Intraocular Pressure Increases in Parallel with Systemic Blood Pressure during Isometric Exercise

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PURPOSE. Normal-tension glaucoma has been found to be related to transient increases in intraocular pressure (IOP). Isometric exercise induces a pressor response with a characteristic increase in blood pressure. The purpose of the present study was to investigate how transient changes in systemic blood pressure, induced by isometric exercise, affect IOP.

METHODS. Nine healthy volunteers participated in the study. Systemic blood pressure, heart rate (ECG) and IOP (electronic continuous-indentation tonometer) were recorded continuously before, during, and after a 2-minute period of isometric exercise (40% maximum voluntary contraction of the forearm).

RESULTS. During the 2-minute isometric exercise, heart rate increased from 74 ± 6 beats/min (mean ± SEM) to 93 ± 6 beats/min (P < 0.005) and systolic and diastolic arterial blood pressure increased from 125 ± 6 to 169 ± 8 mm Hg (P < 0.005) and from 65 ± 3 to 96 ± 5 mm Hg (P < 0.005), respectively. IOP increased from 15 ± 1 to 19 ± 2 mm Hg at rest to 19 ± 2 mm Hg at the end of the isometric exercise (P < 0.005).

CONCLUSIONS. During isometric exercise, IOP increased continuously, as long as the isometric exercise persisted, in parallel to the increase in systemic blood pressure. (Invest Ophtalmol Vis Sci. 2009;50:760–764) DOI:10.1167/iovs.08-2508

The physiological changes in the eye during exercise are not fully understood. Some studies have demonstrated that physical activity has a beneficial effect in lowering intraocular pressure (IOP) both after isometric exercise (static) and dynamic exercise. There are, however, few studies on IOCHanges during exercise, and the results are inconsistent.

Isometric exercise is known to cause a transient increase both in diastolic and systolic systemic blood pressure. Since normal-tension glaucoma has been found to be related to transient increases in IOP, knowledge of how isometric exercise affects IOP may be of clinical importance. The results of the studies on this topic differ. Some studies have found transient increases in IOP during isometric exercise, whereas others have found the opposite. And again, some studies have found no significant changes in IOP during isometric exercise. However, the methods used in the studies are different, and may explain the diversity in findings. To our knowledge, no previous study has measured IOP continuously during isometric exercise.

The purpose of the present study was to gain more knowledge about how transient changes in systemic blood pressure, induced by isometric exercise, affect IOP. Based on the knowledge that systemic blood pressure increases during isometric exercise, our hypothesis was that IOP would increase in parallel with the increase in systemic blood pressure.

METHODS

Subjects

Nine healthy subjects were included in the study, three women and six men. Subject characteristics are presented in Table 1. All subjects were nonmedicated, normotensive, and nonsmokers. The subjects were instructed not to drink coffee or tea, exercise, or eat for at least 2 hours before the start of the experiment. Biometric assessment was obtained before the exercise (axial length, corneal radii, and anterior-chamber depth; IOLMaster; Carl Zeiss Meditec, GmbH, Jena, Germany) and A-Scan pachymetry (model AL-1000; Tomey Corp., Nagoya, Japan). IOP was measured by means of Goldmann applation tonometry. The research adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants, and the study was approved by the local ethics committee in Oslo, Norway.

Handgrip and Experimental Protocol

A custom-made handgrip unit was used to measure and display the force exerted by the test subjects when squeezing the grip with the right hand. A digital display gave the test subjects continuous information, making it possible to maintain the intended force. The test subjects were asked to exert a force corresponding to 40% of their individual and previously measured maximum voluntary contraction (MVC) force. The test subjects were instructed to avoid the Valsalva maneuver and to relax all the muscles not primarily involved in contraction, to avoid recruitment of accessory muscle mass and an increase in venous pressure. MVC was determined approximately 10 minutes before the experimental protocol by asking the test subjects to apply maximum force around the handgrip transducer for 3 seconds. The experimental protocol was as follows: After a rest period of 30 seconds, a 2-minute period followed in which the subjects exerted 40% of maximum voluntary force, before a final rest period of 30 seconds. The subjects were supine during the experimental protocol. Control experiments were conducted on a different day, after the exercise runs, with continuous measurements of IOP for 3 minutes in resting, supine conditions.

