The Relationship Between Corneal Biomechanics and Intraocular Pressure Dynamics in Patients Undergoing Intravitreal Injection

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Purpose: The purpose of this study was to evaluate the relationship between measurable corneal biomechanical properties and acute IOP elevation after rapid intraocular volume expansion from the routine intravitreal injection.

Materials and Methods: A total of 100 patients necessitating unilateral intravitreal injection with 0.05 mL of bevacizumab for retinal pathology were analyzed before injection with Goldmann Applanation Tonometry to measure IOP, Ocular Response Analyzer (ORA) to measure corneal biomechanical properties, and optical biopsy to calculate globe measurements. IOP and ORA were measured again within 5 minutes of the injection and then IOP measurements were taken every 10 minutes until the IOP was ≤ 150% of the preinjection IOP. Linear regression and logistic regression were used to test variables associated with acute IOP increase. A Cox proportional hazard model accounting for pre-injection IOP and postinjection IOP was used to test the effect of CH or CRF on the time required to return to 150% of baseline IOP.

Results: Higher CRF was associated with greater immediate postinjection IOP (P = 0.026) elevation. A preinjection IOP > 15.5 mm Hg moderately predicted postinjection IOP ≥ 35 mm Hg (area under the receiver operating characteristics curve = 0.74). A preinjection IOP > 18.5 mm Hg combined with CH poorly predicted postinjection IOP > 50 mm Hg (area under the receiver operating characteristics curve = 0.67). A higher CH [hazard ratio (HR) = 1.24; 95% confidence interval (CI) = 1.08-1.42; P = 0.002] and preinjection IOP (HR = 1.16; 95% CI = 1.09-1.22; P < 0.001), along with a lower immediate postinjection IOP (HR = 0.93; 95% CI = 0.90-0.95; P < 0.001), were each independently associated with quicker IOP recovery postinjection. Similar results were seen in the Cox model examining CRF and IOP recovery.

Conclusions: Higher CRF and preinjection IOP were independently associated with greater postinjection IOP elevations. ORA metrics did not greatly strengthen the prediction of patients who would have postinjection IOP > 50 mm Hg. Higher CH and CRF were associated with faster IOP recovery after intravitreal injection, demonstrating the dynamic relationship between ocular biomechanical properties and aqueous outflow pathways.

Key Words: corneal hysteresis, corneal biomechanics, glaucoma, intravitreal injection, intraocular pressure

Intravitreal injection of bevacizumab (Avastin; Genentech Inc., South San Francisco, CA) is a commonly used treatment modality for a multitude of ophthalmic conditions associated with abnormal neovascularization, such as diabetic retinopathy1 and macular degeneration.2 Several studies3–6 have reported significant acute intraocular pressure (IOP) increase immediately postinjection, with some eyes experiencing transient IOP as high as 70 or 80 mm Hg.7 IOP increase after bevacizumab injection has been shown to momentarily decrease the mean ocular perfusion pressure,8 and it has been observed that glaucoma patients have slower IOP normalization rates.8 In animal models, acute IOP increase has been shown to block axonal transport to the optic nerve head9 and decrease juxtapapillary retinal and optic nerve head blood flow.8 The clinical significance of transient severe IOP increases with respect to glaucoma progression is largely unknown, and relationships between ocular biomechanical properties and IOP have yet to be elucidated.

Corneal hysteresis (CH) and corneal resistance factor (CRF) are biomechanical parameters that measure the viscoelastic properties of the cornea and are calculated by analyzing the corneal response to air pulse deformation by the Ocular Response Analyzer (ORA; Reichert Instruments, Depew, NY).9 CH reflects the ability of corneal tissue to absorb and dissipate energy,9 whereas the CRF measures the overall viscoelastic resistance of the cornea.10 Low CH has been identified as a risk factor for glaucoma progression in prospective studies and has been associated with increased retinal nerve fiber layer loss in glaucoma patients.11

