# EVALUATION OF CHOROIDAL THICKNESS AND ITS ASSOCIATED FACTORS AMONG AGE-RELATED MACULAR DEGENERATION PATIENTS

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**DISCLAIMER**

I hereby clarify that the work in this dissertation is of my own except for quotations, some figures, and summaries which have been duly acknowledged. I declare that I have no financial of interest in the instruments and the computer software used in this study.

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(Dr. Nur Aliah binti Hassan)

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**ABSTRACT**

**Introduction:**

Age-related macular degeneration (ARMD) continues to be one of the leading cause of visual impairment in elderly populations in developed countries. Enhanced-depth imaging spectral domain optical coherence tomography (EDI-SD-OCT) provides a high definition cross-sectional images of choroid which enables us to quantify the choroidal thickness and gives better understanding of the pathological process of the disease.

**Objectives:**

Our objectives were to compare the mean subfoveal choroidal thickness between early ARMD, late ARMD and control group, and to compare the mean subfoveal choroidal thickness between neovascular ARMD (nARMD), polypoidal choroidal vasculopathy (PCV) and control group. Besides that, we aim to identify the associated factors (demographic data and clinical characteristics) of subfoveal choroidal thickness among ARMD patients.

**Methods:**

A comparative cross-sectional study was conducted in the Ophthalmology Clinic Hospital Universiti Sains Malaysia (USM) and Ophthalmology Clinic Hospital Selayang from January 2021 till January 2022. This study involved patients with early ARMD, late ARMD and control group. The choroidal thickness was measured using EDI-SD-OCT and statistical analysis was done using SPSS Inc Version 26.

**Results:**

A total of 144 patients were recruited into the study and 143 patients were analysed (Early ARMD: 48 patients, late ARMD: 47 patients, control group: 48 patients). The mean subfoveal choroidal thickness was significantly higher in late ARMD (262.76 ± 68.80 $\mu$m) compared to early ARMD (236 ± 28.18 $\mu$m, p=0.025) as well as the control group (244.04 ± 25.76 $\mu$m, p=0.037). The mean subfoveal choroidal thickness was significantly higher in PCV (324 ± 32.13 $\mu$m) than in nARMD (200.17 ± 21.31 $\mu$m) and control group (p<0.001). Factors that showed significant associations with the choroidal thickness were age (p=0.004), Malay ethnicity (p=0.031), nARMD (p<0.001) and PCV (p<0.001).

**Conclusion:**

This study showed there was a significant difference of mean subfoveal choroidal thickness between early ARMD, late ARMD and control group. The mean subfoveal choroidal thickness was significantly higher in PCV compared to nARMD patients and control group. Age, Malay ethnicity, nARMD and PCV were the factors associated with choroidal thickness. Choroidal thickness measurements with OCT device can make a contribution to the understanding the pathophysiology of ARMD as well as providing potential non-invasive biomarker to identify the subtype and assess the progression of ARMD.

**ABSTRAK**

**Pengenalan:**

Degenerasi makula yang berkaitan dengan usia (ARMD) terus menjadi salah satu penyebab kecacatan penglihatan dikalangan warga emas. Mesin imbasan mata *Enhanced-depth imaging spectral domain optical coherence tomography* (EDI-SD-OCT) memberi imej keratan rentas koroid definisi tinggi yang membolehkan kita mengukur ketebalan koroid dan memberi kefahahaman yag lebih baik tentang proses patologi penyakit tersebut.

**Objektif:**

Objektif kami adalah membandingkan min ketebalan koroid subfovea antara ARMD awal, ARMD lewat dan kumpulan kawalan, serta membandingkan min ketebalan koroid subfovea antara ARMD neovaskular (nARMD), *polypoidal choroidal vasculopathy* (PCV) dan kumpulan kawalan. Selain itu, matlamat kami adalah untuk mengenalpasti faktor-faktor yang berkaitan dengan ketebalan koroid subfovea (data demografi dan ciri-ciri klinikal) dikalangan pesakit ARMD.

**Kaedah:**

Sebuah kajian keratan rentas telah dijalankan di klinik Oftalmologi Hospital Universiti Malaysia dan di klinik Oftalmologi Hospital Selayang dari Januari 2021 till Januari 2022. Kajian ini telah melibatkan pesakit ARMD (awal dan lewat) dan kumpulan kawalan. Ketebalan koroid diukur menggunakan mesin imbasan mata EDI-SD-OCT. Analisis statistik telah dilakukan dengan menggunakan SPSS Inc Versi 26.

