• Clinical Research •

Correlation between diastolic function and fundus vascular features in coronary heart disease

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Abstract

● **AIM:** To assess the correlation between cardiac diastolic function and retinal/choroidal vascular features in patients with coronary heart disease (CHD).

● **METHODS:** This observational clinical cohort study included 206 CHD patients (412 eyes). Optical coherence tomography (OCT) and OCT angiography (OCTA) images were obtained from each participant using the AngioVue Imaging System. Each patient also underwent echocardiography to evaluate cardiac diastolic function.

● **RESULTS:** Several correlations were found between cardiac diastolic function and fundus vascular features in CHD patients. Left ventricular end-diastolic diameter (LVED), interventricular septal thickness in diastole (IVSD), left ventricular posterior wall thickness in diastole (LVPWD), and early (E) to atrial (A) wave velocity (E/A ratio) positively correlated with retinal thickness, while early (E) diastolic mitral inflow velocity to early (E') diastolic mitral annular velocity (E/E' ratio) and pulmonary arterial systolic pressure (PASP) negatively correlated. Significant associations were noted for LVED and PASP across several retinal regions, excluding the foveal central subfield. Vessel density in superficial capillary plexus (SCP) and deep capillary plexus (DCP) layers had negative correlations with IVSD, LVPWD, and E/E' ratio, but a positive correlation with E/A ratio. The choriocapillaris (CC) layer's vessel density positively correlated with the E/A ratio and negatively with the E/E' ratio. LVPWD and E/A ratio positively correlated with choroidal perfusion, while E/E' ratio showed a negative correlation. LVED, pulmonary artery diameter (PA), and PASP showed no significant associations with retinal or choroidal perfusion.

● **CONCLUSION:** In CHD patients, macular retinal/choroidal thickness, vascular density across different layers, and perfusion may serve as useful and sensitive predictors of fundus circulatory disturbances resulting from impaired cardiac diastolic function.

● **KEYWORDS:** coronary heart disease; optical coherence tomography angiography; echocardiography; diastolic function; fundus vascular features

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INTRODUCTION

Coronary artery disease (CAD), as called coronary heart disease (CHD), is a significant global health concern, responsible for high rates of morbidity and mortality[1]. The pathogenesis of CHD manifests because of plaque accumulation in the arterial wall, leading to reduced blood flow to the heart muscles. These ischemic conditions not only compromise systolic function but also affect the diastolic phase of the cardiac cycle[2].

In patients with CHD, echocardiography has proven to be a cornerstone diagnostic tool for assessing cardiac function, particularly in the evaluation of diastolic dysfunction. This non-invasive and cost-effective modality allows clinicians to visualize cardiac chambers and assess myocardial relaxation and filling pressures in real-time[3]. Key echocardiographic indices for diastolic function serve as robust biomarkers, helping clinicians to not only diagnose varying grades of diastolic dysfunction but also to guide risk stratification and subsequent therapeutic approaches[4].

As a systemic atherosclerotic disease, emerging research has suggested CHD may not only impacts coronary vessels but also influences peripheral vasculature, such as fundus blood vessels[5]. In our preliminary research, we also found that even in the absence of ocular complications, the retinal and choroidal layers, regional blood flow density, and macular

perfusion in CHD patients were all lower than those in the normal control group[6]. These retinal or choroidal vessel changes are hypothesized to be reflective of systemic vascular health and could potentially serve as a non-invasive window to assess cardiovascular risk. Therefore, studying fundus vasculature in CHD patients may provide insights into the broader cardiovascular health of these individuals.