A proportion of patients who receive intravitreal injections for retinal pathologies may also have decreased juxtapapillary retinal and optic nerve head blood flow12 related to glaucomatous optic neuropathy. As such, these patients may be at greater risk for disease progression, particularly given that therapeutic interventions often require multiple injections for optimal and sustained benefit. Elucidating factors linked with a severe or prolonged IOP increase after the intravitreal injection may help guide clinicians on appropriate prophylactic pressure-lowering interventions and postinjection monitoring. To our knowledge, this is the first study to explore corneal biomechanics and acute IOP changes in the setting of rapid ocular volume expansion after intravitreal injection.
MATERIALS AND METHODS

This prospective interventional study was performed at the Department of Ophthalmology, Henkind Eye Institute at Montefiore Medical Center in the Bronx, NY from November 2018 to March 2020. The study obtained institutional review board approval and was conducted with according to the Declaration of Helsinki. The study protocol was explained to all candidates, and voluntary written consent was obtained from all participants before inclusion.

Eligible participants included adults over the age of 18 undergoing intravitreal bevacizumab injection for maculopathy related to diabetes, macular degeneration, or vasculitis at the discretion of the retina service. Patients who were unable to perform all required measurements for any reason were excluded from the study, as were patients necessitating immediate anterior chamber paracentesis at the discretion of the 2 retina specialists in the study (no patients required paracentesis).

Baseline measurements were taken within 2 hours before intravitreal injection. Each patient had 3 consecutive ORA measurements determining CH, CRF, Goldmann-correlated intraocular pressure (IOPg), and corneal-compensated intraocular pressure (IOPcc). Furthermore, IOP was measured using Goldmann applanation tonometry (GAT), and optical biometry measurements determining axial length were obtained using the Lenstar LS 900 (Haag-Streit AG, Koeniz, Switzerland) for patients without a previous prior measurement on chart review. Baseline IOP was measured using Goldmann applanation for comparison to postinjection Goldmann-applanated IOP alone. To prevent model overfitting from numerous variables, cross-validation was performed where model estimation was done with 80% of the data and then tested on the remaining 20% of the data. This cross-validation process was performed a total of 5 times to generate the final AUCs. To evaluate prolonged postinjection IOP elevation, the bivariate association between a variable and time required to return to 150% of baseline IOP was examined using a Cox proportional hazard model, including 11 censored patients. These 11 censored patients all stopped IOP recording before reaching 150% of preinjection IOP (8 patients decided to leave the study before reaching 150% baseline IOP and 3 patients completed the 30-minute postinjection measurement period without achieving 150% of baseline IOP). The high hazard ratio (HR) indicates the faster recovery to 150% of baseline IOP. Variables are significant at P-value <0.2 in the bivariate association, demographic variables (age, sex, attending for injection), and clinically relevant variables (glaucoma status, glaucoma medication, central corneal thickness (CCT)) were included in the multiple Cox model. As CRF and CH were highly correlated (p = 0.6) and were significantly associated with prolonged IOP increase in the bivariate association, a separate Cox model was assessed including one of CRF and CH and then refined after dropping nonsignificant variables (P > 0.05 and axial length) other than demographic variables, clinically important variables or variable of interest (CH or CRF). To study the ORA’s performance at various IOP levels, ORA measurement qualities were plotted against IOPs for both preinjection and postinjection timepoints and a linear regression model was fitted to examine the association and infer the IOP value expected to have ORA measurement quality <6. Statistical analysis was performed using SPSS25 (Statistical Package for Social Sciences version 25; SPSS Inc., Chicago, IL) and R 3.6.2. (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 100 patients were included in the analysis, and the demographic data is summarized in Table 1. The mean ± SD age of patients was 63.3 ± 11.36 (range: 34 to 89 y), and 49% of patients were male. The right eye was studied in 51% of patients. With respect to self-identified race and ethnicity, patients were 58% white, 33% black, and 8% Asian, with 50% reporting Hispanic ancestry. The vast majority of patients (~90%) were diabetic, and 32% had a preexisting glaucoma diagnosis. The reasons for bev- acizumab injection were diabetic macular edema (81%), retinal vein occlusion (11%), age-related macular degeneration (7%), and cystoid macular degeneration (1%). Glaucoma diagnoses were present in 12% of patients and a diagnosis of glaucoma suspect was present in another 20% of patients, with 17% of all patients treated with at least 1 topical ocular hypertensive medication (latanoprost, bimatoprost, timolol, brimonidine, timolol/brimonidine, dorzolamide/timolol). Four patients with a clinical diagnosis of glaucoma had received glaucoma-related surgery (gonioplasty or an aqueous shunt). Overall, 68% of patients where phakic and the remaining 32% of patients were pseudophakic. Optical biometry demonstrated an average axial
length of 23.6 ± 1.22 mm and a CCT of 531.6 ± 48.94 μm. The Pearson correlation coefficients between preinjection Goldmann-applanated IOP and preinjection IOPg and IOPcc were 0.88 and 0.79, respectively. Although 2 different retina providers performed the injections, there were no differences were noted in outcome between them (P = 0.367 for acute IOP increase analysis; P = 0.942 for IOP recovery analysis).