**Keputusan:**

Seramai 144 pesakit telah direkrut ke dalam kajian dan seramai 143 telah dianalisa (ARMD awal: 48, ARMD lewat: 47, kumpulan kawalan: 48). Hasil kajian telah menunjukkan min ketebalan koroid subfovea adalah jauh lebih tinggi pada pesakit ARMD lewat (262.76 ± 68.80 $\mu$m) daripada pesakit ARMD awal (236 ± 28.18 $\mu$m, p=0.025) dan juga kumpulan kawalan (244.04 ± 25.76 $\mu$m). Min ketebalan koroid subfovea juga tinggi dengan ketara pada pesakit PCV (324 ± 32.13 $\mu$m) berbanding pesakit nARMD (200.17 ± 21.31 $\mu$m) dan kumpulan kawalan ($p<0.001$). Faktor-faktor berkaitan dengan ketebalan koroid subfovea adalah umur ($p=0.004$), kaum Melayu ($p=0.031$), nARMD ($p<0.001$) dan PCV ($p<0.001$).

**Kesimpulan:**

Penyelidikan ini menunjukkan bahawa terdapat perbezaan yang signifikan bagi min ketebalan koroid subfovea antara pesakit ARMD awal, ARMD lewat and kumpulan kawalan. Min ketebalan koroid subfovea didapati tinggi dengan ketara pada pesakit PCV berbanding pesakit nARMD dan kumpulan kawalan. Faktor-faktor yang berkaitan dengan ketebalan koroid subfoeva adalah umur, kaum Melayu, nARMD dan PCV. Pengukuran ketebalan koroid dengan mesin pengimbas mata OCT memberi sumbangan kepada kefahaman tentang patofisiologi ARMD serta menyediakan potensi biomarker yang tidak invasif dalam mengenalpasti subjenis dan menilai perkembangan penyakit ARMD.

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# CHAPTER 1

# INTRODUCTION

# 1. INTRODUCTION

## 1.1 Study Introduction

Age-related macular degeneration (ARMD) is the leading cause of blindness in developed countries (Bourne et al., 2013) which accounts for 8·7% of all blindness worldwide and is likely to increase with age. The number of individuals suffering from ARMD is estimated to increase up to 113 million by 2040, due to the rapid growing elderly population (Wong et al., 2014).

Ronald et al., classified ARMD into early and late. Early ARMD is defined as the presence of drusen with pigmentary abnormalities. Late ARMD is classified into geographical atrophy (GA) and neovascular ARMD (nARMD) (Klein et al., 1991). Geographic atrophy of late ARMD is characterised by geographic retinal atrophy involving foveal centre. Whereas, nARMD is characterised by presence of choroidal neovascularisation (CNV), serous and/or haemorrhagic detachment of the neurosensory retina, subretinal hard exudates, subretinal fibrosis and disciform scar. The main concern about nARMD is that the vision loss progress rapidly due to its main manifestations of CNV.

A study by Chakravarthy et al., showed there was a strong associations of ARMD with increasing age, active cigarette smoking, history of cataract surgery, and a family history of ARMD. Moderate risk factors were higher body mass index (BMI), history of cardiovascular disease, hypertension, and higher plasma fibrinogen (Chakravarthy et al., 2010).

Diagnosis of nARMD is confirmed based on a combination of fundus fluorescein angiography (FFA) and indocyanine green angiography (ICGA) according to evidence of hyperfluorescence

with late leakage associated with pigment epithelial detachment (PED) in the macular region, serous retinal detachment, subretinal exudation, and haemorrhage (Seddon et al., 2006).

Polypoidal choroidal vasculopathy (PCV) is a common subtype of exudative ARMD in Asian populations (C. W. Wong et al., 2016), reaching up to 60% of neovascular ARMD (nARMD) cases in East Asia (T. H. Lim et al., 2010). Meanwhile, CNV secondary to ARMD (CNV-ARMD) is the typical subtype in Western populations (C. W. Wong et al., 2016). They exhibit characteristics of CNV through blood leakage and sub-retinal haemorrhage at the macular region (Sharma et al., 2014). Although the two subtypes share common clinical features and risk factors, they have different epidemiological, history and clinical characteristics, and treatment outcomes (C. W. Wong et al., 2016).

Few studies have studied specific risk factors for PCV, compared to the considerable research on risk factors for ARMD. These findings imply that systemic variables for PCV and conventional ARMD are generally comparable. For instance, smoking is a consistent risk factor for both PCV and conventional ARMD (Cackett et al., 2011). Other studies showed that higher BMI is associated with PCV, as in typical ARMD (Woo et al., 2015).

Traditionally, ICGA has been used to diagnose PCV, however, a validated non-invasive diagnostic system has been developed to identify PCV-specific features using optical coherence tomography (OCT) and colour fundus photography (Fenner et al., 2022). This is supported by Cheung et al. as OCT results are more readily available and genuinely highly reliable (Chui Ming Gemmy Cheung et al., 2018).

Choroid plays an important role in the pathophysiology of many diseases affecting the retina. It provides blood supply to the RPE, outer retina and prelaminar portion of the optic nerve. A compromised volume or flow in its circulation could result in photoreceptor and RPE dysfunction. However, the choroid is one of the most difficult structures to image in vivo, because the RPE and choroid's pigments impede image captured by ophthalmoscopy, 1904 fundus photography, FFA, and conventional optical coherence tomography (OCT) (Kim et al., 2011).

