Ocular Rigidity in Living Human Eyes

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PURPOSE. To measure the rigidity coefficient of a large number of subjects at clinically encountered intraocular pressures (IOPs) and to examine the possible correlation of ocular rigidity with other factors, such as the age of the patients, ocular parameters (axial length and corneal thickness), and pathologic conditions affecting the eye.

METHODS. The pressure–volume relationship and the ocular rigidity coefficient (K) were determined in 79 eyes undergoing cataract surgery, by injecting 200 μL of saline solution (in steps of 4.5 μL) through the limbus into the anterior chamber, while continually monitoring the IOP with a transducer, up to the limit of 60 mm Hg. Data within an IOP range of 10 to 35 mm Hg were used to calculate the scleral rigidity coefficient. All measurements were taken at the same time of day, to eliminate any possible diurnal variation.

RESULTS. The mean ocular rigidity coefficient was 0.0126 mm Hg/μL (95% confidence interval [CI], 0.0112–0.0149). A statistically significant positive correlation between the rigidity coefficient and age of the patient was found (P = 0.02), whereas similar findings were not observed for the examined ocular parameters (axial length, P = 0.09; and corneal thickness, P = 0.12). No correlation was found for patients with diabetes mellitus (P = 0.39), age-related macular degeneration (P = 0.55), and hypertension (P = 0.45).

CONCLUSIONS. The present study provides quantitative data on the ocular rigidity coefficient based on measurements in a large series of living human eyes. A positive correlation between the ocular rigidity coefficient and the patient’s age was documented. (Invest Ophthalmol Vis Sci. 2005;45:409–414) DOI:10.1167/iovs.04-0162

Ocular rigidity is a measurable physical parameter of the eye that expresses the elastic properties of the eye globe. In 1937, Friedenwald1 described the coefficient of ocular rigidity as a "measure of the resistance, which the eye exerts to distending forces," and he developed a formula for ocular rigidity.

Friedenwald’s equation was the first attempt to quantify ocular rigidity and was extracted from the pressure–volume relationship measured in a wide range of pressures. A main obstacle of Friedenwald’s formula is that measurements are performed on enucleated eyes. In addition, when this formula is used in clinical practice, the calculation of the scleral rigidity coefficient is performed indirectly on the basis of only two IOP measurements, using application and indentation tonometers. Other investigators performed direct manometric measurements of the ocular rigidity in living human eyes, in situ.2–4 They determined that rigidity increases with increasing intraocular pressure (IOP) and developed alternative formulas to characterize this change as a function of pressure. Although these formulations are more accurate than Friedenwald’s equations, they are more complicated and present difficulties when applied in daily clinical practice.

There is supporting evidence that ocular rigidity has particular relevance in several clinical situations, such as pathologic myopia (alterations in mechanical properties of myopic sclera), glaucoma, refractive surgery, changes in ocular blood flow, and correlated pathologic conditions.5–7

The purpose of the present study was to measure the rigidity coefficient in a large number of subjects at clinically encountered IOPs and to examine any possible correlation of ocular rigidity with other factors, such as the age of the patient and ocular parameters (axial length and corneal thickness).

SUBJECTS AND METHODS

Ocular rigidity was determined in 79 patients who were undergoing cataract surgery under retrobulbar anesthesia, by injecting 200 μL of a balanced salt solution (in steps of 4.5 μL; BSS, Alcon Laboratories, Fort Worth, TX) through the limbus into the anterior chamber. One eye of each patient enrolled was used in the study (79 eyes). The necessary number of subjects participating in the study was determined by using α = 0.05 and a β = 0.20 and an estimation of the variance of scleral rigidity (K).1 Forty-two of the participants were men (53%).

To minimize the possible effects of the changes in aqueous secretion and outflow (that might alter ocular rigidity measurements), subjects were excluded from the study if they had glaucoma or ocular hypertension or had undergone previous ophthalmic surgery.

