A Longitudinal Study of the Relationship Between Intraocular and Blood Pressures

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The relationship between intraocular and systemic blood pressures was investigated in a prospective study of 572 middle-aged men. There was no consistent relationship between intraocular pressure at first visit and age. Subjects with an intraocular pressure greater than 20 mm Hg had a significantly higher systolic blood pressure than controls matched for age. An autoregressive model was used to examine the relationship between change in intraocular pressure and initial intraocular pressure, age, and blood pressure. When the authors compared data obtained 1 or 2 years apart, a change in intraocular pressure was positively correlated with a change in systolic blood pressure. Thus, the results of this study indicate that changes in intraocular pressure over time are associated with changes in systolic blood pressure and that intraocular pressure does not necessarily increase with age.


Because the development of glaucomatous visual field loss is more likely with higher intraocular pressure,1 it is important to identify factors that may influence the level of intraocular pressure. A number of studies attempted to identify risk factors associated with the development of elevated intraocular pressure.2-7 Two variables that may relate to intraocular pressure are age and systemic blood pressure.8,9

Some reports suggest that intraocular pressure increases with age, perhaps by as much as 0.05 mm Hg per yr.10-13 However, Carel et al2 found that the positive relationship between intraocular pressure and age disappears when the increase in systemic blood pressure with age is taken into account. Similarly, Shiose et al14 reported that intraocular pressure actually declines with age in a Japanese population. There is further evidence of a strong link between blood pressure level and intraocular pressure. In the Framingham Eye Study, mean systolic blood pressures were higher in 340 ocular hypertensives compared with those of 1301 ocular normotensives.3 In another study of 83 patients with primary open-angle glaucoma and 237 (age-matched) controls, there was a positive association between systolic hypertension (equal to or greater than 160 mm Hg) and primary open-angle glaucoma.4

Data from the Baltimore Longitudinal Study of Aging provides a unique opportunity to evaluate the relationship between changes in blood and intraocular pressures in a healthy white male population followed for up to 6 yr. In most previous studies, heterogeneous populations were divided into subgroups that were compared to one another cross-sectionally. The behavior of individuals was thus inferred from differences between groups. Our longitudinal design has the advantage of allowing the study of change in individuals at yearly intervals. We asked the following questions: (1) how does intraocular pressure change with age; (2) is elevated intraocular pressure associated with higher systemic blood pressure; and (3) how does intraocular pressure change with alterations in blood pressure in the same individual over time?

Materials and Methods

Population

The Baltimore Longitudinal Study of Aging (BLSA), an intramural research program of the National Institute on Aging, was established in 1958 to study the effects of aging on a community-dwelling population.15 Participants are self-selected volunteers, most of whom reside in Maryland, Virginia, and Washington, DC. New participants were enrolled in the study to maintain constant age groups over
time. Ninety-six percent of the participants are white. Until 1978, all the participants were men. Throughout the history of the study, the research participants as a group have an above-average educational level and socioeconomic status. Other characteristics of the population have been described in detail in several publications. The participants in the BLSA are scheduled for follow-up visits every 12–24 months during which measurements of various physiologic and psychologic functions are made during a 2½-day period. All procedures and protocols have been reviewed and approved by the Francis Scott Key Hospital Institutional Review Board, and all participants gave informed consent.

A total of 611 men were enrolled in the BLSA in April 1966, all but 39 (6%) of whom underwent tonometry (Fig. 1). None of these 39 had known glaucoma. There were 5892 visits made by the remaining 572 men between April 1966 and May 1972, of which data from 5758 visits were used (98%). Blood pressure data for individual visits were excluded if a difference of 15 mm Hg was recorded between the left and right arm (31 visits, 0.5%) or if a single blood pressure measurement was greater than 180/140 systolic/diastolic (13 visits, 0.2%). These 572 men had at least one intraocular pressure reading, and 413 had at least two intraocular pressure measurements over the period (Fig. 1). The latter 413 cases provide the data for our longitudinal analysis of intraocular and blood pressures. Twelve men (1.9%) at some time over the study period were receiving antihypertensive medications affecting the alpha- or beta-adrenergic nervous systems. These visits were excluded because of the strong likelihood that these agents would change both blood and intraocular pressures. The 20 participants (3.5%) who were receiving diuretics for hypertension were included.

