Short Research Article

Correlations between Quality of Vision, Higher Order Aberrations and Non-Invasive Keratographic Tear Film Break-Up Time in Pseudophakic Eyes after Uncomplicated Phacoemulsification

ABSTRACT

Aims: In this study, we aimed to investigate the intercorrelations between tear film break up time, measured non-invasively using non-invasive keratographic break-up time (NIKBUT), higher order aberrations (HOA) and quality of vision (QoV) in pseudophakic patients.
Study design: Cross-sectional
Methods: Thirty-five pseudophakic aged patients aged 50 years or older, and 35 control phakic patients aged 17 to 23 years with corrected visual acuity of 20/20 were included in this study. All subjects underwent similar examination including QoV questionnaire, aberrometry to measure HOA, and NIKBUT. HOA was measured with the OPD-Scan/ ARK 10000 corneal analyzer (Nidek CO. Ltd), expressed as Root Mean Square (RMS) HOA and NIKBUT was assessed using non-invasive TF-Scan module Keratograph 5M (K5M), equipped with modified tear film scanning function (Oculus, Wetzlar, Germany). Statistical analysis was performed to find the correlation between NIKBUT, HOA and QoV.
Results: Patients in the pseudophakic group were significantly older (median age 66 vs. 20 years; P<0.01), had shorter NIKBUT (10.5 vs. 17.2; P<0.01), lower QoV score (1.63 vs. 0.68; P=0.04), and higher RMS HOA (0.5 vs. 0.26; P<0.01) compared to control group. NIKBUT was inversely correlated with RMS HOA (r = -0.19; p = 0.03) and RMS HOA was significantly correlated with QoV, even after adjustment for age and gender (r = -0.21; P0.04). NIKBUT <9.93s was correlated with lower QoV. The area under the curve was 0.81 (95% CI = 0.67 – 0.95, *p* = 0.012), and had 100% sensitivity and 61% specificity.
Conclusion: Shorter NIKBUT was correlated with greater HOA and greater HOA was correlated with lower QoV. NIKBUT value of shorter than 9.93s could potentially predict pseudophakic patients who will likely experience visual symptoms leading to decreased QoV; thus, the use of artificial tears might be beneficial.

Keywords: Higher Order Aberrations, Non-Invasive Keratographic Break-Up Time, Phacoemulsification, Pseudophakic, Quality of Vision, Tear Film.

1. INTRODUCTION

Cataract is the leading major cause of visual impairment in patients older than 50 years old, contributing to 55% of total blindness and 77% of visual impairment worldwide [1]. Current standard of practice for the treatment of cataract is phacoemulsification with intraocular lens (IOL) implantation [2]. Studies have shown that almost all uneventful cataract surgery with

phacoemulsification will result in refraction target of +/- 1.00 D. However, many patients still reported decreased quality of vision (QoV) due to the presence of visual field artefacts such as halo, glare, or starburst despite excellent visual acuity after cataract surgery [3-5].

Visual disturbance that is experienced by some patients after cataract surgery is often caused by optical higher order aberration (HOA) [3-5]. HOA can occur after cataract surgery due to disturbance in tear film stability. There were few studies reporting the phacoemulsification-induced corneal tear film instability [6]. Pre-corneal tear film as the first refractive media provides a smooth layer on the ocular surface and therefore pre-corneal tear film instability may cause local thinning or irregularity of the tear film and further introduces HOA leading to reduced QoV [7].

Tear film break up time (TBUT), a time elapse between the last blink and the appearance of the first tear film break up on corneal surface observed after fluorescein instillation, has been suggested as one of important markers that reflect the stability of corneal tear film [8]. Previous studies have shown that permanent or transient shortening of TBUT occur in patient after cataract surgery [9-11], which could explain why some patients had reduced QoV despite excellent visual acuity. Whilst TBUT has been widely used to assess tear film stability in previous years, a more recent method using non-invasive keratographic tear film break up time (NIKBUT) has been shown to be more objective and reproducible in assessing corneal tear film stability [12]; however, none has investigated the relationship between QoV, HOA and NIKBUT in pseudophakic patients after cataract surgery.