Evaluation of the choroid using enhanced depth imaging optical coherence tomography (EDI-OCT) and swept source optical coherence tomography (SS-OCT) not only allows for quantification of choroidal thickness but also provides information about the anatomy and pathophysiology of the choroid (Gallego-Pinazo et al., 2014). The changes in the choroidal thickness help to determine the pathologic processes of various retinal diseases. Wood et al. reported that there was no significant difference in choroidal thickness between early ARMD and control. They postulated that choroidal thickness seems to be unaffected in early ARMD (Wood et al., 2011). For late ARMD, Chung et al. found that there was choroidal thinning in nARMD compared to control (Chung et al., 2011). They also found that there was increase in choroidal thickness compared to control in PCV. Thus, the recognition of an underlying choroidal thickness in neovascularised maculopathies may have important implications regarding their pathogenesis and management.

We aim to compare the subfoveal choroidal thickness in early ARMD, late ARMD and PCV, and to evaluate the factors affecting choroidal thickness among ARMD patients.

## 1.2 Study Rationale

In ARMD, vascular insufficiency which contributes to the changes in choroidal thickness may result in loss of RPE and photoreceptors. Improved in vivo visualization of the choroid and measurement of choroidal thickness using EDI-OCT is likely to enhance our understanding of several retinal diseases particularly ARMD and PCV.

EDI-OCT provides measurement of choroidal thickness which helps to determine disease's activity, monitor disease progression, differentiate between ARMD and PCV, and monitor the treatment response. Early detection of high risk early ARMD patients is important to prevent the blinding complication of the advanced diseases. Evaluation of associated factors in relation to choroidal thickness of ARMD patients will help in lifestyle modification in order to delay the progression of disease.

# CHAPTER 2

# LITERATURE REVIEW

## 2. LITERATURE REVIEW

### 2.1 Age-Related Macular Degeneration

ARMD is the leading cause of severe visual impairment and blindness worldwide, given with incidence ranging from 9 to 25% at ages between 65 and 75 years, leading to blindness of over 80% of affected individuals after the age of 70 years. The risk of developing advanced ARMD lesions is ten times higher in people over 85 years compared with those 70–74 years old (Jonasson et al., 2011).

ARMD can be categorised in a number of ways, even though it is most frequently classified by the presence or absence of abnormal neovascularization; exudative (wet) or non-exudative (dry) (Jonisch et al., 2011). ARMD can also be classified based on the extent of visual impairment; early and late (Klein et al., 1991). Early ARMD has multiple small lipid deposits called drusen (< 63 μm) and a smaller number of medium drusen (63-125 μm) under the retina, or mild pigmentation abnormalities of the RPE in at least one eye. Late ARMD is vision-threatening and it is categorised as either pure geographic atrophy involving the foveal centre or nARMD (Mehta, 2015).

Geographic atrophy is characterised by well circumscribed area of RPE atrophy. The atrophy which extends to the choriocapillaris and retina because these three layers are inseparably joined together (Vingerling et al., 1995).

Although nARMD is less common than the non-neovascular form, it carries a more guarded prognosis for vision. nARMD is characterised by the presence of CNV with subretinal fluid or haemorrhage, fluid or haemorrhage beneath the RPE, accompanied with ipsilateral detachment

of RPE, hard drusen, vitreous haemorrhage, a combination of the previous elements or geographic atrophy, and subretinal fibrosis (scar) in the final stages. Presence of CNV in nARMD can be detected as a grey membrane and formation of scar at final stage leads to severe visual loss (Jonisch et al., 2011).

Multimodal imaging FFA has historically been utilised to establish the diagnosis of nARMD. With the advent of technology, usage of fundus photography, OCT, FFA and ICGA has enabled us to differentiate the subtypes of CNV-ARMD, as well as to differentiate PCV from nARMD (Coscas et al., 2014).

OCT is employed to detect subtle sub-RPE and subretinal and retinal material (fluid, haemorrhage, exudates, fibrosis). FFA is particularly useful in identifying leakage from a CNV or pooling of an RPE detachment. Additionally, it aids in pinpointing the site of lesions, size, and for tracking disease activity, progression, and response to treatment. In atypical cases of nARMD, ICGA is helpful for diagnosis, in cases of idiopathic polypoidal choroidal vasculopathy, retinal angiomatous proliferation, or when the diagnosis is uncertain (Jonisch et al., 2011).

Increasing age, smoking, previous cataract surgery, and a family history of ARMD showed strong and consistent associations with late ARMD. Moderate risk factors were higher BMI, history of cardiovascular disease, hypertension, and higher plasma fibrinogen. Risk factors with weaker and inconsistent associations with ARMD were gender, ethnicity, diabetes, iris colour, history of cerebrovascular disease, and serum total and high-density lipoprotein cholesterol and triglyceride levels (Chakravarthy et al., 2010).

