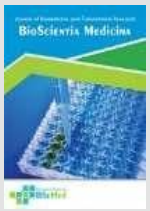
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Comparison of Subfoveal Choroidal Thickness Values with Severity of Diabetic Retinopathy in Type 2 Diabetes Mellitus Patients

Sandiyanto[1*], Weni Helvinda[1], Kemala Sayuti[1]

[1]Department of Ophthalmology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

ARTICLE INFO

Keywords:
Diabetic retinopathy
Subfoveal choroidal thickness
Severity

***Corresponding author:**
Sandiyanto

E-mail address:
sandi081088@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v6i13.653

A B S T R A C T

Background: Changes in choroidal thickness may be associated with increased severity of diabetic retinopathy and may occur simultaneously or even earlier than diabetic retinopathy. This study aims to compare the value of subfoveal choroidal thickness (SCT) with the severity of RD in patients with type 2 DM without RD with NPDR at Dr. M. Djamil General Hospital Padang, Indonesia. **Methods:** This research is a cross-sectional analytic observational study. The study was conducted on 36 eyes obtained from 29 study subjects. Data analysis was performed with the help of SPSS to determine the ratio of SCT thickness in diabetic retinopathy patients, $p<0.05$. **Results:** The thickest mean SCT value was found in the type 2 DM group without RD (328.78 + 14.78 μm) and the thinnest in the severe NPDR group (234,22 + 12,30 μm). **Conclusion:** The more severe the severity of diabetic retinopathy, the thinner the SCT (subfoveal choroidal thickness).

1. Introduction

Diabetic retinopathy (RD) is a microvascular complication of DM affecting the retinal blood vessels, which is the leading cause of visual impairment in middle age and the elderly in the United States. Data from the World Health Organization (WHO) in 2015 stated that around 1.9% of visual impairment and 2.6% of blindness occurred globally due to RD, the biggest cause of which was type 2 DM. Research analysis of 35 studies that collected data on the prevalence of RD Worldwide in 1980-2008, the prevalence of RD in DM patients was around 93 million (34.6%) people, with 28 million (10.2%) of them experiencing Vision Threatening Diabetic Retinopathy (VTDR). One of the causes of visual impairment in DM patients is retinal microvasculature abnormalities. However, some cases show visual acuity does not match or is worse than the severity of the RD suffered. Diabetic choroidopathy is thought to be related to the decrease in visual acuity because the choroidal vascular ischemia causes hypoxia in the RPE tissue and retinal photoreceptors. In addition, the overexpression of vascular endothelial growth factor (VEGF) due to ischemia also plays a role in the process of forming diabetic macular edema (DME).[1-4]

The assessment of choroidal structure related to the involvement of diabetic choroidopathy was previously carried out through histological examination, indocyanine green angiography (ICGA),

and Doppler flowmetry. However, this examination is still limited in interpreting the choroidal vasculature.[5,6] Optical coherence tomography (OCT), as an examination tool with a non-invasive imaging technique, is able to provide cross-sectional images of intraocular tissue quantitatively with high resolution. The application of enhanced depth imaging (EDI) to spectral domain-optical coherence tomography (SD-OCT) can show a detailed view of the choroidal layer structure. The EDI-OCT application also provides a caliper to measure the thickness of the choroid and is able to show the sclera-choroid boundary more clearly by increasing the sensitivity setting of the examination of the sclera.[7-10] A study measured choroidal thickness in healthy subjects using EDI-OCT and found that choroidal thickness decreases with age. In addition, the thickness of the choroid was found to be thickest in the subfoveal, thinner in the temporal, and thinnest at the nasal side. Along with the increasing use of OCT, various studies of measuring choroidal thickness have been carried out to determine its association with other ocular abnormalities.[11-14]

Changes in choroidal thickness may be associated with increased severity of RD and may occur simultaneously or even earlier than RD. Therefore, this study aims to compare the value of subfoveal choroidal thickness (SCT) with the severity of RD in type 2 DM patients without RD with NPDR at Dr. M. Djamil General Hospital Padang, Indonesia.

2. Methods

This study is an observational study with a cross-sectional approach. The study was conducted in the Eye and Internal Medicine section of the General Hospital. Dr. M. Djamil General Hospital Padang, which was held in February 2022-September 2022. A total of 36 eyes from 29 research subjects participated in this study, where research subjects met the inclusion criteria: new patients or controls who had been diagnosed with type 2 DM by a specialist in Internal Medicine, who came or were consulted to the Eye polyclinic of the Dr. M. Djamil General Hospital Padang, the research subject is willing to participate in the study and undertakes to comply with the rules of the examination to be carried out, the age of the research subject is 40-60 years, on fundus examination, the posterior segment is normal or found signs of NPDR based on the ETDRS criteria, intraocular pressure $\leq$ 21 mmHg, the c/d ratio $\leq$ 0.6, and the difference in the c/d ratio between the two eyes $\leq$ 0.2. This study has been approved by the medical and health research ethics committee of Dr. M. Djamil General Hospital Padang, Indonesia.

