Ocular Pulse Amplitude in Healthy Subjects as Measured by Dynamic Contour Tonometry

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Objectives: To test whether dynamic contour tonometry yields ocular pulse amplitude (OPA) measurements that are independent of corneal thickness and curvature, and to assess variables of observer agreement.

Methods: In a multivariate cluster analysis on 223 eyes, the relationship between central corneal thickness, corneal curvature, axial length, anterior chamber depth, intraocular pressure, sex, age, and OPA measurements was assessed. Intraobserver and interobserver variabilities were calculated from repeated measurements obtained from 8 volunteers by 4 observers.

Results: The OPA readings were not affected by central corneal thickness ($P = .08$), corneal curvature ($P = .47$), anterior chamber depth ($P = .80$), age ($P = .60$), or sex ($P = .73$). There was a positive correlation between OPA and intraocular pressure (0.12 mm Hg/1 mm Hg of intraocular pressure; $P < .001$) and a negative correlation between OPA and axial length (0.27 mm Hg/1 mm of length; $P < .001$). Intraobserver and interobserver variabilities were 0.08 and 0.02 mm Hg, respectively, and the intraclass correlation coefficient was 0.89.

Conclusions: The OPA readings obtained with dynamic contour tonometry in healthy subjects are not influenced by the structure of the anterior segment of the eye but are affected by intraocular pressure and axial length. We found a high amount of agreement within and between observers.

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Most of the recent studies on pulsatile ocular hemodynamics are based on the developments of the recording pneumotonometer of Langham and McCarthy,\(^1\) such as the ocular blood flow tonometer (OBF) (OBF Laboratories Ltd, Malmesbury, England) or the ocular blood flow analyzer (Paradigm Medical Industries, Salt Lake City, Utah). The reliability of pressure waves recorded by pneumotonometers has repeatedly been questioned. Intraocular pressure (IOP) measurements obtained by the OBF system have been shown to be even more dependent on central corneal thickness (CCT)\(^2\-\(^4\) and corneal curvature\(^5\) than those of Goldmann applanation tonometry. A similar effect of CCT on IOP measurements has been shown for the OBF analyzer system,\(^6\) and the repeatability of the OBF system compared unfavorably with that of Goldmann applanation tonometry.\(^6\)

Dynamic contour tonometry (DCT) (Pascal; Swiss Microtechnology AG, Port, Switzerland) represents a novel type of continuously recording tonometry giving a reading of IOP and ocular pulse amplitude (OPA) (Figure 1). According to the working principles of DCT, matching up the concave pressure sensor with the cornea provides direct measurements independently of corneal properties.\(^7\) In eyes that have undergone laser in situ keratomileusis, DCT has been shown to measure IOP independently of CCT.\(^8\)-\(^10\) In normal eyes, IOP measurements assessed with DCT are not affected by corneal curvature, and intraobserver and interobserver variabilities compare favorably with those of Goldmann applanation tonometry.\(^11\) Furthermore, IOP values obtained with DCT are closer to the manometric reference pressure than those measured with Goldmann applanation tonometry.\(^12\) However, in a given tonometer, IOP and OPA do not necessarily correlate with regard to dependency on corneal variables. With the OBF analyzer, CCT affects IOP readings but not OPA measurements, whereas corneal curvature affects OPA recordings but not IOP readings.\(^3\) Therefore, the aim of this study was to investigate the factors af-
METHODS