Smoking affects the pathogenesis of ARMD by promoting oxidative damage, inducing new vessels formation (angiogenesis), impairing the choroidal circulation, and by activating the immune system including the complement pathway (Ni Dhubhghaill et al., 2010).

RPE cells are vital for phagocytosis of shed photoreceptor rod outer segments. With increasing age, RPE function becomes less efficient and lead to incomplete degradation of shed photoreceptor rod outer segments or abnormal molecules. Progressive engorgement of RPE with these functionless residues is associated with the extrusion of aberrant materials which accumulate in Bruch's membrane and aggregate in the form of drusen and basal laminar deposits. These excretions contribute to the further deterioration of the RPE. Both basal laminar deposits and drusen cause a reduction in the permeability of Bruch's membrane, thus hinder the nutrients transport from choriocapillaries to the RPE and photoreceptors. It results in ischaemic insults to the RPE and responsible for secretion of vascular endothelial growth factors (VEGF) which contribute to the development of CNV as seen in neovascular late ARMD.

Aging also causes a 50% reduction in the thickness of choroidal vessels and an alteration of the sinusoid structure. A compromised volume or flow in its circulation could result in photoreceptor and RPE dysfunction and death.

## 2.2 Polypoidal choroidal vasculopathy

PCV which is a variant of neovascular AMD presents as a serosanguinous maculopathy (Honda, 2014). It has been established to affect both genders and is most frequently diagnosed in patients between the ages of 50 and 65 years. They discovered higher incidence rates in numerous Asian nations, approximately 23% to 54% in patients with presumed ARMD (Imamura et al., 2010).

PCV patients have unique clinical features, such as more distinct polypoidal lesions, fewer sub-retinal deposits of drusen, a higher risk of massive subretinal haemorrhage, and poorer responses to standard anti-vascular endothelial growth factor (VEGF) treatment, as compared with nARMD (T. H. Lim et al., 2010). PCV has been classified into two categories based on ICGA properties.; type 1 (polypoidal CNV) which is characterised by presence of polyp/s with well-defined BVN (both feeder and draining vessels) and type 2 (typical PCV); polyp with absent BVN (Honda et al., 2014; Kawamura et al., 2013).

The most typical SD OCT features in PCV include PED, double-layer sign, thickened choroid, and sometimes focal choroidal excavation. These features should alert a clinician of the possibility of PCV or in which ICGA is not accessible or performed routinely. In addition to assisting the diagnosis of PCV, SD OCT also is useful in monitoring the changes in subretinal fluid, PED, or both after therapy (Chui Ming Gemmy Cheung et al., 2018).

On FFA, PCV lesions resemble occult CNVM lesions, which can be misinterpreted for nARMD if they are at submacular region. A peripheral notch at the margin of a serous PED may provide a hint to the site of the polyp. RPE atrophy is manifested as window defects. Block fluorescence is caused by subretinal or sub-retinal pigment epithelium haemorrhage. FFA also

aids in eliminating other disparities, such as CNV, microaneurysms and retinal angiomatous proliferans (Tan et al., 2015).

In the EVEREST study, a PCV diagnosis was made on the basis of subretinal focal ICGA hyperfluoresence in the presence of at least one of the following: BVN; pulsatile polyp; nodular appearance on stereoscopic viewing; hypofluorescent halo; orange subretinal nodule on colour fundus photo; presence of massive submacular haemorrhage (Koh et al., 2012).

Even though ICGA is the essential modality for diagnosis of PCV, it is an invasive and time-consuming procedure that may not be available widely (Chui Ming Gemmy Cheung et al., 2018). Majority of studies used a combination of clinical findings and ICGA features in diagnosing PCV, as there is no universally accepted ICGA definition of PCV (C. W. Wong et al., 2016). Recently, the Asia Pacific Ocular Imaging Society (APOIS) PCV Workgroup assessed and verified diagnostic standard based on non-ICGA features for differentiating PCV from typical nARMD (Chui M.Gemmy Cheung et al., 2021).

De Salvo et al. reported that using a combination of three of the following four OCT based signs; multiple PEDs, sharp PED peak, PED notch, and rounded sub-RPE hyporeflective, PCV could be diagnosed with a sensitivity of of 94.6% and specificity of 92.9%. A sensitivity of 89.4% and specificity of 85.3% was discovered in another study using a combination of two of the following three signs; PED, double-layer sign, and thumb-like protrusion to detect PCV (de Salvo et al., 2014). This diagnostic system would be quite beneficial in medical facilities where ICGA is not always accessible.

