible contributing factors namely age group, gender, race, laterality of the operated eyes, surgeon status and intraoperative complications were analyzed.

The study protocol was reviewed and approved by the Medical Research and Ethics Committees of the Ministry of Health Malaysia.

Statistical analysis

Statistical analysis was conducted using IBM SPSS for Windows version 20 (IBM SPSS Statistics, Armonk, NY). The analysis was performed on the available data in the Cataract Surgery Registry from year 2008 to 2011.

All numerical data was expressed as mean and standard deviation, or median and inter-guartile range (IQR). Categorical data was described in the form of frequency and percentage. The dependent variable is cylinder power measurement and the independent variables (factors) included patient's age group, gender, race, and laterality of the operated eyes, surgeon status and intraoperative complications. Kruskal-Wallis and Mann-Whitney U test were performed to determine the difference of the cylinder measurement between each group in the independent variables at both preoperative and postoperative state of cataract surgery. Multiple logistic regression were then carried out at preoperative and postoperative to identify factors associated with cylinder category and to estimate odds ratios (OR) and its 95% confidence intervals (CI) for the association between the dependent variable (cylinder power measurement of more than 1.0 D) and the independent variables. The regression was also carried out to determine the association between visual acuity and cylinder power after cataract surgery. McNemar's Chi-squared test was used to compare proportionality in cylinder category between the preoperative and postoperative state. All reported values are two-sided and p-value of less than 0.05 was considered as statistically significant.

Results

There were 5350 patients included in this study. Patients' demographic features are summarized in Table 1. Patients' refractive assessment data before and after phacoemulsification cataract surgery are shown in Table 2.

Characteristics							
Age							
Mean (SD)	68.0 (7.7)						
Median (IQR)	69 (62-74)						
Min, max	50, 99						
Gender; n (%)							
Male	2521 (47.1)						
Female	2829 (52.9)						
Race; n (%)							
Malay	1932 (36.1)						
Chinese	2602 (48.6)						
Indian	643 (12.0)						
Others*	89 (1.7)						
Surgeon status; n (%)							
Specialist	4398 (82.2)						
Trainee**	566 (10.6)						
Intra-operative complications; n (%)							
Yes	157 (2.9)						
No	5193 (97.1)						
Operative eye; n (%)							
Right eye	2671 (49.9)						
Left eye	2679 (50.1)						

Table 1. Characteristics of cataract surgery patient year 2008 – 2011 (N = 5350).

*Others including Melanau, Kadazan/Murut/Bajau, Iban and other Malaysian.

**Trainee including gazetting specialist and medical officer.

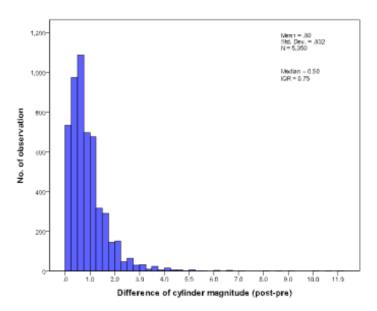
IQR = interquartile range

The frequency is based on available information.

	Preoperatively	Postoperatively	
Visual acuity, n (%)			
6/5 – 6/12	1097 (20.5)	4632 (86.6)	
6/18 – 3/60	2530 (47.3)	291 (5.4)	
2/60 – NPL	414 (7.7)	13 (0.2)	
Cylinder			
Mean (SD)	0.88 (0.83)	1.19 (0.91)	
Median (IQR)	0.75 (0.00 – 1.25)	1.00 (0.50 – 1.50)	
Min, max	0.00, 6.00	0.00, 12.00	
Spherical Equivalent (SE)			
Mean (SD)	-1.16 (2.47)	-0.67 (0.87)	
Median (IQR)	-0.62 (-2.25 – +0.00)	-0.62 (-1.12 – -0.25)	
Min, max	-22.75, +15.62	-10.00, +13.00	

Table 2. Refractive assessment pre- and postoperatively (N = 5350).

The frequency is based on available information.



