Kok-Leong Tan[1,2], Lai-Chan Fhun[1,3], Maizan Yaakub[2], Mei-Fong Chong[3], Ahmad Tajudin Liza-Sharmini[1,*]

[1]Department of Ophthalmology, School of Medical Sciences, Health campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[2]Department of Ophthalmology, Hospital Sultanah Nur Zahirah, 20400 Kuala Terengganu, Terengganu, Malaysia

[3]Department of Ophthalmology, Hospital Raja Permaisuri Bainun, 31400 Ipoh, Perak, Malaysia

Received 07 Sep 2017.
Revised 28 Sep 2017.
Accepted 02 Oct 2017.
Published Online 01 Dec 2017

*Corresponding author:
Liza-Sharmini AT
E-mail: liza@usm.my , sharminiliz@live.com

Stress and Repetitive Visual Field Assessment in Glaucoma Patients

Abstract— Glaucoma is a chronic disease that could affect the quality of life and is a potential stressor for patients. Visual field assessment is important in monitoring disease progression among glaucoma patients. Stress could influence the performance of patients in visual field test that may affect the reliability of the test. Our objective in this study was to determine the association between stress score using Depression, Anxiety and Stress Scale (DASS) questionnaire and reliability indices of Humphrey visual field analysis (HFA). A total of 155 primary and secondary glaucoma patients were recruited in the study. Face to face interview using stress component of DASS questionnaire was conducted after automated HFA test. Reliability indices; i.e. fixation loss, false positive, and false negative error, were used to determine the accuracy of HFA result. Only 12 patients (7.7%) were found to have elevated stress score. No significant correlation was found between DASS stress score and the reliability indices of HFA. There was 0.2 folds (95% confidence interval (CI) [-2.35, -0.06], p = 0.039) reduction of fixation loss for every number of HFA done. For every one year increase in age, there was 0.2 folds (95% CI [-0.38, -0.07], p = 0.006) reduction in false positive error in HFA. Minimal stress may not affect the reliability of HFA assessment. Minimising stress among glaucoma patients is important not only for assessment of visual field but also for improvement of quality of life.

Keywords **- Glaucoma, reliability, stress, visual field.**

1 INTRODUCTION

Stress is often blamed to cause many illnesses including common cold and impaired of cognition [1-6]. Vice versa, illnesses especially chronic illnesses are often responsible for development of individual and family stress [7-9]. Glaucoma is a chronic, progressive optic neuropathy that characterized by changes in the optic nerve head and visual field damage [10]. Glaucoma warrants a long term follow up, repetitive test, and changing in various modalities of treatment as the disease progresses. The fear of being blind, dependency, and inability to drive are among the potential stressors faced by glaucoma patients that may affect their quality of life [11-14].

Visual field assessment is necessary in diagnosis and monitoring progression of glaucoma [15, 16]. Automated visual field is an objective method of quantifying visual field loss using the principle of testing the retinal sensitivity [17]. The most common and popular mode of assessment is automated Humphrey perimetry. The test is based on the patient's response by clicking on seeing light stimuli with different intensities at fixed points.

Interpretation of Humphrey visual field analysis (HFA) relies on reliability of the test. Automated HFA is equipped with reliability indices; i.e. fixation loss, false negatives error and false positive error. Patient-related factors such as age, visual acuity, test time, education background, learning ability, and clarity of instruction from the perimetrist may influence the reliability of HFA result [17, 18]. Learning ability may be affected by emotional stress and anxiety [19, 20]. In addition, similar to other systemic diseases, glaucoma also may induce stress [21]. Frequent follow up, financial difficulty, long term medication, and social support are among the possible stress factors in glaucoma patients.

Understanding and eliminating emotional stress in glaucoma patients is important to ensure compliance and persistent to treatment. In

addition, eliminating stress may help in monitoring the disease accurately using HFA assessment. Our objective in this study was to determine the association between stress score using Depression, Anxiety and Stress Scale (DASS) questionnaire and reliability indices of HFA.

2 METHODS

An observational cross-sectional study was conducted involving 155 glaucoma patients who were receiving regular follow-up check in the eye clinics of tertiary centers in Malaysia. These locations included Hospital Sultanah Nur Zahirah, Hospital Raja Permaisuri Bainun, and 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 5 patients presented with secondary glaucoma (two with pseudoexfoliative, one with neovascular, one with angle recession, and one with thyroid orbitopathy-related glaucoma). 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.

