The Effect of Systemic Hyperoxia on Optic Nerve Head Blood Flow in Primary Open-Angle Glaucoma Patients

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Purpose. To assess the optic nerve head blood flow (ONH BF) response to hyperoxia in glaucoma patients using laser speckle flowgraphy (LSFG), and determine factors influencing vasoreactivity within the ONH.

Methods. We performed oxygen provocation testing in 15 eyes of 15 primary open-angle glaucoma (POAG) patients and 15 eyes of 15 age-matched control subjects. During the test, LSFG-derived tissue mean blur rate (MBRT) and clinical variables, including blood pressure, were recorded. We evaluated differences in MBRT alteration during systemic hyperoxia between the groups. Additionally, we calculated the mean % change in MBRT against baseline and determined contributing factors.

Results. Despite similar clinical variables during systemic hyperoxia in both groups, the mean % change in MBRT against baseline was significantly lower in the POAG than control subjects (P < 0.0001). Multiple regression analysis revealed that baseline MBRT and systolic blood pressure (SBP) were contributing factors to mean % change in MBRT (β = 0.44, β = −0.32, respectively). Additionally, baseline MBRT and SBP were strongly correlated to mean % change in MBRT only in the POAG group (r = 0.85, P < 0.0001; r = −0.60, P = 0.02, respectively).

Conclusions. POAG patients had a weaker vasoreactive response to hyperoxia than controls, and this impaired response was associated with lower basal ONH BF and higher SBP. These findings suggest that pre-existing vasoconstriction in the ONH of eyes with glaucoma might reduce the capacity of the vasoconstrictive response to hyperoxia. Alternatively, the pathways that mediate hyperoxia-induced vasoconstriction could be altered in POAG.

Keywords: ocular blood flow, laser speckle flowgraphy, autoregulation, hyperoxia

Primary open-angle glaucoma (POAG), the second most common cause of blindness worldwide,1 is characterized by progressive retinal ganglion cell death and associated visual field loss.2 High intraocular pressure (IOP) is the only evidence-based risk factor for glaucoma progression,3 but glaucoma can progress even with normal IOP. Many non-IOP risk factors have been investigated,4 but glaucoma pathogenesis remains imperfectly understood.

One suspected non-IOP risk factor for progression is damage to the optic nerve head (ONH) and associated low blood flow (BF). Low BF contributes to glaucoma by interrupting vascular autoregulation, or vasoreactivity,5 the intrinsic ability of vascular beds to maintain constant BF despite fluctuating perfusion pressure and varying metabolic demand.6 Vasoreactivity is usually assessed with oxygen, CO2, or light flicker provocation tests, which measure the capacity of the vessels to constrict during systemic hyperoxia and to dilate during hypercapnia or flicker stimulation. Provocation testing in glaucoma patients shows impaired vasoreactivity in the middle cerebral artery,7 retrobulbar vessels,8–11 retinal arteries and veins12–14 and superficial ONH.15,16

Assessing vasoreactivity is an important part of research into glaucoma pathophysiology, but previous reports could not measure hemodynamics in the deep layers of the ONH. Moreover, laser Doppler flowmetry, used in many reports to measure ONH microcirculation, is slow, has limited reproducibility, and has a limited ability to measure BF within the deep ONH, due to the relatively short wavelength of its laser.17 There is, therefore, a need for a new, convenient, and reproducible way to assess ocular hemodynamics during provocation tests. Recently, optical coherence tomography angiography (OCTA) has been used in glaucoma research to reliably visualize the capillary response to provocation outside the ONH in healthy subjects.18–20 However, OCTA shares the same weaknesses as laser Doppler flowmetry in visualizing deep ONH capillaries, due to image artifacts.21

Laser speckle flowgraphy (LSFG) promises to overcome previous limitations. LSFG is a convenient, reproducible way to assess ocular hemodynamics during provocation tests, and can evaluate BF within the deep ONH, from the posterior tissue to the lamina cribrosa, with high reproducibility.12 LSFG is already gaining popularity in Japan,22–25 and its clinical usability for estimating ocular perfusion has been validated in Caucasian

