



## **Anxiety and Visual Field Assessment Reliability in Glaucoma Patients**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Author ATLS designed the study, wrote the protocol, managed the analyses of the study and comment on the draft of the manuscript.*

*Authors KLT and LCF performed the data collection, statistical analysis, wrote the draft of the manuscript and managed the literature searches. Authors MY and MFC helped in data collection and commented on the draft of the manuscript. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Visual field assessment is very important for the diagnosis and monitoring of glaucoma. Anxiety may affect the quality of a patient's performance when undergoing these assessment tests and influence the reliability of visual field measurement.

**Methods:** A total of 155 primary and secondary glaucoma patients were recruited. Face-to-face interviews using the Beck Anxiety Inventory (BAI) questionnaire were conducted prior to Humphrey visual field analysis (HFA) assessment testing. The reliability indices of fixation loss, false positive error, and false negative error were used to determine the accuracy of the HFA measurement.

**Results:** Based on the BAI, 122 patients were classified with minimal anxiety, 21 with mild anxiety, and 12 patients had moderate to severe anxiety. There was no correlation between BAI score and the reliability indices of the HFA. An increase in the number of previously conducted HFA tests reduced fixation loss by 1.3% (95% confidence interval (CI) [-2.394, -0.110],  $P = .032$ ). There was a negative linear relationship between age and false positive error. For every 1 year increase in age, there was a 0.2% reduction in false positive error (95% CI [-0.376, -0.059],  $P = .008$ ). Higher education level reduced the false negative errors by 3.5% (95% CI [-6.640, -0.279],  $P = .028$ ).

**Conclusions:** Minimal anxiety may not affect the reliability indices of HFA. Age, education level, and number of previous visual field tests are the major factors affecting the reliability of visual field.

*Keywords: Effect; anxiety; reliability; visual field; glaucoma.*

## 1. INTRODUCTION

Glaucoma is a progressive optic neuropathy characterized by structural damage of the optic nerve head (ONH) and distinctive functional damage [1]. The functional damage caused by glaucoma and the progression of the disease are best assessed using perimetry, which measures the visual field. Visual field can be described as an island of vision in a sea of darkness, with different light sensitivities to the area of the retina according to the topography of the island [2]. It is the assessment of the ability of the visual pathway to process information and sending it back to the visual cortex.

Currently, automated static perimetry is regarded as the gold standard for measuring this visual field [3]. Static perimetry tests the light sensitivities of specific retinal locations, like measuring the different topographies of the island, distributed on fixed grid pattern. The most popular automated static perimetry test is the Humphrey visual field analysis (HFA). The HFA is equipped with reliability indices for fixation loss, false negative errors, and false positive errors, and these reliability indices were used in this study to determine the effects of anxiety on testing. Fixation loss rate is an estimation of how steady the patient gazes at the fixation stimulus. It is based on the response given when the light stimuli are projected at blind spot and gaze tracker. False positive measures the tendency of the patients to press response button when there is no light stimulus [4], and the false negative value measures the unresponsiveness toward light stimulus 9 dB above the threshold [5].

Accuracy in the detection of visual field defects depends mainly on the ability of the patient to identify the light stimulus. This ability can be affected by various factors including age; visual acuity; duration of the assessment; severity of glaucoma; educational background; learning curve of patient; and the clarity of the instructions

given by operator; perimetrist, optometrist, or technologist [4,6]. Pupillary size [7] and refractive errors including astigmatism [8] may also affect the accuracy of static perimetry assessment. Uncorrected refractive errors reduce the differential light sensitivity in the visual field and may affect the quality of HFA assessment. This means that because most perimetry is performed using a stimulus located at a reading distance, a near correction should be given to presbyopic patients during assessment. Contact lens wear is also recommended when performing automated perimetry in patients with high refractive errors in order to reduce spectacle rim artefacts [9,10].

Visual field assessment is also affected by a patient's psychological status [11,12]. Glaucoma patients are subjected to multiple visual field assessments as part of their management [13,14]. Less anxious individuals tend to be more proficient and make less error while performing tasks compared to anxious subjects [15]. Anxiety may lead to lack of focus during the HFA assessment that could affect the accuracy of the test. Anxiety and negative thoughts were found to correlate with HFA variability [11].

