Evaluation of Retinal Vessel Diameter Measurement in Coronary Artery Disease

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ABSTRACT

Purpose: To examine the relationship between the stage of coronary artery disease (CAD) and retinal vessel diameters in patients with stable angina pectoris (SAP) and diagnosed with CAD.

Material and Methods: Patients with a diagnosis of CAD are divided into 3 stages according to the results of coronary angiography. Stage 1) Normal coronary artery; stage 2) Non-critical narrowing of coronary arteries (<70% stenosis); stage 3) 70% and above critical narrowing in coronary arteries. The diameters of retinal vascular structures were measured by Optical Coherence Tomography. The relationship between retinal arteriole, venule diameters and arterio-venous ratio (AVR) with CAD stage was evaluated.

Results: One hundred six eyes of 106 CAD patients (36 patients in stage 1, 40 patients in stage 2, and 30 patients in stage 3) were studied (P = 0.539). Demographic characteristics of the groups were similar (P> 0.05). In stage 1, the mean diameter of the retinal arterioles was 119.77 ± 7.24, and the venules were 142.44 ± 7.10; 118.77 ± 6.69 um and 143.01 ± 6.67 in stage 2, 104.60 ± 5.17 and 144.73 ± 12.45 um in stage 3, respectively. There was a significant difference between stage 1-3 and stage 2-3 (P = 0.730; P <0.001; P <0.001, respectively). There was no significant difference in venule diameter between the groups (P>0.05). The mean AVR was 0.84 ± 0.04 in stage 1, 0.83 ± 0.02 in stage 2, 0.72 ± 0.01 in stage 3, and there was a significant difference between stage 1-3 and stage 2-3 (P = 0.301; P<0.001; P <0.001, respectively). It was found that there was a negative and significant correlation between arteriolar diameter and AVR with CAD stage (r = -0.665, P <0.001, r = -0.717, P <0.001, respectively).

Conclusions: It was found that as the CAD stage increased, there was a significant decrease in arteriole diameter and AVR value and a tendency to increase in venule diameter.

Keywords: Coronary Artery Disease, Optical Coherence Tomography, Retinal Vessel Diameter.

INTRODUCTION

Coronary artery disease (CAD) is a disease accompanied by atherosclerosis and is clinically associated with inflammation that can be seen as stable angina, unstable angina, myocardial infarction (MI) and sudden cardiac death.[1] The sedentary lifestyle triggered by improvements in living standards and technological advances is among the essential reasons for the increase in the incidence of CAD. It is one of the most important causes of death in developed and developing countries.

The retina is the only tissue in the body that allows direct observation of the vascular system and non-invasive visualization of its microcirculation within a few seconds. In studies, the central retinal artery and its branches are an actual artery containing intima, media and adventitia layers.[2] In addition, the similarity between these arteries and the structures of other small arteries in the body, especially the brain and heart, is noteworthy.[3] Various systemic conditions can affect the retinal arteriolar and venular diameter. Decreased retinal arteriolar diameter and increased retinal venular diameter are independently associated with mortality of various diseases such as hypertension, cardiovascular disease, and stroke.[4, 5] Today, morphological features such as length, width, curl and branching patterns of retinal vessels are used for screening

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and evaluation of various cardiovascular diseases.[6] Studies report that atherosclerotic changes in retinal arteries characterized by thickening of the vascular wall, lipid accumulation and calcification in the intima are strongly associated with atherosclerotic changes in the coronary arteries.[7, 8]

Spectral Domain-Optical Coherence Tomography (SD-OCT) is a frequently used imaging method that can non-invasively obtain high-resolution cross-sectional images of retinal layers and complex retinal cell architecture.[9] It has been reported that the diameters of the retinal vessels can be measured indirectly using SD-OCT images, as shadows or dark columns are characteristic of the retinal vessels on SD-OCT images (light does not penetrate the blood vessel, so the underlying tissues cannot be visualized).[10] Vessels can be characterized as arteries or veins based on their appearance on fundus images. The arteriovenous ratio (AVR) is a marker of changes in retinal vessel morphology and can be calculated using vessel measurements in SD-OCT.[11]