If a difference in measurement of intraocular pressure greater than 4 mm Hg between right and left eyes was present on only one occasion, we presumed that there was a high probability of measurement error, and the data were excluded (90 visits, 1.5%). For the longitudinal analysis, there were 321 pairs of visits of 191 men 1 yr apart and 324 pairs of visits of 244 men 2 yr apart (84 men were common to both groups). The age distributions of the total population and of those with at least two measurements were similar (Table 1). The mean age of the entire group in whom tonometry was done at first visit was 53.8 yr (range, 19–89); the mean age of those with at least two intraocular pressure measurements at first visit was 54.7 yr (range, 21–85) (difference not statistically significant, P > 0.05). During follow-up visits, 24 participants were found to be receiving glaucoma medications (4% of the sample). Further tonometry data was not obtained on this group.

Measurements

The data presented are limited to the period April 1966 to May 1972 when tonometry data were

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**Study Population**

- 611 Eligible
  - 572 With Tonometry
    - One IOP Measurement: n = 159
      - IOP ≥ 20 mmHg: n = 15 (9%)
      - IOP < 20 mmHg: n = 144 (91%)
    - At least Two IOP Measurements: n = 413
      - IOP ≥ 20 mmHg: n = 54 (13%)
      - IOP < 20 mmHg: n = 359 (87%)
  - 39 Without Tonometry
collected. Both intraocular pressure by Schiotz tonometry and blood pressure were recorded on the same day.

Blood pressure measurements on the left and right arm of each participant were collected at all visits. Readings in the supine position were obtained manually by physicians with a mercury sphygmomanometer in the midmorning. Blood pressures reported are the mean of right and left systolic and diastolic measures.

Tonometry was done in the supine position by one experienced technician with an electronic Schiotz tonometer (model OP 9050; V. Mueller, Chicago, IL). The tonometer was recalibrated after every other patient or after 2 hr, whichever came first. The intraocular pressure was calculated from the scale reading using the Simplified Tonographic Table. The tonometry data gathered from the first (right) eye measured in each person was used for these analyses. This was done to eliminate any error caused by the pressure-lowering effect that tonometry measurements of the first eye have on the second.16 Elevated intraocular pressure was defined as equal to or greater than 20 mm Hg, since Schiotz tonometry gives lower readings.

Information concerning age, medical history, diagnoses, and medications was obtained by questionnaire.

**Analyses**

Three analyses were done. First, a cross-sectional analysis of intraocular and blood pressures by age was done on the entire population of 572 men. The intraocular and blood pressures of each person at the first visit with tonometry were plotted against age at that visit, and linear regressions were analyzed.

Second, a nested case-control analysis was done of the association of blood pressure indices and elevated intraocular pressure. Cases were identified with intraocular pressure equal to or greater than 20 mm Hg (69 of 572 men). Three controls with intraocular pressures less than 20 mm Hg were randomly selected for each case, matched by age (±5 yr) and visit date (±1 yr). A conditional logistic model was used to examine the association between higher blood and intraocular pressures.