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METHODS

Oxygen Inhalation Test

Clinical characteristics were measured before testing. The oxygen inhalation test itself was performed in the same way as our previous investigation. Briefly, the protocol had three phases (shown in Fig. 1): baseline, hyperoxia, and recovery. In the baseline phase, the subjects inhaled room air for no less than 5 minutes; baseline measurements of blood pressure (BP), pulse rate (PR), and saturation of pulse-oximetry oxygen (SpO2) were made once, while MBRF represented the average of five measurements. In the hyperoxia phase, the subjects inhaled pure oxygen (6 L/min) for 12 minutes; MBRF was measured at 1, 2, 3, 4, 8, and 12 minutes after the start of oxygen inhalation. In the recovery phase, the subjects inhaled room air for 4 minutes; MBRF was measured again. Our previous report showed that MBRF already decreased significantly 2 minutes after the start of oxygen inhalation in normal subjects, so we shortened the total oxygen inhalation and recovery time to widen the measurement intervals to minimize the burden on the patients. BP, PR, and SpO2 were monitored every 5 minutes during the protocol. SpO2 was measured with an oximeter (Onyx II Model 9580 Finger Pulse Oximeter, Nonin Medical, Inc., Plymouth, MN, USA). MBP and MOPP were calculated as follows: MBP (t) = DBP (t) + 1/3 (SBP (t) − DBP (t)). MOPP (t) = 2/3 MBP (t) − baseline IOP. *t* indicates minutes after the start of oxygen inhalation (*t* = 0, 5, 10, and 15). The IOP values used to calculate MOPP(t)
Statistical Analysis

All data are shown as mean ± standard deviation. Dynamic changes in MBR$_F$ (%MBR$_F$) were defined as the percentage of baseline (100%). Repeated analyses of variance (ANOVA) were used to analyze the significance of differences in baseline variables in the POAG patients and control subjects. Two-way ANOVA and a post hoc Dunnett’s test were used to analyze the significance of differences in systemic variables in each phase, as well as the %MBR$_F$ alteration in the hyperoxic and recovery phases. We performed an a priori power analysis to determine the necessary total sample sizes for the 2-way ANOVA, with the values $a = 0.05$, power = 0.80, and effect size $= 0.40$. The calculated minimum total sample size was 30 (these calculations were made with G*Power, Version 3.1.9.2; program written by Franz Faul, University of Kiel, Kiel, Germany). Pearson’s correlation coefficient was used to determine the correlation between the mean % change in MBR$_F$ and other ophthalmic and systemic variables. The independent variable in the multiple regression analysis was mean % change in MBR$_F$, and the dependent variables were the variables that the univariate analysis showed were correlated with mean % change in MBR$_F$. The value of mean % change in MBR$_F$ was defined as follows:

$$\text{mean % change in MBR}_F(\%) = 100 - \frac{1}{6} \sum_{i=1}^{12} \frac{\%\text{MBR}_F(t)}{\text{Baseline MBR}_F}$$

All statistical analyses were performed with JMP software (Pro version 11.2.0; SAS Institute Japan Inc, Tokyo, Japan). The significance level was set at $P < 0.05$.

Results

Clinical Characteristics and BF Variables in Both Groups at Baseline

As shown in Table 1, clinical characteristics did not significantly differ in the two groups ($P = 0.12–0.94$), although cpRNFLT ($P < 0.001$) and baseline MBR$_F$ ($P = 0.048$) were significantly lower in the POAG patients.

Changes in BF Variables During Oxygen Inhalation Test

As shown in Table 2, SpO$_2$ rose significantly in both groups during oxygen inhalation ($P < 0.0001$). During systemic hyperoxia, no systemic variables, including SBP, DBP, MABP, MOPP, and PR, changed significantly in either group ($P = 0.51–0.99$).

Differences in the Vascular Response to Hyperoxia

As shown in Figure 2, MBR$_F$ decreased significantly in the control group 2 minutes after the start of oxygen inhalation (%MBR$_F$ = 87.7 ± 6.5%, $P = 0.0006$) and after 3 minutes in the POAG patients (%MBR$_F$ = 90.5 ± 9.3%, $P = 0.02$). The response to hyperoxia was significantly lower in the POAG patients (2-way ANOVA: $P < 0.0001$).