Only 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 history of systemic diseases were obtained from patient medical records. Duration of glaucoma was 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 completed the automated HFA test using DASS questionnaires by two investigators (KLT and LCF) who were masked from the HFA assessment outcome. The DASS is a questionnaire designed to measure the magnitude of three negative emotional states, i.e. depression, anxiety, and stress. Only items related to stress assessment in the DASS questionnaire were used. DASS-stress items focus on tension and irritability [22]. Stress score of DASS ranges from 0 to 42. Based on the DASS-stress score, stress level was divided into five categories: normal, mild, moderate, severe, and extremely severe. A score of 0-14 indicates normal stress level, 15-18 minimal level of stress, 18-25 moderate level of stress, 26-33 severe stress, and 34 or more suggests extremely severe stress level [23]. The results from the DASS questionnaire were compared to the reliability indices from 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% [17]. High fixation loss is considered when the score is ≥20%. High false positive or negative error is defined when the score is ≥33%. The raw data of reliability indices were used for analysis.

2.1 Data Analysis

Data was analyzed with Windows SPSS version 21.0. Spearman correlation was used to determine the relationship between anxiety 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 (84 (54.2%) were male and 71 (45.8%) were female) were included in this study. Majority of them were POAG patients (70.3%), followed by 14.8% NTG, 11.6% PACG, and the remaining were secondary glaucoma (Table I). Their mean age was 69.0 ± 10.3 years old. Only 11.0% received tertiary

Table I: Demographic and clinical data of study subjects

Demographic characteristic	**N = 155**
Mean age (± SD in years)	69.0 ±10.3
Type of glaucoma (n, %)	
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 (± SD in years)	6.1 ± 5.7
Gender (n, %)	
Male	84 (54.2)
Female	71 (45.8)
Race (n, %)	
Malay	44 (28.4)
Chinese	83 (53.5)
Indian	25 (16.1)
Others	3 (1.9)
Education Level (n, %)	
No formal education	12 (7.7)
Primary school	54 (34.8)
Secondary school	72 (46.5)
Tertiary education	17 (11.0)
Best corrected visual acuity (n, %)	
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 ± 4.2
Reliability indices (n, %)	
High fixation loss	50 (32.3)
High false positive	3 (1.9)
High false negative	10 (6.5)
Stress level based on DASS stress score (n, %)	
Normal	143 (92.3)
Mild	5 (3.2)
Moderate	4 (2.6)
Severe	3 (1.9)
Extremely Severe	0 (0.0)

POAG = Primary Open Angle Glaucoma, PACG = Primary Angle Closure Glaucoma, NTG = Normotensive Glaucoma, NVG = Neovascular Glaucoma, HFA = Humphrey Visual Field Analysis, DASS = Depression Anxiety Stress Scale

education and 7.7% without any formal education (Table I). A total of 116 patients have best corrected vision 6/12 or better, 32 patients with vision of 6/18 to 6/24, and only seven patients were between 6/36 to 6/60 (Table I). The average number of previous HFA done by patients was 5.4 ± 4.2 (with range from 1 to 19).

Based on DASS score, only 12 patients (7.7%) were found to have elevated level of stress. None was extremely stressed and three were severely stressed (Table I). Many patients reported to feel impatient if delay or rather touchy, and upset easily and for trivial things (Table II). There was no significant correlation between DASS stress score and reliability indices of HFA (Table III).

Table II: Mean score of each question of DASS stress items

Question	**Mean ± SD**
Upset by quite trivial things	0.42 ± 0.65
Tends to over-react	0.30 ± 0.60
Difficult to relax	0.37 ± 0.68
Upset easily	0.45 ± 0.63
Felt using lot of nervous energy	0.35 ± 0.67
Felt impatient if delayed	0.46 ± 0.71
Felt rather touchy	0.46 ± 0.64
Hard to wind down	0.28 ± 0.61
Very irritable	0.47 ± 0.66
Hard to calm down after upset	0.35 ± 0.66
Difficult to tolerate interruptions	0.31 ± 0.62
In a state of nervous tension	0.27 ± 0.59
Intolerant of anything that kept from getting on with what was doing	0.30 ± 0.64
Agitated	0.34 ± 0.64