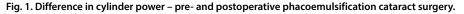


Figure 1 shows the overall data on difference of cylinder power between preoperative and postoperative was skewed to the right. This signifies a very high degree of SIA in a significant number of cases in the study population.

Preoperatively, there were no significant differences in cylinder power for patients of different gender, right or left eyes, assigned surgeons and intraoperative complications grouping. However, all patients aged 70 years and above had median of 1 D cylinder preoperatively. Also, the Chinese patients were found to have a significantly higher preoperative cylinder power compared to other races. Postoperatively, a significantly high cylinder power was found in older patients, Chinese, surgeries performed by trainee ophthalmologists, surgery done in the left eyes and for those encountered with intraoperative complications (Table 3).

Multiple logistic regression analysis revealed significant high postoperative cylinder power in Chinese (p < 0.001), in the left eyes (p < 0.001), surgery performed by trainee ophthalmologists (p = 0.001), and for those encountered intraoperative complications (p < 0.001). Chinese patients had the highest astigmatism among all races both pre- and postoperatively. The cylinder power also increased with age same as their preoperative state. There was no significant difference in cylinder power by gender. The insignificant results for the age group of 90-99 both preoperative and postoperatively was probably due to small sample size (Table 4). McNemar test showed overall significant changes of cylinder power (p < 0.001) following phacoemulsification cataract surgery.

Logistic regression analysis adjusted for intraoperative complications and surgeon status showed significant association between high cylinder power and poor visual acuity (Snellen 6/18-3/60) (Table 5).

		Preoperatively			Postoperatively				
Variable n		Median (IQR)	Test- statistic (df)	<i>P</i> -value	Median (IQR)	Test- statistic (df)	<i>P</i> -value		
Age group (years)									
50 – 59	815	0.50 (0.00 – 1.01)	49.28 (4)ª	< 0.001ª	0.75 (0.50 – 1.25)	260.16 (4)ª	< 0.001ª		
60 – 69	2075	0.75 (0.00 – 1.25)			1.00 (0.50 – 1.50)				
70 – 79	2167	1.00 (0.00 – 1.50)			1.25 (0.75 – 1.75)				
80 - 89	286	1.00 (0.25 – 1.50)			1.25 (0.75 – 2.00)				
90 – 99	7	1.00 (0.00 – 3.50)			1.75 (1.00 – 4.75)				
Gender									
Male	2521	1.00 (0.00 – 1.25)	-1.20 ^b	0.230 [♭]	1.00 (0.50 – 1.50)	-1.09 ^b	0.276 ^b		
Female	2829	0.75 (0.00 – 1.25)			1.00 (0.50 – 1.50)				
Race									
Malay	1932	0.75 (0.00 – 1.25)	43.30 (3)ª	< 0.001ª	1.00 (0.50 – 1.50)	51.66 (3)ª	< 0.001ª		
Chinese	2602	1.00 (0.00 – 1.50)			1.00 (0.75 – 1.50)				
Indian	643	0.75 (0.00 – 1.25)			1.00 (0.50 – 1.50)				
Others	89	1.00 (0.50 – 1.50)			1.00 (0.50 – 1.50)				
Operative of	eye								
Right eye	2671	0.75 (0.00 – 1.25)	-1.98 ^b	0.047 ^ь	1.00 (0.50 – 1.50)	-4.84 ^b	< 0.001 ^b		
Left eye	2679	1.00 (0.00 – 1.25)			1.00 (0.75 – 1.50)				
Surgeon status									
Specialist	4398	0.75 (0.00 – 1.25)	-0.49 ^b	0.624 ^b	1.00 (0.50 – 1.50)	-3.31 ^b	0.001 ^b		
Trainee	566	1.00 (0.00 – 1.25)			1.25 (0.75 – 1.50)				
Intraopera	tive con	nplication							
Yes	157	0.75 (0.00 – 1.25)	-1.53 ^b	0.127⁵	1.50 (0.75 – 2.50)	-6.40 ^b	< 0.001 ^b		
No	5193	0.75 (0.00 – 1.25)			1.00 (0.50 – 1.50)				

Table 3. The difference of cylinder power pre- and postoperatively.