Measurements

Finger arterial pressure was continuously acquired by a photoplethysmographic pressure recording device (Finometer: Finapres Medical Systems BV, Amsterdam, The Netherlands) measured from the left arm. Care was taken to adjust the arm so that the measured finger was at heart level. The Finometer device has been shown to satisfy the validation criteria of the Association for the Advancement of Medical Instrumentation, and it has therefore been recommended for measurements in the clinical setup and for research purposes.

The IOP was continuously acquired in an improved Schiotz electronic tonometer (dynamic tonometer; Nycotron, Oslo, Norway [the company no longer exists; the tonometer is therefore not in commercial production any longer]). The tonometer measures changes in...
corneal indentation pulse and reflects the change in ocular volume produced by the excess of blood entering the eye after each heart beat. The dynamic tonometer works as a tonograph, measuring the IOP continuously with an output of 1 mV/μm of the 5.5-g plunger movement.25 The analog signal (in millivolts) from the electronic tonometer was converted digitally by means of an AD converter and sampled at 300 Hz along with the instantaneous blood pressures, heart rate (HR), and voluntary contraction force.

Hørven22 showed that the linearity of the dynamic tonometer was complete throughout all tension levels (i.e., from 1 to 15 Schiøtz scale readings). The tonometer fulfills the criteria of specification 5 for Schiøtz tonometers, which means that Friedenwald’s table converting tonometer readings into millimeters of mercury IOP can be used.26 After controlling the linearity of the tonometer with the 5.5-g plunger weight (R² = 1.0, n = 13), we converted the millivolt readings into millimeters of mercury by first fitting the values from Friedenwald’s table iteratively for best nonlinear regression (R² = 0.99, n = 27). The millimeters of mercury values were then calculated.

Figure 1 shows average IOP measured continuously during control and isometric exercise. The weight of the Schiøtz electronic tonometer is 16.8 g and during measurement, the IOP declines as fluid in the anterior chamber is drained by the pressure of the tonometer. In the nine control experiments, the average rate of decline was 12% per minute, in accordance with Hørven.22 Linear regression on the nine control experiments showed that the rate of decline of IOP was almost linear during this time period (R² = 0.90 ± 0.03). The IOP measured during isometric exercise was corrected for this drift found during each corresponding control experiment. The bottom curve of Figure 1 shows IOP corrected for the drift caused by the tonographic effect of the tonometer.

Data and Statistical Analyses
Data acquisition was performed with commercial software (LabView, ver. 8.0, National Instruments Corp., Austin, TX). The calculation of rates of change and the slopes of IOP and blood pressure were performed in another program (SigmaPlot ver. 11.0; Systat Software, Inc., San Jose, CA).

Applicable data are presented as the mean ± SEM. Student’s t-test was used to calculate significance between means when the data passed the normality test; otherwise, a Wilcoxon’s signed-rank test was performed. Repeated-measures ANOVA was used to test for significant differences between the exercise and control runs. Linear regression and correlation were performed (SigmaStat ver. 3.10; Systat Software, Inc.) with the correlation coefficient determined by Spearman rank order correlation. P < 0.05 was considered statistically significant.

In our study, the mean IOP change between pre-exercise resting values and the peak values at the end of isometric exercise was 3.6 mm Hg, and the SD of the individual changes was 2.5 mm Hg. Assuming that these results reflect the true values of these parameters, and using a two-sided paired t-test with 5% significance level, it may be shown that the test power in our study with nine subjects is 0.95.

