## COVER LETTER OF EDITED MANUSCRIPT

Date: 27th February 2022

To The Editor,

## VISION JOURNAL

I am enclosing herewith a manuscript entitled "CHOROIDAL THICKNESS IN CORRELATION WITH AXIAL LENGTH AND MYOPIA DEGREE". We would like to inform you that we have revised our manuscript based on academic editor and reviewers' suggestion. Here are we attached point by point response:

Comment/question: Can the authors address the concerns raised by reviewer 2? Response:

Thank you very much for your kind information/question.

Due to <u>reviewer 2 comment in round 1</u>, there are three questions/comments for us:

Point 1 = Introduction, line 32: Although both statements, that myopia is more likely to occur at young age and more frequent in people who are for example microscopists, it should be formulated differently. As it currently stands, it reads as if young people often work as microscopists.

For this comment, we have made a sentence change from "myopia is more likely to occur at young age and more frequent in people who are for example microscopists" become "Myopia is more likely to occur in several condition such as young age (mostly 8 to 15 years old), hereditary person with myopic parent, and persons who work extensively with the eyes such as microscopists, computer users, or university students" (manuscript line 33-35).

Point 2 = Materials and methods section: The authors should add, as stated at the end of the manuscript, that informed consent was obtained, that the study was approved by an IRB and that the study adhered to the Declaration of Helsinki. The authors should also mention which software was used for statistical analysis.

We have added a sentence regarding the ethical statement according to the reviewer's input on the manuscript in line 109-112. It was stated that the study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee for Medical Research of Hasanuddin University (Approval No.: 751/UN 4.6.4.5.31 /PP36/2021).

Point 3 = Table 3: It would be of interest for the readers if a figure showing the most relevant correlations could be provided.

We have added "figure 5" as a form of visualization that shows the correlation between choroidal thickness with axial length and choroidal thickness with myopia degree.

## Point 4 = Maybe it would also be of interest to have a control group with no myopia.

We have already added the examinations result of 10 healthy subjects (20 eyes) as control group. The results are presented in table 1 (line 135-136). We also attach normal OCT photo for figure 1 and figure 2 (line 125 and 130).

### All comments above were replied in round 1 of review.

Furthermore, due to reviewer 2 comment in round 2, there are two questions/comments for us:

- 1. When looking at the categories for myopia, I think it should be: low ( $\geq$  -3.0 dpt), moderate (<-3.0 to  $\geq$  -6.0 dpt) and high (<-6.0 dpt). I think the authors forgot about the "minus" sign, therefore "higher" values would mean "smaller" numbers.
- 2. Although the authors now included a control group as asked for by the referees, they did not include the control group in the statistical analysis in Table 1, since there seems to be no change in p-values. In addition, the control group was not added to the other analyses (i.e. Table 2). This should be clarified and justified in the "Methods" section on statistics or the control group should be part of the analysis set.

We have already replied it as our response to reviewer and explained that:

- 1. For question number one, we were agreed with the reviewer 2 statement in the first comment and have already changed the myopia categories in our manuscript line 111 to 112 from "Low (≤ -3.00 D), moderate (-3.25 to -6.00 D), and high (> -6.00 D) myopias" become "Low (≥-3.00 D), moderate (<-3.00 to ≥-6.00D) and high (<-6.00 D) myopias".
- 2. For question number two, we have already retested the statistics on our manuscript data. These changes can be seen in table 1 (line 133-134) and in table 2 (line 156-157). In addition, we also did a change in table 3 (line 166-167) and figure 5 to synchronize the data results.

However, based on your last email, we then made a correction to the measurement unit in the myopia category which was previously written "D" to become "dpt" according to the reviewer's suggestion (manuscript line 111-112).

In our opinion, these answers have represented the instructions and requests of reviewer 2 comments in the previous round 1 and 2 evaluation. It also means that we have already addressed all concerns raised by reviewer 2.

If there any misunderstanding from us regarding your question or instructions in this section, please give us a further email reply.

Thank you for your kind attention and guidance.

Best regards,

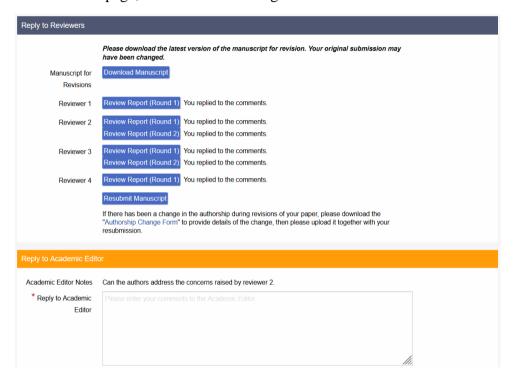
## Andi Muhammad Ichsan

#### REPLY TO ACADEMIC EDITOR

Dear Editor,

Thank you very much for your kind information.

We have already visited the manuscript with the referee reports at this link: <a href="https://susy.mdpi.com/user/manuscripts/resubmit/4162a9fabf5ab650a04d1e847a751b72">https://susy.mdpi.com/user/manuscripts/resubmit/4162a9fabf5ab650a04d1e847a751b72</a>. We only found that there is an academic editor note and there is no any new review report from the reviewers. On the web page, it looks like the image below:



Although, your question is "Can the authors address the concerns raised by reviewer 2?" Response:

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Thank you for your kind attention and guidance.

