ASSOCIATION BETWEEN MOBILITY PERFORMANCE AND SEVERITY OF PRIMARY GLAUCOMA

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DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT FOR THE DEGREE OF MASTER OF MEDICINE (OPHTHALMOLOGY)

SCHOOL OF MEDICAL SCIENCES UNIVERSITI SAINS MALAYSIA

2022

DISCLAIMER

I hereby certify that the work in this dissertation is my own except for the quotations and summaries which have been duly acknowledged. I declare that I have no financial interest in the instruments in this study.

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P-UM0128/18

21/11/2022

ACKNOWLEDGEMENT

I would like to convey my profound gratitude to my supervisor Professor Dr. Liza Sharmini Ahmad Tajudin, senior consultant ophthalmologist (Glaucoma), Department of Ophthalmology, School of Medical Sciences, Universiti Sains Malaysia for her continuous support and guidance during the duration of this study. Her invaluable advice throughout this period of study was deeply appreciated. This accomplishment would not have been possible without her. I would also like to thank my co-supervisor Associate Professor Dr Muhammad Hafiz Bin Hanafi, Rehabilitation Medicine Unit, School of Medical Sciences, Universiti Sains Malaysia for his guidance and patience. I am also grateful to all lecturers and staff of Department of Ophthalmology for their help and support throughout this study period.

My sincere thanks to Dr. Raja Norliza Raja Omar, my out-campus supervisor in Hospital Melaka for her continuous support and dedication.

Last but not least, I would like to place on record my sense of indebtedness towards my family members for their undeterred support spiritually and continuous encouragement throughout my years of study and through the process of researching and writing this dissertation. The accomplishment would not have been possible without them.

TABLE OF CONTENTS

ABSTRAK

PENGENALAN

Glaukoma adalah penyebab utama kebutaan di seluruh dunia dimana glaukoma sudut terbuka (POAG) adalah jenis yang utama diikuti oleh glaukoma sudut tertutup (PACG). Pesakit glaukoma yang merosot mengalami kesukaran untuk melakukan aktiviti harian yang memerlukan penggunaan penglihatan sisi. Ini akan memberi kesan kepada pelbagai aktiviti harian termasuk navigasi dan mobiliti di rumah. Walaupun terdapat intervensi perubatan yang berkesan untuk mengurangkan kemerosotan medan penglihatan bagi pesakit glaukoma, namun kehilangan medan penglihatan yang telah berlaku adalah bersifat kekal. Kekurangan ini berpotensi untuk diatasi melalui simulasi aktiviti harian bagi menguji dan melatih keupayaan fungsi visual.

OBJEKTIF

Untuk membandingkan prestasi mobiliti antara pesakit glaukoma dan kawalan serta hubungkait dengan tahap kemerosotan glaukoma

KAEDAH PENGAJIAN

Satu kajian rentas telah dijalankan melibatkan pesakit glaukoma primer tahap sederhana dan dan subjek kawalan yang mempunyai padanan umur antara Jun 2020 dan Jun 2022 di Hospital Universiti Sains Malaysia (HUSM). Penilaian visual asas termasuk ketajaman penglihatan, kepekaan kontras, penglihatan warna dan ujian medan penglihatan binokular Esterman telah dijalankan. Kawasan ujian mobiliti yang disusun dalam bentuk pagar sesat sepanjang 12 meter beserta halangan yang mewakili objek di rumah telah direka. Kawasan ini dibahagikan kepada empat zon dimana setiap kawasan mempunyai pencahayaan yang tetap serta kamera pengawasan untuk memerhatikan aktiviti yang dijalankan. Prestasi mobiliti akan dinilai

melalui jumlah masa yang diperlukan untuk melengkapkan aktiviti mobiliti (dalam kiraan saat) dan bilangan insiden mobiliti yang berlaku termasuk pelanggaran, tersandung, dan masalah orientasi.