In this study, we aimed to assess the correlations between QoV, HOA and NIKBUT in pseudophakic patients after uncomplicated cataract surgery.

2. MATERIAL AND METHODS

This was a prospective study carried out at JEC Eye Hospitals and Clinics (Jakarta, Indonesia) from May 2020 to December 2020 in accordance with the Declaration of Helsinki. Ethical clearance was given by Ethical Committee of Gadjah Mada University (KE/FK/0379/EC/2020). All patients provided their written consent form prior to their participation.

Thirty five eyes from healthy patients aged 50 years or older who underwent uneventful cataract surgery using phacoemulsification and intraocular lens implantation were included in this study. We included patients with best corrected visual acuity is 20/20 with maximum correction of ± 0.75 D spherical equivalent. The measurement was done using subjective refraction by an optometrist. We ensured that these patients had no posterior capsular opacification, or other posterior segment pathology confirmed using dilated posterior segment examination and imaging. We excluded patients with history of glaucoma, ocular inflammation, diabetes, Sjogren syndrome, severe atopic diseases and systemic immunological disorders.

The cataract surgical procedure was a routine phacoemulsification done by a single surgeon (J.H). The surgery was done under topical anaesthesia using 0.5% pantocaine drop. All patients had a sutureless 2.2 mm and 1 mm clear corneal incision. A single-piece aspheric hydrophobic acrylate IOL (AcrySof SN60WF, Alcon Laboratories) was used for all patients and implanted in the bag at the end of the surgery.

Patients were then subjected to a series of examination (detailed in the following section), at least one month after surgery, during which all ocular medications were discontinued.

1.1. Clinical Examinations

1.1.1. Non-invasive keratographic tear film break-up time (NIKBUT)

Measurement of tear film break up time was done using non-invasive TF-Scan module Keratograph 5M (K5M), equipped with modified tear film scanning function (Oculus, Wetzlar, Germany). All participants underwent similar measurement process, following an established procedure. Briefly, each participant was seated in front of the K5M in a dimmed illuminated room with eye focused on the target. A 22 rings placido disc was projected onto the cornea from the machine. The patient was asked to blink and then keep their eyes open for as long as possible. The machine automatically measured the disruption of the rings reflected on the tear film and the time it occurred as the tear film break up time in seconds and mapped the location and size of the tear-break areas in between blinks. By default, this machine generated the average time of break incidents (NIKBUT-average) (**Figure 1**).

1.1.2. Aberrometry

Higher-order aberrations (HOA) was measured with the OPD-Scan/ ARK 10000 corneal analyzer (Nidek CO. Ltd). The OPD-Scan/ ARK 10000 (NIDEK Co Ltd) by default generated an infrared slit scans across the pupil covering all 3600 corneal meridians and measured the wavefront aberrations from the difference in refractive power. There was no pharmacologic mydriasis during the examination and each individual's HOA was recorded in mesopic conditions. The root mean square (RMS) of the total HOA was obtained from the machine (**Figure 2**).