Best regards,

Andi Muhammad Ichsan





Autial

# CHOROIDAL THICKNESS IN CORRELATION WITH AXIAL LENGTH AND MYOPIA DEGREE

Habibah Setyawati Muhiddin<sup>1</sup>, Andi Ratna Mayasari<sup>1</sup>, Batari Todja Umar<sup>1</sup>, Junaedi Sirajuddin<sup>1</sup>, Ilhamjaya <del>Patellongi<sup>2</sup> Patellongi<sup>2</sup></del>, Itzar Chaidir Islam<sup>1</sup>, Andi Muhammad Ichsan<sup>1</sup>\*

Ophthalmology Department, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia; <sup>2</sup>Physiology Department, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia;

Abstract: Background: Myopia is a condition in which the visual images come to a focus in front of the retina of the eye. This disease is a major cause of visual disability which present in 108 million persons globally. A major cause of visual disability is myopia. It occurs when there is an excessive and continuous expansion of the axial length (AL), resulting in a change in the secondary fundus leading to visual impairment, choroidal neovascularization, retinal detachment, zonal areas of chorioretinal atrophy, myopic macular schisis and hole. Purpose: This study aims to determine the relationship between the degree of myopia, the axial length, and the choroidal thickness (CT). Methods: This is an observational analytical study that made use of a cross-sectional design. A total of 49 59 participants with refractive errors, underwent treatment at Hasanuddin University Hospital and 69-116 eyes were measured and analyzed. The choroidal thickness was measured using the Enhance Depth Imaging OCT (EDI-OCT) tool which is divided into nine observational areas. Furthermore, all data obtained were compared using statistical analysis such as the one-way ANOVA and Pearson correlation test (p<0.05). Results: There was a significant relationship between the choroidal thickness with axial length (p,0.05), and myopia degrees (p<0.05). Conclusions: The thickness of the choroid decreases with an increase in the axial length and degree of myopia which further indicates that the higher the myopia degree the thinner the choroidal vasculature.

Keywords: Choroidal thickness; Myopia; Axial length

Citation: Muhiddin HS et al. CHOROIDAL THICKNESS IN COR-RELATION WITH AXIAL LENGTH AND MYOPIA DEGREE. Vision 2022, 6, x.

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#### 1. Introduction

Myopia, also known as shortsightedness, is a major cause of visual disability around the world. In 1972 and 2004, the prevalence of myopia increased from 25 to 44% in the United States while in Asia, the prevalence is approx. >80%.(1) In 2010, it was noted that the uncorrected refractive error was the major cause of vision impairment and the second most frequent cause of blindness affecting 108 million persons globally. Furthermore, the cases of myopia are expected to increase by more than 5000 million by 2050.(2)

Myopia is more likely to occur in several condition such as young age (mostly 8 to 15 years old), hereditary person with myopic parent, and persons who work extensively with the eyes such as microscopists, computer users, or university students. Myopia is more likely to occur within the ages of 8 and 15 and it is prevalent in persons who work extensively with the eyes such as microscopists. (1,3) According to the World Health Organization, the major cause of vision impairment and blindness around the world are macular degeneration, vitamin A deficiency, infectious disease, uncorrected refractive error with cataracts, and myopia. (4)

Furthermore, myopia has been classified according to anatomical and pathological features, the age of onset, the rate of progression, the degree and theory of development. Physiological myopia occurs when the refractive components of the eye fail to correlate,

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Vision 2022, 6, x FOR PEER REVIEW 2 of 14

unlike pathologic myopia (alternatively, malignant or degenerative myopia) which occurs when the optical system of the eye lies outside the limit of normal biological variations. According to degree, myopia can be grouped into low (<3.00 D), medium (3.00 D 5.00 D), and high (>5.00 D).(5)

According to Okafor et al. (2009), the degree of myopia is could be divided into 3 categories; very low (<-1,0 D), low ( $\ge$  -1 to  $\le$ -3.00 D), moderate (>-3.00 to <-6.00 D), high (>-6.00 D to  $\le$ -10D) and very high (>-10D) myopias.(6)

Myopia and refractive-error disorder may develop when there are irregular contributions of the ocular components to the eye structures. Four structures that contribute to the refractive status of a given human eye are aqueous and vitreous humor, cornea, and lens. When the lens and cornea fail to neutralize the axial length (AL) shortening or elongation, hyperopia or myopia may occur. Therefore, some parameters such as the anterior chamber depth (ACD), corneal curvature, vitreous chamber depth, axial length and, lens thickness are widely analyzed when studying eye diseases. However, among these components, more attention is paid to the axial length which is the major parameter for both hyper myopia and myopia.(7) Furthermore, studies have shown that the alteration of environmental factors and the identification of genetic correlations may play a significant role in axial elongation, myopia progression, and future ocular complications.(8,9)