Optical coherence tomography angiography (OCTA), an advanced, non-invasive imaging technique, allows for high-resolution visualization of the retinal and choroidal vasculature, without the need for dye injection[7]. Studies have revealed that OCTA can identify subtle yet critical vascular abnormalities, such as decreased vessel density and capillary dropouts, across a range of cardiovascular conditions, including atherosclerosis, acute myocardial infarction, non-obstructive coronary artery disease (NOCAD), hypertension, and heart failure[7-8]. These peripheral vascular changes are thought to mirror systemic vascular pathology, offering a relatively intuitive window into cardiovascular health and potential risk stratification. Given these capabilities, OCTA is emerging as a promising adjunctive tool for comprehensive cardiovascular assessment and management.

Indeed, there is a limited but growing body of evidence indicating the interconnectedness of cardiac and retinal health. However, the link between cardiac diastolic function and fundus vascular characteristics as observed through OCTA remains largely unexplored. Thus, this study aims to fill the knowledge gaps by evaluating the correlation between echocardiographic indices of cardiac diastolic function and retinal/choroidal vascular features by OCTA among CHD patients.

PARTICIPANTS AND METHODS

Ethical Approval The study was approved by the Institutional Review Ethics Committee of Huashan Hospital. All procedures performed in the study involving human participants were in accordance with the ethical standards of the committee and with the Helsinki Declaration and its later amendments or comparable ethical standards. The ethical approval number for this study was (No.2022-255). Written informed consent was obtained from all participants before their inclusion in the study.

This cross-sectional observational study was conducted in the Department of Ophthalmology, Huashan Hospital, Fudan University and the Department of Cardiology, Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine.

CHD subjects were diagnosed by cardiologists based on relevant criteria. Patients with conditions that could potentially affect the final outcomes, such as congenital valvular abnormalities, aortic aneurysms, rheumatic and infectious valvular diseases, were excluded. All patients underwent echocardiography performed by experienced technicians. We selected the left ventricular end-diastolic diameter (LVED), interventricular septal thickness in diastole (IVSD), left ventricular posterior wall thickness in diastole (LVPWD), pulmonary artery systolic pressure (PASP), pulmonary artery diameter (PA) early (E) to atrial (A) wave velocity ratio (E/A ratio) and early (E) diastolic mitral inflow velocity to early (E') diastolic mitral annular velocity ratio (E/E' ratio) as representative indices for assessing cardiac diastolic function for subsequent data analysis.

All participants underwent comprehensive ophthalmic examinations. Patients with refractive errors ≥3.0 diopters, amblyopia, uveitis or intraocular infection, glaucoma, macular diseases, diabetic retinopathy, or those who had previously undergone retinal photocoagulation or intraocular surgeries (except for uncomplicated cataract removal such as phacoemulsification) were excluded. Additionally, patients with severe refractive opacities that could result in low-quality OCTA images and affect data recording were also excluded.

Using the AngioVue Optical Coherence Tomography (OCT) instrument and system (Optovue, Fremont, CA, USA), both OCT and OCTA scans of retina and choroid were carried out. For OCT scans, radial scans targeted the foveal region. The integrated software then gauged the thickness of retinal and choroidal capillary layers, generating eight regions (fovea, para fovea, superior hemisphere, inferior hemisphere, temporal, superior, nasal, and inferior). This software assessed the retinal thickness spanning from the inner limiting membrane to the retinal pigment epithelium, subsequently computing the average. In OCTA mode, a high-definition 6 mm×6 mm image centered on the fovea was obtained. The device's proprietary software algorithm produced vascular density maps for the superficial capillary plexus (SCP), deep capillary plexus (DCP), and choriocapillaris (CC) layer. It then automatically derived the mean vascular density in eight regions representing them in percentage terms. Furthermore, values indicating retinal and choroidal perfusion in the macular area were generated. Notably, the retina's outer layer is avascular, so its data was omitted. The delineation for layers like SCP, DCP, CC, eight regions and retinal/choroidal perfusion has been detailed in our prior publication[6].