In studies evaluating the relationship between retinal vascular structure and CAD, measurements of retinal vessels mainly were performed using fundus photographs obtained after dilatation and using additional software.[12] This procedure, which is not easy to apply in clinical practice, can be performed in today's technology with SD-OCT, giving results within seconds and does not require dilatation.[13]

This study compares retinal vessel diameter measurements obtained from SD-OCT images according to CAD stages and investigates whether there is a correlation with the disease stage.

MATERIALS AND METHODS

Study Design

This clinical study was conducted in Kayseri City Training and Research Hospital Ophthalmology Clinic Retina Unit and Cardiology Clinic in accordance with the principles of the Declaration of Helsinki and was carried out after all participants were informed in detail about the study and written informed consent was obtained. Ethical approval of the study was obtained from the ethics committee of Kayseri City Training and Research Hospital (111064898). This observational study included individuals who presented to the cardiology clinic with the complaint of stable angina pectoris (SAP) between February 2019 and February 2020 and were diagnosed with CAD after coronary angiography.

Detailed ophthalmologic examination, including manifest refraction measurement, best-corrected visual acuity measurement (BCVA), and intraocular pressure measurement, biomicroscopic anterior segment and dilated fundus examination, were performed in all patients. During cardiological examinations, anamneses of all patients were taken and systemic physical examinations, fasting blood lipids and fasting blood glucose measurements were performed. Individuals were questioned regarding demographic information such as age, gender, CAD risk factors and drug use. Those who received antihypertensive treatment or whose blood pressure was 140/90 mm Hg and above in the measurements were accepted as hypertension (HT) patients. Patients with a fasting blood glucose level of 126 mg/dl and above, HbA1C values of 6.5% and above, or who received antidiabetic therapy were considered diabetic patients and were investigated for diabetic retinopathy in dilated fundus examination. Those with a total cholesterol level of 200 mg/dl and above and a history of statin drug use within the last 3 months were accepted as hyperlipidemia patients. Smokers were defined as patients who smoked or reported active smoking before hospitalization.

Patients with SAP were typically considered to be patients who described pain in the chest, jaw, shoulder, back or arms manifested by exertion or emotional stress and passed at rest or with nitroglycerin.[14] Coronary angiography was planned to diagnose the presence of CAD and to evaluate its stage. A detailed ophthalmological examination and non-invasive imaging of retinal vessels with SD-OCT were performed in the retina unit of the ophthalmology clinic one day before the coronary angiography for patients who applied with SAP. The cardiology clinic performed CAD staging according to the results of coronary angiography in patients whose retinal vessel diameter was measured.

Coronary angiography

In coronary angiography, the right femoral artery was preferred as the entry site, and puncture with the Seldinger method as the entry technique. During the vascular puncture, a 6 Fr cannula was used; if necessary, a 7 Fr cannula was used. Left coronary system imaging was performed using a left Judkins catheter, and right coronary system imaging was performed using a right Judkins catheter (Siemens Artis Zee Biplane coronary angiography). Coronary arteries were visualized in standard plans. The use of the iodohexol non-ionic contrast agent was preferred in all patients. An average of 6-10 cc contrast agent was used during each angiographic exposure. As a result of the coronary angiography, the patients were divided into 3 groups. Stage 1) Normal coronary artery; stage 2)

Patients with non-critical stenosis in any of the coronary arteries (<70% stenosis) and stage 3) Patients with 70% or more critical stenosis in any of the coronary arteries and underwent percutaneous coronary angioplasty and stenting.