Preinjection versus postinjection findings are summarized in Table 2. IOP increased on average from 18.3 ± 5.24 to 47.4 ± 11.19 mm Hg (mean difference = 29.14 ± 10.95; P < 0.001). CH decreased from 9.5 ± 1.98 to 5.3 ± 3.19 mm Hg (mean difference = −4.07 ± 3.15; P < 0.001). The signal quality of the ORA measurements (waveform score out of 10) decreased from 7.6 ± 1.69 to 3.4 ± 1.74 (mean difference = −4.16 ± 2.11; P < 0.001). Figure 1 shows the change in CH plotted against change in IOP from baseline and immediately after injection. A greater IOP increase was associated with a larger reduction in CH (Pearson correlation coefficient = −0.65; P < 0.001).

A linear regression analysis of factors associated with postinjection IOP elevation severity was performed, with subgroups divided using the following classification system: IOP < 35 mm Hg (minor), IOP 35 to 50 mm Hg (moderate), or IOP > 50 mm Hg (severe). Higher preinjection IOP and higher CRF were significantly associated with increased immediate postinjection IOP (P = 0.014 and 0.026), although there was no association with CH (P = 0.317). Excluding patients diagnosed with glaucoma did not significantly change these results. Preinjection IOP was plotted against postinjection IOP (Fig. 2). Predictive models for immediate postinjection IOP were generated using 2 logistic regression analyses examining postinjection pressures for patients with moderate (≥ 35 mm Hg) and severe (> 50 mm Hg) IOP elevations. Using the ROCs based on GAT alone, the preinjection IOP thresholds to predict moderate and severe IOP increases were determined to be 15.5 and 18.5 mm Hg, respectively. The overall accuracy of the low (< 15.5 mm Hg), middle (15.5 to 18.5 mm Hg), and high (> 18.5 mm Hg) baseline IOP ranges to predict minor, moderate, and severe IOP increase was 43% (Table 3). The addition of the ORA biomechanical metrics to this model increased the accuracy to 48%. Figure 3 shows the cross-validated ROCs of each prediction model for postinjection IOP ≥ 35 mm Hg and for prediction of postinjection IOP > 50 mm Hg. Associated cross-validated AUCs for each prediction model are displayed in Table 4. Using preinjection IOP alone, the AUC35 was 0.74 and the AUC50 was 0.62. The addition of ORA metrics produced slightly lower AUC35’s but slightly increased the predictive value for the AUC50’s (IOP+CH: AUC35 = 0.80; AUC50 = 0.67; IOP+IOPg+IOPcc+CRF+CH: AUC35 = 0.69, AUC50 = 0.65).