## 2.3 Choroid

The choroid is a pigmented vascular tissue which extends from the ora serrata anteriorly to the optic nerve head posteriorly. Anatomically it forms the posterior portion of the uveal tract, which continues anteriorly with the ciliary body and the iris. From retina to sclera, the choroid comprises Bruch's membrane, the choriocapillaris, the medium diameter choroidal vessels (Sattler's layer), the large diameter vessels (Haller's layer), and suprachoroidal space (Figure 2.1). Microscopic examination shows the choroid has a mean thickness of 0.15 mm anteriorly and 0.22 mm posteriorly (Ryan, 2006).

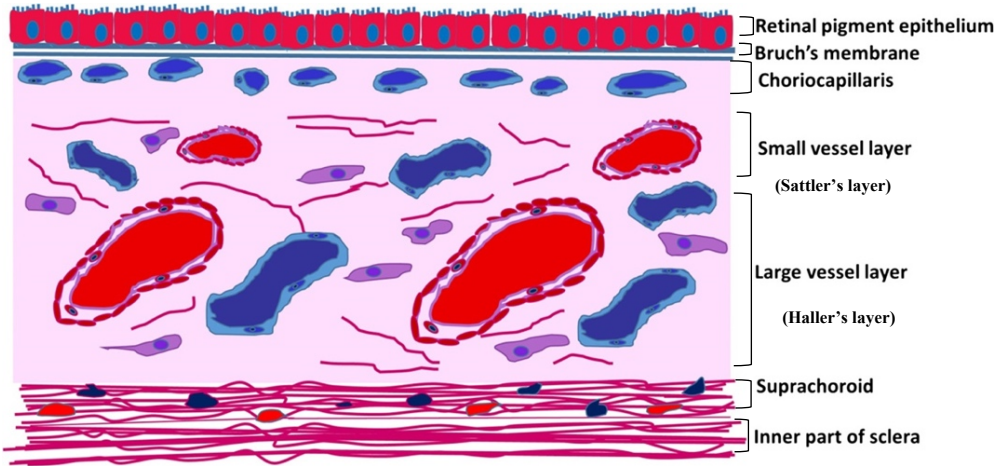


Figure 2.1: Layers of the choroid.

A healthy and functioning choroid is essential for retinal function as abnormal choroidal blood volume or compromised flow may result in photoreceptor and RPE dysfunction and death. The short posterior ciliary arteries (PCA) supply the posterior choroid and the peripapillary region, whereas long PCAs and the anterior ciliary artery supply the anterior parts of the choroid. The anterior ciliary artery is a branch from the ophthalmic artery which accompanies the rectus muscle anteriorly to supply the iris and the anterior choriocapillaris.

Venous drainage from the choriocapillaris is mainly through the vortex veins and also through the ciliary body and the anterior ciliary vein. The vortex veins drain into the inferior and superior ophthalmic veins and later through the superior and inferior orbital fissures as it exit the orbit (Ehrlich et al., 2016).

The choroid is thought to play a significant pathophysiologic role in macular diseases, however, it is one of the most difficult structures to image in vivo, due to the pigments in the RPE and choroid impede image capture by ophthalmoscopy, 1904 fundus photography, FFA and conventional OCT (Kim et al., 2011). Recent technological developments allow for measurement of the choroid layer with spectral-domain OCT, hence revealing new directions in the study of retinal diseases. Evaluation of the choroid using EDI-OCT and SS-OCT not only allows for quantification of choroidal thickness, but also provides information about the anatomy and pathophysiology of the choroid (Gallego-Pinazo et al., 2014).

## 2.4 Enhanced Depth Imaging-Optical Coherence Tomography (EDI-OCT)

OCT is a relatively new method that has enabled the acquisition cross-sectional images of the retina similar to ultrasound (B scan), but uses light waves instead of sound waves resulting in much higher resolution images. Technically, OCT is a partial coherence interferometer. Coherent light refers to light of a single wavelength, like laser light. Partially coherent light includes light of different wavelengths within a narrow range. The partially coherent light used in OCT is of a specific wavelength provided by a laser source (Wong et al., 2011).

The OCT technology used in routine practice is spectral domain (SD) OCT. Unlike the older Time Domain-OCT (TD-OCT), SD-OCT does not use a reference mirror; instead, light reflected from the various tissue layers is detected simultaneously by a high-speed spectrometer

and processed with a Fourier transform. The use of a spectrometer to detect light reflected from tissue allows SD-OCT instruments to acquire 20,000-52,000 A-scans per second and produce images with 5 µm resolution (Adhi and Duker, 2013). SD-OCT is a non-invasive imaging tool that is used commonly to assess retinal thickness, volume, and morphology in pathologic eyes (Domalpally et al., 2010). Recently, EDI-OCT developed to have a longer wavelength to evaluate the choroid and is useful as an additional tool for differentiating typical AMD and PCV (Jirarattanasopa et al., 2012). Figure 2.2 shows the normal retinal and choroidal anatomy using EDI-OCT.