We enrolled 150 healthy hospital staff members. The study group consisted of the same cohort as presented in an earlier report comparing IOP measurements using Goldmann appplanation tonometry and DCT. All study participants gave informed consent to be enrolled in the study, which was approved by the local medical ethics committee and was performed according to the tenets of the Declaration of Helsinki. All participants were asked for bilateral measurements, but the option to have only 1 eye measured was offered as well. Seventy-four volunteers agreed to unilateral measurements only. None of the subjects had any history of ocular disease, trauma, or surgery. Slitlamp findings were unremarkable. Owing to the different calibrations of DCT and Goldmann appplanation tonometry, reference IOP values as measured by DCT are 1.0 to 2.6 mm Hg higher. Because the upper threshold for reference IOP measured with DCT has so far not been defined, all of the IOP values recorded were included in the study. Axial length, corneal curvature, and anterior chamber depth were obtained by means of an optical biometry system (IOL Master; Carl Zeiss AG, Feldbach, Switzerland), followed by ultrasonic pachymetry (SP2000; Tomey Corp, Cambridge, Mass). The pachymeter probe was placed on the center of the cornea, and the mean of 3 readings was calculated for each eye. Finally, DCT was performed in a sitting position according to the manufacturer’s guidelines. A technically identical prototype of the model launched in November 2003 was used; however, it was devoid of auxiliary routines to calculate the grade of measurement quality (Q value). The smallest possible recording time of about 5 seconds per single measurement was used. Every measurement furnished an IOP and an OPA reading on a digital display, with a precision of 1 decimal place. Three consecutive readings were taken and the mean of the values was recorded. In the absence of objective Q values, a set of measurements was excluded from the study in the event that the output routine failed to calculate the OPA for any of the 3 individual readings.

To study the intraobserver and interobserver variability, the OPA was measured in 8 participants by 4 fully masked observers 3 times each, resulting in a total of 96 measurements. The delay between different observers was kept as short as possible (<30 seconds).

For statistical analysis, OPA values were transformed into their logarithm to obtain a normally distributed dependent variable. To avoid the problem of collinearity and overparameterization, we used the strategy proposed by Kleinbaum et al. The variables investigated were CCT, IOP, anterior chamber depth, and axial length. The variables considered to be confounders were sex, age, eye (left or right), and keratometric reading. Data were analyzed to determine whether a linear relationship existed between the OPA measurements and the different independent continuous variables. Dummy variables (indicator variables) were used if nonlinearity was observed. This set of variables was used to fit a first model. In a second step, interaction terms were entered to see whether their inclusion would give a statistically significant better fit of the model (using the log-likelihood ratio test, considering \( P < 0.05 \) as statistically significant). Finally, new models were fitted, leaving out 1 confounder at a time to see how the coefficients of the other characteristics would change.

Because the final data set contained some measurements (n = 73) in both eyes of the same subject, a clustered analysis was applied in which each participant was considered as a cluster to adjust for the dependency of measurements in the fellow eye.

Analyses of variance were performed to study the variability between the different observers and the OPA readings. The contribution of an independent variable (observer, subjects, observer x subject interaction, and residual error) to the variance of the dependent variable (OPA measurement) was estimated using the variance components procedure. On the basis of the variance components, we calculated the intraclass correlation coefficient and the interobserver and intraobserver variabilities. The intraclass correlation coefficient (also referred to as reliability coefficient) represents the proportion of the total variability in a given measure that can be attributed to the true variability among subjects. It assumes values from 0.0 to 1.0, approaching 1.0 when the variation in measurements is solely due to subject-to-subject variability.

Statistical analysis was performed using commercially available software (Stata, version 8.2 [Stata Corp LP, College Station, Tex], and the SPSS statistical software package, version 10 [SPSS Inc, Chicago, Ill]).

RESULTS

We excluded 1 volunteer from the unilateral and 1 volunteer from the bilateral group (total of 3 eyes excluded) because the output routine failed to calculate an accurate OPA from these eyes. Thus, the study included 148 healthy participants (64 women and 84 men) contributing 223 normal eyes. We evaluated measurements taken from 115 right and 108 left eyes. The characteristics of the study group are given in Table 1.