Prolonged postinjection IOP was assessed by time to return to 150% of baseline IOP using a Cox proportional hazard model. Since CRF and CH were highly correlated (P = 0.66), 2 separate Cox models were fitted to test the effect of CH or CRF on the time required to return to 150% of baseline IOP after adjusting for preinjection IOP, postinjection IOP, demographic, and clinically important variables (Table 5). In the final model including CH, which excludes nonsignificant variables, higher CH [HR = 1.24; 95% confidence interval (CI) = 1.08-1.42; P = 0.002], higher preinjection IOP (HR = 1.16; 95% CI = 1.09-1.22; P < 0.001), and lower immediate postinjection IOP (HR = 0.93; 95% CI = 0.90-0.95; P < 0.001) were independently associated with

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### TABLE 1. Demographical and Clinical Characteristics

|                     |       |
|---------------------|-------|
| N                   | 100   |
| Right eye injected  | 51    |
| Male sex            | 49    |
| Age (y)             | 63.26 ± 11.36 |
| Race                |       |
| White               | 58    |
| Black               | 33    |
| Asian               | 9     |
| Ethnicity           |       |
| Hispanic            | 50    |
| Non-Hispanic        | 50    |
| Patients treated by attending #1 | 71 |
| Glaucoma pathology  | 32    |
| Taking glaucoma medications | 17 |
| Diabetes mellitus   | 90    |

Data are represented as mean ± SD for quantitative variables and percentage for qualitative variables.

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### TABLE 2. Preinjection and Postinjection Measurements

|                          | Preinjection | Postinjection | Difference | P       |
|--------------------------|-------------|---------------|------------|---------|
| IOP (mm Hg)              | 18.3 ± 5.24 | 47.4 ± 11.19  | 29.14 ± 10.95 | <0.001  |
| Corneal hysteresis       | 9.5 ± 1.98  | 5.5 ± 3.19    | −4.07 ± 3.15 | <0.001  |
| ORA measurement quality  | 7.6 ± 1.69  | 3.4 ± 1.74    | −4.16 ± 2.11 | <0.001  |

Goldmann-applanated intraocular pressure (IOP) and corneal hysteresis findings before and after injection. Mean IOP significantly increased after injection, while corneal hysteresis and quality of Ocular Response Analyzer (ORA) measurements (waveform score out of 10) significantly decreased.
faster IOP recovery. Similarly, in the final model including CRF, higher CRF (HR = 1.16; 95% CI = 1.004-1.35; \( P = 0.046 \)), higher preinjection IOP (HR = 1.11; 95% CI = 1.03-1.19; \( P = 0.004 \)), and lower immediate postinjection IOP (HR = 0.93; 95% CI = 0.90-0.96; \( P < 0.001 \)) were independently associated with faster IOP recovery. In both CH and CRF models, the use of pressure-lowering eye drops was associated with nonsignificant trends towards a faster time to IOP recovery (HR_{CH}: 1.52; HR_{CRF}: 1.49). When axial length was included in the bivariate analysis (Table 6), CH became marginally significant (\( P = 0.095 \)), while CRF became nonsignificant (\( P = 0.601 \)). Excluding patients diagnosed with glaucoma did not significantly change these results.

Performance of the ORA was evaluated over the range of preinjection and postinjection IOP measurements. A plot of ORA measurement quality versus Goldmann-applanated IOP (Fig. 4) showed that increased IOP was significantly associated with decreased ORA measurement quality (Pearson correlation coefficient = \(-0.74\), \( P < 0.001 \)).

**DISCUSSION**

Intravitreal therapy has dramatically improved the clinical prognosis for patients with retinovascular disease. This study aims to better understand the relationship of acute volume expansion upon IOP to help identify predictive characteristics of eyes at potential risk for severe and prolonged pressure elevation after bevacizumab injection. Specifically, we analyzed a variety of corneal biomechanical properties, IOP, and axial length to determine if we could predict which eyes were at greater risk for both the severity and the duration of pressure elevation after intravitreal injection. As a tertiary objective, we furthermore aimed to analyze the reliability and accuracy of ORA measurements at various IOP levels.

