Evaluation of retinal microvasculature according to stable chronic obstructive pulmonary disease severity and the correlation of pulmonary parameters with optical coherence tomography angiography findings

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Purpose: To evaluate the retinal and optic disc microvascular changes according to disease severity in patients with stable chronic obstructive pulmonary disease (COPD), and the correlation of pulmonary parameters with optical coherence tomography angiography (OCTA) findings. Methods: Forty patients with COPD and 30 age- and sex-matched subjects (control group) were included in this cross-sectional prospective study. The COPD group was then divided into two subgroups according to GOLD classification and disease severity as mild-to-moderate COPD group (group 1) and severe COPD group (group 2). OCTA was performed with 6 mm × 6 mm sections for the macula and 4.5 mm × 4.5 mm sections for the optic disc. Foveal retinal thickness (FRT), peripapillary retinal nerve fiber layer (RNFL) thickness, and vessel density in different sections of the retina and optic disc were analyzed. Results: The mean ages, gender, intraocular pressures, peripapillary RNFL thickness, FRT, and optic disc vessel densities were similar among the groups. Compared to the control group and group 1, group 2 showed significantly lower mean foveal vessel density measurements in superficial and deep capillary plexus (P = 0.014 and P = 0.007, respectively). Cigarette packets/year, exacerbation per year, and Modified Medical Research Council showed significant negative correlations, whereas forced expiratory volume in 1 s (FEV1) and FEV1/forced vital capacity showed significant positive correlations with foveal vessel densities. Conclusion: COPD severity seems to have a negative effect on OCTA measurements. OCTA may reflect the severity of inflammation and hypoxia in COPD and may provide useful detailed information on the role of retinal vascular changes in the follow-up and progression of patients with COPD.

Key words: Chronic obstructive pulmonary disease, optic disc, optical coherence tomography angiography, retina, severity

Chronic obstructive pulmonary disease (COPD) is a common, chronic, inflammatory, and progressive lung disease that leads to obstructed airflow from the lungs.[1,6] Symptoms include breathing difficulty, cough, mucus production, and wheezing. It is caused by long-term exposure to irritating gases or particulate matter, most often from long-term smoking of cigarettes. In addition, there are other factors that play a role in the development of COPD, such as genetic susceptibility, as only about 20%–30% of smokers may develop COPD. Individuals with COPD are at increased risk for developing heart disease, lung cancer, and a variety of other conditions such as ophthalmic problems.[1,6] Chronic hypoxemia, systemic inflammation, vascular and endothelial dysfunction, and increased sympathetic activity are thought to involve ocular structures such as the retina and optic nerve.[2,3] It is necessary to provide appropriate treatment to preserve and monitor visual functions. Optical coherence tomography angiography (OCTA) is a new technique that demonstrates the vascular structure of the retina in a non-invasive, rapid, and high-resolution method. OCTA is thought to be useful in explaining the pathophysiology of ocular disorders other than the retina such as glaucoma or extraocular disorders.[8,9] In previous studies, retinal, choroidal, and optic nerve head changes in patients with COPD have been demonstrated by the optical coherence tomography (OCT) technique.[2,5] Retinal and optic disc vascular changes of patients with COPD by using OCTA[10,11] and correlation of pulmonary parameters with OCT findings in stable COPD[9] were also mentioned by recently published reports. However, microvascular blood flow changes due to chronic hypoxia in patients with COPD are still not clear. Additionally, retinal microvascular changes according to COPD severity and the correlation between pulmonary parameters of patients with COPD and OCTA variables have not been reported yet.

In this study, given the role of chronic hypoxemia and systemic inflammation in COPD, we aimed to determine the retinal microvasculature according to disease severity in...
patients with COPD by OCTA and compare them with age- and sex-matched control subjects as well as the correlation of pulmonary parameters with OCTA findings in patients with stable COPD.