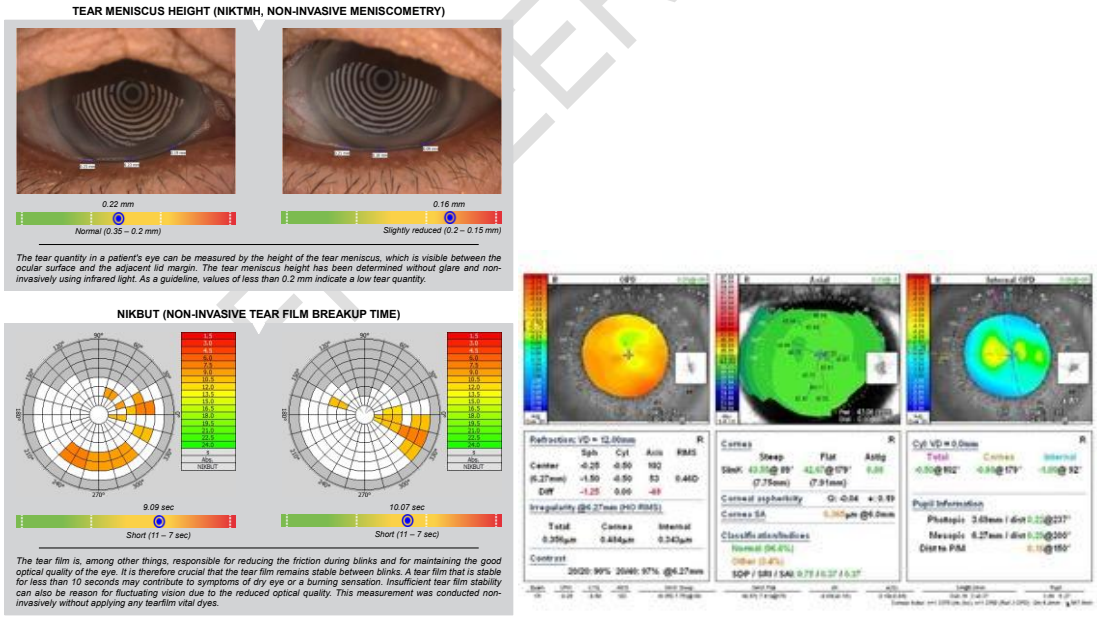
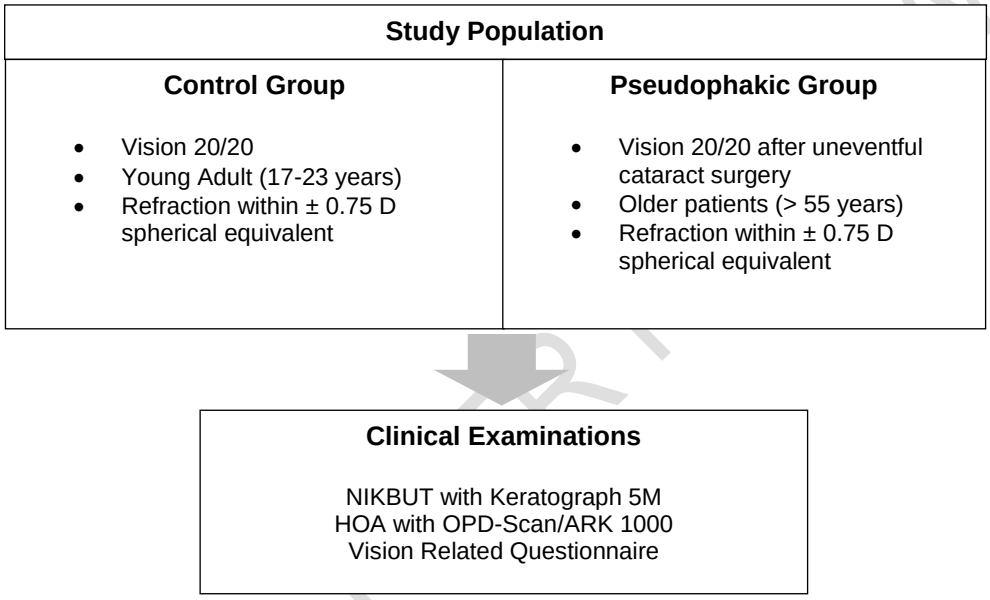


Figure 1. NIKBUT examination (left) and aberrometry (right)

1.1.3. Vision Related Questionnaires

The Indonesian version of the QoV questionnaire (adapted from McAllinden [13]) was developed to quantify patient's subjective perception on their quality of vision. The questionnaire consisted of seven questions covering seven visual symptoms (glare, halo, starburst, hazy, blurred, distortion, and double vision). The patient was directed to cover the fellow eye and asked about the relevant symptoms, assisted by a photo example of each visual symptoms. Answer to each question was scored as follows: never (score: 0), occasionally (less than once a week; score: 1), quiet often (about once a week; score: 2), very often (more than once a week; score: 3). Lower score indicated better QoV.