Central corneal thickness (available in 51 patients) was measured with ultrasonic pachymetry (50 MHz; Corneo-GAGE; Sonogage Inc., Cleveland, OH). Corneal thickness measurement was not included in the initial design of the study. However, due to the increasing interest shown in the recent literature, the inclusion of this parameter was considered essential, and all study participants were recalled retrospectively. Fifty-one of 79 patients responded positively.

The study was performed according to the tenets of the Declaration of Helsinki and approved by the institutional review board. All subjects included in the study were informed of the purpose of the research and the procedures to be used in collecting the data, and all provided informed consent.

Measurement System

The ocular rigidity measurement device consisted of three units: the computer unit and transducer controller, the mechanical dosage sys-
would affect the results of the second measurement, we performed two measurements for each eye. The repeatability was defined as twice the standard deviation of the differences between the two measurements. Plotting the measurement difference between the two methods against the mean ocular rigidity coefficient can demonstrate any relationship (bias) between the measurement error and the mean measurement.

All measurements were performed under retrobulbar anesthesia (1:1 lidocaine-bupivacaine mixture up to a total volume of 5 mL). The procedure usually started 15 minutes after retrobulbar injection. It was performed in a sterile field, and all components (tubing, needle, and syringe) were gas sterilized. Eyes were prepared with povidone-iodine (Betadine; Purdue Frederick, Norwalk, CT) and lids were retracted by a speculum. After insertion of the needle into the anterior chamber of the eye, the IOP was regulated to 10 mm Hg by appropriate irrigation or aspiration of the saline solution. Additional incremental volumes of saline solution were injected automatically via the syringe in bursts of 4.5 µL followed by a 1-second delay, to allow the transducer system to reach equilibrium with the tubule manifold and IOP. This delay was chosen after preliminary experiments with our system in enucleated porcine eyes. The data curves obtained in these experiments when the delay was set to 1 second were sufficiently smooth to ensure that the system had reached equilibrium. Furthermore, this delay also allowed the surgeon to observe the measurement process and terminate it in case of any unexpected adverse event. In addition, the increased infusion rate used compared with the theoretical aqueous secretion and outflow (264 µL/min vs. 4.1 µL/min, respectively) and the exclusion of eyes with several pathologic conditions (such as operated or glaucomatous eyes) minimized the possible effects of variations in aqueous dynamics. After each volume injection, the resultant IOP was measured twice, and the mean pressure was recorded, along with the corresponding amount of the injected volume. The experiment proceeded until a final IOP of 60 mm Hg was reached or 200 µL saline solution was injected into the eye, whichever was achieved first. The system then regulated the IOP to 10 mm Hg, and the measurement was repeated.

All measurements were taken under continuous microscopic monitoring to avoid aqueous leakage from the cannulation site.

**Data Analysis**

Results are expressed as the mean ± SE (range) and the mean with 95% confidence interval. Independent-sample *t*-tests were used to correlate the ocular rigidity coefficient with the corresponding clinical dichotomous parameters, such as the presence of diabetes mellitus (DM), age-related macular degeneration (ARMD), and hypertension, whereas linear regression analyses were used to test the influence of continuous variables such as patient age, ocular axial length, and corneal thickness. Multivariable linear regression analysis was performed to identify independent variables associated with ocular rigidity (all variables included simultaneously). The level of significance was set at 5%. The slope of the pressure-volume curves over the measurements was obtained for the pressure interval of 10 to 35 mm Hg by using linear regression analysis (the least-squares method).

**RESULTS**

**Pressure–Volume Measurements**

None of the examined patients experienced any intra- or postoperative complications. Figure 2 shows the measurements of IOP versus injected volume of saline solution into the eye. Two consecutive measurements on the same eye were made, and the mean ± SD is shown for each data point. The mean data were used for the calculation of the slope that determined the ocular coefficient.

The linear regression procedure was used for the calculation of all rigidity coefficients over the 79 eyes. The average $R^2$ coefficient for all the regression procedures was 0.9203 ±
This level of $R^2$ justified the linear approximation for the pressure range used in the analysis.