Methods

This prospective cross-sectional study was approved by the ethics committee of our institution (protocol number: 2020/09, 16/01/2020) and conducted in accordance with all the relevant tenets of the Declaration of Helsinki. Fifty-one patients with COPD who were referred to the ophthalmology outpatient clinic from the department of chest diseases and 30 age- and sex-matched subjects (control group) who were non-smoking volunteers and admitted to the ophthalmology outpatient clinic for a routine exam with no ocular pathology, no history of smoke, and additional systemic diseases except controlled hypertension were included to the study. We excluded 11 referred patients with COPD because of history of cataract surgery (n = 7), age-related macular degeneration (n = 1), history of bypass surgery (n = 1), leukemia (n = 1), and lung cancer (n = 1). A total of 40 qualified stable patients with COPD were included in the analysis. The forced expiratory volume in 1 s (FEV1%) and forced vital capacity (FVC%) were measured in all patients with COPD. The severity of COPD is evaluated by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). Patients with COPD were divided into two subgroups according to GOLD classification and disease severity as the mild-to-moderate group (group 1, patients of stages A and B) and severe group (group 2, patients of stages C and D). The modified Medical Research Council (mMRC) Questionnaire is widely used for assessing the severity of breathlessness in patients with COPD. The mMRC grade is a five-point scale based on the severity of a patient’s breathlessness related to physical activity. Current guidelines advocate the use of this scale to assess symptoms. In this study, the mMRC grades were assessed by the Chest department.

All participants signed written informed consent forms and underwent complete ophthalmic examinations including measurement of best-corrected visual acuity (BCVA), refractive error (RE), slit-lamp biomicroscopy, non-contact tonometry, and fundoscopy. We included the right eyes of the subjects with BCVA ≥8/10, RE ≤± 2.0 D, and intraocular pressure ≤21 mm Hg. The exclusion criteria were diabetes mellitus, uncontrolled systemic arterial hypertension, undergoing systemic steroid therapy, cases with acute exacerbations, using mechanical ventilator therapy, cardiovasculardisease, dyslipidemia, age-related macular degeneration, a history of intraocular surgery, glaucoma, uveitis, ocular inflammation, optic neuropathy, ocular trauma, and/or amблиопия.

The OCTA images were obtained by a single technician by using a spectral-domain OCT system with the Avanti RTVue OCTA software (Avanti RTVue-XR 100, Optovue Inc., Fremont, CA). This device uses an increased A-scan rate of 70 kHz, which allows the generation of high axial resolution of 5 µm in tissue. The OCTA provides vascular information of retinal layers as an en face angiogram, a vessel density map, and a vessel density percentage (%) calculated as the area covered by flowing blood vessels in the selected region. Volumetric angiograms were semi-automatically segmented into three layers, allowing for separate angiograms of the inner retina, outer retina, and choroid. The OCTA image protocol involved two raster scans acquired by repeated B-scans at 304 raster positions, and each B-scan consisted of 304 A-scans covering a 6 mm × 6 mm area centered on macula and 4.5 mm × 4.5 mm area centered in the optic nerve head. Two volumetric raster scans were taken consecutively, with one in the horizontal priority (x-fast) and one in the vertical priority (y-fast). Motion artifacts, including residual axial motion and transverse saccadic motion, were removed by three-dimensional (3D) orthogonal registration and by merging the pair of scans by using the contained software (ReVue, version 2014.2.0.15; Optovue Inc.). Shadow graphic projection artifacts were removed using a slab-subtraction method, reducing inner retinal projection onto the outer retinal angiogram. En face retinal angiograms were created by projecting the flow signal internal to the retinal pigment epithelium. Foveal retinal thickness (FRT), vessel density in the fovea of superficial and deep capillary plexus, and 300-µm width around the fovea avascular zone (FAZ) were measured. FAZ was defined as the area without vessels that covers the center of the fovea. The fovea was defined as an annulus centered on the foveal avascular zone with inner and outer ring diameters of 1 mm. Flow areas of choriocapillaris were also noted. Radial peripapillary capillary (RPC) densities, including whole image, inside disc, and peripapillary capillary plexus densities, and retinal nerve fiber layer thickness (RNFL) were also obtained. The peripapillary region was automatically defined by the software as a 1.0-mm-wide round annulus extending from the optic disc. OCTA scans with a quality level of less than 7, artifacts, or decentered were not used in the study. All measurements were taken at the same hour of the day (10:00 AM–12:00 PM) in all groups to rule out the effect of diurnal variations on OCTA values.