Our mean CH value of 9.5 ± 1.98 mm Hg falls within the normal range seen in healthy eyes by a literature review (9.3 ± 1.4 to 11.43 ± 0.52 mm Hg).\(^{13}\) The relationship between CH and glaucoma has been well studied in glaucoma patients. In a prospective, interventional case-control study, Meda et al\(^{14}\) found that a 6-week trial of a prostaglandin analogue (PGA) induced IOP lowering in primary open-angle glaucoma patients along with a reversible increase in CH. Bolivar et al\(^{15}\) described a similar increase in CH in a 6-month PGA trial. Pakravan et al\(^{16}\) found that trabeculectomy, phacotrabeculectomy, and glaucoma valve implantation were all associated with significant increases in

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**TABLE 3. Preinjection and Postinjection IOP Groupings**

| Preinjection IOP (mm Hg) | <35 | 35-50 | >50 |
|--------------------------|-----|-------|-----|
| <15.5                    | 8   | 18    | 5   |
| 15.5-18.5                | 3   | 17    | 7   |
| ≥18.5                    | 1   | 22    | 18  |

Patients grouped by both preinjection and postinjection intraocular pressure (IOP) cutoffs. Higher preinjection IOP values were associated with higher postinjection IOP values.
CH. Neuburger et al\textsuperscript{17} found that CH in primary angle-closure glaucoma patients increased with decreases in IOP, while CH decreased with an increase in IOP. This relationship between CH and IOP is further validated by our study, which demonstrated a decrease in CH (mean difference $= -4.07 \pm 3.15$; $P < 0.001$) after intravitreal bevacizumab injection. Moreover, we found that the magnitude of acute IOP increase correlated with the magnitude that CH decreased (Fig. 1). This finding adds to a study from Agarwal et al\textsuperscript{18} that found lower baseline CH was associated with a greater magnitude of IOP reduction following PGA therapy.

One of the primary objectives of the study was to determine if IOP, axial length, or any corneal biomechanical measurements were predictive of the risk of severe IOP elevation after injection of bevacizumab. Linear regression analysis found higher preinjection IOP and higher CRF to be associated with higher postinjection pressures. Figure 2 shows a steep increase in immediate postinjection pressure after the preinjection pressure exceeds 16 to 17 mm Hg. Logistic regression analysis based on preinjection GAT demonstrated that eyes at risk of postinjection IOP $\geq 35$ mm Hg had a preinjection IOP $\geq 15.5$ mm Hg, whereas eyes at risk of a postinjection IOP $> 50$ mm Hg had a preinjection IOP $> 18.5$ mm Hg. With an AUC\textsubscript{35} of 0.74, this model had acceptable discrimination to predict an acute IOP increase to $\geq 35$ mm Hg; however, the ability to predict IOP $> 50$ mm Hg was poor (AUC\textsubscript{50} = 0.62). The addition of CH increased the predictive value of the severe (> 50 mmHg) IOP increase model to an AUC\textsubscript{50} = 0.67, although this is would still be considered poor discrimination (Table 4, Fig. 3). Therefore, corneal biomechanical measurements by the ORA only added modest value in predicting severe IOP elevation beyond simple preinjection IOP measurement by

FIGURE 3. Receiver operating characteristics curves (ROCs) with 5-fold cross-validation based on various models for prediction of IOP $\geq 35$ mm Hg and IOP $> 50$ mm Hg. Models based on single variables independently are on the left, with multivariate models on the right. The addition of multiple ORA biomechanical metrics modestly improved the model for prediction IOP $> 50$ mm Hg. This effect was not seen for the IOP $\geq 35$ mm Hg model. AL indicates axial length; CH, corneal hysteresis; CRF, corneal resistance factor; IOP, Goldmann-applanated intraocular pressure; IOPcc, corneal-compensated intraocular pressure; IOPg, Goldmann-correlated intraocular pressure. Figure 3 can be viewed in color online at www.glaucomajournal.com.
GAT. Interestingly, while smaller axial lengths were expected to coincide with larger IOP increases as they would represent larger percentage volume changes with the injection, we did not find an association between axial length and acute IOP increase. Ultimately, our findings show that in addition to GAT, ORA biomechanical metrics likely do not add significant utility in screening for patients deemed at risk of visual loss from an acute pressure elevation (severe glaucomatous damage, poor vascular perfusion).