The rigidity coefficient ($K = dP/dV$ [in mm Hg/$\mu$L]) was calculated as the slope of the pressure ($P$) versus volume curve ($V$) for the IOP range (10–35 mm Hg) in the analysis. The mean rigidity coefficient ($K$) was found to be 0.0126 mm Hg/$\mu$L (95% CI: 0.0112–0.0149). The coefficient of repeatability (CR; twice the standard deviation of the mean difference between the two measurements) was 0.0023 (Fig. 3).

Ocular Rigidity Versus Age, Axial Length of the Eye, Diabetes Mellitus, Age-Related Macular Degeneration, and Hypertension

The mean age of the subjects was 65.3 $\pm$ 13.9 years (range, 27–91). The mean axial length was 22.9 $\pm$ 1.1 mm (range, 20.0–24.8), and the mean central corneal thickness was 531.6 $\pm$ 20.9 $\mu$m (range, 487–576). Twenty-five (31.6%) of 79 patients had hypertension, 14 (17.7%) had diabetes mellitus, and 12 (15.2%) had age-related macular degeneration.

A statistically significant positive correlation between rigidity coefficient and age of the patient was found ($r = 0.27, P = 0.02$; Fig. 4). A trend for decreased scleral rigidity in correlation with increase in axial length of the eye ($r = -0.24, P = 0.09$) was observed (Fig. 5), whereas no statistically significant correlation was found in central corneal thickness ($r = 0.22, P = 0.12$, type II error = 0.64; Fig. 6). In parallel, there was no statistically significant correlation between the rigidity coefficient and the presence of diabetes mellitus ($P = 0.39$), age-related macular degeneration ($P = 0.55$), and hypertension ($P = 0.45$). In multivariate analyses, none of the examined variables was found to have statistically significant correlation with the ocular rigidity coefficient ($P > 0.05$).

DISCUSSION

Until now, the most commonly used pressure–volume relationship for the calculation of ocular rigidity has been Friedenwald’s equation. This equation has received criticism because the data that were used for its computations were obtained from enucleated eyes. Because of postmortem changes (such as edema and consequent thickening, active flow of blood, effect of extraocular muscles, and vascular rigidity in the intact living eye), marked differences were noted when the ocular rigidity was measured in a live eye and compared with rigidity in the same eye obtained after enucleation.

Several investigators tried to use direct manometric measurements in living human eyes to obtain a more accurate estimate of ocular rigidity. The number of eyes measured, however, was always small, and in all cases these eyes had serious diseases and were scheduled for enucleation. Recently, Silver and Geyer, in an attempt to derive a uniform formula for the calculation of the ocular rigidity coefficient, collected all
the data available in the literature that were obtained with direct manometric measurements from living human eyes. Based on these data, they described a new equation that provides the best fit for the collected data. They also found a larger volume increment for a given increment of pressure than was provided by the Friedenwald equation. The main limitation of this work is that it is based on collected data of different experiments in a relatively small number of pathologic eyes (21 eyes).

Our direct manometric measurements of ocular rigidity did not justify the use of complicated formulas to describe the pressure-volume relationship within the clinically significant

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**FIGURE 4.** Correlation between ocular rigidity and age of the patients ($r = 0.27, P = 0.02$).

**FIGURE 5.** Correlation between ocular rigidity and axial length ($r = -0.24, P = 0.09$).
pressure range of 10–35 mm Hg. The best fit in our experimental data was achieved with a linear regression.

The selection of a pressure range between 10 and 35 mm Hg was chosen because of its high clinical importance, because most individuals have IOPs within this range. Because other investigators have documented a correlation between IOP and scleral rigidity, we used the 10 mm Hg as the common set point for the initiation of measurements in all eyes. In parallel, an automated process adding or removing fluid from the anterior chamber until the desired IOP pressure was achieved at the beginning of our measurements was used. Therefore, ocular rigidity was always measured within the range of interest.

An important factor that might have altered the ocular rigidity coefficient measurements in this study was retrobulbar anesthesia. Retrobulbar anesthesia could affect ocular rigidity measurements by increasing the IOP during measurements or by altering the ocular shape. The time between retrobulbar anesthetic injection and the measurement (15 minutes), as well as the fact that before measurements the IOP was regulated to 10 mm Hg by appropriate irrigation or aspiration of saline solution, minimized these possible effects. In parallel, the alternative anesthesia with topical drops could also affect the ocular rigidity measurements because of eye movements and the patient’s refusal to cooperate, increasing the possibility of intraoperative complications.