DASS = Depression Anxiety Stress Scale, SD = standard deviation

Table III: Correlation between stress score and reliability indices of HFA

	Correlation coefficient (r)	***p* Value**
Stress score and fixation loss	-0.022	0.784*
Stress score and false positive	0.036	0.654*
Stress score and false negative	0.038	0.651*

HFA = Humphrey Visual Field Analysis
*$p < 0.05$ is significant based on Spearman correlation

There was significant linear relationship between number of HFA test and fixation loss of HFA (Table IV). There was 0.2 folds (95% confidence interval (CI) [-2.35, -0.06], $p = 0.039$) reduction of fixation loss for every number of HFA done (Table IV). For every one year increase in age, there was 0.2 folds (95% CI [-0.38, -0.07], $p = 0.006$) reduction in false positive error in HFA (Table V). There was no significant linear relationship between false negative error in HFA and confounding factors such as age, number of HFA test, DASS stress score and duration of glaucoma (Table VI).

Table IV: Multivariate analysis on factors affecting fixation loss in HFA

Variables	Simple Linear Regression		Multiple Linear Regression	
	b [a] [95% CI]	*p* value	b [b] [95% CI]	*p* value
Age	0.390 [0.023, 0.757]	0.037	0.139 [-0.041, 0.691]	0.082
Duration of glaucoma	0.120 [-0.555, 0.794]	0.726	0.181 [-0.081, 1.612]	0.076
Number of HFA	-0.702 [-1.613, 0.209]	0.130	-0.209 [-2.346, -0.060]	0.039
Education level	-2.619 [-4.884, -0.354]	0.024	-0.160 [-4.640, 0.015]	0.052
Stress score	0.354 [-0.282, 0.990]	0.274	0.092 [-0.251, 0.985]	0.242

HFA = Humphrey Visual Field Analysis
[a] Crude regression coefficient
[b] Adjusted regression coefficient
Backward multiple linear regression method applied
Coefficient of determination (R^2) = 0.091
$p < 0.05$ is significant

Table V: Multivariate analysis on factors affecting false positive in HFA

Variables	Simple Linear Regression		Multiple Linear Regression	
	b [a] [95% CI]	*p* value	b [b] [95% CI]	*p* value
Age	-0.213 [-0.369, -0.057]	0.008	-0.226 [-0.384, -0.066]	0.006
Duration of glaucoma	0.152 [-0.137, 0.440]	0.300	0.118 [-0.154, 0.581]	0.252
Number of HFA	0.093 [-0.300, 0.486]	0.640	-0.019 [-0.543, 0.449]	0.851
Education level	0.117 [-0.870, 1.104]	0.816	-0.041 [-1.266, 0.755]	0.618
Stress score	0.191 [-0.081, 0.464]	0.167	0.106 [-0.087, 0.450]	0.184

HFA = Humphrey Visual Field Analysis
[a] Crude regression coefficient
[b] Adjusted regression coefficient
Backward multiple linear regression method applied
Coefficient of determination (R^2) = 0.068
$p < 0.05$ is significant

Table VI: Multivariate analysis on factors affecting false negative in HFA

Variables	Simple Linear Regression		Multiple Linear Regression	
	b [a] [95% CI]	*p* value	b [b] [95% CI]	*p* value
Age	0.180 [-0.066, 0.426]	0.150	0.103 [-0.096, 0.405]	0.225
Duration of glaucoma	-0.309 [-0.736, 0.118]	0.155	-0.062 [0.705, 0.379]	0.554
Number of HFA	-0.428 [-1.017, 0.161]	0.153	-0.056 [-0.942, 0.539]	0.591
Education level	-1.741 [-3.171, -0.310]	0.017	-0.156 [-2.884, 0.125]	0.072
Stress score	0.054 [-0.350, 0.458]	0.793	0.032 [-0.320, 0.478]	0.695

HFA = Humphrey Visual Field Analysis
[a] Crude regression coefficient
[b] Adjusted regression coefficient
Backward multiple linear regression method applied
Coefficient of determination (R^2) = 0.058
$p < 0.05$ is significant

4 DISCUSSION

Performance of HFA is affected by many factors. Understanding the instruction, hand and eye coordination, concentration ability, and other environmental factors are among the factors identified to affect the reliability of the test [17, 18]. Conducting HFA in elderly is challenging due to poor concentration span, dementia, and poor eye and hand coordination secondary to physiological aging or systemic comorbidities [24-27]. It is even more challenging in glaucoma patients with visual field defect.