Statistical analyses were conducted using IBM SPSS 22.0 for Windows (USA). Numerical variables are expressed as mean±standard deviation (SD), and categorical variables are summarized as numbers and percentages. Due to the non-normal distribution and non-linear nature of the data, Mann-Whitney *U* tests or Kruskal-Wallis tests were employed for comparing quantitative variables. To assess the correlation between cardiac diastolic function and retinal vascular changes, we employed the following non-linear regression

model and multinomial logistic regression analysis: The non-linear regression model is formulated as:

$$Y = \beta_0 + \beta_1 X + \beta_2 X^2 + \epsilon$$

where Y represents the quantitative measure of cardiac diastolic function, X represents the associated retinal vascular changes, β coefficients indicate the impact of variables, and ϵ is the error term. The multinomial logistic regression model is expressed as:

$$\log\left(\frac{P(Y_i)}{P(Y_{ref})}\right) = \alpha + \gamma_1 X_1 + \gamma_2 X_2 + \cdots + \gamma_n X_n.$$

Here, $P(Y_i)$ is the probability of cardiac diastolic function being in state i, $P(Y_{ref})$ is the probability of the reference state, X_1, X_2 ... X_n represent various retinal vascular parameters affecting cardiac diastolic function, and γ coefficients represent the influence of these parameters. All analyses considered a P-value of less than 0.05 as statistically significant.

RESULTS

Participants Finally, 206 patients with 412 eyes graciously consented to participate in this study. The cohort exhibited a diverse age range, spanning from 36 to 87y, with a median of 67y and an average age of 66.86y. Intriguingly, our sample predominantly consisted of males, constituting 58.3% (n=120), and 41.7% females (n=86). The most prevalent comorbidities were hypertension and diabetes mellitus, affecting 52.9% (n=109) and 17.0% (n=35), respectively. In our echocardiographic data, we honed in on six key metrics that best represent cardiac diastolic function: LVED, IVSD, LVPWD, mitral valve E/A ratio, E/E' ratio, and PASP. The range, median, and reference value for each parameter were detailed in Table 1.

Cardiac Diastolic Function and Retinal Thickness The correlation estimates between retinal thickness from OCTA and cardiac diastolic function indices in CHD patients were presented in Table 2. The results revealed that LVED, IVSD, LVPWD, E/E' ratio and E/A ratio were positively correlated with retinal thickness, whereas PASP showed a negative correlation. Notably, both LVED and PASP exhibited statistically significant correlations with average retinal thickness in the para foveal, superior hemisphere, inferior hemisphere, superior, inferior, nasal, and temporal regions. Conversely, the foveal central subfield demonstrated no statistically significant correlation. Similarly, no significant associations were found between other diastolic function indices and retinal thickness.

Cardiac Diastolic Function and Retinal/Choroidal Microvasculature The correlation estimates between OCTA-measured retinal and choroidal vascular density (CVD), as well as choroidal perfusion and various diastolic function parameters, were detailed in Table 3 (SCP), Table 4 (DCP), and Table 5 (CC). In SCP, the average vascular density stood at 47.97 (ranging 38.03 from 58.13). There were statistically significant correlations with IVSD, LVPWD, E/E' ratio (negative) and E/A ratio (positive). When examined regionally, aside from the central fovea, all areas showed a statistically significant negative correlation with IVSD, LVPWD, and E/E' ratio. The E/A ratio displayed a significant positive correlation with the SCP's superior hemisphere, temporal, and superior regions.

Table 1 The range, median, and reference value for age and echocardiographic indices

Characteristics	Range	Median	Mean±SD	Reference value
Age (y)	36.00-87.00	67.00	66.86±9.40	-
LVED (mm)	33.00-67.00	49.00	48.39±5.23	42.00-59.00
IVSD (mm)	5.00-13.00	9.00	9.35±1.19	6.00-11.00
LVPWD (mm)	7.00-13.00	9.00	9.25±1.19	6.00-11.00
E/A ratio	0.46-1.79	0.80	0.85±0.26	>1.0
E/E' ratio	3.30-30.20	11.00	11.94±4.58	<8.0
PASP (mm Hg)	13.00-53.00	29.00	21.91±1.99	15.00-25.00

LVED: Left ventricular end-diastolic diameter; IVSD: Interventricular septal thickness in diastole; LVPWD: Left ventricular posterior wall thickness in diastole; E/A ratio: Early (E) to atrial (A) wave velocity ratio; E/E' ratio: Early (E) diastolic mitral inflow velocity to early (E') diastolic mitral annular velocity ratio; PASP: Pulmonary arterial systolic pressure; SD: Standard deviation.