Statistical analysis

Statistical analyses were performed using IBM SPSS for Windows Version 21.0 software. Numerical variables were expressed as mean ± standard deviation or median interquartile range (IQR: 25%–75%) as appropriate. Categorical variables were summarized as numbers and percentages. The normality of the distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test. Independent samples t test or Mann–Whitney U test was used to determine the difference between two independent subgroups. Multiple comparisons of between-group variables were performed using one-way ANOVA. The Tukey post-hoc HSD test was applied as appropriate. Pearson correlation coefficient was used for the correlations between variables, and P ≤ 0.05 was considered to reflect statistical significance.

Results

The mean ages, gender, intraocular pressures, peripapillary RNFL thickness, and FRT were similar among the groups. Demographics and clinical characteristics of the groups are shown in Table 1. There was a significant difference regarding pulmonary parameters between groups 1 and 2. Comparison of pulmonary parameters of group 1 and group 2 patients are shown in Table 2. Compared to the control group and group 1, group 2 showed significantly lower mean foveal vessel density measurements in superficial and deep capillary plexus (P = 0.014 and P = 0.007, respectively) [Table 3]. OCTA images (superficial and deep capillary plexus) of a control,
Table 1: Comparison of demographic and clinical characteristics among the groups

| Characteristics                  | COPD Mild/Moderate Group (n=22) | COPD Severe Group (n=18) | Control Group (n=30) | P     |
|---------------------------------|---------------------------------|--------------------------|----------------------|-------|
| Age, years (Mean±SD)            | 58.7±11.1                       | 59.6±13.8                | 55.1±8.0             | 0.295 |
| Gender, n (male/female)         | 21/1                            | 18/0                     | 29/1                 | 0.677 |
| % (male/female)                 | 95.5/4.5                        | 100.0/0.0                | 96.7/3.3             |       |
| Body mass index (kg/m²) (Mean±SD)| 27.8±4.8                        | 27.1±6.7                 | 27.0±2.9             | 0.795 |
| Hypertension                    | 15 (% 68.1)                     | 13 (72.2%)               | 20 (66.6%)           | 0.554 |
| Intraocular pressure (mmHg) (Mean±SD) | 16.4±4.1                           | 17.0±4.6                 | 16.3±1.5             | 0.822 |
| FRT (µm) (Mean±SD)              | 264.9±22.4                      | 252.6±22.9               | 257.3±15.9           | 0.185 |
| RNFL thickness (µm) (Mean±SD)   | 111.4±14.0                      | 105.5±16.2               | 111.6±11.7           | 0.321 |
| Inferior quadrant (µm) (Mean±SD) | 144.4±20.0                      | 129.1±23.5               | 139.9±18.2           | 0.063 |
| Superior quadrant (µm) (Mean±SD) | 133.1±18.5                      | 126.7±22.3               | 131.6±17.8           | 0.567 |
| Temporal quadrant (µm) (Mean±SD) | 72.7±15.4                       | 69.3±12.4                | 71.2±7.2             | 0.682 |
| Nasal quadrant (µm) (Mean±SD)   | 99.5±18.2                       | 96.8±16.5                | 103.7±18.3           | 0.412 |

COPD: Chronic obstructive pulmonary disease; SD: Standard deviation; FRT: Foveal retinal thickness; RNFL: Retinal nerve fiber layer