 $^{\rm a}$ Kruskal-Wallis test $^{\rm b}$ Mann-Whitney U test df = degree of freedom

Table 4. Distribution of cylinder power using logistic regression.

	Preope	ratively	,				Postoperatively					
	Cylinder ≤ 1.0 (<i>n</i> = 3747)		Cylinder > 1.0 (<i>n</i> = 1603)		Multivariable analysis (n = 4882)		Cylinder ≤ 1.0 (<i>n</i> = 3077)		Cylinder > 1.0 (<i>n</i> = 2273)		Multivariable analysis (n = 4882)	
	n	%	n	%	Adj. OR (95% Cl)	<i>P</i> -value ^a	n	%	n	%	Adj. OR (95% CI)	<i>P</i> -value ^a
Age group	(years)					<0.001						< 0.001
50 – 59	611	16.3	204	12.7	1.00		587	19.1	228	10.0	1.00	
60 – 69	1503	40.1	572	35.7	1.10 (0.90, 1.34)	0.344	1302	42.3	773	34.0	1.57 (1.30, 1.89)	< 0.001
70 – 79	1443	38.5	724	45.2	1.45 (1.19, 1.76)	< 0.001	1059	34.4	1108	48.7	2.77 (2.29, 3.34)	< 0.001
80 – 89	185	4.9	101	6.3	1.61 (1.18, 2.18)	0.002	127	4.1	159	7.0	3.35 (2.49, 4.51)	< 0.001
90 – 99	5	0.1	2	0.1	1.18 (0.22, 6.19)	0.849	2	0.1	5	0.2	6.42 (1.20, 34.19)	0.029
Gender												
Male	1743	46.5	778	48.5	1.09 (0.96, 1.23)	0.172	1433	46.6	1088	47.9	1.06 (0.94, 1.19)	0.361
Female	2004	53.5	825	51.5	1.00		1644	53.4	1185	52.1	1.00	
Race						< 0.001						<0.001
Malay	1427	38.6	505	32.1	1.00		1176	38.9	756	33.7	1.00	
Chinese	1763	47.7	839	53.4	1.35 (1.18, 1.55)	< 0.001	1374	45.5	1228	54.7	1.33 (1.17, 1.52)	< 0.001
Indian	448	12.1	195	12.4	1.33 (1.08, 1.63)	0.007	422	14.0	221	9.8	0.89 (0.72, 1.08)	0.229
Others	56	1.5	33	2.1	1.99 (1.23, 3.22)	0.005	50	1.7	39	1.7	1.25 (0.77, 2.03)	0.366

Table 4 continued.

	Preoperatively						Postoperatively					
Operative eye												
Right eye	1870	49.9	801	50.0	1.00		1593	51.8	1078	47.4	1.00	
Left eye	1877	50.1	802	50.0	0.98 (0.87, 1.11)	0.797	1484	48.2	1195	52.6	1.23 (1.09, 1.38)	0.001
Surgeon status												
Specialist	3080	88.8	1318	88.2	1.03 (0.85, 1.25)	0.743	2570	90.2	1828	86.4	1.44 (1.20, 1.73)	< 0.001
Trainee	390	11.2	176	11.8	1.00		278	9.8	288	13.6	1.00	
Intraoperat	Intraoperative complication											
Yes	111	3.0	46	2.9	0.92 (0.64, 1.34)	0.675	57	1.9	100	4.4	2.84 (1.98, 4.08)	< 0.001
No	3636	97.0	1557	97.1	1.00		3020	98.1	2173	95.6	1.00	

Adj. OR = Adjusted odds ratio. Number and percentage are based on available information. ^aWald statistic.

	Cylind ≤ 1.0 (<i>n</i> = 30		Cylind > 1.0 (<i>n</i> = 22		Multivariable analysis (n = 4935)		
	n	%	n	%	Adj. OR (95% CI)	<i>P</i> -value ^a	
Postoperative visual acuity	/					< 0.001	
6/5 – 6/12	2706	95.4	1926	91.7	1.00		
6/18 - 3/60	123	4.3	168	8.0	1.81 (1.42, 2.31)	< 0.001	
2/60 – NPL	7	0.2	6	0.3	1.16 (0.39, 3.50)	0.787	

Table 5. The association between visual acuity and cylinder power postoperatively.