In the current study, there were only 12 patients (7.7%) who had elevated stress level. Erb et al. [28] reported more psychosomatic symptoms including stress symptoms were detected in NTG patients compared to age-matched controls. There are studies suggesting stress is responsible for the variation of intraocular pressure [29-31]. In addition, there are also reports that acute angle closure was precipitated by stress [6, 32-34]. However, none of our recruited patients experienced extreme stress. Feeling very irritable, impatient and touchy were among the common somatic symptoms experienced by glaucoma patients in the current study.

Stress may also affect the reliability of HFA. To the best of our knowledge, there is no reported relationship between HFA reliability and stress. Based on reliability indices, the most affected was the fixation loss. A total of 50 patients demonstrated high fixation loss (32.3%). Only three patients demonstrated high false positive. However, there was no significant correlation between stress score and fixation loss. Stress-induced learning impairments could impede the performance of task.

Sensorimotor coordination, motor learning, or altered fear conditioning are possible reasons for poor performance [35]. Four types of relationships are possible between job stress and performance: curvilinear/U-shape, negative linear, positive linear or no relationship between the two. Other factor such as commitment could have moderated or masked the effect of stress [36]. Commitment to perform well in HFA test to avoid additional medications or surgery could have partially influenced performance of stressed patients, if any. The patients in the study were generally of older age (mean age 69.0 ± 10.3 years). Co-existing conditions such as joint deformation or inflammation, reduced motor coordination and attention span could have deterred proper response in HFA test. Patients were required to press a button when perceived light during HFA assessment.

Repetitive test may help in improvement of reliability of HFA. The total number of HFA done by subjects in this study varied between 1 to 19 times (mean 5.4 ± 4.2). Learning curve of patient influences HFA performance [17]. On the other hand, repetitive test may also cause stress to glaucoma patients [37]. Existing stress due to the chronicity and nature of the disease, fear of blindness, and financial burden may also aggravate the stress during HFA assessment [11, 12].

Reliability of HFA may also be affected by the clarity of instruction given by the perimetrist. All perimetrists involved in this study were Malays. While 53.5% of patients were Chinese, 16.1% was Indians and 1.9% was others. It was assumed that all Malaysian regardless of race must be able to communicate in Malay language. However, perhaps, there was possibility of miscommunication between patients and perimetrists. Clear and adequate instruction by the perimetrist is crucial during visual field assessment [38]. In addition, 12 patients (7.7%) had no formal education and 54 patients (34.8%) only completed primary school education. Education level also may act as a barrier in understanding the task.

DASS questionnaire is not specific in detecting stress. It evaluates three factors or systems; depression, anxiety, and stress, in a subject. Stress scale in DASS is strongly associated with the construct of general negative affect or distress, which is the common feature shared by anxiety and depression disorders. Stress component of DASS was found to evaluate symptoms related to generalised anxiety disorder [39]. Stress is part of the symptoms of generalised anxiety disorder. Detection of stress through DASS questionnaire may not accurately assess stress in our glaucoma patients. In addition, using a single questionnaire may not be ideal in this study.

Our major limitation is relatively small sample size. Larger number of patients will provide more accurate representation of the actual problem. Severity of glaucoma was

reported to influence the reliability indices of HFA [17, 40]. Patients with more severe glaucoma were associated with reduction in visual field sensitivity, higher fixation losses and false negative errors [17, 40]. However, the severity of glaucoma was not assessed in this study. High fixation loss and false negative error in our subjects may be influenced by the advanced stage of the disease, not just due to stress.

5 CONCLUSION

As a conclusion, minimal stress may not affect the reliability of HFA assessment. Minimizing stress among glaucoma patients is important not only for assessment of visual field but for improvement of quality of life. Previous experience in completing HFA and age of the patients may also influence the reliability of HFA.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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