Table 2: Comparison of the pulmonary parameters between COPD subgroups

| Characteristics                  | Mild/ Moderate COPD Group (n=22) | Severe COPD Group (n=18) | P     |
|---------------------------------|---------------------------------|--------------------------|-------|
| FEV1%                           | 75.5±16.6                       | 54.8±15.3                | <0.001|
| FVC %                           | 89.5±15.5                       | 74.2±22.3                | 0.019 |
| FEV1/FVC                        | 67.8±9.9                        | 59.5±10.7                | 0.018 |
| FEV25-75%                       | 53.0±20.1                       | 31.0±11.9                | <0.001|
| PEF %                           | 70.8±19.7                       | 50.3±15.1                | 0.001 |
| Smoking status (non/active)     | 1/21                            | 4/14                     | 0.080 |
| Cigarette packets/year Median (IQR; 25%-75%) | 30 (20-50)                    | 40 (10-60)               | 0.472 |
| Exacerbation per year Median (IQR; 25%-75%) | 0 (0-0)                      | 1 (0-1)                  | 0.001 |
| Disease duration (year) Median (IQR; 25%-75%) | 3 (1-5)                      | 4 (1-10)                 | 0.064 |
| SaO2, %                         | 96.0±1.1                        | 93.2±4.1                 | 0.004 |

COPD: Chronic obstructive pulmonary disease; SD: Standard deviation; FEV1: Forced expiratory volume in first second; FVC: Forced vital capacity; PEF: Peak expiratory flow, mMRC: Modified Medical Research Council; SaO2: Arterial oxygen saturation

mild/moderate, and severe-COPD patient are shown in Figs. 1–6. Optic disc microvascular parameters showed no significant difference among the groups [Table 4]. Cigarette packets/year showed significant negative correlations with deep foveal vessel density (r = −0.341, P = 0.036). Exacerbation per year showed significant negative correlations with superficial parafoveal density (r = −0.386, P = 0.017) and positive correlations with flow area for outer retina (r = 0.408, P = 0.011). The mMRC showed significant negative correlations with superficial and deep foveal vessel density, and FRT, (r = −0.415, P = 0.018; r = −0.369, P = 0.037; r = −0.391, P = 0.027, respectively), but positive correlations with flow area for outer retina (r = 0.353, P = 0.047). Arterial oxygen saturation showed negative correlations with flow area for outer retina (r = −0.362, P = 0.024) but positive correlations with flow area for choriocapillaris (r = 0.384, P = 0.016). Duration of COPD showed negative correlations with OCTA values, but the difference was not significant. FEV1 and FEV1/FVC showed significant positive correlations with superficial foveal density (r = 0.352, P = 0.030; r = 0.442, P = 0.005, respectively). FEV1/FVC also showed significant positive correlations with deep foveal density (r = 0.333, P = 0.041). Results of correlation analysis between pulmonary parameters and OCTA values of patients with COPD are presented in Table 5.

Discussion

Our study showed that compared to the control group and group 1, group 2 showed significantly lower mean foveal vessel density measurements in superficial and deep capillary plexus. In addition, correlation analysis between pulmonary parameters and OCTA values of patients with COPD were reported for the first time. A significant negative correlation was found on foveal vessel densities regarding cigarette packets/year, exacerbation per year, and mMRC, whereas FEV1 and FVC showed significant positive correlations with foveal vessel densities.

The direct impact of hypoxemia and hypercapnia on the wall of arterioles, venules, and capillaries results in severe vasodilatation along with the increased permeability of the walls causing clinically evident changes in the retina.[13] Palkovits et al.[13] and Elíasdóttir et al.[14] reported hypoxia of retinal vessels in people with severe COPD. Several studies have shown that systemic endothelin-1 levels are elevated in patients with COPD, and increased levels of endothelin-1 have been shown to affect retinal vessels.[15,16] It is well known that decreased NO and increased endothelin-1 synthesis due to endothelial dysfunction causes vasoconstriction.[17] All these reports support why there is a decrease in foveal vessel density measurements in superficial and deep capillary plexus of patients with COPD, and why a positive correlation is found between flow area for choriodapillaris and arterial oxygen saturation in our study. We assumed that the positive correlation between the flow area of the outer retina and clinical parameters as exacerbation per year and mMRC was also for compensation.

