Location of Initial Visual Field Defects in Glaucoma and Their Modes of Deterioration

Joon Mo Kim,1,2 Haksu Kyung,2,3 Seong Hee Shim,1 Parham Azarbod,2,4 and Joseph Caprioli2

1Department of Ophthalmology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
2Stein Eye Institute, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, United States
3Department of Ophthalmology, National Medical Center, Seoul, Korea
4Moorfields Eye Hospital, London, United Kingdom

Correspondence: Joseph Caprioli, Department of Ophthalmology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA 90025; caprioli@ucla.edu.
Submitted: May 19, 2015
Accepted: July 7, 2015
Citation: Kim JM, Kyung H, Shim SH, Azarbod P, Caprioli J. Location of initial visual field defects in glaucoma and their modes of deterioration. Invest Ophthalmol Vis Sci. 2015;56:7956–7962. DOI:10.1167/iovs.15-17297

PURPOSE. To describe the location of initial visual field defects (VFD) in glaucoma, their modes of deterioration, and those factors associated with different modes of deterioration.

METHODS. Patients with POAG were categorized into four groups based on three consecutive initial VFD: (1) superior paracentral defects (PD), (2) inferior PD, (3) superior nasal defects (ND), and (4) inferior ND. According to the worsening of the VF, four further subgroups were identified: (1) superior central worsening (CW), (2) inferior CW, (3) superior peripheral or nasal worsening (NW), and (4) inferior NW. Systemic and ocular factors were analyzed for each of the subgroups to identify possible associations.

RESULTS. One hundred sixty-two eyes of 162 subjects were analyzed. Superior PD (n = 40) were more frequent in females and associated with disc hemorrhage (DH), and were less frequent in patients with systemic hypertension (HT). Inferior PD (n = 35) showed a significant association with cup shape measure and axial length. Superior ND (n = 37) were more highly associated with HT and diabetes. Inferior ND (n = 50) showed a lower incidence of DH. With binary logistic regression analysis, superior PD showed a significant association with both HT and DH. With respect to VF worsening, superior CW showed a significant association with HT and diabetes, whereas superior NW was associated with a high minimum IOP during follow-up, and inferior NW was associated with a high maximum IOP during follow-up.

CONCLUSIONS. The initial location and subsequent direction of worsening of VFD were associated with different systemic and ocular factors.

Keywords: glaucoma, initial visual field defect, visual field progression

Glaucoma is characterized by a chronic progressive optic neuropathy with corresponding and characteristic patterns of visual field (VF) loss. In the majority of patients, VF changes are initially localized and as the disease progresses, these focal areas become wider, deeper, and more numerous. However, there is a great deal of variability in the rate and mode of worsening between patients.1 Failure to treat early to moderate VF changes could lead to a decline in the quality of a glaucoma patient’s life, with various effects depending on the degree and location of the visual loss.2,3 Visual field defects (VFD) near fixation have a greater impact on the level of function compared with peripheral changes, even at an early stage of glaucoma.4,5 It is generally taught that initial glaucomatous VF abnormalities frequently occur in the periphery with relative preservation of the central field. In actuality, one finds a variety of patterns and in some patients the initial defect may be quite centrally located. There is very little published about the exact nature of the initial VFD and the manner in which it subsequently worsens.

Given that glaucoma is a chronic progressive disease, much effort has been dedicated to the study of the factors relating to visual decay and the relationship between structural and functional changes.6–9 The two key elements in the study of glaucomatous VF deterioration are the direction and the rate of decay. If deterioration occurs in the central direction (toward fixation), one would expect a greater impact on the patient’s function with increasing functional loss in cases of rapidly centrally deteriorating VFs, even in those with relatively small initial defects.

The current study was undertaken to investigate the location of initial glaucomatous VFD, and the possible ocular and systemic factors associated with (1) the location of the initial VFD, and (2) the direction of worsening relative to the initial defect.