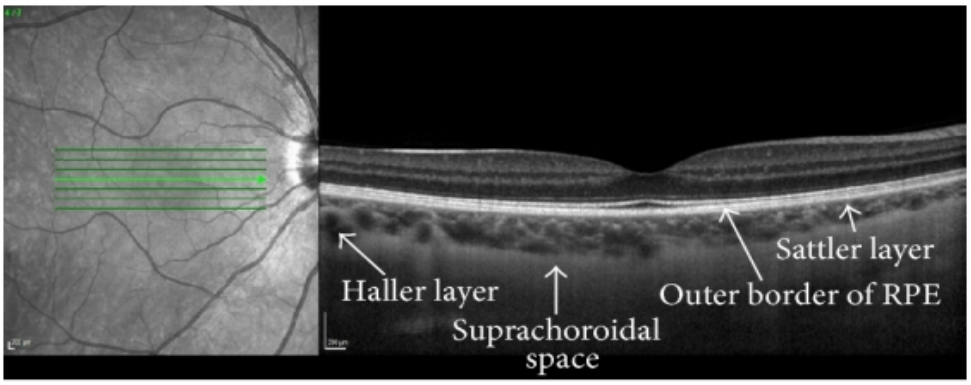


Figure 2.2: Enhanced Depth Imaging-Optical Coherence Tomography (EDI-OCT) using a Heidelberg Spectralis OCT (Heidelberg Engineering, Germany). (a) Near-infrared fundus image. (b) Corresponding EDI-OCT demonstrating normal retinal and choroidal anatomy at the macula (Baltmr et al., 2014).

## 2.5 Choroidal Thickness and Retinal Diseases

EDI-OCT can be used to obtain high-quality choroidal images for choroidal thickness and volume measurements including three-dimensional imaging. Choroidal volume measurement by manual segmentation using built-in automated retinal segmentation software on EDI Spectralis OCT is highly reproducible and repeatable and has a very small range of variability

(Chhablani et al., 2012). Although this measurement is currently performed manually on all devices, the intervisit, interobserver and intersystem agreement is very good, and highly reliable measurements can be obtained. The most common measurement used in daily practice is subfoveal choroidal thickness, by using the software's caliper tool to draw a line connecting the outer border of the RPE and the inner border of the sclera (Figure 2.3). The same tool can also be used to take thickness measurements at different points in the choroid (Koizumi et al., 2011).

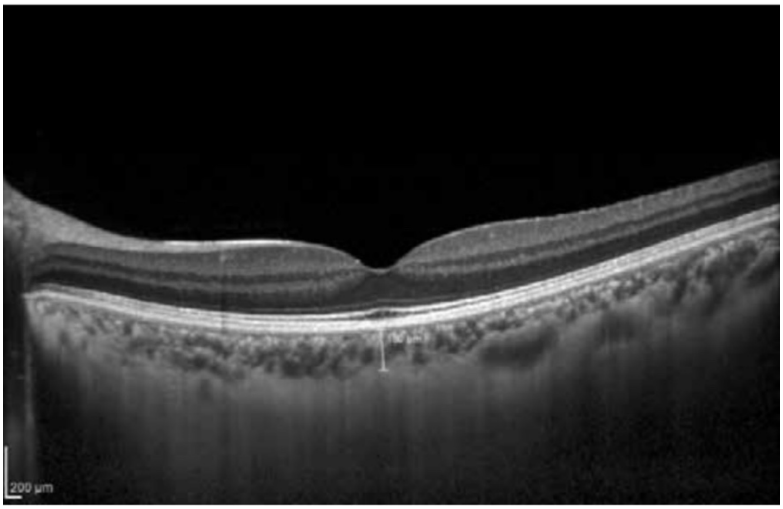


Figure 2.3: Choroidal thickness is measured manually as the vertical distance between the outer edge of the hyperreflective retinal pigment epithelium and the inner edge of the choroidoscleral junction (Sezer et al., 2016).

Choroidal thickness seems to vary topographically within the posterior pole. The mean subfoveal choroidal thickness was found to be between 272 ± 81 µm and 287 ± 76 µm in normal eyes (Spaide, 2009; Manjunath et al., 2010).

### 2.5.1 Diseases with Increased Choroidal Thickness

Retinal diseases with increased choroidal thickness include nARMD, PCV and central serous chorioretinopathy (CSCR). Koizumi et al. discovered thicker choroidal thickness in PCV patients which measured 293.4 ± 48.8 μm (Koizumi et al., 2011) (Figure 2.4).