The main objective in the present study was to determine the correlation between anxiety and the accuracy of HFA as relates to false negatives, false positives, and fixation loss. Factors affecting the reliability indices were also studied.

## 2. METHODOLOGY

An observational cross-sectional study was conducted involving 155 glaucoma patients who were receiving a regular follow up check in the eye clinics of tertiary centers in Malaysia. These locations included the Hospital Raja Permaisuri Bainun, the Hospital Sultanah Nur Zahirah, and the Hospital Universiti Sains Malaysia. A total of 109 patients presented with primary open angle glaucoma (POAG), 18 had primary angle closure

glaucoma (PACG), 23 had normal tension glaucoma (NTG), and five patients presented with secondary glaucoma (two with pseudoexfoliative, one with neovascular, one with angle recession, and one with thyroid orbitopathy-related glaucomas). All patients were recruited between January and June 2014. This study received ethical approval from the research ethics committee (human) at the Universiti Sains Malaysia and was conducted in accordance to Declaration of Helsinki for human research.

Patients with confirmed diagnoses of primary and secondary glaucoma were recruited. Patients with glaucoma suspect and ocular hypertension were excluded. Those who have visual acuity less than 6/60 and history of recent ocular surgery, including phacoemulsification and glaucoma surgery less than six months prior to recruitment were excluded. Only patients with the ability to understand the instructions for visual field assessment were included. In this study, only the right eye was chosen for analyzing the reliability of the visual field if both eyes were eligible.

The duration of glaucoma, the number of visual field assessments conducted, and systemic diseases were obtained from patient medical records. Duration of glaucoma is defined as the time between when the initial diagnosis of glaucoma was made and the recruitment period when the interview was conducted. The number of visual field assessments was based on the number of HFA tests that were conducted on the patient regardless of the reliability or learning curve of the patients.

Face-to-face interviews were conducted after the subjects took the automated HFA test using Beck Anxiety Inventory (BAI) questionnaires by two investigators (KLT and LCF) who were masked from the HFA assessment outcome. BAI questionnaire is a tool for the assessment of anxiety, which provides good discrimination from depression [16]. Based on the score, anxiety level was divided into categories: minimal, mild, moderate, and severe. A score of 0-7 indicates minimal level of anxiety, 8-15 mild anxiety, 16-25 moderate anxiety, and 36 or more suggests severe anxiety. A BAI score of 16 or more indicated clinically significant anxiety [17]. The results from the BAI tests were compared to the reliability indices from the HFA test results. According to the criteria used by the HFA software, a visual field is reliable if the fixation losses score less than 20%, the false positive response scores less than 33%, and the

false negative response scores less than 33% [4].

## 2.1 Data Analysis

Data was analyzed with Windows Statistical Package for Social Science (SPSS) version 21.0. Spearman correlation was used to determine the relationship between anxiety (using the raw scoring of BAI questionnaire) and the reliability indices of HFA. Multivariate analysis using multiple linear regression was also conducted to determine the factors affecting the reliability indices of HFA.

## 3. RESULTS

A total of 155 glaucoma patients were recruited. The majority (70.3%) were POAG patients (Table 1). There were slightly more men (54.2%) compared to women (45.8%), and their ages ranged from 20.0 to 88.3 years old. Of the patients studied, 53.5% were Chinese, followed by Malays (28.4%), Indians (16.1%), and others (1.9% comprised of 1 Siamese, 1 Sikh and 1 Kadazan Dusun indigenous person). Only a small number (12 patients, 7.7%) of patients did not receive any formal education (Table 1). Mean duration of glaucoma in this study was  $6.1 \pm 5.7$  years. The average number of HFA conducted by each patient was  $5.4 \pm 4.2$ .

Based on the BAI score, dizziness or light headedness, numbness or tingling sensations, wobbliness in the legs, the inability to relax, and the fear of worst-case scenarios were among the most common anxiety symptoms reported by glaucoma patients (Table 2). A total 122 (78.7%) of patients were classified as having minimal anxiety, followed by 21 (13.5%) with mild anxiety, 6 (3.9%) with moderate anxiety, and 6 (3.9%) with severe anxiety (Table 1). Twelve patients (7.7%) experienced clinically significant anxiety (BAI score 16 or more).