KEPUTUSAN

Sebanyak 318 subjek (159 glaukoma utama dan 159 subjek kawalan) telah menyertai kajian ini. Julat waktu bagi pesakit glaukoma primer (53 tahap ringan, 54 tahap sederhana dan 52 tahap teruk) untuk melengkapkan aktiviti mobiliti adalah 31.5 $\pm$ 13.5 saat berbanding 17.0 $\pm$ 2.2 saat oleh subjek kawalan ($p<0.001$). Pesakit yang mempunyai masalah glaukoma pada tahap teruk mengambil masa yang lebih lama (46.8 $\pm$ 15.2 saat) berbanding tahap ringan (25.1 $\pm$ 1.3 saat) dan tahap sederhana (23.0 $\pm$ 2.2 saat) ($p<0.001$). Pesakit glaukoma mempunyai bilangan insiden mobiliti yang lebih ketara ($p<0.001$) dimana pesakit glaukoma pada tahap teruk mempunyai insiden mobiliti tertinggi (4.9 $\pm$ 3.2). Ujian medan penglihatan Esterman menunjukkan kadar negatif yang selari dengan keupayaan mobiliti ($r=-0.932$) dan kepekaan kontras menunjukkan kadar selari yang sederhana ($r=-0.520$). Jarak terbaik antara perabot adalah 1.5 meter, manakala jarak 0.5 meter mempunyai 48 $\pm$ 30.2 bilangan insiden mobiliti di kalangan pesakit glaukoma.

KESIMPULAN

Pesakit glaukoma berjalan lebih perlahan dan sering mengalami insiden mobiliti. Kemerosotan medan penglihatan dikaitkan dengan tahap mobiliti dan navigasi yang lebih rendah di rumah. Susunan perabot yang teratur, pencahayaan serta aturan kontras di persekitaran yang baik boleh meningkatkan navigasi mereka di rumah.

ABSTRACT

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide with primary open angle glaucoma (POAG) as the predominant subtype followed by primary angle closure glaucoma (PACG). Patients with advancing glaucoma suffer from increasing difficulty with daily living activities requiring peripheral vision which affects a broad array of activities that includes navigation and mobility at home. While there are effective medical interventions to minimize the progression of peripheral visual field loss in glaucoma, there is no cure the acquired field loss is irreversible. These limitations could be potentially be overcome by objective simulation of functional visual ability.

OBJECTIVE

To compare mobility performance between patients with glaucoma and control and to associate with severity of glaucoma

METHODOLOGY

A cross sectional study was conducted involving patients with primary glaucoma and age-matched controls between June 2020 and June 2022 at Hospital Universiti Sains Malaysia (HUSM). Baseline visual assessment including visual acuity, contrast sensitivity, colour vision and Esterman binocular visual field were conducted. Patients with primary glaucoma were divided into severity of glaucoma based on the modified Hodapp-Anderson-Parish criteria on the visual field of their better eye. A mobility course arranged in a maze of 12-meters long and seeded with obstacles that represent furniture at home was created. The course was divided into four zones with fixed illumination and surveillance camera to observe the activities. Mobility

performance was assessed by the time required to complete the course (in seconds) and number of mobility incidents which include bumps, stumbles, and orientation problem.

RESULTS

A total of 318 subjects (159 primary glaucoma and 159 controls) were recruited in this study. The mean time required by patients with primary glaucoma (53 mild, 54 moderate, and 52 severe) to complete the mobility course was 31.5 $\pm$ 13.5 sec compared to 17.0 $\pm$ 2.2 sec by the age-matched control ($p<0.001$). Those with severe glaucoma took longer time (46.8 $\pm$ 15.2 sec) compared to mild (25.1 $\pm$ 1.3 sec) and moderate (23.0 $\pm$ 2.2 sec) ($p<0.001$). Patients with glaucoma have significant more mobility incidences ($p<0.001$). Mean mobility incidents were 4.9±3.2 and all were documented in patients with severe visual field of the better eye. Esterman visual field test showed strong negative correlation with mobility performance ($r=-0.932$) and contrast sensitivity showed moderate correlation ($r=-0.520$). The best distance between the furniture is 1.5 meter, while the distance of 0.5 meter reported 48 $\pm$ 30.2 mobility incidence among patients with glaucoma.

CONCLUSION

Patients with glaucoma walk slower than the age-matched controls of which those with severe glaucoma walk the slowest. Mobility incidents were reported among those with severe glaucoma. Proper arrangement of furniture, good illumination and contrast sensitivity in their home environment may improve their navigation especially among those with severe disease.