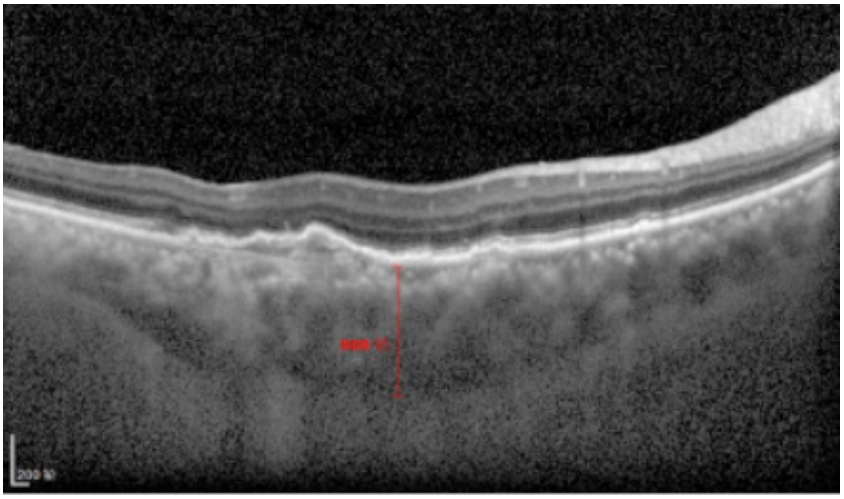

Figure 2.4: Subfoveal choroidal thickness is remarkably increased in Polypoidal choroidal vasculopathy (PCV) (Chui Ming Gemmy Cheung et al., 2018).

### 2.5.2 Diseases with Decreased Choroidal Thickness

Ocular diseases with decreased choroidal thickness include nARMD, pathological myopia, and idiopathic macular hole (Xie et al., 2021).

Clinical studies by Jonas et al. and Yiu et al., have shown that choroidal thickness in patients with advanced ARMD is thinner than the control group, which reflects the degree of choroidal atrophy (Jonas et al., 2014; Yiu et al., 2015). A study by Manjunath and colleagues discovered that the mean subfoveal choroidal thickness was 194.6 ± 88.4 μm in the nARMD group and 213.4 ± 92.2 μm in the dry ARMD group (Manjunath et al., 2011) (Figure 2.5 & Figure 2.6).

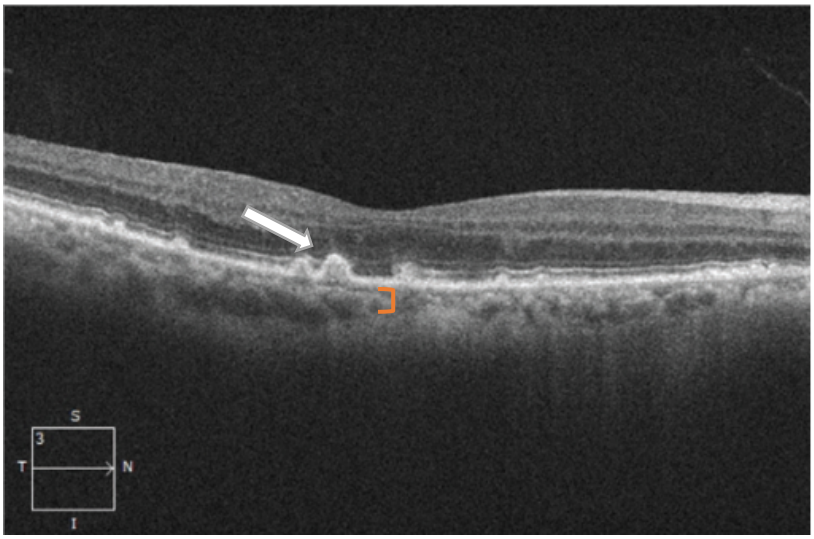


Figure 2.5: Subfoveal choroidal thickness in early age-related macular degeneration with drusen (white arrow).

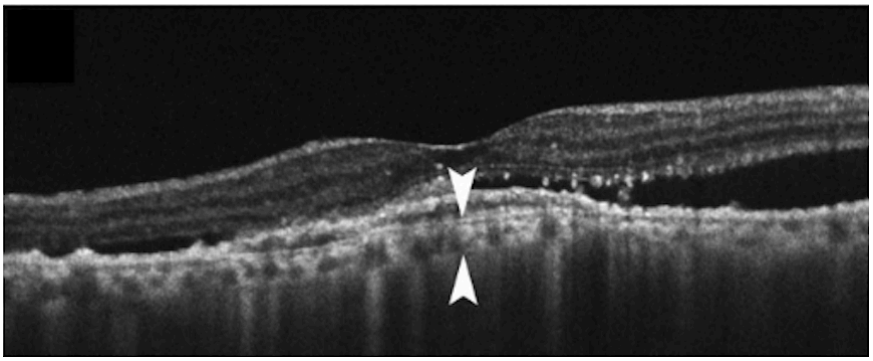

Figure 2.6: Subfoveal choroidal thickness is thinner in neovascular ARMD (white arrows)

Thus, the recognition of an underlying choroidal thickness in retinal diseases may have important implications regarding their pathogenesis and management.