Myopia is known to be the cause of multiple eye fatalities around the globe and investigation conducted on a particular population in various hospital have shown that when the axial length or refractive error is ~26.5 mm or ~8.00 D, the parapapillary atrophy and optic disc becomes enlarged gradually. However, when these values are higher, the prevalence of glaucomatous optic neuropathy and myopic retinopathy is increased. Myopia is identified as the excessive and continuous expansion of the axial length, resulting in a change in the secondary fundus which leads to visual impairment, as well as choroidal neovascularization, retinal detachment, zonal areas of chorioretinal atrophy, myopic macular schisis, and hole.(10)

In high myopic eyes, recent changes start in the choroid therefore, studies have shown that the choroid is a very valuable structure that is required in the pathophysiology of high myopia.(11) The choroidal vasculature helps nourish the outer retina (including the photoreceptors), however, when there is a loss of the vascular tissue and an extreme thinning of the choroid, it leads to visual impairment and damage to the photoreceptors. The thickness of the choroidal is an essential parameter used for studying the pathogenesis of high myopia.(12) Furthermore, measurement of CT in vivo is suitable for determining the onset of diseases and their progression which causes thinning of the choroidal.(13) The presence of lacquer cracks and choroidal neovascularization (CNV) is seen mostly in eyes with thinner macular choroids.(14) Therefore, this study aims to determine the relationship between the degree of myopia, the axial length, and the choroidal thickness.

#### 2. Materials and Methods

#### 2.1 Study design

This is an observational analytical study that made use of a cross-sectional design. A total of 59 participants were included. There are 49 patients with refractive errors and underwent treatment at Hasanuddin University Hospital and 10 normal subjects as a control group. A total of 116 eyes were measured and analyzed. In this study, our criteria for recruiting subjects were patients aged 20-50 years, had a refractive error  $\geq$  0.5D, did not suffer from anterior segment abnormalities during examination, no history of eye infection or eye surgery. A total of 49 participants with refractive errors, underwent treatment at Hasanuddin University Hospital and 69 eyes were measured and analyzed. Each patient who meets the criteria was asked to fill out and sign an informed consent form after then examined according to applicable standards.

Vision 2022, 6, x FOR PEER REVIEW 3 of 14

#### 2.2 Ophthalmology examination

The examination was carried out by measuring the patient's visual acuity and correction using a Snellen chart projector, trial lens, and retinoscopy. The results obtained from retinoscopy were in the form of a spherical equivalent (SE). The anterior segment of the eye was then examined with a slit lamp biomicroscope, then the patient was made to undergo an indirect funduscopic examination with a 90D ocular lens to view the posterior segment of the eye. Subsequently, the length of the patient's eyeball axis was obtained using A-Scan Ultrasound which measures from the top of the cornea to the posterior segment, and the results were represented in millimeters (mm). The choroidal thickness was measured using the Enhance Depth Imaging OCT (EDI SD-OCT) tool which is divided into nine observation areas. The type of OCT used is Heidelberg Spectralis® OCT (3-mode), Germany. It was carried out by 2 technicians (two graders) then the results were blindly confirmed by the research team (HSM and AMI). It-The test was performed semi-automatically by drawing a perpendicular line between the outermost part of the hyper-reflective line that represents the RPE with the hypo-reflective line that represents the choroid-scleral surface using a calipers software tool.

#### 2.3 Data analysis and interpretation

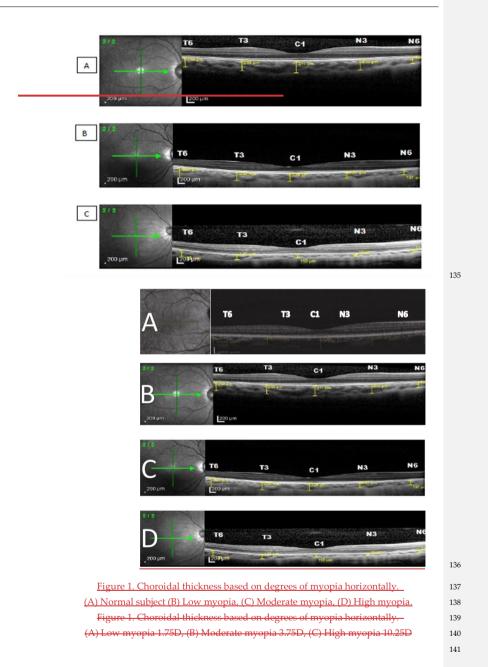
All results obtained were recorded and compared using SPSS for windows ver. 24.0 using the with One-way ANOVA and Spearman-Pearson correlation test (sig. p<0.05) which was represented in tables and figures. The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee for Medical Research of Hasanuddin University (Approval No.: 751/UN 4.6.4.5.31 /PP36/2021).