The measurement of the retinal vessel (arteriole and venule) diameters of the patients was performed with SD-OCT (Spectralis, Heidelberg Engineering, Inc., Heidelberg, Germany), and the measurement of the axial length of the eyes was performed with the help of non-contact partial coherence interferometry (IOL Master, Zeiss, Jena, Germany). When the image quality was appropriate, the right eye of each patient was evaluated for SD-OCT based vascular analysis, and in conditions where the image quality was not suitable, the other eyes of the patients were included in the study.

The diagnosis and staging of CAD were performed by an experienced cardiologist (SK) who performed coronary angiographies. Patients with complete ophthalmological examination records and coronary angiography records were included in the study.

Patients with concomitant retinal vascular pathology such as diabetic retinopathy or retinal vascular occlusion in any eye, patients with BCVA below 20/20, patients with systemic diseases affecting vascular structures (Behçet's, systemic lupus erythematosus-like connective tissue diseases), patients with a previous history of heart disease (heart failure, rheumatic heart disease, valvular heart disease, arrhythmia, cardiomyopathy), patients with primary vascular pathology such as an aortic aneurysm or peripheral vascular disease, patients with a history of heavy alcohol use (> 40 grams/day) which may affect vascular structures, patients with a history of migraine, patients were taking medications that affect the diameter of their blood vessels such as angiotensin receptor inhibitors and vasodilators in the last 1 month, patients younger than 40 years old, patients with spherical refractive errors above ± 5 diopters or astigmatic refraction above ± 2 diopters were excluded.

The Framingham risk score, which helps to calculate the risk of having a cardiovascular event within the next 10 years, with the parameters of age, gender, smoking status, total cholesterol, HDL cholesterol, systolic blood pressure and diabetes, among cardiological risk factors, were performed in all patients[15] and any correlation between risk scoring and AVR in each group was investigated.

Spectral Domain-Optical Coherence Tomography and Retinal Vessel Diameter Measurement

The SD-OCT system takes high resolution, microscopic, cross-sectional images of the retina non-invasively. It has a scanning speed of up to 40,000 A-scans per second, a depth resolution of 7 µm and a cross-resolution of 14 µm using an 870 nm wavelength diode laser beam.

SD-OCT imaging of all patients was performed by an experienced nurse (SE) at the same time of the day (between 9 - 11 am). A cube scan of seven horizontal scans was placed at the lower border of the disc to include the large retinal vessels (inferior temporal retinal arcade) emerging from the disc (Figure 1). There is a scanning range of 240 µm between 7 scan lines placed on the inferior border of the optic disc. The vessel diameters were measured from SD-OCT scans using vessel associated shading (lumen + vessel wall) as previously described.[16,17] The shadow widths of the vessels on SD-OCT scanning were determined, assuming that retinal vascular blood flow attenuates the SD-OCT signal beneath the vessel. Since possible difficulties in determining the border of retinal vessels in the first and second scan sections (at the optic disc border and at 240 µm) and sometimes secondary branching can be observed in the 6th and 7th scan sections, the statistical analysis was performed on the other 3 scan