Table 2 Association estimates of retinal thickness with cardiac diastolic function indices

Region	LVED	IVSD	LVPWD	E/A ratio	E/E' ratio	PASP
Fovea						
r	0.14	0.13	0.12	0.01	0.02	-0.04
P	0.05	0.09	0.11	0.85	0.78	0.54
Para fovea						
r	0.26	0.09	0.05	0.08	0.07	-0.16
P	<0.001[a]	0.25	0.53	0.30	0.36	0.03[c]
Superior hemisphere						
r	0.23[b]	0.08	0.04	0.06	0.07	-0.16
P	0.001[b]	0.29	0.57	0.40	0.34	0.04[c]
Inferior hemisphere						
r	0.27	0.09	0.05	0.09	0.06	-0.17
P	0.001[b]	0.21	0.48	0.24	0.47	0.02[c]
Temporal						
r	0.24	0.11	0.06	0.04	0.09	-0.17
P	0.001[b]	0.13	0.45	0.62	0.22	0.02[c]
Superior						
r	0.23	0.06	0.02	0.05	0.10	-0.16
P	0.001[b]	0.40	0.75	0.51	0.17	0.03[c]
Nasal						
r	0.26	0.08	0.05	0.10	0.03	-0.13
P	<0.001[a]	0.30	0.49	0.19	0.74	0.04[c]
Inferior						
r	0.29	0.09	0.05	0.10	0.07	-0.15
P	<0.001[a]	0.24	0.53	0.19	0.39	0.04[c]

LVED: Left ventricular end-diastolic diameter; IVSD: Interventricular septal thickness in diastole; LVPWD: Left ventricular posterior wall thickness in diastole; E/A ratio: Early (E) to atrial (A) wave velocity ratio; E/E' ratio: Early (E) diastolic mitral inflow velocity to early (E') diastolic mitral annular velocity ratio; PASP: Pulmonary arterial systolic pressure. [a]P<0.001; [b]P<0.01; [c]P<0.05.

Table 3 Association estimates of SCP vessel density with cardiac diastolic function indices

SCP	LVED	IVSD	LVPWD	E/A ratio	E/E' ratio	PA	PASP
Whole							
r	0.07	-0.28	-0.31	0.15	-0.21	-0.14	-0.03
P	0.32	<0.001[a]	<0.001[a]	0.04[c]	0.004[b]	0.06	0.64
Fovea							
r	0.10	0.03	-0.07	0.06	-0.14	0.08	-0.08
P	0.17	0.66	0.36	0.46	0.07	0.27	0.26
Para fovea							
r	0.07	-0.22	-0.23	0.14	-0.22	-0.12	-0.08
P	0.33	0.002[b]	0.001[b]	0.07	0.003[b]	0.10	0.30
Superior hemisphere							
r	0.12	-0.22	-0.23	0.15	-0.24	-0.12	-0.06
P	0.11	0.002[b]	0.002[b]	0.05	0.001[b]	0.11	0.44
Inferior hemisphere							
r	0.03	-0.22	-0.23	0.12	-0.20	-0.12	-0.08
P	0.74	0.002[b]	0.001[b]	0.10	0.009[b]	0.12	0.28
Temporal							
r	0.08	-0.18	-0.20	0.15	-0.17	-0.08	-0.09
P	0.30	0.01[c]	0.005[b]	0.04[c]	0.02[c]	0.28	0.23
Superior							
r	0.05	-0.21	-0.22	0.15	-0.26	-0.13	-0.03
P	0.48	0.004[b]	0.002[b]	0.04[c]	0.001[b]	0.08	0.74
Nasal							
r	0.10	-0.21	-0.20	0.13	-0.23	-0.14	-0.08
P	0.17	0.004[b]	0.007[b]	0.08	0.002[b]	0.06	0.27
Inferior							
r	0.01	-0.23	-0.24	0.11	-0.17	-0.12	-0.06
P	0.85	0.002[b]	0.001[b]	0.16	0.02[c]	0.10	0.39