Figure 2. Flow diagram of the patients included in the study



1.2. Statistical analysis

Data analyses were performed using IBM SPSS Statistics 26.0© for Mac. All variables in this study were treated as continuous variables. The difference in HOA, QoV questionnaire score, and NIKBUT between groups was analysed using unpaired student-t test. Correlation between variables was analyzed using Spearman's rank correlation and multivariate linear regression. Receiver operating curve was constructed to assess the discriminative ability of NIKBUT in detecting patients with visual symptoms based on QOV questionnaire. For this analysis, all patients who reported any visual symptoms of any frequency in QoV questionnaire were considered symptomatic. Any difference with p value <0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

There were 35 eyes included in the final analyses. The demographic characteristics of each group were shown in Table 1. Gender distribution and laterality of patients were similar

between the two groups. Patients in the pseudophakic group were significantly older (median age 66 vs. 20 years; P<0.01), had lower NIKBUT (10.5 vs. 17.2; P<0.01) and lower QoV score (1.63 vs. 0.68; P=0.04) compared to the control group. The RMS HOA in pseudophakic group was higher (0.5 vs 0.26;P<0.01) in control group.

Table 1. Patient characteristic among groups

Variable	Control	Pseudophakic	P value
No. of eyes	35	35	
Gender, n (%)			
Male	22 (62.9)	21 (60)	
Female	13 (37.1)	14 (40)	0.806
Age [median (range)]	20 (17-23)	66 (50-84)	**<0.01***
Laterality, n (%)			
Right	17 (48.5)	14 (40)	
Left	18 (51.5)	21 (60)	0.470
NIKBUT	17.2 (6.57)	10.5 (4.76)	<0.01[a]
QoV	0.68 (1.18)	1.63 (2.22)	0.04[b]
RMS HOA	0.26 (0.17)	0.5 (0.17)	<0.01[b]

NIKBUT was inversely correlated with RMS HOA (r = -0.19; p = 0.03) (Figure 1) and RMS HOA was significantly correlated with QoV, even after adjustment for age and gender (r = -0.21; P0.04). However, NIKBUT was not correlated with patients' subjective QoV (Table 2). We performed additional analysis to explore possible non-linear correlation between NIKBUT and QoV. We found potential threshold value of NIKBUT shorter than 9.93 s, in which pseudophakic patients were likely to experience visual symptoms. The receiver operative characteristic curve of NIKBUT value shorter than 9.93 s in discriminating which patient was likely to experience visual symptoms was illustrated in Figure 2. The area under the curve was 0.81 (95% CI = 0.67 – 0.95, p = 0.012), and this value discriminated patient who experienced visual symptoms with 100% sensitivity and 61% specificity.