MATERIALS AND METHODS

Patient and Visual Field Data
A retrospective case review of open-angle glaucoma (OAG) patients of the University of California at Los Angeles (Los Angeles, CA, USA) Glaucoma Division with 6 or more years follow-up, and who had at least eight VF examinations was conducted. Visual fields were performed with a Humphrey Visual Field Analyzer (Carl Zeiss Ophthalmic Systems, Inc., Dublin, CA, USA) with the 24-2 SITA standard test strategy. Visual fields with acceptable VF reliability scores (according to the Advanced Glaucoma Intervention Study [AGIS] protocol)
Definitions

Initial VF Defect. These were divided into two groups, paracentral (PD) and nasal (ND) defects based on probability map locations in at least three out of the four Humphrey VF print outs. These two groups were then divided into two subgroups (superior and inferior) based on the affected hemifield. This yielded four initial defect arms for the study: (1) superior PD, (2) inferior PD, (3) superior ND, and (4) inferior ND.

Paracentral defects were defined as three or more adjacent points with an abnormal probability score of $P$ less than 2%, or at least one point with a $P$ less than 1% within the two paracentral locations nearest to fixation. Nasal defects were defined as three or more adjacent points with an abnormal probability score of $P$ less than 2%, or one or more points with $P$ less than 1% within the three nasal-most points of the Humphrey VF (Figs. 1, 2). Horizontally, PD was for points lying from 0° to 10°, and ND was for points beyond 20°.

The Direction of VF Deterioration. Deterioration was defined with modified Anderson’s criteria as contiguous points on a Humphrey 24-2 SITA standard VF with $P$ less than 2% on the total deviation plot, or the development of new scotoma (at least 1 point of $P < 1\%$ or 3 contiguous points of $P < 2\%$) in the same hemifield.

The direction of worsening was recorded as either central (CW), or peripheral/nasal (NW) depending on the initial location of the VFD (Fig. 2). Deterioration required confirmation in at least three consecutive VFs. Patients were divided into four groups, depending on the direction of the worsening of the defect: superior CW, (2) inferior CW, (3) superior NW, and (4) inferior NW. Cases were excluded from these groups if (1) worsening could not be detected, or (2) the direction of worsening could not be defined such as the occurrence of a new scotoma in the opposite hemifield, a change in the location of a scotoma with repeated VF testing, deepening of a scotoma without spatial expansion, or the development of multiple scotoma, such as from a branched retinal vein occlusion or occurring after a long period of loss to follow up.

Data Analysis

The relationships between both the initial VFD and the direction of subsequent decay with demographic, systemic, and ocular factors were evaluated. Demographic factors included age at the onset of initial VF defect, sex, and family history of glaucoma. Systemic factors included a history of diabetes mellitus (DM), systemic hypertension (HT), and migraine. Ocular factors included disc hemorrhage (DH), CCT, axial length, maximum IOP, minimum IOP, IOP range during follow up, MD, PSD, cup to disc ratio (CDR), retinal nerve fiber layer (RNFL) thickness, cup shape measure (CSM), and disc area. Intraocular pressure range was defined as the difference between maximum IOP and minimum IOP during follow-up. Depending on the sample size, a $\chi^2$ test or a Fisher’s
The Direction of Worsening of VF Defect

As shown in Table 2, in the group with an initial superior paracentral defect (PD), 14 eyes worsened nasally (superior NW) and three worsened centrally (superior CW). In the group with the initial inferior paracentral defects (PD), two deteriorated centrally (inferior CW) and 14 deteriorated nasally (inferior NW). In the group with initial superior nasal defects (superior ND), 20 eyes deteriorated toward a central direction (superior CW) and six eyes deteriorated toward a nasal direction (superior NW). In the groups with initial inferior nasal defects (inferior ND), 20 eyes deteriorated centrally (inferior CW) and three deteriorated nasally (inferior NW).

Central Worsening Group.
Superior CW subgroup. This group had a significant association with HT \((P = 0.039, OR = 2.65, 95\% CI: 1.032 \sim 6.803, \chi^2\) test) and DM \((P = 0.048, OR = 0.167, 95\% CI: 0.039 \sim 0.973, Fisher exact test), and there was a higher minimum IOP \((10.88 \text{ mm Hg} \sim 2.33\)) during the follow-up period compared with the other groups \((9.44 \text{ mm Hg} \sim 2.07, P = 0.017, \text{ independent } t\text{-test})\).

Inferior CW subgroup. There was a higher maximum IOP \((21.55 \text{ mm Hg} \sim 6.25)\) during the follow-up period compared with the other groups \((18.53 \text{ mm Hg} \sim 4.45, P = 0.019, \text{ independent } t\text{-test})\).

Peripheral/Nasal Worsening Group. There were no factors that were significantly associated with either of the subgroups in these patients.