Table 1. Subjects’ Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>23.6</td>
<td>0.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.5</td>
<td>0.6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175</td>
<td>2.6</td>
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<tr>
<td>Weight (kg)</td>
<td>68</td>
<td>3.4</td>
</tr>
<tr>
<td>CCT (μm)</td>
<td>562</td>
<td>12</td>
</tr>
<tr>
<td>IOP by Goldmann (mm Hg)</td>
<td>12</td>
<td>0.1</td>
</tr>
<tr>
<td>AL (mm)</td>
<td>24.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Mean K (D)</td>
<td>43.1</td>
<td>0.5</td>
</tr>
<tr>
<td>ACD (mm)</td>
<td>3.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

BMI, body mass index; CCT, central corneal thickness; AL, axial length; Mean K, mean keratometric power; ACD, anterior chamber depth.

RESULTS
Figure 2 shows the development of all recorded variables throughout the experiment. The systemic blood pressures, HR and IOP at the different time points are presented in Table 2. During isometric contraction, there was a gradual increase in blood pressure and HR. IOP increased in parallel with the increase in systemic blood pressure. After exercise, blood pressure, HR and IOP declined to pre-exercise levels during the next 30 seconds (Fig. 2). Two minutes of 40% voluntary force caused the averaged systolic (SP) and diastolic blood (DP) pressure to increase significant by 36% (P < 0.005) and 49%.
where \( y \) is IOP (or blood pressures) as a function of time, \( t \) is time (in seconds), \( e \) is the mathematical constant, \( T \) is the time constant, and \( a \) is IOP or blood pressure, at the start of the decline. Measured pressure data during the start of the postexercise relaxation period was fitted to this model to obtain an estimation of the time constant. The coefficient of determination for nonlinear regression, \( R^2 \), was 0.99 ± 0.0004, 0.998 ± 0.0009, and 0.996 ± 0.0017 for IOP, SP, and DP, respectively, indicating a very good fit. The time constant, \( T \) (the time required to complete 63.2% of the total decay), of the fitted IOP curves was 56.4 ± 9.5 seconds. The time constants of the curve fit of the decline of SP and DP were 63.0 ± 7.4 and 33.0 ± 4.5 seconds, respectively. In the last 20 seconds of the postexercise resting period DP and IOP levels were not significantly different from the pre-exercise resting period.

**DISCUSSION**

The main finding in the present study was that IOP changed in parallel with systemic blood pressure during isometric exercise.

**Methodological Considerations**

Different types of tonometers have different ranges of accuracy and precision. Repeated applanation measurements have been shown to induce IOP lowering on remeasurement. This IOP lowering can be explained as a forced drainage of anterior chamber fluid due to indentation of the tonometer. Stocker found the standard Mueller electronic tonometer (Schiotz) to give average lowering of 1.9 mm Hg at remeasure after 4 minutes. He also found additional lowering of IOP when the tonometer had been resting on the contralateral eye between the measurements. In the present study, we used an improved Schiotz electronic tonometer. When measuring continuously with this tonometer, we therefore expected a lowering of the IOP. To measure the degree of IOP lowering induced by the tonometer, we applied the tonometer on all subjects in a separate control run without any isometric effort. These measurements showed a continuous, gradual lowering of the IOP during indentation. The average rate of decline of 12% per minute found in our study is in accordance with the rate of decline found by Horven (11.3%). By correcting for this decrease in IOP, we could calculate the relative IOP changes during isometric exercise. Ideally, it would be preferable to measure the IOP by means of nonindentation/applanation, but to our knowledge no such tonometer is available for continuous measurements. The actual IOP response to isometric exercise can be revealed only by direct manometry, but such direct measurements cannot be performed in humans for ethical reasons. The IOP responses to mechanical elevation of arterial pressure have been studied in animals and, consistent with our results, mechanical elevation of blood pressure in cats and rabbits elicit modest increases in IOP. Bill proposed that this effect is due to increased sympathetic nerve activity to the