Relationship Between Mean % Change in MBR$_F$ and Other Variables

In the total group of POAG and control subjects ($n = 30$), a single regression analysis showed that mean % change in MBR$_F$ was significantly correlated with cpRNFLT ($r = 0.47$, $P = 0.007$), baseline MBR$_F$ ($r = 0.68$, $P < 0.0001$), baseline SBP ($r = -0.52$, $P = 0.005$), and baseline MABP ($r = -0.37$, $P = 0.033$),

Figure 1. Oxygen inhalation test protocol. The protocol had three phases: baseline, hyperoxia, and recovery. The hyperoxia phase is shown in gray; recovery comprised the 4 minutes after pure oxygen inhalation ended. During hyperoxia, pure oxygen (6 L/min) was inhaled for 12 minutes. The circles indicate the measured time points for each variable. During baseline, BP, PR, SpO$_2$, IOP, and MBR$_F$ were measured. MBR$_F$ was measured five times while the subjects inhaled room air for no less than 5 minutes, and the average was used as the baseline MBR$_F$.

Table 1. Clinical Characteristics and BF Variables in Both Groups at Baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>POAG, $n = 15$</th>
<th>Control, $n = 15$</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCVA, logMAR</td>
<td>−0.13 ± 0.06</td>
<td>0.12 ± 0.05</td>
<td>0.94</td>
</tr>
<tr>
<td>Refractive error, diopter</td>
<td>−2.1 ± 2.6</td>
<td>−2.2 ± 2.9</td>
<td>0.92</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>24.5 ± 1.1</td>
<td>24.8 ± 1.7</td>
<td>0.54</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>12.6 ± 1.5</td>
<td>14 ± 3.0</td>
<td>0.12</td>
</tr>
<tr>
<td>CpRNFLT, μm</td>
<td>88.8 ± 12.6</td>
<td>111.8 ± 9.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MBR$_F$, a.u.</td>
<td>11.3 ± 3.1</td>
<td>13.5 ± 2.7</td>
<td>0.048</td>
</tr>
<tr>
<td>Age, y</td>
<td>54.7 ± 12.9</td>
<td>55.6 ± 7.6</td>
<td>0.82</td>
</tr>
<tr>
<td>Gender, male, female</td>
<td>7 : 8</td>
<td>8 : 7</td>
<td>1.0*</td>
</tr>
<tr>
<td>Diabetes mellitus, $n$</td>
<td>2</td>
<td>0</td>
<td>0.48*</td>
</tr>
<tr>
<td>Dyslipidemia, $n$</td>
<td>4</td>
<td>2</td>
<td>0.65*</td>
</tr>
<tr>
<td>Hypertension, $n$</td>
<td>3</td>
<td>1</td>
<td>0.60*</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>138.4 ± 5.9</td>
<td>131.1 ± 5.9</td>
<td>0.39</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>86.2 ± 3.3</td>
<td>87.4 ± 3.3</td>
<td>0.81</td>
</tr>
<tr>
<td>MABP, mm Hg</td>
<td>103.6 ± 15.4</td>
<td>101.9 ± 14.7</td>
<td>0.77</td>
</tr>
<tr>
<td>MOPP, mm Hg</td>
<td>56.6 ± 9.6</td>
<td>54.6 ± 10.2</td>
<td>0.60</td>
</tr>
<tr>
<td>PR, bpm</td>
<td>68.5 ± 7.7</td>
<td>71.0 ± 9.0</td>
<td>0.44</td>
</tr>
<tr>
<td>SpO$_2$, %</td>
<td>97.6 ± 1.3</td>
<td>97.4 ± 0.9</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Unmarked $P$ values, ANOVA test. * $\chi^2$ test.
vasoreaction to hyperoxia might be due to pre-existing vasoconstriction. Additionally, SBP was a dependent contributing factor to mean baseline MBRT, low SBP, and high mean % change in MBRT in the upper panel and low baseline MBRT, high SBP, and low mean % change in MBRT in the lower panel.