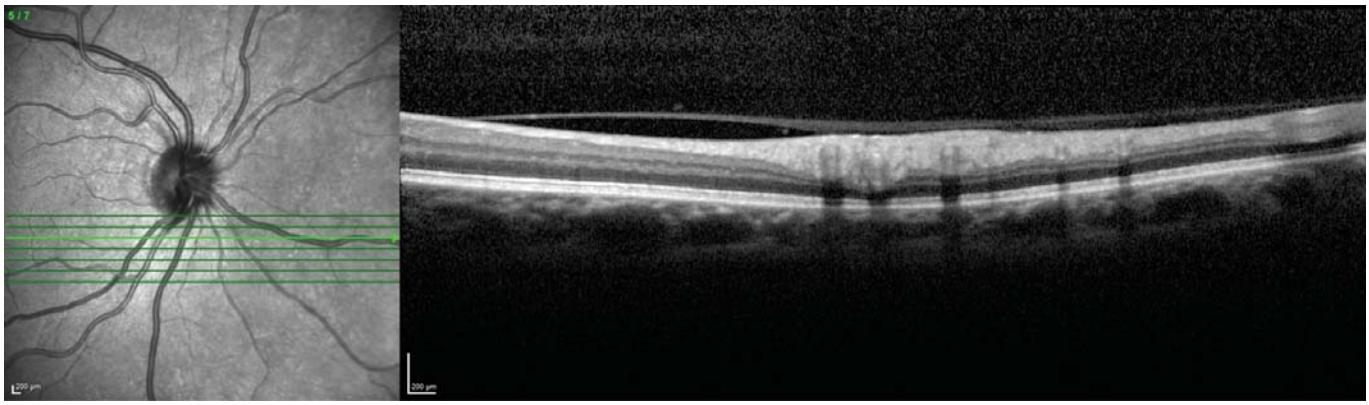

Figure 1: *Placing 7 horizontal grids with a distance of 240 microns to the lower border of the optic disc.*

sections (3, 4, and 5. scans) (480-960 µm from optical disc border). In addition, morphologically, the characteristics of the blood vessels in the 3rd and 5th horizontal section are more compatible with the definition of small arteries and venules, and less arteriovenous crossing and arterial pulsation are observed in this area. All measurements were performed manually and on SD-OCT images by two independent, masked clinicians (CO, YY) who did not know the CAD stage (Figure 2). Then, the average of the measurements of 3 sections on the same vessel was accepted as the average diameter of that vessel. The cases in which the SD-OCT section passes through the artery-vein crossing point or the common trunk instead of the temporal branches, which may prevent the determination of vessel boundaries accurately, were not included in the analysis due to technical difficulties.

Outcome measures

The primary outcome measure is to investigate whether there is a difference in retinal vessel diameters in patients with CAD at different stages. The secondary outcome is to investigate the presence of a correlation between mean retinal arteriole and venule diameters and CAD stage.

Statistical Analysis

All analyzes were performed with the Windows SPSS V.24.0 software package (SPSS Inc., Chicago, IL). The distribution of variables was checked with the Shapiro-Wilk test. Descriptive data are presented as a percentage and mean ± standard deviation (sd). ANOVA test was used for parametric numerical data and Chi-Square /Fisher tests were used to analyze quantitative data in the comparison between stages. The effects of cofactors such as diabetes, HT, hyperlipidemia and smoking, which may affect vessel diameters, were evaluated using a generalized linear model. Post hoc comparison between stages was carried out with the help of the Tukey test for parametric data and Pearson's correlation test was used for the correlation of parametric variables. In the power analysis performed with G*power 3.1, it was calculated that there should be at least 24 patients in each group in order to calculate the difference of at least 1 micron between the groups with 0.5 effect size and 5% margin of error from 3 groups in which cofactors were also taken into account. $P< 0.05$ was considered statistically significant.

RESULTS

Features of Participants

One hundred six eyes of a total of 106 CAD patients were included in this study. According to the results of coronary angiography, there were a total of 36 patients with a mean age of 64.15 ± 8.94 in the stage 1 CAD group, a total of 40 patients with a mean age of 66.33 ± 7.87 in the stage 2 CAD group, and a total of 30 patients with a mean age of 66.40 ± 12.88 in the stage 3 CAD group (P=0.539). The demographic characteristics of the groups such as gender, diabetes, HT, smoking and hyperlipidemia rates and axial length values were statistically similar. The demographic and descriptive information of the groups is shown in Table 1. The mean Framingham risk score was 7.09±4.05. in the stage 1 CAD group, 9.66±2.78 in the stage 2 CAD group, and 11.57±3.08 in the stage 3 CAD group. While a significant difference was detected between stage 1-2 and stage 1-3 CAD groups in terms of the average Framingham risk score, no significant difference was detected between stage 2-3 CAD groups ($P = 0.022$, $P <0.01$, $P = 0.126$, respectively).