Chapter 1
Introduction

1.1 PRIMARY GLAUCOMA

Glaucoma is the leading cause of irreversible blindness worldwide with primary open angle glaucoma (POAG) as the predominant subtype followed by primary angle closure glaucoma (PACG) (Zhang et al., 2021). Primary glaucoma affects those above 40 years old and the number of population affected increased exponentially with age (Tham et al., 2013). In Malaysia, which is a developing country with improved healthcare system and increased life expectancy among the population, the number of glaucoma patients were expected to rise and increasing throughout time which may pose burden to the current healthcare support. Globally, about 4.5 million people estimated to become blind due to glaucoma and up to 50% of people affected without even aware of having glaucoma in developed countries. (WHO and World Glaucoma association 2016). According to a research conducted on Chinese residents in Singapore, the rate of uniocular blindness is 27% for POAG and 50% for PACG, while the rates of binocular blindness from POAG and PACG are 9% and 29% respectively (Foster et al., 2000). Singapore Malay Eye Study revealed POAG accounted for 69.3% of glaucoma cases and PACG accounted for only 5.3% cases (Shen et al., 2008). These two studies demonstrate a lower prevalence of PACG in Malays compared with Chinese residents in Singapore. (Foster et al., 2000 and Shen et al., 2008).

Primary open angle glaucoma (POAG) is a chronic, progressive optic neuropathies that characterised by structural changes in the optic nerve head and/ or with visual field defect without identifiable causes (Asia Pacific Glaucoma guidelines, 2008). Whereas, primary angle closure glaucoma (PACG) is characterized by an occludable drainage angle and features indicating that trabecular obstruction by the peripheral iris has occurred, such as peripheral anterior synechiae with elevated intraocular pressure and optic neuropathy (Foster et al., 2002).

Glaucoma patients may need lifelong treatment as it is a disease of longevity. The main goals of glaucoma treatment are to slow down disease progression and preserved the quality of life (Weinreb et al., 2015). Lowering the intraocular pressure has been shown to be effective in preventing the development and slowing the disease's progression in multicentre clinical trials. Despite having the surgical and medical options to reduce intraocular pressure, current therapies remain imperfect, and novel treatment options are desired. The patient may experience gradual deterioration of vision, initially peripherally but eventually affecting the central vision (Khadka et al., 2013). The rates of visual field progression in manifest glaucoma with field loss were highly variable with a mean rate of −0.80 dB/year and 5.6% of patients 16 progressed at rates worse than −2.5 dB per year (Heijl et al., 2012). Despite receiving treatment, the majority of glaucoma patients still experience disease progression (Rossetti et al., 2010).

Patients with advancing glaucoma suffer from increasing difficulty with daily living activities requiring peripheral vision, contrast discrimination and light/dark adaptation. Studies have suggested that glaucoma affects a broad array of activities, where it can impact driving, walking, venturing from home, reading, seeing at night, judging distance and seeing peripheral objects. While there are effective medical interventions to minimize the progression of peripheral visual field loss in glaucoma, there is no cure the acquired field loss is irreversible (Heather et al., 2014). These limitations could be potentially be overcome by objective simulation of functional visual ability. (Skalicky et al., 2016)

1.2 Glaucoma and quality of life

Quality of life (QOL) is defined as individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns (Quaranta et al., 2016). The ultimate goal of glaucoma management is to slow down disease progression, preservation of visual function and QOL (Weinreb et al., 2014, Quaranta et al., 2016). As a major cause of vision loss, glaucoma can affect several aspects of QOL in the long run. Impaired activities of daily living including reading, walking and driving have been reported in several studies (Friedman et al., 2007, Ramulu., 2009). People with visual impairment also at higher risk than healthy population for accidents, social withdrawal, anxiety and depressions (Brundle et al., 2015, Demmin and Silverstein, 2020).