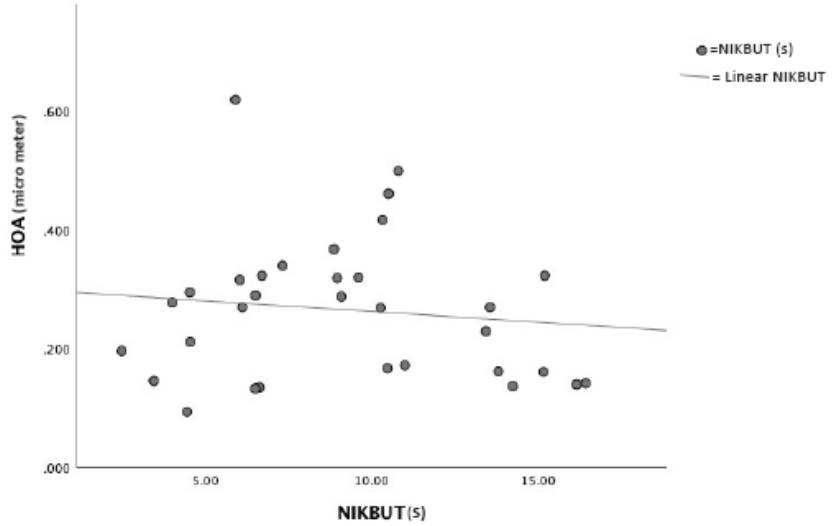


Figure 3. Inverse correlation between NIKBUT and HOA

Table 2. Correlations between NIKBUT and HOA with patients subjective QoV

Clinical Feature	Univariate Analysis		Multivariate Analysis	
	Correlation Coefficient	*p*	Correlation Coefficient*	*P**
RMS HOA (μm)	-0.21	0.03	-0.21	0.04
NIKBUT (s)	-0.22	0.24	-0.36	0.27

*Adjusted for age and gender

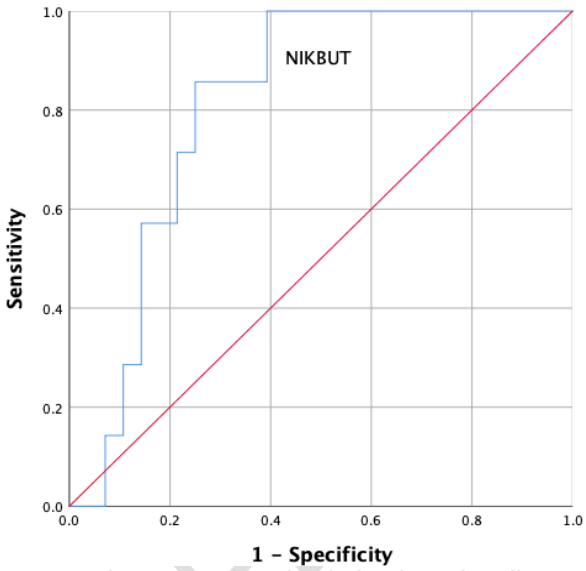


Figure 4. Receiver Operating Curve for Discriminating Visually Symptomatic Patient

To our knowledge, this is the first study reporting the inter-correlations between QoV, HOA and NIKBUT in patients after cataract surgery. We found that the lower the NIKBUT, the higher the HOA and the higher the HOA, the lower the QoV in pseudophakic patients independent of age and gender. Importantly, we documented a possible threshold value of NIKBUT shorter than 9.93 s which could potentially predict pseudophakic patients who will likely experience visual symptoms leading to reduced QoV.

Inverse correlation between tear film break-up and higher HOA was plausible and was consistent with previous study [14]. Tear film is the outermost refractive surface of the eye, which is also key in stabilising HOA [15]. Irregular optical surface due to tear film break-up involving central cornea has been speculated to increase HOA [16]. In support of this, a study by Koh et al. suggested that higher HOA was related to short tear film break up time in patients with dry eye with central corneal keratopathy compared with patients without central corneal keratopathy [17]. This study measured sequential changes in HOA for 10 seconds duration and found that the HOA increased with time but returned to baseline after blinking [17]. Our study also found that increased HOA was correlated with poorer QoV, which led to a logical sequence that lower NIKBUT was associated with lower QoV. Though we failed to demonstrate that NIKBUT was linearly correlated with QoV, we documented potential threshold value of NIKBUT which could potentially predict patients who will likely experience visual disturbance after cataract surgery. This was consistent with few studies that have previously reported associations between tear film stability and vision. For example, Kaido

and colleagues found that patient with dry eye, with or without superficial punctate keratopathy, had lower ability to maintain visual acuity over 10 second period [18].