SCP: Superficial capillary plexus; LVED: Left ventricular end-diastolic diameter; IVSD: Interventricular septal thickness in diastole; LVPWD: Left ventricular posterior wall thickness in diastole; E/A ratio: Early (E) to atrial (A) wave velocity ratio; E/E' ratio: Early (E) diastolic mitral inflow velocity to early (E') diastolic mitral annular velocity ratio; PA: Pulmonary artery diameter; PASP: Pulmonary arterial systolic pressure. [a]*P*<0.001; [b]*P*<0.01; [c]*P*<0.05.

Table 4 Association estimates of DCP vessel density with cardiac diastolic function indices

DCP	LVED	IVSD	LVPWD	E/A ratio	E/E' ratio	PA	PASP
Whole							
r	0.06	-0.19	-0.19	0.19	-0.27	-0.16	-0.07
P	0.42	0.008[b]	0.009[b]	0.009[b]	<0.001[a]	0.33	0.34
Fovea							
r	0.05	0.12	0.001	0.007	-0.04	0.08	-0.10
P	0.50	0.09	0.99	0.93	0.63	0.29	0.18
Para fovea							
r	0.07	-0.18	-0.22	0.17	-0.24	-0.13	-0.07
P	0.32	0.01[c]	0.003[b]	0.03[c]	0.001[b]	0.08	0.38
Superior hemisphere							
r	0.10	-0.18	-0.22	0.18	-0.25	-0.13	-0.06
P	0.18	0.01[c]	0.003[b]	0.02[c]	0.001[b]	0.10	0.45
Inferior hemisphere							
r	0.06	-0.17	-0.21	0.14	-0.22	-0.12	-0.08
P	0.46	0.02[c]	0.004[b]	0.04[c]	0.004[b]	0.11	0.31
Temporal							
r	0.08	-0.13	-0.19	0.17	-0.21	-0.09	-0.10
P	0.25	0.04[c]	0.009[b]	0.02[c]	0.006[b]	0.23	0.19
Superior							
r	0.05	-0.17	-0.20	0.19	-0.28	-0.15	-0.04
P	0.47	0.03[c]	0.006[b]	0.01[c]	<0.001[a]	0.05	0.59
Nasal							
r	0.10	-0.16	-0.21	0.17	-0.24	-0.14	-0.04
P	0.18	0.03[c]	0.004[b]	0.02[c]	0.001[b]	0.06	0.58
Inferior							
r	0.02	-0.19	-0.21	0.11	-0.18	-0.12	-0.08
P	0.78	0.01[c]	0.004[b]	0.03[c]	0.02[c]	0.10	0.26

DCP: Deep capillary plexus; LVED: Left ventricular end-diastolic diameter; IVSD: Interventricular septal thickness in diastole; LVPWD: Left ventricular posterior wall thickness in diastole; E/A ratio: Early (E) to atrial (A) wave velocity ratio; E/E' ratio: Early (E) diastolic mitral inflow velocity to early (E') diastolic mitral annular velocity ratio; PA: Pulmonary artery diameter; PASP: Pulmonary arterial systolic pressure. [a]*P*<0.001; [b]*P*<0.01; [c]*P*<0.05.