There was no significant correlation between the BAI score and the reliability indices of HFA (Table 3). The BAI was also not found to directly affect the reliability indices of the HFA based on a multivariate analysis. The score for fixation loss was shown to be most affected by the number of previous HFA assessments (Table 4). Each increase in the number of these assessments conducted on the patient reduced the fixation loss by 1.3% (95% confidence interval (CI) [-2.394, -0.110],  $P = .032$ ). The score for false positive error was mainly affected by age

(Table 5). For each year increase in age, the false positive error was reduced by 0.2% (95% CI [-0.376, -0.059],  $P = .008$ ). Education level was found to be a significant factor ( $P = .028$ ) affecting the scores for false negative errors (Table 6), with higher education levels reducing the false negative error by 3.5% (95% CI [-6.640, -0.279]).

**Table 1. Demographic and clinical data of glaucoma patients**

Demographic characteristic	N = 155
Mean age ( $\pm$ SD)	69.0 $\pm$ 10.3
<b>Type of glaucoma (n, %)</b>	
POAG	109 (70.3)
PACG	18 (11.6)
NTG	23 (14.8)
NVG	1 (0.6)
Pseudoexfoliation	2 (1.3)
Other secondary glaucoma	2 (1.3)
Mean duration of glaucoma ( $\pm$ SD in years)	6.1 $\pm$ 5.7
<b>Gender (n, %)</b>	
Male	84 (54.2)
Female	71 (45.8)
<b>Race (n, %)</b>	
Malay	44 (28.4)
Chinese	83 (53.5)
Indian	25 (16.1)
Others	3 (1.9)
<b>Education level (n, %)</b>	
No formal education	12 (7.7)
Primary school	53 (34.2)
Secondary school	72 (46.5)
Tertiary education school	18 (11.6)
<b>Best corrected visual acuity (n, %)</b>	
6/6-6/12	116 (74.8)
6/18-6/24	32 (20.6)
6/36-6/60	7 (4.5)
Mean of number HFA done before	5.4 $\pm$ 4.2
<b>Anxiety level based on Beck score (n, %)</b>	
Minimal	122 (78.7%)
Mild	21 (13.5%)
Moderate	6 (3.9%)
Severe	6 (3.9%)

*SD = Standard Deviation, POAG = Primary Open Angle Glaucoma, PACG = Primary Angle Closure Glaucoma, NTG = Normotensive Glaucoma, NVG = Neovascular Glaucoma, HFA = Humphrey Visual Field Analysis*

#### 4. DISCUSSION

Visual field assessment is essential for the diagnosis and management of glaucoma because it can help determine visual field

changes over the course of the patient's lifetime. The accuracy of the visual field analysis may be affected by anxiety, especially because anxiety among glaucoma patients is not uncommon [18]. Anxiety may also escalate in a busy clinic with long waiting times, which often occur in glaucoma clinics [19]. It was hypothesized that the anxiety experienced by these glaucoma patients may cause short attention spans [20], affecting the outcome of the measurements because attention span can dramatically affect eye contact and hand gestures. Because the response input in HFA relies on clicking the test button once the eye is in contact with the light stimulus [4], an adequate attention span is important to ensure the reliability of HFA.

**Table 2. Mean score of each question of modified beck anxiety inventory**

Question	Mean $\pm$ SD
Numbness or tingling	0.37 $\pm$ 0.68
Feeling hot	0.25 $\pm$ 0.61
Wobbliness in legs	0.37 $\pm$ 0.69
Unable to relax	0.37 $\pm$ 0.66
Fear of worst happening	0.32 $\pm$ 0.69
Dizzy or lightheaded	0.38 $\pm$ 0.68
Heart pounding/racing	0.26 $\pm$ 0.57
Unsteady	0.25 $\pm$ 0.54
Terrified or afraid	0.24 $\pm$ 0.54
Nervous	0.34 $\pm$ 0.62
Feeling of choking	0.14 $\pm$ 0.39
Hands trembling	0.12 $\pm$ 0.34
Shaky/ unsteady	0.17 $\pm$ 0.45
Fear of losing control	0.18 $\pm$ 0.52
Difficulty in breathing	0.25 $\pm$ 0.58
Fear of dying	0.18 $\pm$ 0.49
Scared	0.25 $\pm$ 0.56
Indigestion	0.21 $\pm$ 0.54
Faint/lightheaded	0.14 $\pm$ 0.48
Face flushed	0.14 $\pm$ 0.48
Hot /cold sweat	0.20 $\pm$ 0.50