The second major objective of this study was to explore factors associated with prolonged IOP elevation after injection. The final Cox proportional hazard models of Postinjection IOP Prediction Models Including Axial Length

| Model With CH | Model With CRF |
|---------------|----------------|
| Race (reference = white) | HR 95% CI P | HR 95% CI P |
| Black | 0.63 0.36-1.09 0.099 | 0.62 0.36-1.09 0.096 |
| Asian | 1.65 0.69-3.9 0.258 | 1.44 0.62-3.36 0.400 |
| Attending, #2 vs. #1 | 1.05 0.59-1.85 0.880 | 1.01 0.57-1.8 0.975 |
| Age | 1.00 0.98-1.02 0.841 | 1.00 0.97-1.02 0.778 |
| Sex, male vs. female | 0.89 0.49-1.59 0.685 | 0.87 0.47-1.58 0.637 |
| Central corneal thickness | 1.00 0.99-1.01 0.869 | 1.00 0.99-1.01 0.821 |
| Glaucoma | 0.61 0.19-1.98 0.411 | 0.63 0.19-2.02 0.435 |
| Glaucoma | 1.72 0.6-4.92 0.311 | 1.55 0.56-4.3 0.399 |
| medication | | |
| Preinjection IOP | 1.15 0.75-1.78 0.549 | 1.01 0.67-1.52 0.569 |
| Postinjection IOP | 0.93 0.56-1.51 0.399 | 0.90 0.54-1.51 0.399 |
| Axial length | 0.86 0.75-0.98 0.302 | 0.86 0.75-0.98 0.302 |
| CH | 1.15 0.99-1.35 0.095 | 1.07 0.98-1.26 0.095 |
| CRF | — | 1.05 0.88-1.24 0.601 |

Two Cox regression models analyzing factors (including axial length) associated with time to recovery of 150% of baseline IOP. HRs over 1 indicated a direct relationship with the variable and quicker rates of IOP recovery. With the inclusion of axial length, CH became marginally significant ($P = 0.066$), while CRF became nonsignificant ($P = 0.459$).

CH indicates corneal hysteresis; CI, confidence interval; CRF, corneal resistance factor; HR, hazard ratio; IOP, intraocular pressure.

FIGURE 4. Goldmann-applanated intraocular pressure (IOP) plotted against corresponding Ocular Response Analyzer (ORA) measurement quality (waveform score out of 10). Blue circles indicate preinjection values, while red X’s indicate immediate postinjection values. The solid line is a regression line representing the relationship between measurement quality and IOP (ORA measurement quality $≥ 9.4-0.11$ IOP). The dotted horizontal line represents a waveform score threshold of 6. IOPs $> 30$ mm Hg were expected to have a quality score below 6. Figure 4 can be viewed in color online at www.glaucomajournal.com.
preinjection CH or CRF, preinjection IOP, and postinjection IOP on the time required to achieve ≥50% of preinjection IOP are shown in Table 5. The results showed that higher CH, higher CRF, higher preinjection IOP, and lower postinjection IOP were independently associated with a faster rate of IOP recovery. Both CH and CRF IOP recovery models showed that the use of glaucoma medication was associated with trends towards faster times to IOP recovery. This may be partially explained by the fact that 9/17 of the patients on pressure-lowering medications were taking PGAs, which would be expected to increase aqueous outflow and thereby reduce time to IOP recovery. In addition, as suggested by our model, lower preinjection IOP was associated with faster rates of recovery. Therefore, all of these pressure-lowering drops may have contributed to this trend. When axial length was also included in the model, CH became marginally significant, while CRF became nonsignificant, suggesting CH is a more robust predictor of prolonged IOP increase than CRF. The changes associated with the addition of axial length to the models are likely due to a combination of correlated effects between axial length, CH, and CRF as well as a decreased sample size. Our study is likely underpowered to determine the differences in the effect of CH and axial length. The bivariate analysis did not find CCT, glaucoma diagnosis, or patient demographics to be associated with prolonged IOP recovery after injection; however, the study was not designed or powered to determine these relationships. Our findings suggest that CH is more predictive than CCT for prolonged IOP elevation in the limited number of patients where this was seen. Further investigation is warranted to determine the true clinical significance of this finding.