Third, an autoregressive model was constructed as described by Rosner et al.18 This model investigates the dependence of a change in intraocular pressure on the initial intraocular pressure, initial blood pressure, a change in blood pressure, and the age of the subject. The unit of analysis was pairs of visits. The autoregressive model requires that data pairs be evenly spaced in time. Therefore, pairs comprised of visits between 1 yr and 18 months apart were placed into a 1-year group (n = 321 pairs), while pairs comprised of visits between 19 and 29 months apart were placed into a 2-year group (n = 324 pairs). The groups were analyzed separately. The data for each group was fit into the model: \[ IOP_{T1} - TO = \beta_0 + \beta_1 (IOP_{T0}) + \beta_2 (BP_{T0}) + \beta_3 (BP_{T1} - TO) + \beta_4 (Age_{T0}) \] where \( IOP = \) intraocular pressure, \( \beta_3 = \) regression coefficient, \( BP = \) average systolic, diastolic, or mean blood pressure, \( TO = \) first visit, and \( T1 = \) second visit.

**Results**

The mean intraocular pressure at first visit with tonometry was 16.05 mm Hg (standard error, 0.12), with no difference by decade of age (Fig. 2). There was no evidence of an increase in intraocular pressure with age in this population, using a linear-regression model of intraocular pressure at first visit versus age (slope, -0.003; standard error, 0.009; \( P = 0.7 \)).

There was an increase in blood pressure with age in our cross-sectional data. Mean systolic blood pressure increased by 0.5 mm Hg per yr as judged by linear regression (\( P < 0.0001 \)). Mean systolic blood pressure therefore increased by approximately 20 mm Hg between the fourth and eighth decades (Table 2). Mean diastolic blood pressure increased only 0.06 mm Hg

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>N</th>
<th>IOP (mmHg)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>29</td>
<td>15.51 ± 0.44</td>
<td>120.03</td>
<td>78.26</td>
</tr>
<tr>
<td>30-39</td>
<td>65</td>
<td>15.47 ± 0.29</td>
<td>123.99</td>
<td>82.35</td>
</tr>
<tr>
<td>40-49</td>
<td>136</td>
<td>16.14 ± 0.25</td>
<td>124.29</td>
<td>80.86</td>
</tr>
<tr>
<td>50-59</td>
<td>151</td>
<td>16.65 ± 0.24</td>
<td>131.46</td>
<td>85.26</td>
</tr>
<tr>
<td>60-69</td>
<td>105</td>
<td>16.33 ± 0.29</td>
<td>136.35</td>
<td>83.82</td>
</tr>
<tr>
<td>70-79</td>
<td>73</td>
<td>15.12 ± 0.35</td>
<td>144.19</td>
<td>83.46</td>
</tr>
<tr>
<td>&gt;79</td>
<td>13</td>
<td>15.23 ± 0.91</td>
<td>140.38</td>
<td>77.50</td>
</tr>
<tr>
<td>Total</td>
<td>572</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are given as mean; IOP values also indicate SE.
Table 3. Comparison of differences in blood pressures between cases with intraocular pressure >20 mmHg and controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean differences</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases vs. controls</td>
<td>6.20</td>
<td>1.39</td>
</tr>
<tr>
<td>t-test</td>
<td>2.50 (P &lt; 0.01)</td>
<td>0.92 (NS)</td>
</tr>
<tr>
<td>Regression analyses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-coefficient</td>
<td>0.022</td>
<td>0.013</td>
</tr>
<tr>
<td>Standard error</td>
<td>0.003 (P &lt; 0.01)</td>
<td>0.013 (NS)</td>
</tr>
</tbody>
</table>

per yr, and this was of borderline significance (P = 0.06, linear regression).

Comparison of the difference in blood pressures for cases of elevated intraocular pressure (equal to or greater than 20 mm Hg) and matched controls suggested that systolic blood pressure was 6.20 mm Hg higher in cases than in controls (P < 0.01; Table 3). Likewise, the conditional logistic-regression model suggested that systolic blood pressure was significantly higher in cases than in controls (P < 0.01). Diastolic pressure was not significantly different between the two groups. Converting the regression coefficient to an odds ratio, we found that subjects with a systolic blood pressure of 160 mm Hg had a 2.2 times greater chance of having an intraocular pressure of 20 mm Hg or more than did a subject with systolic blood pressure of 120 mm Hg.