Retinal Vessel Parameters

Table 2 shows the results of retinal vessel parameters between groups. According to the analysis, the mean diameter of retinal arterioles in the stage 1 CAD group was 119.77 ± 7.24 µm, in the stage 2 CAD group, it was 118.77

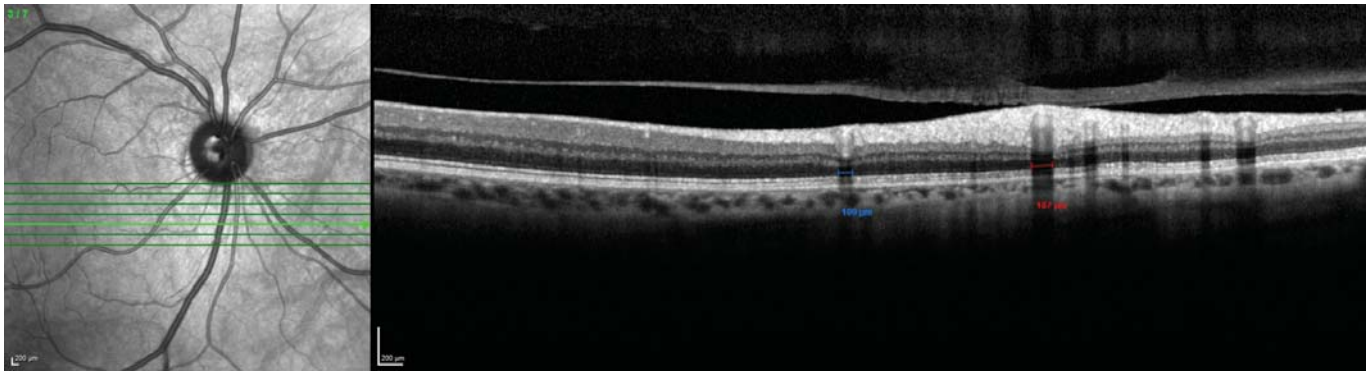

Figure 2: *Measurement of arteriole and venule diameter from section 5 of the grid placed at the lower border of the optic disc.*

Table 1: *Demographic and descriptive data of the patients.*

PARAMETER	STAGE 1 CAD n: 36	STAGE 2 CAD n:40	STAGE 3 CAD n:30	P
	mean±sd	mean±sd	mean±sd	
AGE (years)	64.15±8.94	66.33±7.87	66.40±12.88	0.539
GENDER (M/F)[α]	20/16	24/16	24/6	0.095
DIABETES	16 (%44.4)	19(%47.5)	15/15 (%50)	0.704
HYPERTENSION	22 (%61.1)	27 (%67.5)	22(%73.3)	0.581
SMOKING	17 (%47.2)	19 (%47.5)	16 (%53.3)	0.861
HYPERLIPIDEMIA	12 (%33.3)	12 (%30)	11(%36.7)	0.686
AXIAL LENGTH (mm)	24.3 ± 0.9	24.4 ± 1.1	24.0 ± 0.7	0.316

CAD; coronary artery disease

Table 2: *The results of retinal vessel parameters in coronary artery patients according to the stages.*

PARAMETER	STAGE 1 CAD n: [a]	STAGE 2 CAD n: [b]	STAGE 3 CAD n: [c]	F	P
	mean±sd	mean±sd	mean±sd		
Retinal arteriole diameter	119.777±7.244	118.775±6.696	104.600±5.170	4.767	**0.031**
Retinal venule diameter	142.444±7.109	143.015±6.674	144.733±5.451	1.558	0.179
Arterio-venous ratio (AVR)	0.842±0.041	0.832±0.025	0.727±0.019	4.949	**0.028**

Retinal arteriole diameter p [a-b]: 0.730, p [a-c]: <0.001, p [b-c]: <0.001
Retinal venule diameter p [a-b]: 0.909, p [a-c]: 0.148, p [b-c]: 0.057
AVR p [a-b]: 0.301, p [a-c]: <0.001, p [b-c]: <0.001

± 6.69 µm, and in the stage 3 CAD group, it was 104.60 ± 5.17 µm. There was no significant difference in arteriolar vessel diameters between stage 1-stage 2 CAD groups. However, there was a significant difference between stage 1-stage 3 and stage 2-stage 3 CAD groups (*P*=0.730; *P*<0.001; *P*<0.001, respectively).

