ORIGINAL RESEARCH

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Retinal Microvascular Changes in Patients with Chronic Heart Failure due to Idiopathic Dilated Cardiomyopathy

İdiyopatik Dilate Kardiyomiyopatiye Bağlı Kronik Kalp Yetmezliğinde Retinal Mikrovasküler Değişiklikler

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Abstract

Objective: Idiopathic dilated cardiomyopathy (IDCM), one of the major causes of chronic heart failure, is a disorder that causes impairment of the systolic function due to left ventricular dilatation without coronary artery disease. In this study, we aimed to investigate retinal vascular density (VD) and the foveal avascular zone (FAZ) area changes in patients with IDCM using optical coherence tomography angiography (OCTA).

Method: Forty-eight patients with IDCM and a left ventricle ejection fraction below 50% (Group 1) and 50 healthy individuals (Group 2) were evaluated using OCTA. FAZ area, superficial and the deep parafoveal VDs and peripapillary area VDs were measured and compared between the groups.

Results: The FAZ values were significantly higher in Group 1 (0.29±0.09, 0.20±0.05; p<0.001, respectively). Moreover, the mean VD values were significantly lower in the deep capillary plexus of the parafoveal area in Group 1 (49.05±3.81, 54.81±2.88; p<0.001, respectively). The mean VD values were also significantly lower in the peripapillary area in Group 1 (50.54±3.38, 54.66±1.42; p<0.001, respectively).

Conclusion: OCTA may possess the potential to be used in the follow-up of this patient group.

Keywords: Dilated cardiomyopathy, heart failure, microvascular density, optical coherence tomography angiography

Öz

Amaç: Kronik kalp yetmezliğinin en önemli nedenlerinden biri olan idiyopatik dilate kardiyomiyopati (KMP), koroner arter hastalığı olmaksızın sol ventrikül genişlemesine bağlı olarak, sistolik fonksiyonun bozulmasına neden olan bir hastalıktır. Bu çalışmada, optik koherens tomografi anjiyografi (OKTA) kullanarak KMP'si olan hastalarda foveal avasküler zon (FAZ) alanı ve retinal vasküler dansite (VD) değişikliklerini araştırmayı amaçladık.

Yöntem: Sol ventrikül ejeksiyon fraksiyonu %50'nin altında olan KMP'li 48 hasta (Grup 1) ve 50 kişiden oluşan sağlıklı kontrol grubu (Grup 2) OKTA ile değerlendirildi. FAZ alanı, yüzeyel ve derin parafoveal VD değerleri ve peripapiller alan VD değerleri ölçülerek, gruplar arasında karşılaştırma yapıldı.

Bulgular: FAZ değerleri Grup 1'de anlamlı olarak daha yüksekti (sırasıyla 0,29±0,09, 0,20±0,05; p<0,001). Ayrıca Grup 1'de parafoveal alanın derin kapiller pleksus ortalama VD değeri anlamlı olarak daha düşüktü (sırasıyla 49,05±3,81, 54,81±2,88; p<0,001). Peripapiller alanın ortalama VD değeri de Grup 1'de anlamlı olarak daha düşük bulundu (sırasıyla 50,54±3,38, 54,66±1,42; p<0,001).

Sonuç: Çalışmamızın sonuçları bu hasta grubunun takibinde OKTA'nın kullanılabileceğini düşündürmektedir.

Anahtar kelimeler: Dilate kardiyomiyopati, kalp yetmezliği, mikrovasküler dansite, optik koherens tomografi anjiyografi

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Introduction

Chronic heart failure (CHF) is a severe disease in which the feeding of tissue is impaired as a result of the loss of the heart's pumping function due to various reasons (1). Although the pathogenesis of CHF remains uncertain, it is thought to be associated with microvascular dysfunction (2-6). Idiopathic dilated cardiomyopathy (IDCM), one of the major causes of CHF, is a disorder that causes impairment of the systolic function due to left ventricular dilatation without coronary artery disease (CAD) (7,8). As a spontaneous consequence of the impaired pumping function of the heart, the circulation in the tissues is also impaired (1).

The retina is unique in that it allows for the monitoring of the effects of systemic diseases *in vivo*. Retinal vascular alterations can be evaluated using different imaging methods. For this reason, many previous studies have been conducted to reveal the effects of cardiac diseases, such as CHF and hypertension (HT), on retinal and choroidal tissues (9-13).