*Logistic regression was adjusted for intraoperative complication and surgeon status.

Adj. OR = Adjusted odds ratio.

Number and percentage are based on available information. ^aWald statistic.

Discussion

Cataract surgery today aims not only to restore vision; but also to minimize patients' pre-existing astigmatism and SIA for better refractive outcome and visual quality. Optimal visual acuity (6/12 and better) could only be achieved with accurate intraocular lens (IOL) power calculation and minimization of astigmatism.

Astigmatism is defined as unequal radius of curvature of the refractive surface of the eye with resultant failure to focus point source of light on the retina. The image is thus not sharp as it is being spread over a diffuse area.² Correction of pre-existing astigmatism and minimization of SIA is crucial in modern day cataract surgery, particularly with the popularization of toric IOL and multifocal IOL. The success in effectively reducing astigmatism with toric IOL is very much affected by SIA,⁴ while implantation of multifocal IOL with significant SIA impairs both near and distance visual acuity. Significant SIA impairs quality of vision by causing blur vision, image distortion and difficulty in binocular vision. It also defeats the benefits of spectacle independence.

SIA contributing factors like patients' preexisting astigmatism, cornea optical power, axial length, intraocular pressure, patients age and gender had been evaluated in some studies.^{5,6} In this study, we studied other possible contributing factors namely patients' age, gender and race, laterality of the operated eye, surgeon status and intraoperative complications.

Our study revealed significant high pre-existing astigmatism among the Chinese population. This finding is similar to a population-based study done on the clinical Chinese population in Hong Kong where 41.8% in the > 60 years age group had refractive astigmatism of more than 1 D cylinder.⁷ According to a study done by Matsumoto and colleagues,⁸ eyes with pre-existing astigmatism have higher chance of getting residual astigmatism after cataract surgery. Our finding is in total agreement with this study as the Chinese patients were also noted to have

high astigmatism preoperatively. We also found that all patients aged 60 years and above had significant high postoperative cylinder power of more than 1.0 D. The rising trend of astigmatism power with age also corresponded with their preoperative status.

Besides age and race, we concluded that the laterality of the operated eye had significant influence on the SIA. The operated left eyes had significantly higher SIA compared to the right eyes. This is probably due to the fact that majority of our surgeons are right-handed and they normally perform cataract surgery sitting in their comfortable superior position. Thus, the most commonly cited location of the main incision on the cornea in our settings is superotemporal for the right eye and superonasal for the left eye. When a surgeon sits superior to a patient; a high nasal bridge makes a peripheral cornea incision on the left eye difficult to achieve. A more central cornea incision closer to the pupillary axis is usually made and this induces more cornea astigmatism. Phacoemulsification cataract surgeries performed by qualified surgeons were noted to have lower SIA compared to those operated by the trainees. This could be explained by the overall better surgical technique, better wound construction and less incidence of intraoperative complications. Cornea wound extension is required in the event of intraoperative complications and this ultimately results in more SIA compared to the uneventful cases.

The finding of a significant increase in mean cylinder power after phacoemulsification cataract surgery in all age groups, genders, races, by all surgeons including qualified ophthalmologists and trainees, in both right and left eyes, and cases with or without intraoperative complications is pretty alarming. The insignificant differences among the variables noted in preoperative statistical analysis clearly pointed to a significant SIA in all phacoemulsification cataract surgeries performed within the study period.

The majority of the cataract surgeries were performed with small limbal or cornea incision wound less than three mm in size. Limbal relaxing incisions are rarely performed due to the lack of surgical skills and surgical tools in the government hospital settings here. The variability in the degree of SIA among the surgeons could be due to type of incision either scleral, limbal or cornea; location of cornea wound (distance from the optical zone), length of cornea tunnel and different technique in wound construction.^{9,10}

This important finding should alert us clinician to be more cautious with the issue of astigmatism in cataract surgery. Attempts should be made to rectify the pre-existing astigmatism and effort to minimize it by various surgical techniques should be sought after. It is very important on the surgeon's part to identify his own degree of SIA and to attempt modulating the preexisting astigmatism during cataract surgery.