This study collects socio-demographic data of research subjects in the form of age, gender, and address. The study also assessed the clinical eye, namely visual acuity, anterior segment conditions, intraocular pressure, and posterior segment conditions. SCT measurements are carried out using the app-enhanced depth imaging (EDI) on SD-OCT with the HD 1-5 Line Raster method. SCT examination was carried out in a dark room with a time span between 09.00-15.00 WIB. The method of examination is by asking the patient to sit facing the OCT, placing the chin and forehead on the backrest, and making the patient's sitting position as comfortable as possible. The patient is asked to look at the fixation point in the form of green light. Next, the examiner optimizes and captures when the OCT screen is focused. The best OCT results with signal strength $\geq$ 6 were saved. SCT was measured perpendicularly below the fovea using the calipers provided on the app EDI-OCT with the inner border of the RPE hyperreflexivity and the outer limit of the inner hyperreflexivity of the sclera.

Data processing is done computerized in the form of tables and the average standard deviation. The results of the study are presented in the form of categorical data assessing the severity of diabetic retinopathy in type 2 DM patients and numerically assessing the thickness of the choroid. Categorical variable data is presented in terms of frequency and percentage, while numerical variables are presented in tabular form with a mean and standard deviation. After that, the data was analyzed using SPSS 25. The research data were tested for normality of the data and then analyzed using the one-way ANOVA test if the

data were normally distributed with the significance of the test results based on the p value<0.05. If the one-way ANOVA test obtained significant results, a post hoc test was carried out to see the comparison between groups.

3. Results

Age of research subjects between 50-60 years more than the age of 40-49 years with 63.8%. Of the 29 research subjects, the most gender was female, namely 16 people (55.17%). Then, based on the duration of suffering from DM in each study group, the group without RD had a known mean length of time suffering from the shortest DM, namely 4.78 ± 1.98, and the severe NPDR group with a known mean duration longest sufferer of DM is 9.11 ± 3.01 years, (Table 1).

Table 1. Characteristics of RD severity in type 2 DM patients based on age, gender, and long-known suffering from DM.

Variable	Frequency (n)	Percentage (%)
Age		
40-49 years	13	36.2
50-60 years	23	63.8
Gender		
Male	13	44.83
Female	16	55.17
	Mean (years)	**Standard Deviation (SD)**
Long-known suffering from DM		
Without RD	4.78	1.98
Mild NPDR	5.89	1.69
Moderate NPDR	7.44	2.45
Severe NPDR	9.11	3.01

Table 2. Characteristics of the severity of RD in type 2 DM patients based on visual acuity and time of EDI-OCT examination.

Severity of RD									
Visual acuity (BCVA)	**Without RD**		**Mild NPDR**		**Moderate NPDR**		**Severe NPDR**		**Total**
	N	%	N	%	N	%	N	%	
20/20-20/30	8	88.9	7	77.8	5	55.6	2	22.2	22 (61.1)
20/40-20/60	1	11.1	2	22.2	4	44.4	6	66.7	13 (36.1)
20/70-20/200	0	0.0	0	0.0	0	0.0	1	11.1	1 (2.8)
Total	9	100.0	9	100.0	9	100.0	9	100.0	36 (100.0)
Examination time (WIB)									
09.00-11.00	3	33,3	2	22.2	2	22.2	2	22.2	9 (25.0)
11.01-13.00	3	33.3	3	33.3	2	22.2	2	22.2	10 (27.7)
13.01-15.00	3	33,3	4	44.5	5	55.6	5	55.6	17 (47.3)
Total	9	100.0	9	100.0	9	100.0	9	100.0	36 (100.0)

Based on Table 2, it can be seen that the characteristics sharp the time and duration of the EDI-OCT examination in each study sample group. The results showed that the best visual acuity (BCVA) was mostly between 20/20-20/30 in 22 samples (61.1%). Visual acuity in the type 2 DM group without RD, mild NPDR, and moderate NPDR obtained the most between 20/20-20/30, namely 8 samples (88.9%) in the group without RD, 7 samples (77.8%) in the mild NPDR group, and 5 samples (55.6%) in the

moderate NPDR group. In contrast, the type 2 DM group with severe NPDR obtained the most visual acuity between 20/40-20/60, namely in 6 samples (66.7%). Based on the time of the EDI-OCT examination, most examinations were carried out between 13.01-15.00 WIB, namely on 17 samples (47.3%). Type 2 DM group without RD underwent EDI-OCT examination as much as between time groups with 3 samples each. In contrast, the type 2 DM group with mild NPDR, moderate NPDR, and severe NPDR underwent EDI-OCT examination at most between 13.01-15.00 WIB with 4 samples (44.5%) in the mild NPDR group, 5 samples (55 .6%) in moderate NPDR, and 5 samples (55.6%) in severe NPDR.