Because the cross-sectional data suggested that higher systolic blood pressure was associated with elevated intraocular pressure, the next step was to examine the relationship between change in systolic blood pressure and change in intraocular pressure over time in individuals. Changes in intraocular pressure over time may also be related to initial blood pressure (ie, subjects with blood pressure of 160 mm Hg might be more likely to have a change in IOP than those with 120 mm Hg). Likewise, change in intraocular pressure may be related to age (although intraocular pressure itself appears to be unrelated to age in these data). The autoregressive model was used to examine changes over 1- and 2-yr periods. In all analyses, initial blood pressure was not associated with a change in intraocular pressure, so the data are presented for the other predictors (Table 4). A change in intraocular pressure was correlated with initial intraocular pressure in a manner that represented regression to the mean (P < 0.001; Table 4). When initial intraocular pressure was low, the next reading was more likely higher, and vice versa. The negative coefficient suggests that the higher the initial intraocular pressure, the more likely that subsequent readings will change. This phenomenon has been well described and is a factor not only of measurement and instrumentation, but also of physiologic variability.

Changes in intraocular pressure were positively correlated with changes in systolic blood pressure over both the 1- and 2-yr periods (P < 0.05; Table 4). Changes in intraocular pressure were correlated with changes in diastolic blood pressure only over the 1-yr period (P < 0.05). In visits 2 yr apart, initial age was inversely correlated with changes in intraocular pressure (P < 0.05).

Table 4. Autoregressive model: association between change in intraocular pressure and age, intraocular pressure and change in blood pressure

<table>
<thead>
<tr>
<th>Variable</th>
<th>1-Year period</th>
<th>2-Year period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>Standard error</td>
</tr>
<tr>
<td>Systolic</td>
<td>0.16</td>
<td>0.008</td>
</tr>
<tr>
<td>Diastolic</td>
<td>0.04</td>
<td>0.013</td>
</tr>
<tr>
<td>Initial IOP</td>
<td>-0.41</td>
<td>0.04</td>
</tr>
<tr>
<td>Age</td>
<td>-0.002</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Discussion

In cross-sectional studies of adults, mean intraocular pressure appears to rise with increasing age. There is evidence that the increase in intraocular pressure in older persons is related to factors other than age alone. Bengtsson found that the increase in intraocular pressure with age was largely dependent on a concomitant rise in systemic blood pressure with age in a Swedish population. Klein and Klein found that the variability in eye pressure in an American population was more highly correlated with systolic blood pressure than with age. Shiose et al reported that intraocular pressure actually decreased with age in a Japanese population, and this decline was accentuated when only those with normal blood pressure were considered.

Our cross-sectional data show no statistically significant association between intraocular pressure and age. It is important to consider whether this conclusion is influenced by the selection of persons in our study group. Two percent of our subjects with ele-
vated blood pressure were excluded due to therapy with alpha- or beta-adrenergic medications. Since these persons represent a small minority of our population, they probably do not influence the conclusion. We cannot exclude the possibility that in the oldest age groups, subjects with hypertension may not have volunteered for the study. For the cross sectional data, of the 86 subjects in the age group 75 and older, about 40% were new recruits into the longitudinal study. However, the levels of blood pressure in our study group and the increase with age are comparable to those of the Framingham Heart Study population.20 Thus, they are indicative of the middle class American population regarding this parameter.

The mean eye pressure data in our study are comparable or even slightly higher than those of other studies that examined unselected populations. For example, 69 persons (12% of our group) had intraocular pressure equal to or greater than 20 mm Hg. This is close to the expected frequency of ocular hypertension in a general population.10,11 Thus, the characteristics of our group do not differ from those of other studies, with regard to elevated eye pressure or systemic hypertension. It seems valid to conclude that age does not seem to be the most important determinant of eye pressure in populations similar to our study group.