With respect to the tertiary objective of characterizing the accuracy of ORA measurements during acute IOP elevation, we found that as IOP increased, the measurement quality of ORA significantly decreased (Fig. 4). When IOPs were in the range of 60 to 70 mm Hg, the ORA frequently generated an error message stating the values were out of the scale of the machine and recorded a CH of 0. Our findings suggested a decreased utility of the ORA in eyes with IOP > 30 mm Hg.

This prospective study has several limitations, beyond the relatively small sample size of patients with glaucoma diagnoses. First, while results examining the effect of diabetes on corneal biomechanics have been mixed, the majority of studies found diabetes to be associated with increases in CH. With 81% of patients diagnosed with diabetic macular edema, our sampled population may limit the application of our results to other nondiabetic populations. However, the average preinjection CH of 9.5 ± 1.98 mm Hg found in this study was in the lower range of previously reported values (9.3 ± 1.4 to 11.43 ± 0.52 mm Hg), suggesting that application of our results should not be exempt from nondiabetic populations based on mean CH values alone. Second, while the injection volume and medication remained constant, there were variations in techniques between the 2 retina specialists in the study. However, the univariate analysis did not demonstrate outcome differences between their patients with respect to severity or duration of IOP elevation. Third, the patients who had prior glaucoma surgery or who were taking a PGA may have had artificially reduced initial IOP increases as well as quicker IOP recovery times due to increases in aqueous outflow rates. However, only 10 patients fit these criteria so these treatments likely do not significantly affect the overall results. However, HRs specifically for the patients with a clinical diagnosis of glaucoma should be interpreted with caution. Fourth, since the eyes were not comprehensively examined after the patient received the injection, it is possible that the decreases in postinjection ORA measurement quality were due to factors other than increased IOP. For example, corneal edema or surface compromise from the anesthetics/antiseptics could also be responsible. As such, further analysis of ORA performance as a function of IOP should be performed. Last, measurements of corneal biomechanics and axial length have an associated increased test-retest variability, which may be of significance for the ORA at high IOPs.

In conclusion, higher CRF and preinjection IOP were found to be associated with greater severity of postinjection IOP elevation. ORA biomechanical metrics did not add significant value to the prediction of postinjection IOP over GAT. With respect to the duration of IOP elevation, higher CH and CRF values were associated with faster IOP recovery after acute intraocular volume expansion with bevacizumab in models excluding axial length. Our results suggest that CH may be more useful than CRF in predicting patients who experience a prolonged IOP elevation after intravitreal injection. Therefore, both pretreatment IOP measurements and measurements of corneal biomechanics may add complementary information in predicting the magnitude and duration of pressure elevations after intravitreal injections and may be clinically useful to prevent acute pressure-related visual loss in susceptible patients. A decrease in ORA utility was correlated with eyes that had an IOP > 30 mm Hg; further studies should be performed to evaluate ORA performance as a function of IOP.