#### 3. Results

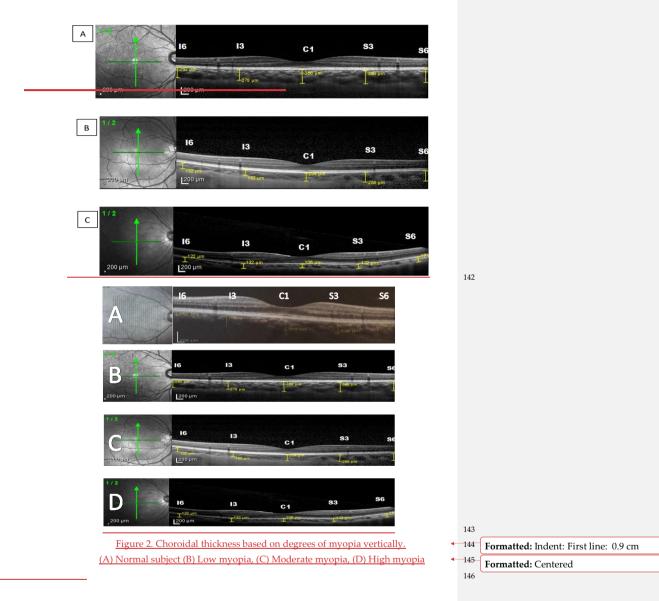
The degree of myopia is divided into 3 categories;  $low (\le 3.00 \, D)$ , moderate (  $3.25 \, lov (\le -6.00 \, D)$ , and high (>  $6.00 \, D$ ) myopias  $low (\ge -3.00 \, dpt)$ , moderate (<- $3.00 \, lov \ge -6.00 \, dpt$ ) and high (<- $6.00 \, dpt$ ) myopias. This was compared with the choroidal thickness found in various areas of the macula. The result obtained showed a significant difference except for the 1.5 mm temporal region (T3) (Table 1). This result indicates a significant relationship between the choroidal thickness and the degree of myopia. A high degree myopia showed a thinner choroidal vasculature.

From the horizontal image (Fig.1), the choroid found in the low myopia is thickest in the subfoveal unlike in medium and high myopia where it is thickest in the temporal. The thinnest area in all groups was the nasal area. Vertically (Fig.2), in low and moderate myopia, the choroid is thickest in the superior area while in high myopia it is thickest in the subfoveal area. The thinnest area in each group was the inferior region. Comparison of the choroidal thickness based on the axial length showed a significant difference (p<0.05), except for the superior region (S6).

Vision 2022, 6, x FOR PEER REVIEW 4 of 14



Vision 2022, 6, x FOR PEER REVIEW 5 of 14



Vision 2022, 6, x FOR PEER REVIEW 6 of 14

> Figure 2. Choroidal thickness based on degrees of myopia vertically. (A) Low myopia 1.75D, (B) Moderate myopia 3.75D, (C) High myopia 10.25D

Table 1. Comparison of choroidal thickness and the degrees of myopia

Choroidal	Myopia degree (D)				
Thickness based on area (Mean ± SD) µm	Normal (n=20)	Low myopia (n=50)	Moderate myopia (n=31)	High myopia (n=15)	р
C=Sub Fovea	296.70±69.62	307.52±79.30	253.39±64.84	267.33±104.01	<u>0.021</u> <del>0.010</del>
T6=Temporal 3	273.35±46.82	280.22±76.18	255.06±47.20	231.07±59.52	0.0470.028
T3=Temporal1.5	295.45±66.94	298.12±78.30	262.58±54.02	267.80±83.84	<u>0.136</u> <del>0.076</del>
N3=Nasal 1.5	274,15±71.70	252.50±64.89	208.23±48.70	196.07±89.16	<u>0.001</u> <del>0.002</del>
N6=Nasal 3	219.25±77.72	173.00±50.72	151.06±47.20	132.33±77.61	<u>0.001</u> <del>0.027</del>
S6=Superior 3	319,90±84,54	306.02±72.50	269.13±56.69	258.67±89.28	0.0390.022
S3=Superior 1,5	299,40±76,45	314.18±80.06	261.52±52.95	257.73±93.38	0.0080.003
I3=Inferior 1.5	293.95±77.33	307.12±71.74	249.97±62.72	244.73±76.31	<u>0.001</u> < <del>0.001</del>
I6=Inferior 3	278,50±86,19	282.04±62.99	237.84±47.31	226.00±65.93₩	0.003 <del>0.001</del>

<sup>\*</sup>One-way Anova test

The mean choroid thickness of the short\_normal (<22.5 mm), medium (22.5 to 25.0 mm) and long (>25.5 mm) axis in the horizontal section (Fig.3) were thickest in the fovea, while the thinnest in each group was found in the nasal area. Furthermore, vertical measurement (Fig.4) on the short normal axis, showed that the thickest area is on subfoveal area while on the medium and long axis it is thickest in the superior area. The thinnest area in the  $\frac{1}{2}$  short  $\frac{1}{2}$  and medium axis groups was the inferior region, while for the long axis it was the sub fovea area.

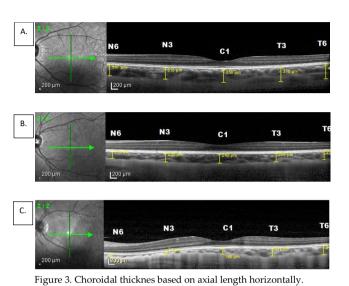
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Vision 2022, 6, x FOR PEER REVIEW 7 of 14



(A) Short axis-Normal axis (22,47 mm)<sub>2</sub> (B) Medium axis-(23,75 mm), (C) Long axis (27,60 mm)

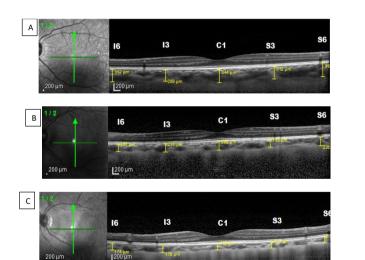


Figure 4. Figure 3. Choroidal thicknes based on axial length vertically.