DISCUSSION

The current study was carried out to identify systemic and ocular factors associated with the location of the initial VF defect and its subsequent direction of worsening in glaucoma. The results suggest that factors associated with the location of the initial VF defect are different from those associated with the subsequent direction of worsening. With regard to the initial location of glaucoma damage, the superior paracentral group had a female preponderance, a higher incidence of disc hemorrhages, and was significantly less frequently associated with HT compared with other groups. The inferior paracentral...
Worsening direction

Systemic factors

Worsening direction

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects

Subjects
Table 3. Clinical Characteristics of the Study Population of Progression Direction

<table>
<thead>
<tr>
<th></th>
<th>Superior NW</th>
<th>Superior CW</th>
<th>Inferior NW</th>
<th>Inferior CW</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>17</td>
<td>17</td>
<td>23</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.23 ± 10.41</td>
<td>69.53 ± 7.50</td>
<td>62.70 ± 13.45</td>
<td>64.60 ± 11.12</td>
<td>0.242</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>5/12</td>
<td>9/8</td>
<td>15/8</td>
<td>15/11</td>
<td>0.144</td>
</tr>
<tr>
<td>Family history (+/- M/F)</td>
<td>6(2/4)</td>
<td>6(3/5)</td>
<td>12(7/9)</td>
<td>15(10/13)</td>
<td>0.418</td>
</tr>
<tr>
<td>Ocular factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axial length</td>
<td>24.07 ± 0.87</td>
<td>25.55 ± 1.34*</td>
<td>25.05 ± 1.15*</td>
<td>24.39 ± 1.01</td>
<td>0.008</td>
</tr>
<tr>
<td>CCT</td>
<td>559.5 ± 39.4</td>
<td>552.9 ± 30.9</td>
<td>562.9 ± 39.10</td>
<td>544.5 ± 40.0</td>
<td>0.599</td>
</tr>
<tr>
<td>FU minimum IOP, mm Hg</td>
<td>11.00 ± 2.28</td>
<td>9.15 ± 2.75</td>
<td>9.86 ± 2.27</td>
<td>10.24 ± 2.05</td>
<td>0.143</td>
</tr>
<tr>
<td>FU maximum IOP, mm Hg</td>
<td>21.56 ± 5.87</td>
<td>18.47 ± 5.74</td>
<td>20.27 ± 5.33</td>
<td>21.46 ± 5.22</td>
<td>0.301</td>
</tr>
<tr>
<td>Disc area, mm</td>
<td>1.97 ± 0.60</td>
<td>2.13 ± 0.51</td>
<td>2.07 ± 0.57</td>
<td>2.03 ± 0.74</td>
<td>0.912</td>
</tr>
<tr>
<td>CDR</td>
<td>0.42 ± 0.22</td>
<td>0.50 ± 0.15</td>
<td>0.46 ± 0.18</td>
<td>0.47 ± 0.19</td>
<td>0.754</td>
</tr>
<tr>
<td>RNFL thickness, mm</td>
<td>0.19 ± 0.97</td>
<td>0.17 ± 0.19</td>
<td>0.19 ± 0.09</td>
<td>0.21 ± 0.28</td>
<td>0.914</td>
</tr>
<tr>
<td>CSM</td>
<td>-0.127 ± 0.094*</td>
<td>-0.134 ± 0.093*</td>
<td>-0.092 ± 0.098</td>
<td>-0.056 ± 0.074*</td>
<td>0.037</td>
</tr>
<tr>
<td>Disc hemorrhage</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>5</td>
<td>0.731</td>
</tr>
<tr>
<td>PPA</td>
<td>12</td>
<td>13</td>
<td>15</td>
<td>21</td>
<td>0.803</td>
</tr>
<tr>
<td>Baseline MD, dB</td>
<td>-2.79 ± 2.4</td>
<td>-6.15 ± 6.1</td>
<td>-3.82 ± 3.2</td>
<td>-3.86 ± 2.94</td>
<td>0.072</td>
</tr>
<tr>
<td>Baseline PSD, dB</td>
<td>3.87 ± 2.32</td>
<td>4.48 ± 2.55</td>
<td>4.42 ± 3.06</td>
<td>4.10 ± 2.49</td>
<td>0.69</td>
</tr>
<tr>
<td>Systemic factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>13</td>
<td>6</td>
<td>16</td>
<td>13</td>
<td>0.048</td>
</tr>
<tr>
<td>Migraine</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Comparing Each Subgroup in Turn With all the Other Groups Combined Together