Based on meta-analysis of the effect of glaucoma related vision impairment on QOL using Glaucoma Quality of Life-15 Questionaire (GQL-15), patients with glaucoma showed significantly higher GQL-15 summary scores (SMD = 0.94, 95% CI=0.73 to 1.16) compare to control participants. As glaucoma severity worsened, patient's QOL also decreased (Wang et al., 2017). Glaucoma patients also had a significantly higher risk of impaired activity of daily living (OR 2.06; 95% CI: 1.14, 3.71) compared to healthy participants. Subjects with bilateral glaucoma have been reported to have driving cessation and limitation, bumping into objects, slower walking, and falls. Some studies also demonstrating higher accident rates in glaucoma (Ramulu., 2009)

1.2.1 Mobility and navigation

Mobility is the issue of greatest importance to glaucoma patients. There is ample of evidence that suggest glaucoma affect mobility. Difficulty in walking, navigation and mobility is the common difficulty reported by glaucoma patients (Maharajah et al., 2007). Glaucoma patients tend to walk slower with greater difficulty and more likely to bump into things than age-matched controls (Ramulu et al., 2012). Visual field defect play major role in navigation and balance compared to visual acuity and contrast sensitivity (Freeman et al., 2006).

In a prospective observational study comparing patients with and without glaucoma, it was shown that subjects with severe glaucoma engaged in 66% less physical activities than controls and took 31% fewer steps/day ($p=0.001$) (Ramulu et al., 2012). The average walking speed of glaucoma patients was also 10% slower than controls, based on a cross sectional study comparing walking in glaucoma and normal vision subjects ($p<0.01$) (Turano et al., 1999). According to a population-based observational study assessing the impact of glaucoma on mobility, participants with bilateral glaucoma walk 2.4 m/minutes slower and experienced 1.65 times number of bumps compared normal participants ($p<0.05$) (Friedman et al., 2007). The problem with navigation and mobility increases as the disease deteriorates (Tharmathurai et al., 2021). Improvement in navigation perhaps may increase the physical activities in glaucoma (Niven et al., 2019).

Glaucoma has been noted to cause impairment of balance and walking ability and has been implicated as a risk factor of fall. These condition may result in the two- to fourfold higher risk of falls in glaucoma patients compared to healthy subjects, as noted in previous studies (Ivers et al., 1998, Haymes et al., 2007). Falls are the leading cause of injury-related death in elderly. Glaucoma related visual field loss is associated with a higher rate of injurious falls and fractures. Nearly half of those with glaucoma fall over the course of a year (Black et al., 2011).

Falls may have a profound psychological impact on the individual due to change in their perception of capability. Even in people who have not recently fallen, fear of falling is a commonly used metric that captures this impact and is seen as an important health outcome. (Jorstad et al., 2005). The fear of falling has been measured using several questionnaires, and greater fear of falling is associated with decreased physical activity, loss of independence, reduction of social activity, lower quality of life and depression (Yardley et al., 2002, Cumming et al., 2000).

Based on a cross sectional study conducted in Japan using the Fall Efficacy Scale-International (FES-I), it was suggested that older age, female gender and inferior peripheral visual field damage we associated with increased fear of falling (Yuki et al., 2020). Despite of these associations, evidence has shown only a relatively weak correlation between peripheral visual field loss measure by standard automated perimetry and risk of falls. It may be related to inadequate ability of this test to evaluate the complex visual demands made for adequate postural control during daily activities and in challenging lighting conditions (Diniz-Filho et al., 2015). A recent strategy using virtual reality and assessment of postural reactions to dynamic stimuli in glaucoma patients performed better than standard automated perimetry in predicting risk of fall. Balance control was evaluated using a force platform, and the postural reactivity to dynamic information was assessed using an immersive virtual environment with head mounted goggles. The postural reactivity metrics showed a significant association with self-reported history of falls in the 1-year period (Diniz-Filho et al., 2015).

1.2.2 Driving

Inability to drive is a significant concern among glaucoma patients. According to number of studies, patients who stop driving may experience a higher number of depressive symptoms, social isolation and reduced access to healthcare services, which can negatively affect their QOL (DeCarlo et al., 2003, Ragland et al., 2005). Previous studies also have indicate that glaucoma patients are at increased risk of motor vehicle accidents. (Haymes et al., 2008, McGwin et al., 2004, McGwin et al., 2005)

Visual acuity is the most common visual parameter assessment performed by motor vehicle regulatory agencies for acquiring driver's license. However, several studies have demonstrated only minimal to no correlation between visual acuity and motor vehicle accidents (Owsley et al., 2001, Cross et al., 2009). The gold standard test to assess functional damage in glaucoma is the visual field examination. It is most frequently performed with standard automated perimetry (SAP). However, previous studies have found only a relatively weak association between SAP results in patients with glaucoma and risk of motor vehicle accidents (Haymes et al., 2007, Tanabe et al., 2011, Tatham et al., 2015).