(A) Short axis Normal axis (22,47 mm) (B) Medium axis (23,75 mm), (C) Long axis (27,60 mm)

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Vision 2022, 6, x FOR PEER REVIEW 8 of 14

Table 2 showed that there is a significant correlation between choroidal thickness and axial length (p<0,05), except on S6 area. This indicates that the thickness of the choroid decreases with increasing axial length.

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Vision 2022, 6, x FOR PEER REVIEW 9 of 14

Table 2. Comparison of choroidal thickness and axial length

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Coroidal thickness based on area (Mean±SD) μm	Short Normal Moderate (n=7481) (n=46)		Long (n= <u>1829</u> )	p*
C=Sub Fovea	329.50±27.28	291.62±76.94 <del>294,04</del>	253.28±86.84	<u>0.029</u> 0.002
	345,00±16,31	±79,83	227,89±77,30	
T6=Temporal 3	315.17±75.89	269.99±62.44 <del>270,20</del>	236.34±55.72	0.0060.001
	34 <del>7,25±73,3</del>	±65,20	222,22±51,0	
T3=Temporal 1,5	320.00±37.06	285.42±71.87 <del>289,12</del>	261.76±70.54	<u>0.120</u> <del>0.020</del>
	328,75±35,76	<del>±75,56</del>	241,83±55,25	
N3=Nasal 1,5	288.17±42.97	241.38±67.44 <del>233,09</del>	206.52±71.63	0.0100.008
	307±39,43	±65,93	<del>196,89±68,55</del>	
N6=Nasal 3	216.83±60.60	171.73±60.47 <del>160,69</del>	147.93±62.65	<u>0.029</u> <del>0.001</del>
	247,25±49,14	±52,17	<del>135,44±55,50</del>	
S6=Superior 3	327.00±40.71	298.06±78.31 <del>291,73</del>	262.45±72.23	0.0490.074
	332,75±49,25	±71,58	255,83±74,45	
S3=Superior 1,5	320.83±36.40	298.53±76.42 <del>298,03</del>	256.14±79.89	0.0240.006
	<del>336±31,76</del>	±76,48	238±76,04	
I3=Inferior 1,5	310.50±45.47	293.37±73.36 <mark>287,24</mark>	239.79±68.67	0.0020.008
	330,5±41,06	<del>±73,33</del>	233,22±70,31	
I6=Inferior 3	278.33±64.76	274.07±67.91264,58	225.48±56.06	0.0030.012
	311,25±14,7	±63,82	224,5±52,34	

\*One-way ANOVA test

Table 3 shows the correlation coefficient between the axial length of the eyeball and the thickness of the choroid (r= 0.270-453) which is higher than the degree of myopia (r= 0.230-407).

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Vision 2022, 6, x FOR PEER REVIEW 10 of 14

Table 3. Correlation between axial length, degree of myopia and choroidal thickness in various regions

iii various regions					
Choroidal	Axial lengt	h (mm)	Myopia degree (D)		
Thickness based on area (Mean±SD) µm	Coefficient correlation (r)	p*	Coefficient correlation (r)	p*	
C=Sub Fovea	<u>-246</u> -0,400	<u>0.008</u> < <del>0,001</del>	<u>-175</u> -0,274	0.0600.003	
T6=Temporal 3	<u>-293</u> -0,385	<u>0.001</u> < <del>0,001</del>	<u>-180</u> -0,317	<u>0.053</u> <del>0.001</del>	
T3=Temporal1,5	<u>-190</u> -0,307	<u>0.041</u> < <del>0,001</del>	<u>-124</u> -0,230	<u>0.186</u> <del>0.012</del>	
N3=Nasal 1,5	<u>-278</u> -0,427	0.0030,001	<u>-347</u> -0,361	<0.001<0.001	
N6=Nasal 3	<u>-238-0,343</u>	<u>0.010</u> < <del>0,001</del>	<u>-368</u> -0,332	<0.001<0.001	
S6=Superior 3	<u>-288-0,270</u>	<u>0.014</u> <0,001	<u>-248</u> -0,300	<u>0.007</u> <del>0.002</del>	
S3=Superior 1,5	<u>-249</u> -0,389	0.0070,004	<u>-227</u> -0,308	<u>0.014</u> 0.001	
I3=Inferior 1,5	<u>-310</u> -0,453	<u>0.001</u> < <del>0,001</del>	<u>-284</u> -0,388	<u>0.002</u> <0.001	
I6=Inferior 3	<u>-289</u> -0,431	<u>0.002</u> < <del>0,001</del>	<u>-299</u> -0,407	<u>0.001</u> <0.001	

<sup>\*</sup>Pearson correlation test

The choroidal thickness showed a significant relationship (p<0.05) with the axial length and degree of myopia found in various areas of the macula and this has a negative correlation coefficient; Therefore, means, the longer the axis of the eyeball the higher the degree of myopia which will lead to choroidal thinning (Fig.5).