For DCP, the correlation dynamics were largely similar to those of the SCP, boasting an average vascular density of 52.69 (ranging 32.49 from 64.46) and statistically significant correlations with IVSD, LVPWD, E/E' ratio (negative), and E/A ratio (positive). Regionally, excluding the central fovea, all areas had a statistically significant negative correlation with IVSD, LVPWD, and E/E' ratio. As for the E/A ratio, a significant positive correlation was seen in all DCP regions except the foveal central subfield, inferior, and inferior hemisphere.

CC layer had an average vascular density of 65.15 (ranging 53.66 from 70.67). Here, only the positive correlation with the E/A ratio and the negative correlation with the E/E' ratio reached statistical significance. Regional data unveiled that IVSD positively correlated with the CC's inferior region, LVPWD with the CC's inferior hemisphere, the E/A ratio with the CC's foveal central subfield and inferior hemisphere, and the E/E' ratio negatively correlated with the CC's superior region. These correlations were all statistically significant. Furthermore, both LVPWD and E/A ratio showed a statistically significant positive correlation with choroidal perfusion, while the E/E' ratio negatively correlated in a statistically significant manner. However, no significant associations were detected for LVED, PA, and PASP in terms of retinal and choroidal vessel density and choroidal perfusion.

DISCUSSION

In our study, OCTA findings demonstrated a positive correlation between retinal thickness and LVED, and a negative correlation with PASP. The retinal vascular density (RVD), as identified in both the SCP and DCP layers, showed a significant negative association with IVSD, LVPWD, and the average E/E' ratio, but a positive association with the E/A

Table 5 Association estimates of CC vessel density and perfusion with cardiac diastolic function indices

CC	LVED	IVSD	LVPWD	E/A ratio	E/E' ratio	PA	PASP
Whole							
r	0.06	0.04	0.11	0.22	-0.16	-0.121	0.02
P	0.40	0.61	0.14	0.003[b]	0.03[c]	0.109	0.84
Fovea							
r	0.04	0.08	0.14	0.22	-0.10	-0.105	0.09
P	0.62	0.27	0.05	0.004[b]	0.18	0.165	0.20
Para fovea							
r	0.11	0.10	0.13	0.13	-0.11	0.005	-0.03
P	0.14	0.17	0.07	0.09	0.15	0.949	0.69
Superior hemisphere							
r	0.10	0.08	0.09	0.09	-0.13	0.019	-0.02
P	0.17	0.27	0.21	0.23	0.09	0.799	0.84
Inferior hemisphere							
r	0.10	0.12	0.17	0.15	-0.08	0.003	-0.02
P	0.19	0.09	0.20	0.04[c]	0.31	0.966	0.77
Temporal							
r	0.08	0.08	0.06	0.12	-0.03	-0.07	-0.04
P	0.29	0.28	0.39	0.10	0.69	0.35	0.60
Superior							
r	0.05	0.09	0.14	0.09	-0.17	0.06	0.01
P	0.48	0.22	0.06	0.22	0.03[c]	0.43	0.94
Nasal							
r	0.14	0.002	0.11	0.13	-0.12	-0.03	-0.006
P	0.06	0.98	0.13	0.08	0.12	0.68	0.94
Inferior							
r	0.03	0.17	0.13	0.12	-0.04	0.02	-0.01
P	0.66	0.32	0.09	0.11	0.60	0.84	0.91
Choroidal perfusion							
r	0.05	0.05	0.15	0.23	-0.14	-0.11	0.09
P	0.53	0.49	0.04[c]	0.002[b]	0.04[c]	0.13	0.22

CC: Choriocapillaris; LVED: Left ventricular end-diastolic diameter; IVSD: Interventricular septal thickness in diastole; LVPWD: Left ventricular posterior wall thickness in diastole; E/A ratio: early (E) to atrial (A) wave velocity ratio; E/E' ratio: Early (E) diastolic mitral inflow velocity to early (E') diastolic mitral annular velocity ratio; PA: Pulmonary artery diameter; PASP: Pulmonary arterial systolic pressure. [b]P<0.01; [c]P<0.05.

ratio—except in the foveal region. CVD exhibited scattered correlations with various diastolic function parameters, predominantly in the inferior hemisphere, superior, and mean density. Additionally, choroidal perfusion was found to be linked to the LVPWD, average E/E' ratio, and E/A ratio. Notably, no significant associations were observed between the PA diameter and measurements related to retinal thickness, vascular density, or choroidal perfusion.