**DISCUSSION**

In this study, we attempted to determine whether patients with glaucoma had an impaired vasoreactive response to hyperoxia. We used LSFG to test the vasoreactive response, which allowed us to obtain a detailed assessment of dynamic changes in ONH BF. We found that the response to hyperoxia was significantly reduced in POAG patients compared to control subjects. Additionally, we investigated factors influencing vasoreactivity within the ONH. We found that in eyes with POAG, mean % change in MBRT was highly associated with MBRT and SBP at baseline. These findings, which demonstrate the usefulness of LSFG in this field of research, suggest that an impaired vasoreactive response to hyperoxia might be due to pre-existing vasoconstriction in the eyes of glaucoma patients.

In this study, LSFG measurements of MBRT were significantly lower in glaucoma patients than control subjects (Table 1), confirming our previously reported results. SpO2 increased significantly during hyperoxia, confirming that systemic hyperoxia was successfully achieved, and that there were no significant changes in SBP, DBP, MBP, MOPP, or PR, confirming that the changes we observed in MBRT during hyperoxia were caused specifically by breathing pure oxygen, not by coincidental changes in other clinical variables. A detailed examination of time-course changes in MBRT showed that MBRT decreased significantly after 2 minutes in the control subjects (Fig. 3). These results are consistent with our previous research.

One of the new findings in this study was that vasoreactivity to systemic hyperoxia was impaired within the deep ONH in POAG patients (Fig. 3). The vascular response to hyperoxia in glaucoma has not been widely studied. Hosking et al.9 used color Doppler imaging to show that hyperoxia resulted in reductions in both peak systolic velocity and end diastolic velocity in the ophthalmic arteries, and that this occurred only in normal subjects, not glaucoma patients. Harris et al.7 used transcranial Doppler imaging to show that hyperoxia significantly decreased both mean and peak systolic velocities in the middle cerebral artery of control subjects, but it did not cause any significant change in open-angle glaucoma patients.7 Our finding that the vascular response to systemic hyperoxia is significantly reduced in the ONH of eyes with POAG is consistent with these reports. MBRT is considered to represent BF in the short posterior ciliary artery in the ONH,22 suggesting that vasoreactivity within the deep ONH is reduced in POAG patients. This novel finding is particularly significant because the deep ONH supplies the lamina cribrosa, which is thought to be the primary site of lesion in glaucoma.36

In this study, we also investigated factors influencing the vasoreactivity to systemic hyperoxia in a mixed group of subjects, comprising both healthy and glaucoma subjects. We set a novel variable, mean % change in MBRT, as the independent variable in a multiple regression analysis, and found that baseline MBRT was the strongest dependent factor (Table 3). Additionally, baseline MBRT was correlated with mean % change in MBRT only in the POAG patients. This result supports the hypothesis that pre-existing vasoconstriction limits the capacity of the glaucomatous eye to moderate blood velocity.37 During hyperoxia, ET-1, which acts via the endothelin receptors, might be the primary actor in the mechanism underlying the BF response to hyperoxia in the ONH and the retinal vessels.

### Table 2. Changes in BF Variables During Oxygen Inhalation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>5 min</th>
<th>10 min</th>
<th>Recovery</th>
<th>16 min</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POAG, n = 15</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>138.4 ± 7.7</td>
<td>140.4 ± 7.7</td>
<td>140.2 ± 7.7</td>
<td>139.4 ± 7.7</td>
<td>0.99 (&lt; 0.0001)</td>
<td></td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>86.2 ± 4.1</td>
<td>89.7 ± 4.1</td>
<td>86.5 ± 4.1</td>
<td>89.0 ± 4.1</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>MBP, mm Hg</td>
<td>103.6 ± 15.4</td>
<td>104.4 ± 20.0</td>
<td>105.8 ± 19.8</td>
<td>106.6 ± 20.8</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>MOPP, mm Hg</td>
<td>56.6 ± 9.6</td>
<td>58.6 ± 13.1</td>
<td>57.2 ± 12.7</td>
<td>51.8 ± 12.5</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>PR, bpm</td>
<td>68.5 ± 7.7</td>
<td>66.8 ± 7.5</td>
<td>64.8 ± 7.2</td>
<td>69 ± 9.4</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>SpO2, %</td>
<td>97.6 ± 1.3</td>
<td>99.1 ± 0.9</td>
<td>99.1 ± 0.6</td>
<td>97.1 ± 1.4</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