The OPA readings ranged from 0.9 to 7.2 mm Hg (median, 3.0 mm Hg; 10th-90th percentile range, 1.8-4.3 mm Hg). The OPA difference in the 75 pairs of eyes examined ranged from 0.0 to 2.5 mm Hg (median, 0.4 mm Hg; 10th-90th percentile range, 0.1-1.2 mm Hg). There was no significant difference in the OPA between right and left eyes (\( P = .71 \)). Multiregression analysis showed no significant effect of CCT (\( P = .08 \)) (Figure 2), keratometry (\( P = .47 \)), anterior chamber depth (\( P = .80 \)), or sex (\( P = .73 \)) on OPA readings. The mean OPA was 0.2 mm Hg higher in the group older than 50 years compared with the group younger than 30 years. However, this difference was not significant (\( P = .60 \)).
There was a positive correlation between OPA and IOP (0.12 mm Hg/1 mm Hg of IOP; 95% confidence interval, 0.07-0.18; *P* < .001) and a negative correlation between OPA and axial length (0.27 mm Hg/1 mm of length; 95% confidence interval, −0.14 to 0.41; *P* < .001).

When the OPA was measured repeatedly in the same eye, the intraclass correlation coefficient was 0.89, the intraobserver variability was 0.08 mm Hg, and the interobserver variability was 0.02 mm Hg (Table 2).

The purpose of continuously measuring tonometry such as DCT is to record IOP oscillations as an indirect measure for intraocular pulsatile hemodynamics. Corneal curvature and CCT have been shown to interfere with the pristine detection of this signal by means of pneumatonometry. 2,5,11 However, the present study is the first, to our knowledge, to describe OPA measurements unaffected by these corneal variables. This finding reproduces what has already been demonstrated for IOP measurements with the same instrument on the same cohort. 11

The independence of corneal dimensions is attributed to the concave shape of the dynamic contour tracing the eye. The independence of corneal dimensions is attributed to the concave shape of the dynamic contour tracing the eye. When in touch with the tip, the contour-matched cornea is thought to be tension free, allowing for direct IOP measurements across its wall.

Other factors altering the signal of IOP oscillations may not be neutralized by contour matching alone. Filling of the orbital vessels causes a pulsatile protrusion of the whole bulbus, allowing for pressure wave recordings even from enucleated eye sockets. 19 Furthermore, the IOP response to the increase in ocular volume during cardiac systole depends on the elastic properties of the ocular shell, 22 a phenomenon that may explain our finding of the positive correlation between OPA and IOP. With higher IOP levels, scleral wall tensions increase, and the injection of a given volume of blood results in a distinct pressure increase rather than a further elastic extension of already prestressed bulbus walls. 19 Similar results have been published, 21-23 but there are reports indicating no such correlation. 24,25 In this study, there was a tendency toward higher OPA in thinner and therefore potentially more elastic corneas.

Moreover, OPA and IOP are not only linked by the elastic properties of the bulbus walls but also by ocular blood flow. The difference between the pressure in the ophthalmic artery and IOP represents the pressure gradient maintaining ocular perfusion. Elevated IOP levels may therefore affect pulsatile ocular blood flow, although the direction of the net effect (increase or decrease) is difficult to predict owing to regulatory mechanisms. 26

Unlike DCT, the OBF and OBAnalyzer use instantaneous IOP measurements to mathematically derive an estimate of pulsatile ocular blood flow (in microliters per second). Based on experimental pressure-volume relations and the heart rate, pulsatile ocular blood flow is approximated by transforming the OPA measurements into a disturbance to the OPA signal, and such an inverse correlation has been described. 29,30 It is a limitation of the present study that the effect of the heart rate has not been investigated. The second correlation found in this study, the OPA's dependence on axial length, has already been documented in the literature. 22-25 These findings are generally attributed to the size of the large myopic bulbus for which a given inflow of blood represents a smaller relative volume change than for a shorter emmetropic eye. Myopia...
is also associated with thinning of the sclera,\(^5,6\) which consequently offers less resistance to expansion brought about by a pulsatile volume change. In addition, there is evidence suggesting that ocular blood flow in myopic eyes is decreased, probably owing to the reduced diameter of straightened vessels.\(^3,13\)

In systemic hemodynamics, transcutaneous tonometer readings derived from peripheral arteries show an elevated pulse amplitude with age secondary to an increase in artery stiffness and pulse-wave velocity.\(^34,35\) In the ophthalmological literature, however, the correlation between OPA and age shows a contrasting trend\(^23,36\) or is not significant at all,\(^4,5,37\) as confirmed by the present study. This apparent paradox might be explained by the vascular resistance of the bulbus that acts as a hemodynamic transducer\(^38\) between peripheral arteries and the tonometer head. A reduced inflow of blood due to an age-related loss and hyalinization of arterioles\(^39\) is likely to dampen the pulse transmitted via the ophthalmic artery.