Alternative methods for assessing driving risk in glaucoma patients have been proposed in more recent studies. These methods include useful field of view, driving simulator metrics and mobile platforms that evaluate visual processing speed, attentiveness and contrast sensitivity. These tests evaluate aspects of vision relevant to driving that are not fully assessed by simple white-on white testing of standard automated perimetry (Gracitelli et al., 2015, Tatham et al., 2015, Rosen et al., 2015).

1.2.3 Reading

Reading is another important pleasure and essential to our everyday life. Problems with reading have been reported as one of the main cause of anxiety for patients with glaucoma (Apinall et al., 2008). Difficulties with reading, following lines of text and other near-vision tasks also have been consistently reported by patients in other interview and questionnaire studies (Nelson et al., 1999, Viswanathan et al., 1999, Freeman et al., 2008). Patients with glaucoma, even at early stage read slowly and with more errors as compared with normal subjects (Rolle et al., 2019). The ability to read well is not primarily determined by having a good visual acuity alone. Visual field defect in glaucoma patients has been reported to associate with slower reading speed, saccade rate and visual span that involved all reading tasks (Ramalu et al., 2009; Kwon et al., 2017).

Studies using spectral-domain optical coherence tomography (SD-OCT) have demonstrated even early glaucomatous injury involves the macula. Such damage include loss of retinal ganglion cells and significant shrinkage of dendritic structures and cell bodies of remaining cells in the macula (Hood et al., 2012, Hood et al., 2013). Disruption of the magnocellular pathway of retinal ganglion cells eventually causes reduced perceptual span, increase saccadic frequency and fixation instability that impair reading speed among glaucoma subjects. (Rolle et al., 2019). Previous studies also have shown that deficiencies of letter recognition such as acuity limit or loss of contrast sensitivity lead to a significant reduction in reading speed (Legge et al., 2011, Kwon et al., 2012). Despite of that, there is no specific rehabilitation program to improve reading abilities among glaucoma patients.

1.3 Visual rehabilitation to improve mobility

Vision rehabilitation is the process of therapy and education that aids visually impaired individuals in achieving their maximum level of function, sense of well-being, a personally satisfactory level of independence and a good quality of life (American Optometric Association Board of Trustees, 2004). In general, a visual rehabilitation programs can be divided into low vision therapy and occupational therapy (Wilkinson and Shahid, 2018). Irreversible vision loss due to severe glaucoma and age-related macular degeneration has a significant impact on quality of life and functional abilities (Bethesda et al., 1998). Low-vision rehabilitation may be the only choice for patients to enhance functional vision when pharmacological or surgical therapy are ineffective for treating advanced vision loss (Patodia et al., 2017). The primary goal of low vision aid is not to restore lost vision but rather to completely utilise the remaining vision to the best extent possible. This enables patient to regain their ADLs and optimize their quality of life (MacKeben, 2009).

The most common form of visual rehabilitation is orientation and mobility training that involves the use of remaining vision and other senses, commonly in conjunction with sighted guides or long or short canes (Blasch, 1997). Orientation is the ability to locate oneself in one's environment. It is a skill that is related to the use of the remaining senses of a person to establish one's position in and to significant objects in the environment (Sage Clinical Rehabilitation, 2013). While, mobility is defined as physical "movement" and the negotiation of any obstacles and hazards. It is the aim of obtaining the freedom of movement without coming to any harm, safety in traveling as well as minimizing the level of stress placed upon a visually impaired person (Sage Clinical Rehabilitation, 2013). Eye movement (scanning) training for mobility rehabilitation has also been investigated for visual field defects such as hemianopia and tunnel vision (Kerkhoff, 1992; Webster, 1984). However there is still limited knowledge on the effects

of visual rehabilitation in patients with glaucoma. Thus, the importance of visual rehabilitation on quality of life in patients with glaucoma is not well established.