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REFERENCES
1. Jorge R, Costa RA, Calucci D, et al. Intravitreal bevacizumab (Avastin) for persistent new vessels in diabetic retinopathy (IBEPE study). Retina. 2006;26:1006–1013.
2. Avery RL, Pieramici DJ, Rabena MD, et al. Intravitreal bevacizumab (Avastin) for neovascular age-related macular degeneration. Ophthalmology. 2006;113:363.e5–372.e5.
3. Hollands H, Wong J, Bruen R, et al. Short-term intraocular pressure changes after intravitreal injection of bevacizumab. Can J Ophthalmol. 2007;42:807–811.
4. Kato A, Okamoto Y, Okamoto F, et al. Short-term intraocular pressure changes after intravitreal injection of bevacizumab. Jpn J Ophthalmol. 2019;63:262–268.
5. Lee JW, Park H, Choi JH, et al. Short-term changes of intraocular pressure and ocular perfusion pressure after intravitreal injection of bevacizumab or ranibizumab. BMC Ophthalmol. 2016;16:69.
6. Kim JE, Mantravadi AV, Hur EY, et al. Short-term intraocular pressure changes immediately after intravitreal injections of anti-vascular endothelial growth factor agents. Am J Ophthalmol. 2008;146:930.e1–934.e1.
7. Quigley HA, Anderson DR. Distribution of axonal transport blockade by acute intraocular pressure elevation in the primate optic nerve head. Invest Ophthalmol Vis Sci. 1977;16:640–644.
8. Michelson G, Groh MJ, Langhans M. Perfusion of the juxtapapillary retina and optic nerve head in acute ocular hypertension. Ger J Ophthalmol. 1996;5:315–321.
9. Moshirfar M, Motalagh MN, Murri MS, et al. Advances in biomechanical parameters for screening of refractive surgery
candidates: a review of the literature, part III. Med Hypothesis Discov Innov Ophthalmol. 2019;8:219–240.

10. Lau W, Pye D. A clinical description of Ocular Response Analyzer measurements. Invest Ophthalmol Vis Sci. 2011;52: 2911–2916.

11. Zhang C, Tatham AJ, Abe RY, et al. Corneal hysteresis and progressive retinal nerve fiber layer loss in glaucoma. Am J Ophthalmol. 2016;166:29–36.

12. Michelson G, Langhans MJ, Groh MJ. Perfusion of the juxtapapillary retina and the neuroretinal rim area in primary open angle glaucoma. J Glaucoma. 1996;5:91–98.

13. Shoeibi N, Ansari-Astaneh MR, Sedaghat MR, et al. Effect of intravitreal bevacizumab injection on corneal in vivo biomechanics: a pilot study. J Ophthalmic Vis Res. 2019;14:151–156.

14. Meda R, Wang Q, Paoloni D, et al. The impact of chronic use of prostaglandin analogues on the biomechanical properties of the cornea in patients with primary open-angle glaucoma. Br J Ophthalmol. 2017;101:120–125.

15. Bolivar G, Sanchez-Barahona C, Teus M, et al. Effect of topical prostaglandin analogues on corneal hysteresis. Acta Ophthalmol. 2015;93:e495–e498.

16. Pakravan M, Afroozifar M, Yazdani S. Corneal biomechanical changes following trabeculectomy, phaco-trabeculectomy, ahmed glaucoma valve implantation and phacoemulsification. J Ophthalmic Vis Res. 2014;9:7–13.

17. Neuburger M, Bohringer D, Reinhard T, et al. Recovery of corneal hysteresis after reduction of intraocular pressure in chronic primary angle-closure glaucoma. Am J Ophthalmol. 2010;149:687–688; author reply 688.

18. Agarwal DR, Ehrlich JR, Shimmyo M, et al. The relationship between corneal hysteresis and the magnitude of intraocular pressure reduction with topical prostaglandin therapy. Br J Ophthalmol. 2012;96:254–257.

19. Del Buey MA, Casas P, Caramello C, et al. An update on corneal biomechanics and architecture in diabetes. J Ophthalmol. 2019;2019:7645352.