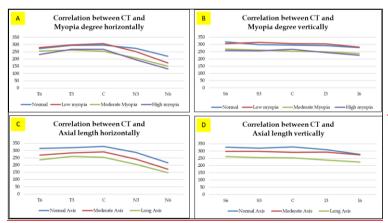


Figure 5. (A, B) Correlation between choroidal thickness and myopia degree (C, D) Correlation between choroidal thickness and axial length.

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Vision 2022, 6, x FOR PEER REVIEW 11 of 14

#### 4. Discussion

Historically, some opticians have thought that myopia is a hereditary abnormality, whereas others have imagined it to be environmentally induced. However, several studies conducted on animals and humans over the last four decades have suggested that the occurrence of myopia is controlled by both genetic and environmental factors.(3)

The comparison between the degrees of myopia and choroidal thickness showed a significant correlation (p<0.05) that indicates that a higher degree of myopia will lead to thinning of the choroidal layer. Moreover, the mean choroidal thickness obtained by OCT examination was based on the degree of myopia found in the horizontal area. The low degree myopia was found to be thickest in the sub\_foveal area, while the moderate and high degree myopia was thickest in the temporal region. The thinnest choroid was found in the nasal area of all degrees of myopia. Study by Shin (2012) reported that the choroid become thinner about 13.62  $\mu$ m for each diopter of refractive error and also decreased about 1.31  $\mu$ m for each year of age.(15)

Based on studies conducted, it is known that the thinning of the choroid reduces ischemia and perfusion of the choroid which leads to the upregulation of the angiogenic factors in the eyes and this may also lead to the formation of myopic choroidal neovascularization and other features of macular degeneration.(16)

In a cross-sectional study by El-Shazly *et al.* (2017) Macular CT was measured in different degrees of myopia and in normal control eyes, and a similar result was obtained which is significantly lower in myopes than in emmetropes. Moreover, it varies by location, where the thickest CT in low myopic eyes, is found in the sub-foveal area, while the thinnest is located in the nasal region. However, for eyes with moderate myopia, the thickest is found in the temporal region while the thinnest region remained in the nasal direction.(17)

Another study by Deng *et al.* (2018) showed that the mean CT in the perifoveal, parafoveal, and central foveal regions where  $215 \pm 50 \, \mu m$ ,  $227 \pm 60 \, \mu m$ , and  $229 \pm 65 \, \mu m$  respectively while the mean spherical equivalent (SE) of the patient was  $-1.71 \pm 2.22$  diopter (D) (range from -7.63 to 4.25 D). Furthermore, the mean global peripapillary choroidal thickness (PPCT) was  $136 \pm 33 \, \mu m$ .(18)

Based on the result obtained from different studies carried out on animals, an alteration in the thickness of the choroid may occur when maintaining a clear vision. Earlier studies on macaques, marmosets, and chicks have led to the hypothesis which states that the thickening of the choroid may occur when myopic defocus is induced due to changes in the position of the retina when maintaining a clear vision. This is possible because, in myopic defocus, the retina is at the back of the image plane so when thickening of the choroid occurs it moves the retina forward.(11)

Furthermore, this study also indicates that an increase in axial length leads to a decrease in the thickness of the choroid. (Table 2). Moreover, the choroidal thickness showed a significant relationship (p<0.05) between the axial length and the degree of myopia found in various areas of the macula that has a negative correlation coefficient. Therefore, this indicates that the longer the axis of the eyeball and the higher the degree of myopia the more choroidal thinning will occur.

In general, the Axial length increases rapidly at the early stage of life but slowly in adulthood and decreases in old age.(7) According to Lee *et.al* (2020) the best-corrected visual acuity (BCVA), baseline axial length, anterior chamber depth, and age were significantly associated with changes in axial length (p=0.005, p<0.001, p=0.006, and p=0.045 respectively).(19)

Furthermore, the choroid may stimulate axial growth by regulating the remodeling of the scleral extracellular matrix, which is important for emmetropization during eye

Vision 2022. 6. x FOR PEER REVIEW 12 of 14

formation. In experimental animals induced with hyperopia and myopia, a change in the thickness of the choroid exceeds that of axial length and scleral remodeling.(12)

According to histologic, clinical, and population-based investigations, it was shown that an increase in axial elongation led to a significant thinning of the choroid. Furthermore, in emmetropic subjects, the mean CT was 250  $\mu$ m while in highly axially myopic patients it decreases to <30  $\mu$ m. Therefore, this indicates that an increase in the axial elongation led to a decrease in the distance between the Bruch membrane and sclera.(17)

Based on Jin et al. (2016), the myopic retinas were thinner than those of emmetropic or hyperopic subjects, especially in the superior parafoveal and all 4 perifoveal subfields (P<.05). But, the results of previous studies on factors influencing the thickness of the ganglion cell layer and nerve fiber layer have been conflicting. While some suggested that the thickness of the ganglion cell layer and peripapillary nerve fiber layer is correlated with spherical equivalent refraction and axial length in adults, others did not observe this relationship.(12)

Karahan (2013) reported that choroidal change plays a major role in the development and progression of many retinal disease. Thickening of the choroid could affect the nutrition supply to the retina, because outer retina layer is nourished by the choroidal vasculature. Thus, choroidal thickness provides useful information to clinicians (20)