Drawing comparisons between OPA standard values in the literature must take into account the different techniques by which the data were obtained. With the original pneumatometer of Langham and McCarthy,\(^1\) the reference mean±SD OPA was found to be 1.5±0.11 mm Hg.\(^42\) With the more recent OBF and OBF analyzer pneumotonometers, mean±SD values ranging from 2.2±0.8 to 3.0±1.2 mm Hg\(^5,41\) were found. The present study demonstrated a median OPA value of 3.0 mm Hg (10th-90th intercentile range, 1.8-4.3 mm Hg)\(^5,41\) which is in agreement with a previous report on DCT that described a mean±SD OPA value of 3.08±0.92 mm Hg in a smaller set of 19 healthy subjects aged 45 to 73 years.\(^42\)

In the present study, we found no significant difference between an individual’s eyes, which is in keeping with earlier reports that described significant differences only in cases of anisometropia of 2 or more diopters.\(^23,25,41\)

Knowledge about the reference range of OPA in healthy individuals permits one to suspect systemic or bilateral disease, even if no difference between sides is detected.\(^44\) However, a significant asymmetry in OPA may indicate vascular stenosis\(^45,46\) or arteriovenous fistulas.\(^47,48\)

Intraobserver and interobserver variabilities in this study were 0.08 and 0.02 mm Hg, respectively, indicating that repeated readings within and between observers are reproducible. Accordingly, we calculated an intraclass correlation coefficient of 0.89, suggesting that the total variation in OPA measurements depends mainly on subject-to-subject variability, ie, on actual differences in OPA among volunteers.

Reports about observer agreements with respect to OPA are sparse, and measuring conditions differ. With a modified slitlamp-mounted OBF tonometer, 2 observers performed 272 measurements on 34 healthy volunteers on different days and reported an intraclass correlation coefficient of 0.66.\(^41\) With a handheld dynamic observing tonometer (SmartLens; Ophthalmic Development Company AG, Zürich, Switzerland), a coefficient of 0.86 was found by 3 examiners performing 5 measurements on 10 volunteers within 2 hours. Intraobserver and interobserver variability were 0.39 and 0.40 mm Hg, respectively.\(^40\)

While the indices of observer agreement that we found for DCT compare favorably with those earlier reports, some limitations of this study must be taken into consideration. Although there is no agreed-upon method to determine a sufficient sample size, the range of data derived from the 8 subjects included in this subanalysis may not be representative of a large collective. Furthermore, the nonrandomized sequence of observers may have led to unequal measuring conditions owing to a tonographic effect associated with repeated corneal distortion. Finally, although it seems unlikely that the corneal contact during ultrasonic pachymetry induced a significant tonographic effect, it has been reported that a decline in pressure may also result from accommodation or extracocular muscular or vascular influences.\(^50\) Therefore, it cannot be excluded that even biometry and pachymetry have interfered to some extent with the subsequent detection of the OPA signal.

**CONCLUSIONS**

The present study did not show any statistically significant influence of corneal curvature, CCT, or anterior chamber depth on OPA readings obtained using DCT in healthy subjects. However, OPA readings are affected by axial length and IOP. With these limitations in mind, DCT might not only provide clinically relevant information in an individual patient, but its independence of anterior segment structure might prove to be useful in determining differences between groups. As the estimation of pulsatile ocular blood flow is mainly based on the OPA, the implementation of a routine that links OPA to volume change may provide blood flow estimates that are largely independent of corneal variables.

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**REFERENCES**


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