| **Control, n = 15** | | | | | | |
| SBP, mm Hg | 131.1 ± 4.8 | 128.2 ± 4.8 | 125.4 ± 4.8 | 127.4 ± 4.8 | 0.86 |
| DBP, mm Hg | 87.4 ± 2.9 | 84.7 ± 2.9 | 85.0 ± 2.9 | 86.6 ± 2.9 | 0.90 |
| MBP, mm Hg | 101.9 ± 14.7 | 98.5 ± 10.8 | 100.2 ± 12.3 | 99.2 ± 12.2 | 0.90 |
| MOPP, mm Hg | 54.6 ± 10.2 | 52.6 ± 8.6 | 51.9 ± 7.5 | 53.4 ± 7.7 | 0.87 |
| PR, bpm | 71.0 ± 9.0 | 69.3 ± 11.3 | 68.7 ± 10.0 | 71.8 ± 12.4 | 0.86 |
| SpO2, % | 97.4 ± 0.9 | 98.9 ± 0.5 | 99 ± 0.6 | 97.6 ± 0.9 | < 0.0001 |

Unmarked P values, ANOVA test.
Previously, a meta-analysis of ET-1 showed that ET-1 blood concentration is elevated in glaucoma, and another study showed that endothelin B receptor immunoreactivity was elevated in the ONH of human glaucoma patients.\textsuperscript{41,42} ET-1 has also been shown to induce astroglial proliferation in cultured human ONH astrocytes, acting via ET (A/B) receptor activation.\textsuperscript{35} Furthermore, in a pigmented rabbit-eye model, the intravitreous injection of ET-1 decreased ONH BF and increased optic disc cupping.\textsuperscript{44} Taken together, these findings suggest that endothelin is associated with both decreased BF and the reduction of redundant vessel constriction capacity in eyes with glaucoma, factors that might underlie glaucomatous neurodegeneration. Further assessment will be required to clarify the relationship between abnormal vasoreactivity to hyperoxia and the endothelin pathway in glaucoma patients.

Other interesting findings in this study were that SBP independently contributed to mean % change in MBR\textsubscript{T}, and that there was a significant negative correlation between SBP and mean % change in MBR\textsubscript{T} seen only in eyes with POAG. There have been various etiologic studies on the influence of BP and OPP on the prevalence, incidence, and progression of glaucoma.\textsuperscript{35} However, these studies have disagreed, finding that both high and low BP and OPP were risk factors for glaucoma. Meanwhile, several other studies have found no association. A solution to this disagreement was suggested by the Los Angeles Latino Eye Study, which found that low DBP and high SBP were both associated with an increased prevalence of POAG. Thus, any kind of extreme change in BP whether high or low, may cause ischemic damage to the ONH. Specifically, low DBP may cause low OPP and high SBP may cause hypertensive vasoconstriction.\textsuperscript{45} High SBP can also cause chronic narrowing of the vessels,\textsuperscript{46–49} creating a pre-existing degree of vasoconstriction that might reduce constrictive capacity during the response to hyperoxia.

There were several limitations to this study. First, the sample size was small. However, as described in statistical analysis section, the study included the minimum necessary sample size. We limited the sample size to this number to avoid placing an unnecessary burden on our patients. Second, although LSFG measurements in the ONH have recently been validated using the microsphere technique and the hydrogen gas clearance method in animal experiments,\textsuperscript{52,56} an adequate understanding of the penetration depth of the laser into the ONH has not been established. Third, the use of anti-glaucoma eye drops might have contributed to altered vasoreactivity during hyperoxia in our POAG subjects. In particular, PGs have been reported to have a direct, IOP-independent effect on BF, improving it by relaxing the vasoconstriction induced by ET-1.\textsuperscript{51,52} Considering that all POAG patients in this study were being treated with PGs, it follows that PGs might have reduced ET-1-induced vasoconstriction during hyperoxia, affecting our results. However, we found that lower vasoreactivity was closely associated with lower baseline BF, making it unlikely that any dysfunction in autoregulation was caused by PG use, which would have improved baseline BF. Other glaucoma eye drops have been reported to either protect BF or to have unclear effects.\textsuperscript{53,54} Thus, their effect on vasoreactivity is likely similar to that of PGs. In fact, the POAG subjects showed no significant correlation between the number of antiglaucoma eye drops and the mean % change in MBR\textsubscript{T} (\(P = 0.19\)) and no significant difference between users and nonusers of each drug (\(P = 0.15–0.93\)). Fourth, our hypothesis that a chronic increase in ET-1 concentration is associated with a decrease in vasoreactivity is contradicted by several studies that found no significant difference in ET-1 concentration in eyes with glaucoma.\textsuperscript{55,56} Nevertheless, as we mentioned in a previous report, we consider that this disagreement between existing studies as to the involvement of ET-1 concentration in the pathogenesis of glaucoma may best be resolved by a hyperoxic provocation assessment. In the future, we therefore plan to measure ET-1 concentration not just at baseline, but also after oxygen provocation. We believe that this should shed new light on blood concentration dynamics and help resolve current disagreements. Fifth, it remains unclear whether an