*SD = Standard Deviation*

**Table 3. Correlation between Beck score (raw score) and reliability indices of HFA**

	Correlation coefficient (r)	P value
Beck score and fixation loss	-0.022	.785*
Beck score and false positive	0.027	.742*
Beck score and false negative	0.017	.842*

*HFA = Humphrey visual field analysis, \*P < 0.05 is significant based on Spearman correlation*

**Table 4. Multivariate analysis on factors affecting fixation loss in HFA**

Variables	Simple linear regression		Multiple linear regression	
	b <sup>a</sup> [95% CI]	P value	b <sup>b</sup> [95% CI]	P value
Age	0.384 [0.016, 0.751]	.041	0.323 [-0.043, 0.689]	.083
Duration of glaucoma	0.031 [-0.544, 0.806]	.703	0.789 [-0.050, 1.647]	.065
Number of HFA	-0.688 [-1.599, 0.224]	.138	-1.252 [-2.394, -0.110]	.032
Education level	-5.254 [-10.004, -0.503]	.030	-4.765 [-9.593, 0.062]	.053
Beck score	0.201 [-0.364, 0.767]	.483	0.086 [-0.704, 0.875]	.831

HFA = Humphrey visual field analysis, <sup>a</sup> Crude regression coefficient, <sup>b</sup> Adjusted regression coefficient, Backward multiple linear regression method applied, Coefficient of determination (R<sup>2</sup>) = 0.058  
P < .05 is significant

**Table 5. Multivariate analysis on factors affecting false positive in HFA**

Variables	Simple linear regression		Multiple linear regression	
	b <sup>a</sup> [95% CI]	P value	b <sup>b</sup> [95% CI]	P value
Age	-0.200 [-0.357, -0.044]	.012	-0.217 [-0.376, -0.059]	.008
Duration of glaucoma	0.164 [-0.124, 0.453]	.262	0.232 [-0.136, 0.600]	.214
Number of HFA	0.101 [-0.293, 0.495]	.613	-0.027 [-0.523, 0.470]	.916
Education level	-0.069 [-2.138, 2.001]	.948	-0.832 [-2.930, 1.265]	.434
Beck score	-0.040 [-0.283, 0.203]	.748	-0.267 [-0.608, 0.074]	.123

HFA = Humphrey visual field analysis, <sup>a</sup> Crude regression coefficient, <sup>b</sup> Adjusted regression coefficient, Backward multiple linear regression method applied, Coefficient of determination (R<sup>2</sup>) = 0.034  
P < .05 is significant

**Table 6. Multivariate analysis on factors affecting false negative in HFA**

Variables	Simple linear regression		Multiple linear regression	
	b <sup>a</sup> [95% CI]	P value	b <sup>b</sup> [95% CI]	P value
Age	0.168 [-0.079, 0.415]	.181	0.139 [-0.111, 0.388]	.274
Duration of glaucoma	-0.308 [-0.736, 0.120]	.167	-0.136 [-0.679, 0.407]	.621
Number of HFA	-0.440 [-1.031, 0.150]	.143	-0.223 [-0.966, 0.519]	.553
Education level	-4.084 [-7.084, -1.083]	.008	-3.509 [-6.640, -0.279]	.028
Beck score	-0.880 [-0.445, 0.269]	.627	-0.186 [-0.691, 0.318]	.467

HFA = Humphrey visual field analysis, <sup>a</sup> Crude regression coefficient, <sup>b</sup> Adjusted regression coefficient, Backward multiple linear regression method applied, Coefficient of determination (R<sup>2</sup>) = 0.041  
P < .05 is significant