An increase in the axial length led to an increase in the retina thickness which aid in blood supply. This, however, caused an increase in length of the ocular axis resulting in a compensatory thickening of the choroidal capillary layer in the fovea centralis and an increase in the number of capillaries and volume. Moreover, an increase in the myopia degree will cause the axial length of the eye to increase as well. However, the retina may fail to compensate causing the capillary layer and choroid to become thinner.(21)

### 5. Conclusions

There was a significant correlation between the degree of myopia and choroidal thickness. Therefore, a higher degree of myopia will cause a decrease in the thickness of the choroid. Furthermore, it is necessary to screen for choroidal thickness in myopic patients using SD-OCT, especially in moderate and high degrees to prevent complications, because a significant increase in myopia degree will lead to a decrease in the choroidal thickness. Also, it is necessary to measure the length of the eyeball axis in myopic patients because a decrease in choroidal thickness is significant to the elongation of the eyeball. All of these examinations are to prevent some further complication such as the progressivity of myopic choroidal neovascularization (CNV) which will eventually lead to worsening of vision.

Author Contributions: HSM, ARM, AMI: Conception and design of the work, performing the medical examination, analysis and interpretation of data, drafting the work. BTU, JS, IP, AMI: performing the medical examination, giving Giving supervision and quality control of the medical examination as a team, review and editing of the manuscript draft. ICI: project administration, drafting the work and revising it for publication.

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**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee for Medical Research of Hasanuddin University (Approval No.: 751/UN 4.6.4.5.31 /PP36/2021).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

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Vision 2022, 6, x FOR PEER REVIEW 13 of 14

Data Availability Statement: The data that support the findings of this study are available from the 301 corresponding author upon reasonable request. 302 303 Acknowledgments: All authors would like to thank and appreciate the team of nurses and staff of 304 Hasanuddin University Hospital who were involved in the preparation, examination and follow up 305 of our patients. We also thank Goodlingua for English preparation review. 306 307 Conflicts of Interest: The authors declare no conflict of interest. 308 References 309 Kaur K, Gurnani B, Kannusamy V. Myopia: Current concepts and review of literature. ◆ 1. 310 TNOA J Ophthalmic Sci Res. 2020;58(4):280. 311 Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global 312 Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 313 Ophthalmology [Internet]. 2016;123(5):1036-42. Available 314 http://dx.doi.org/10.1016/j.ophtha.2016.01.006 315 3. Cooper J, Tkatchenko A V. A Review of Current Concepts of the Etiology and 316 Treatment of Myopia. Eye Contact Lens. 2018;44(4):231-47. 317 Fredrick DR. Myopia. Br Med J. 2002;324(7347):1195-9. 4. 318 Kaiti R, Shyangbo R, Sharma IP, Dahal M. Review on current concepts of myopia and 5 319 its control strategies. Int J Ophthalmol. 2021;14(4):606-15. 320 Okafor M, O FO, I EB. Myopia: a Review of Literature Aetiology Progression of 321 Myopia. Niger J Med. 2009;18(2):134-8. 322 7. Meng W, Butterworth J, Malecaze F, Calvas P. Axial length of myopia: A review of 323 current research. Ophthalmologica. 2011;225(3):127-34. 324 Pugazhendhi S, Ambati B, Hunter AA. Pathogenesis and prevention of worsening 325 axial elongation in pathological myopia. Clin Ophthalmol. 2020;14:853-73. 326 Yotsukura E, Torii H, Ozawa H, Hida RY, Shiraishi T, Corso Teixeira I, et al. Axial length and prevalence of myopia among schoolchildren in the equatorial region of 328 brazil, I Clin Med. 2021:10(1):1-11. 329 10 Teberik K. Kaya M. Retinal and Choroidal Thickness in Patients with High Myopia 330 without Maculopathy. Ocul Immunol Inflamm. 2017;25(2):1438-9. 331 Lee GY, Yu S, Kang HG, Kim JS, Lee KW, Lee J-H. Choroidal Thickness Variation 11. According to Refractive Error Measured by Spectral Domain-optical Coherence Tomography in Korean Children. Korean J Ophthalmol. 2017;31(2):151. 334 Jin P, Zou H, Zhu J, Xu X, Jin J, Chang TC, et al. Choroidal and Retinal Thickness in 12. 335 Children with Different Refractive Status Measured by Swept-Source Optical 336 Coherence Tomography. Am J Ophthalmol [Internet]. 2016;168:164-76. Available 337 from: http://dx.doi.org/10.1016/j.ajo.2016.05.008 13. Fujiwara T, Imamura Y, Margolis R, Slakter JS, Spaide RF. Enhanced Depth Imaging 339 Optical Coherence Tomography of the Choroid in Highly Myopic Eyes. Am J 340 Ophthalmol 2009:148(3):445-50. [Internet]. Available 341 http://dx.doi.org/10.1016/j.ajo.2009.04.029 342 Wang S, Wang Y, Gao X, Qian N, Zhuo Y. Choroidal thickness and high myopia: A

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Vision 2022, 6, x FOR PEER REVIEW 14 of 14