The mean vessel diameter of retinal venules was 142.44 ± 7.10 µm in the stage 1 CAD group, 143.01 ± 6.67 µm in the stage 2 CAD group, and 144.73 ± 12.45 µm in the stage 3 CAD group. There was no significant difference in venule diameter between the groups (P = 0.909; P = 0.148; P = 0.057, respectively).

In the AVR analysis obtained by the ratio of arteriole and venule diameter, the mean AVR was 0.842 ± 0.041 in the stage 1 CAD group, 0.832 ± 0.025 in the stage 2 CAD group, and 0.727 ± 0.019 in the stage 3 CAD group. There was no significant difference between stage 1-stage 2 CAD groups in terms of AVR as well as in arteriolar vessel diameters. There was a significant difference between stage 1-stage 3 and stage 2-stage 3 CAD groups (P = 0.301; P <0.001; P <0.001, respectively).

The results of the sub-analysis performed on 50 diabetic patients and 56 non-diabetic patients to investigate the possible effects of diabetes on vascular structures were found to be consistent with the results of all patients. Significant differences were found in arteriole diameter and AVR parameters between stage 2-3 and stage 1-3 CAD groups in patients with and without DM, but no significant difference was found in venule diameter parameters.

Correlation Analysis

In the correlation analysis between the mean value of the retinal vessel diameters and the CAD stage, a negative and significant correlation was found between arteriole diameter and CAD stage (r= -0.665, *P*<0.001). Similarly, a negative and strong correlation was observed between AVR and CAD stage (r=-0.717, *P*<0.001). There was no significant correlation between retinal venule diameter and CAD stage (r=-0.172, *P*=0.078) (Table 3). In addition, there was a significant and negative correlation between the degree of coronary artery stenosis and AVR in the stage 2 CAD group (r=-0.525, P=0.047).

Table 3: *Correlation analysis of coronary artery disease severity and retinal vessel parameters.*

PARAMETER	STAGE 1 CAD n: [a]	STAGE 2 CAD n: [b]	STAGE 3 CAD n: [c]	r	P
	mean±sd	mean±sd	mean±sd		
Retinal arteriole diameter	119.777±7.244	118.775±6.696	104.600±5.170	-0.665	**<0.001**
Retinal venule diameter	142.444±7.109	143.015±6.674	144.733±5.451	-0.172	0.078
Arterio-venous ratio (AVR)	0.84215±0.041	0.832±0.025	0.727±0.019	-0.717	**<0.001**

While arteriolar vessel diameter and AVR value decreased statistically significantly as the CAD stage increased, that the retinal venule diameter tended to increase, but this difference was not significant.

There was no correlation between Framingham risk score and AVR value in stage 1 CAD (r = 0.218, P = 0.330); there was a negative and significant correlation between Framingham risk score and AVR in stage 2 CAD (r = -0.416, P = 0.043) and in stage 3 CAD (r = -0.565, P = 0.023).