Table 3. The mean value of SCT in patients with type 2 DM is based on severity RD.

Severity RD	**Average SCT value (μm)**	***p-value****
Without RD	328,78 + 14,78	-
Mild NPDR	300,11 + 11,79	0,001
Moderate NPDR	264,11 + 16,93	0,000
Severe NPDR	234,22 + 12,30	0,000

*Post hoc, Bonferroni test VS without RD, p<0.05.

Table 3. SCT values vary with mean SCT values are the thickest in the type 2 DM group without RD (328,78 ± 14,78 μm) and the thinnest in the severe NPDR group (234,22 ± 12,30 μm). In this study, it was found that the SCT values were getting thinner in proportion to the severity of the NPDR severity.

4. Discussion

Chronic hyperglycemia in DM patients is thought to cause changes in choroidal vascularization, including pericytic and vascular endothelial damage, narrowing of the vascular lumen, decreased choroidal blood flow, tissue hypoxia, to choroidal capillary atrophy resulting in choroidal thinning in proportion to the increase in RD severity.[15] The results of this study follow the study where the value of SCT decreases in proportion to the severity of RD severity. The mean values of SCT in each group were DM without RD (216,22 ± 72,46 μm), mild NPDR (213,57 ± 68,24 μm), moderate NPDR (211,91 ± 77,39 μm), severe NPDR (178,47 ± 61,47 μm), and PDR (168,15 ± 61,47 μm), the results were statistically significant in all groups ($p < 0.001$) compared to the control group in healthy people (223,40 ± 89,38 μm). The study conducted on Chinese residents between the ages of 40-89 years used SS-OCT in 1,027 healthy people as control and 1,250 types 2 DM patients.[16,17] When compared to this study, the study obtained a thinner average of SCT values and greater standard deviation in groups with the same variable. This can be caused by several factors, such as a larger age range of patients (40-89 years), the higher mean age of 68.06 ± 7.12 years, using different types of OCT. It can also be because it is carried out on different ethnicities. The results of this study are also consistent with the results of other studies that conducted SCT examinations on ethnic Indians. SCT examination using EDI-OCT in the age range of 43-73 years with a mean of 57.0 ± 9.37 years. The mean value of SCT decreases with the increasing severity of RD. The SCT values in the group without RD were 267.3 ± 51.8 μm, the NPDR group 248.0 ± 56.3 μm, and the PDR group 243,9 ± 56,2 μm.[18]

Another study showed different results from this study, where the SCT value in patients with mild-moderate NPDR (244,6 ± 77,0 μm) was thinner than the group without RD (262,3 ± 68,4 μm), but in the severe NPDR (291,1 ± 107,7 μm) and PDR (363,6 ± 74,9 μm) groups, the SCT values were thicker with statistically significant results. However, from the 195 eye samples in his study, 67 of them had DME. Samples with DME also obtained thicker SCT values than samples without DME ($p<0.05$). SCT thickening in RD patients with advanced severity as a result of tissue ischemia that produces cytokines, including

VEGF, causes dilatation of choroidal blood vessels, increases choroidal blood flow, and enlarges capillary lumen size.[19]

Another study found differences in SCT scores of DME patients, where EDI-OCT examinations were performed on the same patients with DME and after improvement, before and after receiving intravitreal anti-VEGF injections. In this study, the SCT value of DME patients was found to be thicker than after DME improvement ($p<0.001$). The mechanism of changes in SCT values in patients with type 2 DM is still under debate, with mixed findings in previous studies. Various factors mentioned can affect choroidal vasculature. Although still under debate, ischemic tissue factors and the role of VEGF are thought to be the main factors that cause changes in SCT values in DM patients. Recent studies are also still being developed to find out various things that can cause changes in SCT values in DM patients.[20]

Currently, with the widespread development of OCT, assessment of the choroid can be performed using OCT angiography (OCTA). OCTA can be used as an examination to determine the severity of RD or follow-up therapy in RD patients. Another study that monitored SCT using OCTA in PDR patients before and after treatment with an intravitreal anti-VEGF injection or laser photocoagulation found statistically significant attenuation of SCT. In another study, SCT examination using EDI-OCT and foveal avascular zone using OCTA. Although the results of the study did not find a correlation between SCT and the foveal avascular zone, this study has shown a new method to determine the association of SCT changes in patients with type 2 DM.[21]

5. Conclusion

The more severe the severity of diabetic retinopathy, the thinner the SCT (subfoveal choroidal thickness).