In this study, only 7.7% of patients experienced clinically significant anxiety. This was lower than the prevalence of reported clinically significant anxiety among glaucoma patients in Korea, Japan, China, and Turkey (20.8%, 13.0%, 22.9%, and 14.0%, respectively) [21-24]. There is a possibility that the patients may not be truthful in answering the questionnaire, especially if the interviewers are also among the team of treating doctors. Different measurement techniques may also contribute to the difference in the measured prevalence, as questionnaire-based evaluation is usually subjected to recall bias [25]. Some patients may not be able to accurately recall their symptoms, which is especially true among elderly patients as in our present study. This study could also be affected

by the nature of the BAI test, which is reliable for detecting anxiety but is unable to differentiate anxiety from mood disorders [26]. Coexisting mood disorders could have confounded the outcome.

Anxiety was postulated to affect performance by reducing or shifting control of attentiveness and impairing function [27,28]. In this study, however, there was no significant association between anxiety and HFA reliability. This corresponds to the results of Eysenck [29], who reported that the adverse effects of anxiety on performance were apparent only on the more complex versions of the letter transformation task. It is possible, therefore, that performing an HFA test may not be too complex for anxious patients. Repetitive

testing, especially in HFA, may also reduce anxiety in patients and help improve their test results.

Determination of the accuracy and reliability of the HFA is quite challenging, especially in glaucoma patients. Until now, the reliability of the visual field measurement has been partially based on reliability indices. The total number of HFA each patient has previously experienced in this study varied between 1 to 19 times (mean  $5.4 \pm 4.1$ ), which is a very wide range. Fixation loss rates may reflect the attention span of the subjects and the clarity of the instruction given by the perimetrist [4,6]. Repetitive HFA tests not only help to improve the learning curve but also the accuracy of the test [30], and the patient's learning curve was shown to affect the accuracy of the HFA [4]. As expected, improvements in fixation loss rate were seen with increased numbers of HFA tests in this study, though there was no correlation between the BAI score and fixation loss, indicating that this improvement is probably not due to decreased anxiety.

Age was found to affect fixation loss rate in a study conducted by Birt et al. [4]. However, in our study, age was found to affect the false positive rate but not fixation loss. High false positive clicks, measuring the tendency of the patient to press the response button without a light stimulus [4], are usually seen in trigger happy patients [5], and younger patients are more likely to have this trait [31]. The mean age of glaucoma patients in this study was  $69.0 \pm 10.3$  years, indicating that the patients were older and less likely to be trigger happy. Systemic comorbidities such as diabetes mellitus are common among elderly, which may affect their physical coordination and mental ability [32]. Moreover, age-related changes such as osteoarthritis may also affect the ability to respond to light stimulus. Slower responses are therefore expected in elderly patients. There is no plausible explanation for the relationship between age and false positive rates in this study.

The false negative value measures the unresponsiveness toward light stimulus 9 dB above the threshold [4], and the measurement of this rate is also believed to be a better early indicator of glaucoma than the reliability index [5]. Education level was found to be the factor that most affected the false negative rate in this study, with higher education levels reducing the false negative rate. There are studies reported the influence of glaucoma severity on the

reliability indices of HFA [4,33]. Patients with higher degree of visual field sensitivity loss had a greater rate of fixation losses and false negative errors [4,33]. It was one of the limitations of this study: the severity of glaucoma was not evaluated. Perhaps, in the future, analysis on the effect of glaucoma severity on HFA reliability will help to clarify the potential relationship.

Communication and clarity of the instruction given by perimetrist is vital for ensuring accuracy of HFA [6]. In many practices, optometrists and technicians were trained as perimetrists. Proper training must be provided to the optometrists and technicians to ensure a high quality HFA test. A good and reliable HFA is important to provide guidance in clinical decision making for glaucoma patients.

## 5. CONCLUSION

The reliability of HFA may not be affected by anxiety. Repetitive testing and education levels were shown to affect fixation loss and false negative rates in glaucoma patients. More frequent HFA testing may improve the accuracy of HFA in less educated patients.

## CONSENT

All authors declare that informed consent of patient was obtained in this study.

## ETHICAL APPROVAL

All authors hereby declare that this study was 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.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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