![Figure 2](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933448/)
choroid, while Kiel\textsuperscript{31,32} proposed that it is due to chorioidal myogenic autoregulation. Both mechanisms would minimize the choroidal engorgement that would otherwise cause a large increase in IOP. It is clear that the choroid's capacity for engorgement is large, as noted by Duke-Elder\textsuperscript{33,34} when he tied the vortex veins in a dog and the IOP immediately rose to 80 to 90 mm Hg, but more physiologic challenges like head-down tilt\textsuperscript{34} fail to elicit such catastrophic choroidal engorgement.

There has been some discussion of whether the eye's rigidity coefficient is altered at different levels of systemic blood pressure and thereby also a question of the validity of tonometers at different levels of systemic blood pressure. Kiel\textsuperscript{15} found that higher levels of mean arterial blood pressure are associated with increasing rigidity coefficients. Saline was infused into the vitreous to increase the ocular volume and IOP. In our study, indentation of the eye leads to a gradual reduction of the eye volume. According to Kiel, we therefore should expect the differences in pressure-volume relationships to be minor, and consequently we believe any bias in our IOP measurements caused by changes in the rigidity coefficients to be negligible in our study.

### IOP Changes Related to Exercise

The cardiovascular response to isometric exercise has been studied extensively since first described by Lindhard in 1920. There is a gradual increase in blood pressure until exhaustion occurs.\textsuperscript{19,36-38} The current view is that the blood pressure set point is continuously regulated upward as long as the isometric exercise persists.\textsuperscript{39,40} During isometric exercise, it has been demonstrated that blood pressure in the ophthalmic and brachial arteries rise in parallel.\textsuperscript{15} The major finding in the present study is that IOP changed transiently in parallel with blood pressure during isometric exercise. In the limited number of studies on IOP changes during isometric exercise, there have been discrepancies between the findings.\textsuperscript{4,12-15,17} The methods and means of measuring the IOP differ in these studies, as shown in Table 3 and may explain the differences in results.

Blood pressure increase during exercise is shown to be related to the strength of contraction,\textsuperscript{41} and probably also the size of muscle mass involved.\textsuperscript{42} The type and intensity of isometric exercise therefore probably influenced the reported IOP changes in the different studies. Some investigators have used squatting as isometric exercise,\textsuperscript{13,14,17} but the length of contraction differed; 90 seconds,\textsuperscript{14} 150 seconds,\textsuperscript{13} and 6 minutes.\textsuperscript{17} Riva et al.\textsuperscript{14} and Movaffaghy et al.\textsuperscript{15} found increased IOP during squatting, whereas Wimpissinger et al.\textsuperscript{17} found no significant difference in IOP.

Others,\textsuperscript{7,4} including our study, have used handgrip isometric exercise, but the strength of contraction varied between 20% and 55% MVC. Lanigan et al.\textsuperscript{2} found a decrease in IOP, whereas Marcus et al.\textsuperscript{3} reported no significant change in IOP. Robinson et al.\textsuperscript{15} used squatting, leg extension, and handgrip in the same study, but found no significant changes in IOP. Dickerman et al.\textsuperscript{12} observed a prominent increase in IOP by applying maximum contractions in arms combined with the Valsalva maneuver, but the Valsalva maneuver is known in itself to elevate IOP.\textsuperscript{43}