<table>
<thead>
<tr>
<th>Positive Association</th>
<th>Negative Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior PD</td>
<td>Female (P = 0.011), DH (P = 0.018)</td>
</tr>
<tr>
<td>Inferior PD</td>
<td>cs (P = 0.002), axial length (P = 0.038)</td>
</tr>
<tr>
<td>Inferior ND</td>
<td>HT (P = 0.074), DM (P = 0.05)</td>
</tr>
<tr>
<td>Inferior ND</td>
<td>None</td>
</tr>
<tr>
<td>Superior CW</td>
<td>HT (P = 0.039), DM (P = 0.048), higher minimum IOP (P = 0.017)</td>
</tr>
<tr>
<td>Inferior CW</td>
<td>Higher maximum IOP (P = 0.019)</td>
</tr>
<tr>
<td>Superior NC</td>
<td>None</td>
</tr>
<tr>
<td>Inferior NC</td>
<td>None</td>
</tr>
</tbody>
</table>

* Highlight statistical significant differences following Bonferroni correction.

According to a recently presented study that analyzed initial VFD as either central and peripheral, the central cases showed a higher association with systemic risk factors and with DH than the peripheral ones. The differences between those results and those of this study may largely be due to the study design. Their subjects mainly included high IOP glaucoma patients (including chronic angle closure glaucoma); however, our study was in OAG patients (including normal-tension patients), and those with chronic angle closure glaucoma were excluded. Furthermore, our patients were subdivided into four groups rather than two. Considering that IOP-independent factors may preferentially affect the neuroretinal rim or RNFL closer to the papillomacular bundle in the inferior half of optic nerve head or retina compared with high IOP, the negative association between HT and the superior PD group is interesting. The glaucoma patients with HT had superior nasal defects and that tended to progress centrally. Generally, most of initial VF defects, particularly initial parafocal scotomas, developed in the superior hemifield. In the early stages of systemic HT, blood flow to the eye may be enhanced. With longstanding systemic HT, smaller arterioles may be affected earlier than larger arterioles. We hypothesize that although there may be a high ocular perfusion pressure of the large arteries, decreased perfusion in the smaller, diseased vessels may produce peripheral VFD earlier than central VFD. As the effects of systemic HT or its treatment evolve, even central retinal ganglion cells may become vulnerable to decreased perfusion, and the VFD may progress centrally. According to our findings, the central VF in patients...
with systemic HT remains relatively preserved during the initial stage of the disease as compared with those without systemic HT.

There are some limitations of this study. The data were collected retrospectively and information such as the initial history, and the systemic risk factors were dependent on patient reporting and medical record documentation during clinic visits. All study patients were recruited from a tertiary care glaucoma clinic, which could create a sampling bias. Some patients were excluded from analysis because of missing data, such as axial length, CCT, and records at the initial visit. The effect of this selection of patients on our results is not known. A confounding factor in the design of the study is that the central most locations of the VF may preferentially deteriorate toward the periphery and the peripheral most points may do so centrally, and this could have introduced a bias into the results.

In our study, patients with an initial paracentral VFD had different characteristics than those with other patterns of defects. In particular, systemic factors (more migraine and less HT) were closely associated with inferior paracentral defects. However, ocular factors (steeper cup and longer axial length) were more closely associated with inferior paracentral defects. Glaucoma patients with normal blood pressure appear to show a greater loss of superior central VF as compared with their hypertensive counterparts. These findings may help clinicians identify glaucoma phenotypes that may help anticipate the course of worsening patients and guide appropriate treatment.

Acknowledgments

Supported by grants from Pfizer, Inc. (New York, NY, USA), Allergan, Inc. (Irvine, CA, USA), Alcon, Inc. (Fort Worth, TX, USA), an unrestricted grant from Research to Prevent Blindness, Inc. (New York, NY, USA), and the National Eye Institute/National Institutes of Health (Bethesda, MD, USA) Grant R01-EY018644 (all JC).

Disclosure: J.M. Kim, None; H. Kyung, None; S.H. Shim, None; P. Azarbod, None; J. Caprioli, Pfizer, Inc. (F); Allergan, Inc. (F.C.); Alcon, Inc. (F)

References