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## **FIGURES**

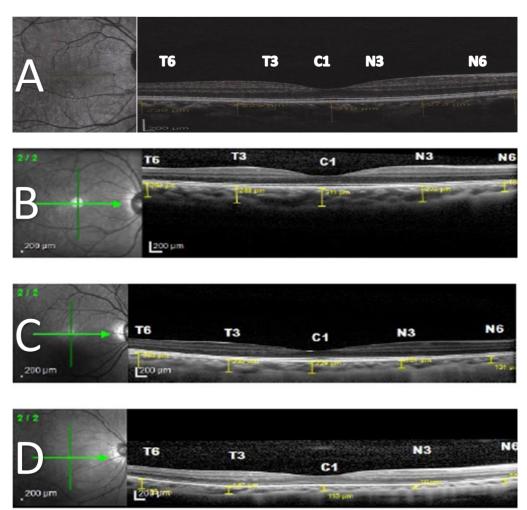


Figure 1. Choroidal thickness based on degrees of myopia horizontally. (A) Normal subject (B) Low myopia, (C) Moderate myopia, (D) High myopia.

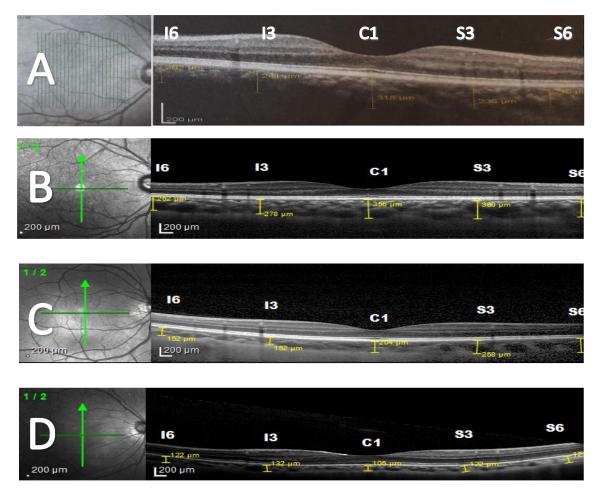
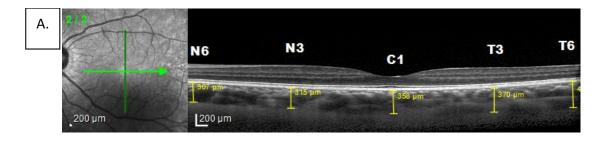
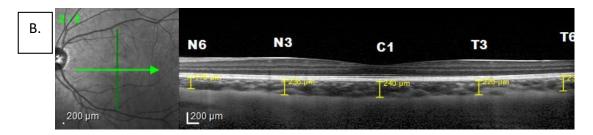


Figure 2. Choroidal thickness based on degrees of myopia vertically. (A) Normal subject (B) Low myopia, (C) Moderate myopia, (D) High myopia





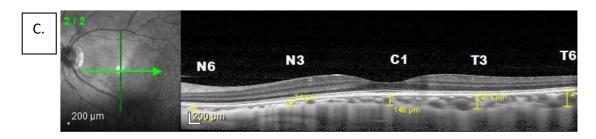


Figure 3. Choroidal thicknes based on axial length horizontally. (A) Normal axis(22,47 mm) (B) Medium axis (23,75 mm), (C) Long axis (27,60 mm)

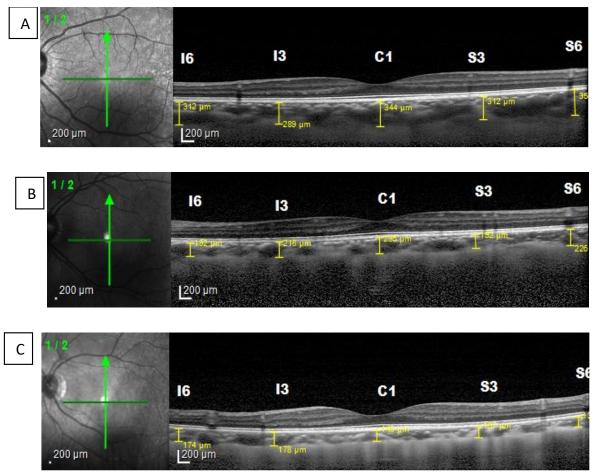


Figure 4. Figure 3. Choroidal thicknes based on axial length vertically. (A) Normal axis(22,47 mm) (B) Medium axis (23,75 mm), (C) Long axis (27,60 mm)

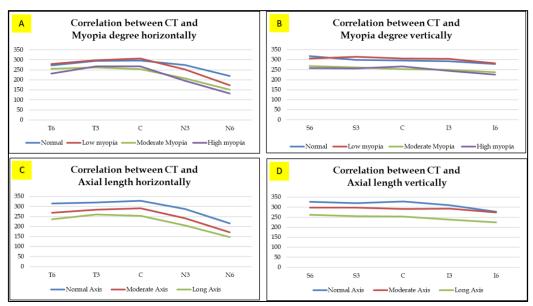


Figure 5. (A, B) Correlation between choroidal thickness and myopia degree (C, D) Correlation between choroidal thickness and axial length.