Optical coherence tomography angiography (OCTA) is a new imaging method to assess retinal vascularization. In recent years, many OCTA studies have reported that retinal microvascularization is affected by systemic diseases. OCTA studies have also revealed retinal vascular impairment in patients with CAD, congenital heart disease, (CHD), and CHF (14-16).

In the current study, we tried to reveal the changes in the retinal vascular network quantitatively in patients with IDCM for the first time.

Materials and Methods

This study received approval from the Ethics Committee of University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital and was conducted under the Declaration of Helsinki (05/02/2019; 2245). Based on a study conducted with a similar subject and methodology, at least 37 participants in each group should be included in the study, according to the power analysis result when α: 0.05, and power (1-β): 0.80 were taken with the G*Power 3.1 program. All participants stated that they agreed to participate in the study with written consent. Patients who are followed in cardiology clinic between February 2019 and June 2019 have been evaluated. Patients with no CAD were determined by coronary angiography and a dilated left ventricle cavity with left ventricle ejection fraction (LVEF) below 50% were documented by echocardiography (echo) included in the study. All patients were stratificated according to New York Heart Association (NYHA) functional classification (17,18). Exclusion criteria were: 1) history of congenital diseases, 2) systemic diseases and conditions that might affect the retina [HT, diabetes mellitus (DM), systemic inflammatory diseases, systemic corticosteroids], 4) history of ocular trauma or surgeries, uveitis, optic nerve pathologies, macular degeneration or another ocular pathology, respectively.

Patients were referred from the cardiology clinic to the ophthalmology clinic for the study. An ophthalmological examination was performed for each patient. Patients who are involved in this study had 1) a refractive error < ±2D, 2) a best corrected visual acuity of 20/20, 3) an intraocular pressure lower than 21, 4) a cup-to-disc ratio ≤0.3.

The control group formed by volunteers without additional pathology. Two groups were thus formed: 1) a IDCM group, 2) a control group.

Imaging Protocol

OCTA images were obtained using the AngioVue Imaging System version 2017.1 (Optovue, Inc., Fremont, CA, USA). Foveal avascular zone (FAZ) area, foveal and parafoveal vascular density (VD) determined by the device. Superficial capillary plexus (SCP) and the deep capillary plexus (DCP) were segmented automatically. VDs measured in the optic disc region contained the radial peripapillary capillary (RPC) density. Scans with a signal strength index <70 were excluded. Previous articles have describe the algorithm (19,20).

Statistical Analysis

SPSS version 26.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for analyses. Mean, standard deviation and percentage were used for descriptive statistics. Chi-square test and independent t-test were used to comparison of the datas.

Results

Right eyes of 98 participants were included in the study. The IDCM group included 48 patients and the control group were formed with 50 patients. Table 1 represents the demographic and clinical features of the participants.

Table 2 shows the imaging results. FAZ values in the IDCM group were significantly higher ($p<0.001$). There was no significant difference between the SCP density values of the two groups ($p>0.05$ for all). However, the DCP and RPC density values of the IDCM group were significantly lower in all quadrants of peripapillary area (Figure 1).

Discussion

Decreases in ocular blood flow and choroidal thickness in patients with CHF as well as retinal arteriolar narrowing due to HT, myocardial infarction, and CHF have been reported in previous studies (9,10,21-23). It has also been shown that retinal arteriolar narrowing and retinopathy findings can be used to predict CHF risk in patients with HT and CHD (22-24).

The low cardiac output due to impaired ventricular function causes compensatory vasoconstriction in the peripheral tissues to ensure feeding in more critical tissues, such as the brain and heart (25,26). Low perfusion also causes vasospasms and vasoconstriction in the ocular vessels. In addition, Almeida-Freitas et al. (21) showed ophthalmic artery blood flow impairment in patients with CHF in their Doppler study. Alnawaiseh et al. (16) found that retinal perfusion was correlated with LVEF in their OCTA study on CHF.

Based on these findings, we evaluated the data of IDCM patients considering that OCTA may reveal peripheral microvascular changes in patients with CHF. Our study revealed FAZ enlargement and an impairment in the DCP and RPC densities in patients with IDCM.

In their research on patients with CAD, Wang et al. (14) found a decrease in parafoveal VD and proposed that this was associated the location of the occluded coronary artery. However, coronary microvascular dysfunction has been shown in patients with signs of myocardial ischemia without CAD via angiography and even in asymptomatic patients with cardiovascular risk factors in previous studies (4,27). An animal study supports these results (28). In addition, left ventricular dysfunction and heart failure are thought to occur as a result of microvascular processes (5,6). Wang et al. (14) stated that OCTA can be used to detect early-stage CHF. As in our study, the results of the OCTA study of Li et al. (29) on patients with CHD revealed decreased VD in the DCP and RPC, especially among cyanotic patients, although there were no decreases in the SCP density.