Various mechanisms might underpin this relationship between retinal thickness and LVED or PASP. As heart and retina both have high metabolic demands, changes in cardiac function, especially in its diastolic phase, might reflect parallel alterations in the microcirculation of the retina[9]. Research indicates that the perivascular cell system of the heart is analogous to that of retina or central nervous system[10]. Pericytes play a crucial role in maintaining the vascular function of cardiac system. When these pericytes are compromised, there's an evident impairment in the cardiac vascular diastolic function and a reduction in coronary blood flow reserve[11]. To date, no studies have delineated a definitive correlation between LVED and retinal thickness. In patients with type 2 diabetes and those with gestational hypertension, abnormalities in left ventricular (LV) diastolic function can lead to peripheral vascular dysfunction, likely resulting from compromised vascular elasticity and reduced compliance[12]. Thus, we hypothesize that the thickening of the retina might be a compensatory response to an increased blood volume or vascular remodeling due to altered hemodynamics in patients with elevated LVED. Conversely, increased PASP often denotes pulmonary hypertension (PH), which can be consequent to left heart diseases leading to congestive backpressure changes. Such systemic changes might induce retinal vascular dysregulation, thereby influencing retinal thickness[13]. Gu *et al*[14] also observed that patients with PH demonstrated a significant reduction in the thickness of ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL), which aligns consistently with our finding. A review of the literature indicates that most reports of morphological changes in retinal microvasculature are related to PH[13]. These vascular abnormalities include a decrease in vascular density of retina and increase in choroidal thickness. The increase in PA pressure initially leads to an increase in superior vena cava pressure, followed by an increase in intraocular pressure, which leads to damage to the retinal and choroidal circulation. Subsequently, the increase in intraocular venous pressure affects perfusion and increases the risk of hypoxia and retinal edema[15].

Our analysis showed that the VD of both SCP and DCP layers is linked to IVSD, LVPWD, and the average E/E' and E/A ratios. The negative correlation of VD with IVSD, LVPWD, and the average E/E' ratio might indicate systemic microvascular changes. The ratio of early diastolic velocity of mitral inflow (E) to early diastolic velocity of the mitral annulus (E') is one of the key indices for evaluating cardiac diastolic function. It can accurately reflect the LV filling pressure and pulmonary arterial hypertension. Therefore, clinically, the E/E' ratio is often used as a biomarker to gauge the severity of diastolic dysfunction[16]. Increased IVSD or LVPWD suggests a less compliant ventricle[17]. A stiffer ventricle then elevates the E/E' ratio, signifying higher diastolic filling pressures. A large-scale cross-sectional study has shown that in patients with CHD, alterations in cardiac structure (such as increased LV mass, LV diameter, LV post wall thickness, and LV septum thickness, along with decreased right ventricular mass and volume, increased right ventricular mass) are associated with retinal arteriolar narrowing and/or

venular widening[18]. Additionally, indices of retinal vascular morphology are also linked with inflammation, endothelial dysfunction, and certain microvascular and macrovascular diseases. Previous research suggests that alterations in LV parameters can lead to modifications in retinal blood flow. These changes are potentially linked to endothelial dysfunction, impaired systemic perfusion and oxygenation, or compromised microvascular adaptability[19].