Alkan et al.[10,11] mentioned that vascular density measured by OCTA decreased in the parafoveal area due to COPD-related...
hypoxemia and endothelial dysfunction, and reported that OCTA may have the potential to be used in the follow-up of patients with COPD. However, they did not evaluate OCTA measurements according to the COPD severity. In our study,
Ozon et al.\[3\] studied the correlation of some pulmonary function test results with the serial structural changes in the OCT of patients with COPD. Disease duration, mMRC, and attacks/year showed significant negative correlations, whereas FEV1 and FEV1/FVC showed significant positive correlations with OCT values in their study. Different from this study, we investigated the correlations between pulmonary parameters and retinal and optic disc microvasculature evaluated by OCTA of patients with COPD. Based on our findings, OCTA may provide us with more detailed information in patients with COPD compared to OCT.

It has been shown that the deep capillary plexus is particularly sensitive to systemic or ocular diseases affecting the retina.\[18\] We found not only deep but also superficial foveal vessel densities significantly decreased in the severe COPD group compared to others.

### Table 3: Comparison of retina microvascular parameters among the groups by OCTA

| Characteristics±SD | Mild/Moderate COPD Group (n=22 eyes) | Severe COPD Group (n=18 eyes) | Control Group (n=30 eyes) | P     |
|---------------------|-------------------------------------|-----------------------------|--------------------------|-------|
| **Superficial Vessel Density (%)** |                                    |                             |                          |       |
| Whole image         | 49.9±3.0                            | 48.3±4.8                    | 49.3±4.1                 | 0.460 |
| Fovea               | 22.1±7.0                            | 16.3±5.7                    | 19.9±5.3                 | 0.014 |
| Parafovea           | 52.7±3.4                            | 51.2±5.8                    | 52.0±5.0                 | 0.624 |
| Perifovea           | 50.3±2.9                            | 48.7±4.9                    | 49.8±4.4                 | 0.488 |
| **Deep Vessel Density (%)** |                                    |                             |                          |       |
| Whole image         | 51.7±5.7                            | 49.9±6.7                    | 50.8±7.3                 | 0.712 |
| Fovea               | 38.2±7.8                            | 30.7±7.6                    | 38.0±8.8                 | 0.007 |
| Parafovea           | 55.0±3.8                            | 53.4±5.3                    | 53.6±5.8                 | 0.559 |
| Perifovea           | 53.1±5.9                            | 51.3±7.5                    | 52.6±7.8                 | 0.710 |
| FAZ area (mm\(^2\)) | 0.3±0.4                             | 0.3±0.1                     | 0.2±0.1                  | 0.185 |
| Flow area for outer retina (mm\(^2\)) | 0.4±0.2                             | 0.6±0.4                     | 0.5±0.2                  | 0.635 |
| Flow area for choriocapillaris (mm\(^2\)) | 2.1±0.1                             | 2.0±0.1                     | 2.0±0.1                  | 0.121 |

OCTA: Optical coherence tomography angiography; COPD: Chronic obstructive pulmonary disease; FAZ: Area of 300-µm width around the foveal avascular zone; SD: Standard deviation
Figure 4: OCTA image (deep vessel density) of a 61-year-old male patient with mild/moderate COPD

Figure 5: OCTA image (superficial vessel density) of a 61-year-old male patient with severe COPD
Table 4: Comparison of optic disc microvascular parameters among the groups by OCTA

| Characteristics±SD | Mild/Moderate COPD Group (n=22 eyes) | Severe COPD Group (n=18 eyes) | Control Group (n=30 eyes) | P  |
|-------------------|--------------------------------------|------------------------------|----------------------------|----|
| RPC density (%)   |                                      |                              |                            |    |
| Whole image       | 49.4±4.5                             | 47.9±4.4                     | 49.3±2.5                   | 0.355 |
| Inside disc       | 50.5±5.3                             | 50.5±4.7                     | 50.2±5.0                   | 0.957 |
| Peripapillary     | 51.0±4.7                             | 49.8±5.0                     | 51.4±2.8                   | 0.405 |