The difference between the SCP and the DCP ischemic findings could be due to their specific structures and locations. In their OCTA study on rhegmatogenous retinal detachment, Woo et al. (30) proposed that perfusion pressure may be higher in the SCP, as its branches leave the retinal artery earlier than those of the DCP, and the DCP may be particularly vulnerable to tissue hypoxia and pressure changes (31,32). OCTA studies on DM and HT have shown that VD decreases specifically in the DCP as well as FAZ enlargement, similar to our results (33,34). In contrast, Rakusiewicz et al. (35) found a decrease in the SCP (not the DCP) density in their OCTA study in children with IDCM, stating that this was an unexpected result. We believe that the difference between the results is due to the difference between the patient groups. Although there is no consensus yet, VD decreases due to LVEF decreases can

Table 1. Demographic features

		IDCM group (n=48) Mean ± SD/n-%		Control group (n=50) Mean ± SD/n-%		p
Age		43.43±10.24		45.32±10.58		0.373*
Gender	Male	33	68.75%	33	66.00%	0.774**
	Female	15	31.25%	17	34.00%	
Systolic BP (mmHg)		116.97±9.38		115.1±9.23		0.320*
Diastolic BP (mmHg)		75.20±9.72		73.50±7.96		0.343*
BMI		21.97±0.97		22.22±1.34		0.311*
AL (mm)		22.56±0.85		22.85±0.76		0.073*
IOP (mmHg)		14.47±1.54		14.00±1.91		0.177*
Hb (g/dL)		14.33±0.87				
Htc (%)		41.97±2.62				
LVEF (%)		30.00±7.57				
Disease duration (year)		3.58±1.79				
NYHA	**Class 1**	30	62.50%			
	Class 2	11	22.92%			
	Class 3	7	14.58%			

*Independent t-test, **chi-square test, IDCM: Idiopathic dilated cardiomyopathy, SD: Standard deviation, BP: Blood pressure, BMI: Body mass index, AL: Axial lenght, IOP: Intraocular pressure, Hb: Haemoglobin, Htc: Haematocrit, LVEF: Left ventricle ejection fraction, NYHA: New York Heart Association

be demonstrated quantitatively with OCTA; therefore, we presume that OCTA may be useful in the follow-up of this patient group in addition to echo.

Although there are several possible explanations, underlying etiological mechanisms in the relationship between optic neuropathies and ocular ischemia remain unknown. In terms of vascular factors, it has been suggested that there may be insufficient blood supply to nourish the optic nerve (36,37). OCTA is insufficient to demonstrate the aetiology of decreased VD in the RPC. Nevertheless, in regard to our study, two possible explanations for this decrease are the loss of vascular structure and vasoconstriction as a result of chronic hypoxia and endothelial dysfunction. Excessive overlapping of radial capillaries near the optic disc may have caused errors in our results. In addition, the fact that retinal nerve fibre layer thickness was not evaluated in our study may have negatively affected our results.

Study Limitations

There was another limitation in our study. The number of participants decreased due to the exclusion of patients with additional systemic disease and poor-quality images. Prospective studies are needed to better understand microvascular changes in this patient group. With continued advances in technology, peripheral retinal VD changes may perhaps be observed via OCTA in the future.