Under pathological conditions, the positive link between the E/A ratio and RVD may arise from interconnected mechanisms. In echocardiography, the E wave signifies early diastolic inflow velocity in the left ventricle, while the A wave represents atrial contraction flow velocity. A heightened E/A ratio usually indicates LV diastolic dysfunction. Shiba *et al*'s[20] work with laser speckle flowgraphy showed a decrease in blood flow velocity in the optic nerve region, corresponding to the central retinal artery, with ventricular diastolic abnormalities. Research by Cornuault *et al*[21] revealed that decreased pericytes in cardiac microvessels of mice result in increased vascular permeability and diastolic dysfunction. Similar pericyte changes have been observed in cerebral and retinal microvessels, suggesting potential analogous impacts in pathological conditions.

Interestingly, the foveal region appeared to be an exception in these relationships. The specialized structure and function of the fovea, with its high concentration of photoreceptors, relative avascularity and its unique "dual circulation" blood supply system, might render it less susceptible to systemic hemodynamic changes, or might respond differently compared to other retinal regions[22].

The dispersion observed in CVD and its varied associations with distinct diastolic function indicators are intriguing. The choroid, rich in blood vessels, plays a pivotal role in supplying nutrients and oxygen to the outer retina. Originating from the ophthalmic artery, the choroidal vascular system might be more responsive to cardiovascular dysfunctions, manifesting early structural and functional changes[23]. Literature suggests that patients with cardiac stents or histories of angina, myocardial infarction, or other CAD exhibit thinner choroidal layer compared to healthy individuals[6,24]. As coronary artery narrowing intensifies, choroidal blood flow density and perfusion tend to decrease. Notably, even in patients without significant coronary narrowing, choroidal thickness correlates with blood flow velocity: slower flow results in thinner choroid, especially when vascular walls thicken and lumens narrow[25].

However, our results underscored a lack of significant association between the PA diameter and retinal thickness, vascular density, and choroidal perfusion. To the best of our knowledge, there is scant literature that establishes a direct correlation between PA diameter and microvasculature of fundus. There has been only a case report suggesting that a patient who underwent left PA stent surgery experienced central retinal artery occlusion. It is hypothesized that this surgery might lead to the migration of microthrombi into the superior vena cava and right atrium, and subsequently, through an atrial septal defect, into the left atrium, eventually entering the systemic and retinal circulation[26]. Typically, alterations in PA diameter are commonly seen in pulmonary embolism. Severe pulmonary embolism can lead to cardiac remodeling, resulting in right ventricular dilation, hypertrophy, and dysfunction[27]. Thus, PA stands as an independent predictor of right ventricular failure[28]. Diseases of the left ventricle can also precipitate right ventricular dysfunction, likely due to PH. However, whether it's pulmonary arterial hypertension or right ventricular dysfunction, both primarily result in elevated jugular venous pressure and tissue edema[29], which may not be as closely related to the retinochoroidal vascular system, which originates from the carotid artery.

The insights from our study highlight the potential value of OCTA as a non-invasive tool in auxiliary diagnosing and assessing cardiac function. Given the observed correlations between retinal parameters and diastolic function indicators, OCTA may serve as an adjunctive tool, complementing traditional cardiac assessments in determining the severity of diastolic impairments. Additionally, understanding these associations can pave the way for novel preventive and therapeutic strategies targeting both ocular and cardiac wellness. Future interventions might focus on modulating systemic hemodynamics to favorably influence retinal and choroidal parameters, which could indirectly reflect improved cardiac diastolic function.

It's paramount to acknowledge potential biases and limitations inherent to our research. Our study design might not capture all the dynamic interactions between ocular and cardiac parameters, and the correlations observed do not necessarily imply causation. Moreover, potential confounding factors might have influenced our findings, necessitating cautious interpretation. For future studies, a larger and more diverse cohort, coupled with longitudinal tracking, could provide a more comprehensive understanding of the interplay between these physiological systems.

In summary, our findings emphasize the intriguing intersections between cardiology and ophthalmology, revealing that fundus parameters can mirror aspects of cardiac function. This interdisciplinary exploration not only advances our knowledge in both fields but also hints at the broader systemic connections that underpin human health.

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