The mean ocular rigidity coefficient in our sample was 0.0126 mm Hg/μL. The frequency distribution was skewed toward the high rigidity coefficients. In his original work, Friedenwald reported an average scleral rigidity coefficient of 0.021 mm Hg/μL. The difference in these results may be due to differences in rigidity coefficient calculation and measurement methodology, as well as to sample size and composition. Investigators who used direct manometric measurements reported ocular rigidity coefficients similar to ours.

In our study, we found a statistically significant increase in ocular rigidity with this increase may affect several parameters of ocular function by alterations in the biomechanical properties of the ocular matrix (sclera, cornea, and choroid). According to Friedman’s theory, the sclera becomes increasingly more rigid and noncompliant with age, because of the aging process or other causes. A rigid sclera limits the filling of the vortex veins and thereby increases the resistance to venous outflow. This relative obstruction ultimately leads to dilatation and decompensation of the choroidal venous system at the posterior pole, compromising Bruch’s membrane, the choriocapillaris, and the retinal pigment epithelium of the macular area. This aging process could be an explanation for the development of ARMD. In our study, we did not observe increased ocular rigidity in patients with ARMD (12 patients). Because of the small number of these patients, however, it is difficult to draw reliable conclusions about ARMD. Future studies enrolling more patients with ARMD are needed.

Ocular rigidity did not correlate with other pathologic conditions, such as diabetes mellitus and hypertension. There was a trend for an increase of ocular rigidity in eyes with small axial length (hyperopic eyes were more rigid than myopic), but this correlation did not reach a statistically significant level.

An important parameter that may affect the ocular rigidity coefficient is the corneal thickness. Several studies have correlated corneal thickness with IOP measurements and the possible effect on corneal rigidity. In our study, we did not find any statistically significant correlation between the ocular rigidity coefficient and central corneal thickness. It seems that differences in corneal thickness over the applanation area (3.06 mm in diameter for a Goldmann instrument) may have an increased effect in IOP measurement through alterations in topical corneal rigidity and corneal elastic properties, but may have less impact in ocular rigidity (total response of the eye) measured in the present study. However, this finding cannot be considered conclusive, since the power to detect such a correlation was low (type II error = 0.64). Further studies (including more patients in whom corneal thickness is estimated prospectively) are needed, to elucidate the possible correlation of corneal thickness and ocular rigidity.
Other sclera shell parameters may affect the ocular rigidity coefficient measurements. Friberg and Fourman found that changes in the shape and stress distribution of the scleral shell are the main factors of the observed reduction of ocular rigidity after scleral buckling. In our study, the measured ocular rigidity coefficient described the total response of the eye without separate evaluation of the function of the two major contributory components: morphologic and material. Although a complex approach that would take into consideration these parameters may be more accurate, it requires complex calculations that make it less functional.

In conclusion, the present study provides quantitative data regarding the pressure-volume relationship in the living human eye, measured in persons with a wide range of ages and eye sizes and in a large number of eyes. To the best of our knowledge, this is the largest series of living eyes that have been assessed with direct manometric measurements for the calculation of ocular rigidity. A positive correlation between ocular rigidity and age of the patients was found. Ocular rigidity measurement may be of clinical significance, as it seems to affect such eye parameters as IOP, ocular pulsation, blood flow, effect of topical medications, and post-refractive surgery complications. Future studies are needed to elucidate the clinical impact of ocular rigidity. Our device for direct manometric measurement of ocular rigidity could be a uniform instrument for use in the future to calibrate instruments for noninvasive estimation of ocular rigidity.

References


In footnote 2, the present affiliation of Jason E. Coleman was misprinted. Dr. Coleman is currently at The Picower Center for Learning and Memory, Howard Hughes Medical Institute, Massachusetts Institute of Technology, Cambridge, Massachusetts.