DISCUSSION

The ageing of the population and developments in living conditions cause the prevalence of cardiovascular and cerebrovascular diseases (myocardial infarction, hypertension, stroke) to increase every year and become one of the most important causes of morbidity and mortality.[18] CAD causes ischemia/hypoxia on the myocardium due to structural changes such as stenosis, dysplasia in the coronary artery structure or dysfunction leading to spasm.[19] Individuals with CAD are more prone to myocardial infarction than the general population. The finding early detection tools of myocardial infarction are needed to minimize the infarction's serious effect on the quality of life and decrease the burden on health systems with the need for repeated medical treatment. The relationship between small vessel disease (microvascular disease) and subclinical and clinical cardiovascular disease is increasingly recognized. Retinal vessels, the only blood vessels that can be directly observed in the body, provide a valuable method to study early structural changes and pathological features of the human microcirculation.[20] Examining and viewing retinal vessels is straightforward and non-invasive. Therefore, in clinical practice, it is important to assist in diagnosing CAD by observing changes in the structure and morphology of retinal blood vessels and evaluating the development of the disease. Therefore, this study investigates the relationship between retinal blood vessels and cardiovascular diseases and whether retinal vessels can be used as a reference in assessing their correlation with the cardiovascular disease stage.

In a study comparing colour fundus photographs of 117 patients with ischemic heart disease (IHD) and 76 healthy individuals, it was reported that the incidence of fundus arteriosclerosis was higher in patients with IHD than in the normal population, and this was associated with coronary atherosclerosis in the heart. However, this study was a study that evaluates retinal vascular morphology qualitatively, and the results may differ between individuals.[21] The need for quantitative measurements arose to evaluate retinal blood vessels more objectively. Parr and Hubbard used semi-automatic vascular measurement software on the fundus photo image for quantitative measurement of retinal blood vessels and measured blood vessels in the 0.5 disc-1 disc region from the edge of the optic disc.[22]

In recent years, accompanying clinical fundus examination, SD-OCT can be used in quantitative and qualitative analysis of retinal tissues and vascular structures. With the quantitative measurement of retinal vessel diameters, the effect of systemic, environmental and genetic factors on the retinal vascular system will be more readily understood. The mechanisms underlying changes in retinal vessel diameter are still unknown, and it is thought that changes in retinal vessel diameter may result from a combination of factors such as race, age, gender, inflammation, and other vascular factors. However, standard reference levels for retinal vessel diameters such as age, gender and blood pressure levels have not been established.[23] It is also difficult to explain the confounding effects of systemic diseases (HT, diabetes ...) on retinal vascular measurements in the adult population. Therefore, this study investigates the relationship between retinal vessel diameter and CAD severity rather than defining standard normal values of retinal vessel diameter.

One hundred six patients diagnosed with CAD according to coronary angiography results were included in this study, and retinal vascular data obtained by SD-OCT were compared to investigate the relationship between CAD and retinal

vascular structures. Retinal blood vessels have anatomical and physiological properties similar to coronary circulation, and it is thought that their morphological changes may have a certain predictive effect on cardiovascular diseases. As a matter of fact, in our study, we observed that the diameter of the retinal arterioles significantly decreased as the CAD stage progressed. While there was no significant relationship between retinal venule diameter and CAD stage, we observed that AVR obtained by proportioning arteriole and venule diameters showed a strong negative correlation with CAD, similar to arteriolar vessel diameter. Analysis of retinal vessel diameter showed that in this population, the retinal arteriole might have developed a pathological morphology similar to the coronary artery, and this change was primarily reflected in the reduction in retinal artery diameter. Studies suggest that this change in vessel diameter may be associated with impaired endothelial function. Endothelial cells have endocrine and metabolic effects. Active substances such as endothelin (ET) and nitric oxide (NO) secreted by endothelial cells play an essential role in vasoconstriction and vasodilation. ET promotes vasoconstriction in vascular structures and the proliferation of vascular smooth muscle cells. On the other hand, NO has the effect of providing vasodilation of blood vessels and inhibiting the proliferation of vascular smooth muscle cells.[24] Therefore, dynamic changes in ET and NO effect regulating vascular tone and altering blood vessel morphology. About 25 years ago, it was suggested that high plasma ET levels might play a role in developing cardiovascular diseases.[25] The literature reports and vascular disease physiology suggest that the result we obtained in our study may also be associated with endothelial dysfunction because there is no sympathetic system-related vasoconstriction to control the change of vascular tone in retinal vessels.[26] Imbalance in the ratio of ET to NO leads to the proliferation of vascular smooth muscle cells, vascular hypertrophy and inhibition of diastolic function, and thus smaller inner and outer vessel diameters. In our study, we think that increasing ET / NO imbalance with the CAD stage is one of the mechanisms explaining the decreased retinal arteriole diameter. Before the 2000s, changes in blood vessels were thought to be related only to metabolically-induced vascular degeneration, but later on, how inflammation plays a role in the formation of vascular changes began to be described.[27] It is currently believed that vasodilation of retinal venules may be associated with systemic inflammatory factors and ischemia/hypoxia. Studies have shown that more dilated retinal venules are associated with higher C-reactive protein levels (CRP), interleukin-6 and plasma fibrin, suggesting that inflammation is one of the major causes of cardiovascular disease.[28] It has also been shown that dilated vessels lead to increased NO production and the release of inflammatory factors from vascular endothelial cells, which contribute to microvascular dysfunction. In another large population-based study, larger retinal venule diameters were reported to be independently associated with higher levels of aortic atherosclerosis and inflammation.[29] In our study, as the CAD stage increases, it was observed that retinal vein diameters tended to increase, and a significant and negative correlation has been oberved between the degree of coronary artery stenosis and AVR in the stage 2 CAD group. Although the enlargement in the diameter of the venules was not significant in our study, it suggests that inflammation may be one of the factors that play an important role in the development of CAD on the narrowing of arterioles and the expansion of the venules. It remains to be investigated whether there is a significant relationship between the change in retinal venular structures and the CAD stage in future studies with larger cases.