Our report presents a new view of the strong association between intraocular and systemic blood pressures. Changes in intraocular pressure from 1 yr to the next were positively correlated with changes in systolic blood pressure at both time points and with diastolic blood pressure in the 1-yr group. The association of the change in intraocular pressure with alteration in blood pressure is unlikely to be due to independent regression to the mean for both parameters, because the change in intraocular pressure was not associated with initial blood pressure measurement. It has been adequately demonstrated that elevated intraocular pressure and systemic hypertension are related. Our results constitute the initial documentation of a linkage between these two physiologic parameters in persons with largely normal levels of eye and blood pressure. There are several reports suggesting an increased risk of open-angle glaucoma in persons with systolic blood pressures greater than 160 mm Hg.4-6 The Framingham Eye Study indicated that higher systolic blood pressure predated ocular hypertension by up to 25 yr.7 Our cross-sectional data confirmed previous reports of an increased probability of elevated systolic blood pressure in persons with elevated intraocular pressure (defined as greater than 20 mm Hg).7

Our data are inconclusive on the relationship between age and change in intraocular pressure. Over a 2-yr period, the older the person, the smaller the change in pressure; in the 1-yr group, changes in eye pressure was not significantly related to age. It appears that in a normal population in which intraocular pressure does not increase with age, its variability likewise may not increase with age.

Although we showed a longitudinal association between changes in intraocular and blood pressures, we cannot estimate the relative magnitude of such changes. The data available to us span 6 yr, and we were only able to compartmentalize comparisons over 1- and 2-yr periods. The expected change in these measures are of the order of a fraction of millimeters per yr for intraocular pressure and millimeters per yr for blood pressure. Thus, we cannot obtain an accurate estimate of magnitude without data points more widely separated in time.

Our study group consisted almost exclusively of white men. It is well known that the prevalences of both glaucoma and systemic hypertension are lower in whites than in blacks.6 In particular, glaucoma in blacks has an earlier age of onset, and higher intraocular pressure and more severe optic nerve damage at the time of diagnosis.4,6 Data on glaucoma in women are sparse and conflicting regarding sex differences in glaucoma rates.21 Hence, conclusions from our data must be confined to men and should be interpreted with caution for other racial groups and in women.

The Schiotz tonometer was selected by the BLSA researchers for this study because in 1958 it was the most commonly used instrument for intraocular pressure measurement. Subsequently, it has been appreciated that its calibration gives a lower intraocular pressure than applanation tonometry.17 Furthermore, it may be inaccurate at the extremes of intraocular pressure and in highly myopic eyes with unusual ocular rigidity, although there were few high myopic patients in this study. In this regard, it is reassuring that the mean intraocular pressure of our population is similar or slightly higher than those of studies using applanation tonometry.10,11,19 In fact, if it is correct that Schiotz tonometry should read artificially higher than true eye pressure with increasing age, then we should have been more likely to find higher pressure in older persons with this tonometer.22 More importantly, our analysis concentrated on comparative intraocular pressures rather than absolute values. This was especially true in the longitudinal phase of the study that compared one eye to itself over time. Under these conditions, a calibrated Schiotz instrument, used consistently, should give reliable comparative data.

If intraocular and blood pressures are correlated with each other over periods of 1-2 yr and if elevated eye and blood pressures occur together, does this
mean that the two parameters are governed by similar mechanisms and lose homeostatic control by related abnormalities? We might speculate that increased blood pressure leads to increased ciliary artery pressure, increasing the ultrafiltration component of aqueous humor formation and thus increasing intraocular pressure. Alternatively, their association may result from a common physiologic factor such as the effect of generalized sympathetic tone or serum corticosteroids. There is increasing evidence that factors that beneficially influence blood pressure, such as aerobic exercise, may have therapeutic effects on elevated eye pressure. This research direction deserves renewed effort.

Key words: intraocular pressure, blood pressure, prospective study

Acknowledgments

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References