6. References

1. Ogurtsova K, da Rocha FJD, Huang Y, Linnenkamp U, Guariguata L, et al. IDF diabetes atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract. 2017; 128: 40-50.
2. Care D, Suppl SS. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care. 2020; 43: 14-31.
3. Cantor LB, Rapuano CJ. Retinal vascular disease: Diabetic retinopathy. In: Retina and vitreous: Basic and Clinical Science Course. San Francisco; 2019-2020; 91-120.
4. Sayin N, Kara N, Pekel G. Ocular complications of diabetes mellitus. World J Diabetes. 2015; 6(1): 92-108.
5. Balaji R, Duraisamy R, Santhosh KMP. Complications of diabetes mellitus: A review. Drug Invent Today. 2019; 12(1): 98-103.
6. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012; 35(3): 556-64.
7. Flaxman SR, Bourne RRA, Resnikoff S, Ackland P, Braithwaite T, et al. Global causes of blindness and distance vision impairment 1990–2020: a systematic review and meta-analysis. Lancet Glob Heal. 2017; 5(12): 1221-34.
8. Klein R, Klein BEK. The epidemiology of diabetic retinopathy In: Retina. 5th ed, Vol. 2. USA: Elsevier. 2012; 907-24.
9. Kusuhara S, Fukushima Y, Ogura S, Inoue N, Uemura A. Pathophysiology of diabetic retinopathy: The old and the new. Diabetes Metab J. 2018; 42(5): 364-76.
10. Yang QH, Zhang Y, Zhang XM, Li XR. Prevalence of diabetic retinopathy, proliferative diabetic retinopathy and non-proliferative diabetic retinopathy in Asian t2dm patients: A systematic review and meta-analysis. Int J Ophthalmol. 2019; 12(2): 302-11.
11. Wiley HE, Ferris FL. Non-proliferative diabetic retinopathy and diabetic macular edema. In:

Retina. 5th ed, Vol. 2. USA: Elsevier; 2012; 940-68.
12. Antonelli DA, Klein R, Gardner TW. Diabetic retinopathy. N Engl J Med. 2012; 366: 1227-39.
13. Fetriyanita S, Hendriati, Helvinda W. Relationship of long-suffering with type 2 diabetes mellitus with retinal ganglion cell layer thickness and retinal nerve fiber layer in patients without diabetic retinopathy. Thesis. Padang: Faculty of Medicine, Universitas Andalas; 2018; 1-63.
14. Huang X, Zhang P, Zou X, Xu Y, Zhu J, et al. Thinner average choroidal thickness is a risk factor for the onset of diabetic retinopathy. Ophthalmic Res. 2020; 63(3): 259-70.
15. El Ghonemy K, Rajab G, Ibrahim A, Gohar II. Comparison between choroidal thickness in patients with diabetic retinopathy and normal individuals using enhanced-depth imaging spectral-domain optical coherence tomography. Delta J Ophthalmol. 2018; 19(1): 53.
16. Ambiya V, Kumar A, Baranwal VK, Kapoor G, Arora A, et al. Change in subfoveal choroidal thickness in diabetes and in various grades of diabetic retinopathy. Int J Retin Vitr. 2018; 4(1): 1-7.
17. Kim JT, Lee DH, Joe SG, Kim JG, Yoon YH. Changes in choroidal thickness in relation to the severity of retinopathy and macular edema in type 2 diabetic patients. Investig Ophthalmol Vis Sci. 2013; 54(5): 3378-84.
18. Sudhalkar A, Chhablani JK, Venkata A, Raman R, Rao PS, et al. Choroidal thickness in diabetic patients of Indian ethnicity. Indian Journal of Ophthalmology. 2016; 63: 912-6.
19. Mathis T, Mendes M, Dot C, Bouteleux V, Bentaleb ZM, et al. Increased choroidal thickness: a new indicator for monitoring diabetic macular edema recurrence. Acta Ophthalmol. 2020; 98: 968-74.
20. Ren Q, Yu H, Li L. Analysis of choroidal thickness in patients with proliferative diabetic retinopathy by optical coherence tomography angiography. Pak J Med Sci. 2021; 37(7): 1943-7.
21. Ghassemi F, Berijani S, Babeli A, Faghihi H, Cholizadeh A, et al. The quantitative measurements of choroidal thickness and volume in diabetic retinopathy using optical coherence tomography and optical coherence tomography angiography; correlation with vision and foveal avascular. BMC Ophthalmology. 2022; 22(3): 1-11.