### Table 3. Dependent Factors Contributing to Mean % Change in MBR\textsubscript{T}; \(N = 50\), \(\text{POAG} = 15\); \(\text{Control} = 15\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Independent</th>
<th>Dependent</th>
<th>(\beta)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean % change in MBR\textsubscript{T}</td>
<td>CpRNFLT</td>
<td>0.23</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline MBR\textsubscript{T}</td>
<td>0.44</td>
<td>0.0096*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline SBP</td>
<td>−0.32</td>
<td>0.030*</td>
<td></td>
</tr>
</tbody>
</table>

\(\beta\) indicates the standard partial regression coefficient. * Indicates statistical significance.
abnormal ONH BF response to hyperoxia is associated with glaucoma progression. Therefore, a prospective study should be performed in the future, including a larger number of glaucoma subjects.

In conclusion, this study used LSFG to show that POAG patients have a weaker vasoreactive response to hyperoxia than healthy controls. Furthermore, this impaired vasoreactivity was associated with lower ONH BF and higher SBP. These findings suggest that eyes with glaucoma have a pre-existing degree of vasoconstriction in the ONH, and that this might reduce the capacity of the vasoconstrictive response to hyperoxia. Alternatively, the pathways that mediate hyperoxia-induced vasoconstriction could be altered in POAG.

![Figure 3](image-url)

**FIGURE 3.** The relationship of mean % change in MBR f to baseline MBR f and SBP in the two groups. Mean % change in MBR f was significantly correlated with baseline MBR f in the subjects overall and in the POAG group (r = 0.68, P < 0.0001; r = 0.83, P < 0.0001, respectively). Furthermore, mean % change in MBR f was significantly correlated with SBP in the subjects overall and in the POAG group (r = -0.52, P = 0.0052; r = -0.60, P = 0.02, respectively). However, there was no significant correlation between mean % change in MBR f and baseline MBR f or SBP in the control group (r = 0.19, P = 0.48; r = -0.36, P = 0.40, Pearson’s correlation coefficient).

![Figure 4](image-url)

**FIGURE 4.** Representative fundus photographs, LSFG images, and %MBR f alteration during the protocol. This figure shows representative fundus photographs, LSFG images, and %MBR f alteration during the protocol. The upper panel shows a patient with high baseline MBR f, low SBP, and high mean % change in MBR f, while the lower panel shows a patient with low baseline MBR f, high SBP, and low mean % change in MBR f. A, B, E, and F show representative baseline fundus photographs and LSFG images for each patient. C and G show representative LSFG images during the hyperoxic phase, while D and H show the recovery phase. The average %MBR f against baseline during hyperoxia was calculated; the gray double arrow indicates mean % change in MBR f. Upper panel: The left eye of a 45-year-old male glaucoma patient (MD: -7.88 dB, MBR f: 15.5 a.u., BP 126/86 mm Hg, PR 70 bpm, mean % change in MBR f: 10.2%). Lower panel: The left eye of a 66-year-old male glaucoma patient (MD: -2.81 dB, MBR f: 8.6 a.u., BP 180/105 mm Hg, PR 65 bpm, mean % change in MBR f: -5.1%).
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