OCTA: Optical coherence tomography angiography, SD: Standard deviation, COPD: Chronic obstructive pulmonary disease; RPC: Radial peripapillary capillary

In a study, OCTA did not detect decreased optic nerve head, RPC, or macular blood vessel density in eyes with obstructive sleep apnea syndrome as another pulmonary disease characterized by repeated or prolonged episodes of hypoxia.[19] Similar to this study, there was no significant decrease regarding optic disc microvascular parameters among the groups by OCTA. COPD does not seem to lead to direct quantitative optic nerve head vascular damages. On the contrary, OCTA showed a significant decrease in foveal vessel densities in patients with severe COPD in our study. The optic nerve head may be affected later or more resistant to hypoxia and inflammation than the fovea; thus, fovea may be more sensitive. The small number of patients may also be a possible reason for the optic nerve head to appear unaffected.

Smoking is a major cause of endothelial dysfunction and microvascular changes.[20] Nicotine stimulates the sympathetic nervous system and causes vasoconstriction. Here, supporting this hypothesis, a significant negative correlation was found on deep foveal vessel densities regarding cigarette packets/year. This may be as a result of ischemia that causes decreased vascular density in the foveal area.

This study has some limitations. First, it is a single-center study and has a relatively small number of patients. Second, the presence of hypertension in both groups may affect the retinal vascular parameters. However, there was no significant difference in the frequency of hypertension among COPD and control groups, and uncontrolled hypertensive ones were excluded from the study; thus, we thought that this would not affect the outcome of the study. Finally, it would be better to analyze the correlation with the treatment modalities; this can be studied in a future study. Our results need to be verified with a further prospective clinical trial in a larger cohort.
Table 5: Results of correlation analysis between pulmonary parameters and OCTA values of patients with COPD