# CHAPTER 3

# OBJECTIVES

# 3. OBJECTIVES

## 3.1 Objectives

3.1.1 General Objectives

To evaluate the subfoveal choroidal thickness and its associated factors among the ARMD patients.

3.1.2 Specific Objectives

i. To compare the mean subfoveal choroidal thickness between early ARMD, late ARMD and control group.

ii. To compare the mean subfoveal choroidal thickness between nARMD, PCV and control group.

iii. To identify the associated factors (demographic data and clinical characteristics) of subfoveal choroidal thickness among ARMD patients.

## 3.2 Research Questions

3.2.1 Is there any significant difference of mean subfoveal choroidal thickness between early ARMD, late ARMD and control group?

3.2.2 Is there any significant difference of mean subfoveal choroidal thickness between nARMD, PCV and control group?

3.2.3 What are the associated factors (demographic data and clinical characteristics) of subfoveal choroidal thickness among ARMD patients?

### 3.3 Research Hypotheses

3.3.1 There is a significant difference of mean subfoveal choroidal thickness between early ARMD, late ARMD and control group.

3.3.2 There is significant difference of mean subfoveal choroidal thickness between nARMD, PCV and control group.

3.3.3 The demographic data and clinical characteristics are the factors associated with subfoveal choroidal thickness in ARMD patients.

# CHAPTER 4

# RESEARCH METHODOLOGY

# 4. RESEARCH METHODOLOGY

## 4.1 Study Design

A comparative cross-sectional study was conducted in the Ophthalmology Clinic Hospital Universiti Sains Malaysia (USM) and Ophthalmology Clinic Hospital Selayang from January 2021 till January 2022. The study population involved all ARMD patients attending Ophthalmology Clinic Hospital USM and Hospital Selayang during the study duration and fulfilled the selection criteria. A control group of non-ARMD patients, who attended Ophthalmology Clinic Hospital USM and Hospital Selayang were recruited in the study for comparison.

## 4.2 Ethical Approval

This study was conducted after approval by the local Human Research Ethics Committee (Universiti Sains Malaysia [USM]/ Jawatankuasa Etika Penyelidikan Manusia [JEPEM]; Registration Number: 20030156] (Appendix A), and National Medical Research Ethics Committee (MREC) [KKM/NIHSEC/P20-2532(12)]; Registration Number: 53998] (Appendix B), with the highest respect for subjects according to the study protocol, the ethical principles that have their origin in the Declaration of Helsinki, and the International Conference on Harmonisation (ICH) – Harmonised Tripartite Guideline for Good Clinical Practice (GCP).

## 4.3 Selection Criteria

The study group included newly diagnosed patients with early and late ARMD, and PCV aged 45 years old and above. Any ARMD patients who have received treatments (anti-VEGF or photodynamic therapy or retinal photocoagulation or intravitreal Steroid), any patients with retinopathy or maculopathy such as diabetic retinopathy or myopic maculopathy were

excluded. Other ocular exclusion criteria were: (a) History of ocular surgery e.g., vitrectomy and cataract surgery in the last 6 months, (b) History of ocular trauma e.g., corneal laceration or traumatic choroidal rupture, (c) ocular media that obscure OCT assessment e.g., cataract or vitreous haemorrhage and (d) patients with refractive error -6.0D power or more.

For the control group, the non-ARMD patients, aged 45 and more with the same exclusion criteria as the study group were selected.

### 4.4 Sample Size Estimation

This study involved 3 group of patients; the early ARMD, late ARMD and control group. Sample size for each group was calculated accordingly.

**Objective 1: To compare the mean subfoveal choroidal thickness between Early ARMD, Late ARMD and Control group.**

The sample size was calculated based on ANOVA formula using G*Power software version 3.1.9.2 (Copyright 1992-2014 by Franz Faul), accessible for free download via the website http://www.gpower.hhu.de/en.html. Level of significance, α of 0.05 and power of 0.8.

α – level of significance : 0.05

β – power of study : 0.8

Standard deviation (SD) : 66 (Yoon et al, 2016)

Effect size : 0.30

Number of groups : 3

Sample size = 37 for each group

Total = 111 patients (Early ARMD: 37, Late ARMD: 37, Control: 37).

**Objective 2: To compare the mean subfoveal choroidal thickness between nARMD, PCV anc control group.**

The sample size was calculated based on two mean formula using G*Power software version 3.1.9.2 (Copyright 1992-2014 by Franz Faul), accessible for free download via the website http://www.gpower.hhu.de/en.html. Level of significance, α of 0.05 and power of 0.8.

α – level of significance : 0.05

β – power of study : 0.8

SD (standard deviation)

Mean group 1 : 184.36 (Saito et al., 2015)

Mean group 2 : 250.03 (Lee et al., 2017)

Effect size : 0.60

Number of groups : 2

Sample size = 44 for each group

Total sample size: = 44 x 3 + 10%

= 144 patients (Early ARMD: 48,

Late ARMD: 48, Control: 48)