1.4 Glaucoma and performance based assessment

It is a measurement of patient performance for a task or set of tasks. These tasks may only be surrogates for the task in real life. Ability to perform the challenging tasks can be measured and form part of an objective, functional analysis to complement self-reported questionnaire data. (Weinreb., 2019)

Assessment of glaucoma-related disability by using questionnaire to subjectively evaluates patient's ability to perform visually related task has been shown to correlate with clinical markers of glaucoma severity. However, the limitation of questionnaire-based assessment such as physiological aging factors, personality and recall bias may influence their responses (Skalicky et al., 2016). These limitations could be potentially overcome by objective simulation of functional visual ability using performance-based method. In performance-based method, patients are asked to perform surrogate tasks of daily activities such as ambulation and locating objects while being evaluated in a standardized manner. Performance-based testing offers several advantages including partially eliminating the subjectivity and provide direct observation of the patients' functional ability for a given task. It will allow the researchers to obtain objective data on measurement of glaucoma related visual disability. This method also provides a baseline data for subsequent correlation analysis on questionnaire-based assessment and other clinical tests.

Persons with advanced glaucoma have significantly reduced peripheral vision as measured by visual field tests. As residual visual field is a significant predictor of mobility performance, it is expected that mobility performance would be affected in advanced glaucoma. However, there were still limited study has addressed this issue and it is unknown wether mild

glaucoma damage might decrease mobility performance (Turano et al., 1999). Several studies have found that glaucoma patients report greatest restriction with mobility compared to the other domains (Turano et al., 1999; Fontana et al., 2016). In fact, other investigators have also found that the highest impact of glaucomatous visual field loss is on mobility or driving difficulty.

Few studies had been done to objectively analyze functional visual disability among glaucoma patients. There is composite functional test available, such as the assessment of disability related to vision (ADREV), the computer-based Cambridge visual function test and various method of 3-D visual stimulation of virtual reality. (R.N Weinreb., 2019). There were stronger correlation noted between clinical tests and performance based assessment compared to patient-reported outcome. Study done by Richman et al using ADREV and NEI-VFQ-25 questionnaire to objectively and subjectively establish the relationship in glaucoma patients between standard vision tests, quality of life and ability to perform daily activities has found that the clinical test had higher correlations with ADREV than with the NEI-VFQ-25. There was a moderate, but not strong connection between how patients rated their own visual ability with how they performed when objectively tested. (Richman et al., 2010). Therefore, performance-based assessment is a potential method that can be used in assessment of glaucoma related visual disability. Besides, it also can become a therapeutic measures as it serve a function as a training tools for patients to develop adaptive gaze strategy to cope with their real life daily activities especially in terms of mobility. Performance based testing is not new to medicine, it is commonly used in the diagnosis and monitoring of stroke and other neurological conditions. However the practise of the test in ophthalmology field to assess the functional abilities of low vision patients such as in glaucoma were still limited.

1.5 RATIONALE OF STUDY

Glaucoma will be a major health problem as Malaysia is moving toward aging country soon. As a major cause of vision loss, glaucoma can affect broad array of activities in the long run. Navigation and mobility is one of the domain which mostly affected by primary glaucoma patients based on quality of life (QOL) questionnaires (Tharmathurai et al., 2019). A previous study also discovered that physical activity is a potential modifiable risk factor in reducing progression and severity of glaucoma. However, the severity of glaucoma may prevent glaucoma patients from engaging in their daily physical activities, which may cause psychosocial impact on their daily lives. These include anxiety and depressions (Niven et al., 2019).

These limitations could potentially be overcome by objective simulation of functional visual ability (Skalicky et al., 2016). QOL assessment using questionnaire is subjected to various biases especially in term psychological influence, recall bias and the impact of physiological aging process. Thus, this performance-based study may provide an objective understanding of the mobility and navigation related difficulty among patients with glaucoma. The outcome of this study may provide an important reference for development of visual rehabilitation module for patient with glaucoma. The mobility course may also be a good home simulation module for patients to overcome their fear of falling and to develop their own skills and strategy in fulfilling their mobility needs at home.

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Chapter 2
Objective

2. STUDY OBJECTIVES

2.1 GENERAL OBJECTIVE

1. To evaluate the association between mobility performance and severity of glaucoma using mobility course module

2.2 SPECIFIC OBJECTIVES:

1. To compare the mobility performance between patients with primary glaucoma and age-matched controls using mobility course module
2. To compare the mobility performance according to severity of visual field defect in patients with primary glaucoma using mobility course module
3. To identify the correlation between visual acuity, visual field, contrast sensitivity and colour vision with mobility performance in patients with primary glaucoma using mobility course module

Chapter 3: Manuscript