We also noted that the percentage of patients with against-the-rule astigmatism increased from 57.4% preoperatively to 71.3% postoperatively. It is worthwhile to investigate if this could be due to natural course of wound healing in phacoemulsification cataract surgery; or could it be due to a shift of astigmatism axis postoperatively. The strength of this study is the large sample size and complete preoperative and postoperative data. However, keratometry-reading, which is the better means of measuring SIA, is not incorporated in this study. We did not have data on the actual location of main incisions either scleral, limbal or cornea including their axis of entry to the eye. We should also consider variability in the elastic property of the cornea, variability in response of cornea to incision and the individual variation in wound healing as factors reducing the predictability of surgical and refractive outcome.¹¹ A longer follow-up period is recommended as SIA is a dynamic feature which may show changes in axis and magnitude up to months and even years.^{9,10}

In conclusion, SIA is an important issue compromising the refractive outcome and quality of vision following phacoemulsification cataract surgery. A large majority of patients in this study had been shifted from the insignificant astigmatism category (Cylinder power ≤ 1 D) into the spectacle-dependent category (Cylinder power > 1 D) due to significant SIA. The shift is contributed by factors like patients' old age, operated left eyes, operations by trainee ophthalmologists and occurrence of intraoperative complications. The need for spectacle corrections for significant astigmatism inevitably results in patients' dissatisfaction and poses a hefty toll on the technical support and healthcare expenses. Minimization of SIA in phacoemulsification cataract surgery should not be overlooked in our continuous quest in targeting a good postoperative vision, good refractive outcome and spectacle independency.

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Ethics Approval: Ethic approval was obtained from Medical Research Ethic Committee, Ministry of Health Malaysia

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Competing Interest: None declared

References

- Ernest P, Hill W, Potvin R. Minimizing Surgically Induced Astigmatism at the Time of Cataract Surgery Using a Square Posterior Limbal Incision. J Ophthalmol 2011. Doi:10.1155 /2011 /243170.
- 2. Adio AO, Aruotu N. Induced astigmatism after cataract surgery a retrospective analysis of cases from the University of Port Harcourt Teaching Hospital, Nigeria. S Afr Optom 2011;70:75-80.

- Goh PP, Elias H, Nor Fariza N, Mariam I. National Eye Database A Web Based Surveillance System. Med J Malaysia 2008;63(Supp):20-23.
- 4. Hill W, Potvin R. Monte Carlo simulation of expected outcomes with the AcrySof toric intraocular lens. BMC Ophthalmology 2008;8:22.
- 5. Ninn-Pedersen K. Relationship between preoperative astigmatism and cornea optical power, axial length, intraocular pressure, gender and patient age. J Cataract Refract Surg 1996;12:472-478.
- 6. Storr-Paulsen A, Madsen H, Perriard A. Possible factors modifying the surgically induced astigmatism in cataract surgery. Acta Ophthalmol Scand 1999;77:548-551.
- 7. Leung TW, Lam AK, Deng L, Kee CS. Characteristic of Astigmatism as a function of age in Hong Kong clinical population. Optom Vis Sci 2012;89(7):984-992.
- 8. Matsumoto Y, Hara T, Chiba K, Chikuda M. Optimal incision sites to obtain an astigmatism free cornea after cataract surgery with a 3.2mm sutureless incision. J Cataract Refract Surg 2001;27(10):1615-1619.
- 9. Neuman AC, McCarty GR, Sander DR, Raanan MG. Small incision to control astigmatism during cataract surgery. J Cataract Refract Surg 1989;15:78-84.
- 10. Cho YK, Kim MS. Perioperative modulating factors on astigmatism in sutured cataract surgery. Korean J Ophthalmol 2009;23(4):240-248.
- 11. Tejedor J, Murube J. Choosing the location of corneal incision based on preexisting astigmatism in phacoemulsification. Am J Ophthalmol 2005;139(5):767-776.