| Characteristics±SD | Duration of COPD | Cigarette packets/year | Exacerbation per year | mMRC | SaO₂ | FEV₁ | FVC | FEV₁/FVC |
|--------------------|-----------------|-------------------------|-----------------------|-------|------|------|-----|----------|
| Superficial Vessel Density (%) | | | | | | | | |
| Whole image | ‑0.242 | ‑0.176 | ‑0.315 | ‑0.169 | 0.031 | 0.185 | 0.232 | 0.022 |
| \( r \) | 0.143 | 0.292 | 0.054 | 0.354 | 0.850 | 0.266 | 0.160 | 0.896 |
| Fovea | ‑0.121 | ‑0.278 | ‑0.141 | ‑0.415 | 0.255 | 0.352 | 0.109 | 0.442 |
| \( r \) | 0.466 | 0.091 | 0.399 | 0.018 | 0.117 | 0.030 | 0.517 | 0.005 |
| Parafovea | ‑0.196 | ‑0.111 | ‑0.386 | ‑0.241 | 0.223 | 0.141 | 0.204 | ‑0.045 |
| \( r \) | 0.238 | 0.508 | 0.017 | 0.184 | 0.172 | 0.400 | 0.220 | 0.789 |
| Perifovea | ‑0.206 | ‑0.116 | ‑0.318 | ‑0.101 | 0.019 | 0.196 | 0.262 | ‑0.006 |
| \( r \) | 0.214 | 0.489 | 0.052 | 0.583 | 0.910 | 0.239 | 0.112 | 0.971 |
| Deep Vessel Density (%) | | | | | | | | |
| Whole image | ‑0.007 | ‑0.078 | ‑0.152 | 0.157 | ‑0.011 | 0.057 | 0.175 | ‑0.092 |
| \( r \) | 0.969 | 0.642 | 0.362 | 0.390 | 0.947 | 0.736 | 0.294 | 0.583 |
| Fovea | ‑0.298 | ‑0.341 | ‑0.201 | ‑0.369 | 0.194 | 0.313 | 0.121 | 0.333 |
| \( r \) | 0.069 | 0.036 | 0.226 | 0.037 | 0.237 | 0.056 | 0.469 | 0.041 |
| Parafovea | 0.000 | ‑0.092 | ‑0.267 | 0.120 | 0.058 | 0.071 | 0.171 | ‑0.102 |
| \( r \) | 0.999 | 0.582 | 0.105 | 0.512 | 0.728 | 0.670 | 0.305 | 0.544 |
| Perifovea | ‑0.013 | ‑0.083 | ‑0.179 | 0.134 | ‑0.006 | 0.068 | 0.172 | ‑0.070 |
| \( r \) | 0.938 | 0.619 | 0.283 | 0.465 | 0.970 | 0.683 | 0.300 | 0.674 |
| Foveal retinal thickness | ‑0.185 | ‑0.227 | ‑0.058 | ‑0.391 | 0.020 | 0.205 | 0.084 | 0.257 |
| \( r \) | 0.266 | 0.171 | 0.731 | 0.027 | 0.905 | 0.217 | 0.617 | 0.120 |
| FAZ area (mm²) | ‑0.048 | 0.121 | ‑0.061 | ‑0.196 | ‑0.010 | 0.149 | 0.228 | ‑0.094 |
| \( r \) | 0.775 | 0.470 | 0.716 | 0.283 | 0.952 | 0.371 | 0.169 | 0.576 |
| Flow area for outer retina (mm²) | 0.013 | 0.246 | 0.408 | 0.353 | ‑0.362 | ‑0.162 | ‑0.105 | ‑0.130 |
| \( r \) | 0.939 | 0.137 | 0.011 | 0.047 | 0.024 | 0.331 | 0.532 | 0.437 |
| Flow area for choriocapillaris (mm²) | 0.073 | ‑0.034 | ‑0.126 | 0.046 | 0.384 | 0.277 | 0.298 | 0.019 |
| \( r \) | 0.663 | 0.840 | 0.451 | 0.803 | 0.016 | 0.093 | 0.069 | 0.909 |
| RPC density (%) | | | | | | | | |
| Whole image | ‑0.153 | ‑0.015 | ‑0.232 | 0.045 | ‑0.011 | 0.206 | 0.231 | 0.046 |
| \( r \) | 0.360 | 0.928 | 0.162 | 0.806 | 0.948 | 0.214 | 0.164 | 0.786 |
| Inside disc | ‑0.048 | 0.009 | ‑0.220 | ‑0.039 | 0.061 | 0.032 | 0.034 | 0.076 |
| \( r \) | 0.775 | 0.956 | 0.185 | 0.834 | 0.625 | 0.850 | 0.842 | 0.649 |
| Peripapillary | ‑0.155 | 0.057 | ‑0.180 | 0.016 | ‑0.011 | 0.170 | 0.171 | 0.056 |
| \( r \) | 0.354 | 0.733 | 0.281 | 0.931 | 0.946 | 0.308 | 0.306 | 0.740 |

OCTA: Optical coherence tomography angiography; COPD: Chronic obstructive pulmonary disease; SD: Standard deviation; FEV₁: Forced expiratory volume in the first second; FVC: Forced vital capacity; mMRC: Modified Medical Research Council; SaO₂: Arterial oxygen saturation; FAZ: Area of 300 µm width around the foveal avascular zone; RPC: Radial peripapillary capillary
Conclusion

In conclusion, the results of the present study showed that patients with severe COPD seem to have significantly lower foveal vessel density measurements in superficial and deep capillary plexus. Additionally, this study showed significant correlations between the pulmonary examinations of clinical/functional parameters accessing severity of COPD and OCTA measurements for the first time. In the light of our findings, ophthalmologists should be aware of retinal microvascular changes in patients with COPD. OCTA may provide useful detailed information on the role of retinal vasculature in the follow-up and progression of patients with COPD, even during the preoperative and postoperative period of any ocular surgery. Further prospective studies are needed to confirm the relationship between COPD and OCTA parameters.

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Conflicts of interest
There are no conflicts of interest.

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