Table 2. OCTA imaging results

	IDCM group (n=48)	Control group (n=50)	p*
	Mean ± SD/n-%	Mean ± SD/n-%	
FAZ (mm^2)	0.29±0.09	0.20±0.05	**<0.001**
SCP density (%)			
Parafovea	48.92±2.11	50.51±2.73	0.624
Superior-hemi	49.79±2.95	50.24±2.81	0.448
Inferior-hemi	50.21±2.73	50.61±2.87	0.474
Parafoveal temporal	48.16±2.93	48.78±2.98	0.3
Parafoveal superior	51.33±3.36	51.85±3.03	0.421
Parafoveal nasal	48.59±2.34	47.29±5.59	0.138
Parafoveal inferior	51.46±2.77	51.98±3.04	0.382
DCP density (%)			
Parafovea	49.05±3.81	54.81±2.88	**<0.001**
Superior-hemi	49.17±3.91	54.62±2.80	**<0.001**
Inferior-hemi	49.71±3.67	54.78±3.10	**<0.001**
Parafoveal temporal	49.02±4.04	54.69±2.97	**<0.001**
Parafoveal superior	49.37±4.05	54.44±3.33	**<0.001**
Parafoveal nasal	50.09±3.59	54.77±3.56	**<0.001**
Parafoveal inferior	49.01±3.67	54.38±3.48	**<0.001**
RPC density (%)			
Peripapillary	50.54±3.38	54.66±1.42	**<0.001**
Superior-hemi	51.52±3.54	54.78±1.78	**<0.001**
Inferior-hemi	49.85±4.32	53.52±1.78	**<0.001**
Superotemporal	55.22±4.56	56.02±3.83	**0.355**
Superonasal	48.68±5.11	52.34±4.21	**<0.001**
Nasal superior	47.83±3.87	52.34±4.28	**<0.001**
Nasal inferior	47.68±4.15	50.42±2.79	**<0.001**
Inferonasal	49.77±4.29	52.88±4.84	**0.001**
Inferotemporal	53.22±6.24	56.98±3.46	**<0.001**
Temporal inferior	50.27±4.24	53.82±2.85	**<0.001**
Temporal superior	54.60±3.76	56.67±3.89	**0.009**

*Independent t-test, OCTA: Optical coherence tomography angiography, IDCM: Idiopathic dilated cardiomyopathy, SD: Standard deviation, FAZ: Foveal avascular zone, SCP: Superficial capillary plexus, DCP: Deep capillary plexus, RPC: Radial peripapilllary capillary

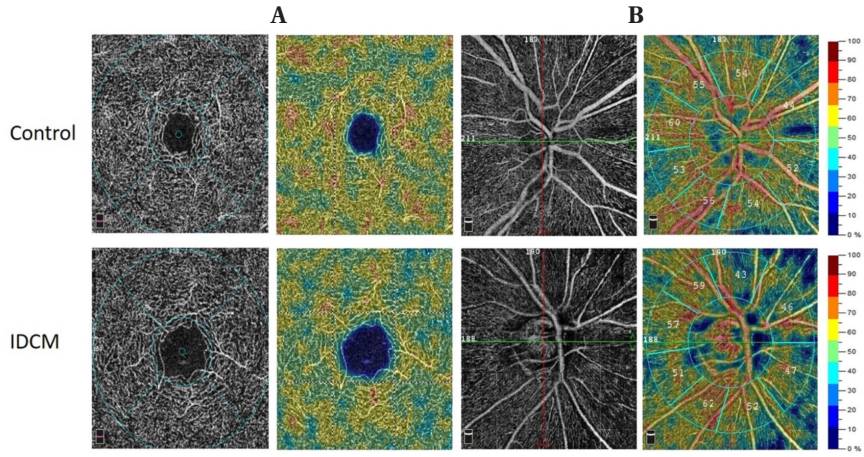

Figure 1. Images taken using the AngioVue Imaging System version 2017.1 (Optovue, Inc., Fremont, CA, USA)

A) DCP angiogram of 3×3 mm^2 and deep macular capillary network of healthy control and patient with IDCM, B) RPC angiogram of 4.5×4.5 mm^2 and peripapillary capillary network of healthy control and patient with IDCM

DCP: Deep capillary plexus, IDCM: Idiopathic dilated cardiomyopathy, RPC: Radial peripapillary capillary, ST: Superotemporal, SN: Superonasal, NS: Nasal superior, NI: Nasal inferior, IN: Inferonasal, IT: Inferotemporal, TI: Temporal inferior, TS: Temporal superior

Conclusion

The results of our study revealed a VD decrease in the DCP and RPC in addition to FAZ enlargement in patients with IDCM. Our results suggest that OCTA may possess the potential to be used in the follow-up of this patient group.

Ethics

Ethics Committee Approval: This study received approval from the Ethics Committee of University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital (05/02/2019;2245).

Informed Consent: All participants stated that they agreed to participate in the study with written consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.A.A., E.D., M.K., M.E.K., D.Ö., S.S., Concept: A.A.A., E.D., M.K., M.E.K., D.Ö., S.S., Design: A.A.A., E.D., M.K., M.E.K., D.Ö., S.S., Data Collection or Processing: A.A.A., E.D., M.K., M.E.K., D.Ö., S.S., Analysis or Interpretation: A.A.A., E.D., M.K., M.E.K., D.Ö., S.S., Literature Search: A.A.A., E.D., M.K., M.E.K., D.Ö., S.S., Writing: A.A.A., E.D., M.K., M.E.K., D.Ö., S.S.

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