AVR is the ratio of retinal artery diameter to the diameter of the accompanying venous blood vessel. It is a comprehensive index for evaluating retinal blood vessels. In a large-scale study of patients aged 50-70 years, it was reported that the AVR value provides essential information to clinicians to predict cardiovascular disease. In parallel with AVR, Framingham risk scoring also appears to be a meaningful predictive parameter for the development of cardiovascular events in patients who develop non-critical (stage 2) and critical (stage 3) stenosis of the coronary arteries. Because, there was a significant difference between the mean risk scores between the stage 1 CAD group and the patients who started to develop stenosis in the coronary arteries, and a significant correlation was found between the risk score and AVR in stage 2 and stage 3 CAD patients.

It has been shown that a low AVR value is associated with the incidence of IHD and stroke and that a decrease in this value may lead to a higher risk of IHD.[30] The data in our study also showed that as the CAD stage increased, the AVR rate decreased significantly and AVR was the parameter showing the strongest correlation with the CAD stage, in accordance with the literature. We suggest that both the microvascular dysfunction caused by the ET / NO imbalance and the different effects of inflammation in the narrowing of arterioles and dilating venules make the AVR value a more predictive parameter in clinical practice.

Our study has limited aspects. First, the sample size is small. Second, if the patients had functional myocardial blood measurements such as microvascular resistance index and

coronary flow reserve, it would be possible to diagnose the presence of microvascular dysfunction directly rather than indirectly due to vessel diameters. The third is that the vessel diameters are not measured by automatic software, but are obtained by manual calibration method. One of the relatively strong aspects of our study is to try to minimize the possibility of error and bias by taking the average of the measurements made by 2 masked ophthalmologists from the areas that best reflect the retinal vessel diameter and microcirculation. In addition, although cofactors such as diabetes, HT, HL, and smoking, which may affect vessel diameters, were found at similar levels among the stages of CAD, the effect of these cofactors was also evaluated with the generalized linear model.

CONCLUSION

In our study, we observed that there was a relationship between the CAD stage and retinal arterioles and venules, and the AVR value most strongly reflected this relationship. With the widespread use of SD-OCT technology and the effortless observation of retinal blood vessels, the relationship between retinal blood vessels and systemic vascular diseases can be better understood, and valuable data can be provided to clinicians through SD-OCT to evaluate systemic microvascular conditions and to prevent and treat systemic vascular diseases.

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