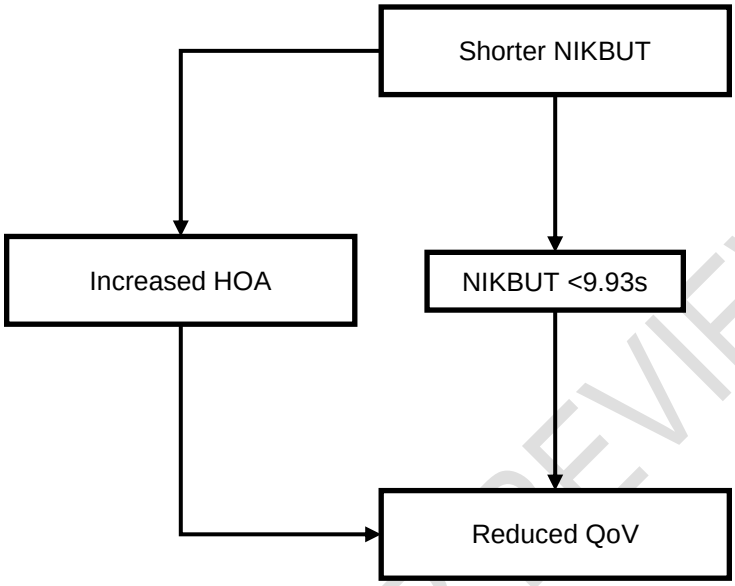


Figure 5. Intercorrelations between NIKBUT, HOA and QoV

Our result was also consistent with recommended value of NIKBUT in dry eye disease. Guideline from the Tear Film and Ocular Surface Dry Eye Workship II (TOFS DEWS-II) has recommended the use of non-invasive methods in assessing tear film stability and at the same time also recommended the use of value <10s in determining dry eye disease [19]. Similar value was also reported by another study suggesting that the NIKBUT value in normal population was >10s and that NIKBUT value of <9s could detect dry eye disease [12]. Notably, result from this study might also suggest that the use of artificial tear may be advantageous in pseudophakic patients whose NIKBUT value is <9.9s to prevent any visual symptoms despite the absence of dry eye symptoms.

There were some limitations in this study. First, we used subjective QoV which might be less accurate than objective visual acuity measurement. However, this measurement was well used in previous study which may accommodate daily symptoms experienced by patients after cataract surgery which are not measurable by objective visual acuity assessment [13]. Second, we did not record the blink rate in our patients, therefore, blink rate was not considered in our analysis. Finally, predicting a trend between groups above the age of 50 years was also difficult considering unequal samples between age groups. The majority of our pseudophakic patient fell between the age of 50 to 70 years (60%). Only 9 (26%) pseudophakic patients were 71-80 years old, and only 2 patients (5.7%) patients were older than 80 years old.

4. CONCLUSION

In conclusion, we documented intercorrelations between NIKBUT, HOA and QoV in our study population. Forty two percent of the pseudophakic patients experienced visual symptoms. Shorter NIKBUT was correlated with greater HOA and greater HOA was correlated with lower QoV. More importantly, there was a possible threshold value of NIKBUT <9.93 s which if confirmed, could be widely used as a cut-off to identify patients who will likely experience visual symptoms leading to reduced QoV. Thus, the use of artificial tears may be beneficial despite the absence of dry eye symptoms.

CONSENT

All authors declare that 'written informed consent was obtained from each participant of this study.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Abbreviations used in this manuscript

Abbreviation	Abbreviated Term
HOA	Higher Order Aberrations
IOL	Intraocular Lens
K5M	Keratograph 5M
NIKBUT	Non-Invasive Keratograph Break-up Time
QoV	Quality of Vision
RMS	Root Mean Square
TBUT	Tear Break-up Time
TFOS-DEWS	Tear Film & Ocular Surface Society - Dry Eye Workshop

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