From these different studies there seems to be no clear connection between changes in IOP and strength of contraction or size of muscle mass involved. In the three studies in which increased IOP was found, pressure was measured with a handheld tonometer (Tono-pen; Reichert Inc., Philadelphia, PA) or a noncontact tonometer. The studies measuring IOP by applanation have either found decreased\textsuperscript{3} or no change\textsuperscript{4,17} in IOP during isometric exercise. Lanigan et al.\textsuperscript{2} measured IOP repeatedly during the exercise. Wimpissinger et al.\textsuperscript{17} also measured IOP repeatedly by applanation, and although the test subjects squatted for 6 minutes, the investigators found no change in IOP. From these studies and in accordance with our findings as well as previously reports in the literature,\textsuperscript{39,44} it seems apparent that repeated measurements by applanation or indentation significantly lower IOP on remeasurement. We believe that this IOP-lowering effect may explain the differences in the findings in these studies. In our study, using handgrip and continuous indentation IOP measurement, we also found a small decrease in IOP during isometric exercise; if not corrected for the IOP lowering caused by the measurement method. In studies using repeated or continuous measurements, a methodological bias resulting in IOP lowering, must be taken into account when evaluating the data.

Krist et al.\textsuperscript{20} found a relationship between normal-tension glaucoma and activities or diseases causing increase in intrathoracic and -abdominal pressure, such as weight lifting and obstruction of the urinary system. Schueman et al.\textsuperscript{15} investigated the IOP response during wind instrument playing. IOP was measured continuously with a pneumotonometer while musicians played different wind instruments, and the IOP increase correlated well with the degree of exhalation. However, there was only a modest correlation with risk of glaucoma and musicians with the greatest IOP response.

Krist et al.\textsuperscript{20} postulated that patients with normal tension glaucoma might have an increased sensitivity for IOP fluctuations. Since our study showed that IOP increases during isometric exercise, this type of effort therefore could be a potential risk factor for the development or progression of normal-tension glaucoma. However, the present study found a modest 3.6 mm Hg IOP response to isometric exercise, which is unlikely to cause glaucoma. Since IOP increases continuously during isometric exercise, more exhausting effort will probably induce higher IOP levels. It has been demonstrated that isometric exercise induces a postexercise IOP-lowering effect,\textsuperscript{1,2,17} and all in all we therefore believe such physical activity should be recommended to patients with glaucoma.

### Table 3: Studies of IOP Changes during Isometric Exercise

<table>
<thead>
<tr>
<th>Study</th>
<th>IOP Measurement</th>
<th>IOP Change</th>
<th>Isometric Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcus et al.\textsuperscript{4}</td>
<td>Applanation</td>
<td>➔</td>
<td>Handgrip, 20% and 55% MVC</td>
</tr>
<tr>
<td>Robinson et al.\textsuperscript{15}</td>
<td>Applanation</td>
<td>➔</td>
<td>Squatting, handgrip, leg extension</td>
</tr>
<tr>
<td>Lanigan et al.\textsuperscript{2}</td>
<td>Applanation, repeated</td>
<td>➔</td>
<td>Handgrip, 33% MVC</td>
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<tr>
<td>Riva et al.\textsuperscript{14}</td>
<td>Tono-pen</td>
<td>➔</td>
<td>Squatting for 90 s</td>
</tr>
<tr>
<td>Dickerman et al.\textsuperscript{12}</td>
<td>Noncontact (Pulsair 2000)</td>
<td>➔</td>
<td>Max contraction arms, including Valsalva</td>
</tr>
<tr>
<td>Movaffaghy et al.\textsuperscript{15}</td>
<td>Tono-pen</td>
<td>➔</td>
<td>Squatting for 150 s</td>
</tr>
<tr>
<td>Wimpissinger et al.\textsuperscript{17}</td>
<td>Applanation (Perkins), repeated</td>
<td>➔</td>
<td>Squatting for 6 min</td>
</tr>
<tr>
<td>Present study</td>
<td>Continuous (improved Schiøtz), indentation</td>
<td>➔</td>
<td>Handgrip, 40% MVC</td>
</tr>
</tbody>
</table>

CONCLUSION

The present study showed that IOP increases in parallel with the transient, continuous changes in systemic blood pressure during isometric exercise. Clinicians should be aware that a patient exerting isometric effort during IOP measurement may have misleadingly high IOP levels.

References