Effects of Valsalva Maneuver on Anterior Chamber Parameters and Choroidal Thickness in Healthy Chinese: An AS-OCT and SS-OCT Study

Xingyi Li, Wei Wang, Shida Chen, Wenbin Huang, Yaoming Liu, Jiawei Wang, Mingguang He, and Xiulan Zhang

Zhongshan Ophthalmic Center, State Key Laboratory of Ophthalmology, Sun Yat-Sen University, Guangzhou, People’s Republic of China

Correspondence: Xiulan Zhang, Zhongshan Ophthalmic Center, State Key Laboratory of Ophthalmology, Sun Yat-sen University, 54 S. Xianlie Road, Guangzhou, China 510060; zhangxl2@mail.sysu.edu.cn.

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PURPOSE. This study concurrently evaluated the effects of the Valsalva maneuver (VM) on the anterior and posterior ocular biometric parameters in a healthy Chinese cohort.

METHODS. This prospective, cross-sectional study used anterior segment optical coherence tomography (AS-OCT) and swept-source optical coherence tomography (SS-OCT) to measure the anterior and posterior ocular biometric parameters before and during the VM. Sixty-three volunteers (126 eyes; 17 males and 46 females) were enrolled. The IOP, blood pressure (BP), and refractive error were recorded before and during a VM.

RESULTS. The mean IOP showed a statistically significant increase (from 13.86–14.25 mm Hg, \(P = 0.005\)), but the different layers of the retina and the choroidal thickness (CT) showed no significant changes. The anterior chamber parameters decreased sharply from the baseline, with a smaller angle opening distance (AOD500; from 0.35–0.31 mm, \(P < 0.001\)), AOD750 (from 0.44–0.39 mm, \(P = 0.007\)), trabecular-iris space area (TISA500; from 0.14–0.13 mm, \(P = 0.027\)), TISA750 (from 0.25–0.23 mm, \(P = 0.007\)), and anterior chamber volume (ACV; from 143.09–139.84 mm\(^3\), \(P = 0.036\)). Regression analyses revealed an association between \(\Delta\)IOP and the baseline IOP (\(\hat{\beta} = 0.26\ [0.15, 0.37], P < 0.001\)) and \(\Delta\)ACW (\(\hat{\beta} = -3.24\ [-5.65, -0.83], P = 0.008\)).

CONCLUSIONS. This study is the first to provide simultaneous evaluation of the effects of the VM on anterior and posterior ocular biometric parameters. The VM caused a significant IOP increase and narrowing of the angles in healthy subjects. However, it did not change the CT in the macular region. The relationship between IOP elevation and choroidal expansion during the VM needs further investigation.

Keywords: ocular biometry, Valsalva maneuver, anterior segment optical coherence tomography, swept-source optical coherence tomography
tory pressure against the hand and the glottis. The participant sustained during the examinations by maintaining the expira-
the VM, and then conducted the examinations. The VM was examiner counted 15 seconds after the participant performed
against his/her hand and the closed glottis, while squeezing
participant to take a deep breath and then blow forcefully

All subjects underwent detailed ocular examinations, including
Examinations

We performed all examinations following standard operating
procedures and all were conducted on the same morning with
the participants in a seated position. The influence of cornea contact on the anterior chamber parameters was avoided by ensuring that all examinations performed were noncontact.

AS-OCT Imaging and Measurements

METHODS

Subject Recruitment

This prospective cross-sectional study recruited healthy Chinese volunteers from the Zhongshan Ophthalmic Center of Sun Yat-sen University in Guangzhou, China. The study was approved by the Ethical Review Committee of the Zhongshan Ophthalmic Center and was conducted in accordance with the Declaration of Helsinki for research involving human subjects. All participants involved in the study signed informed consent forms before examination.

The participants were recruited from students of Sun Yat-Sen University, employees at the Zhongshan Ophthalmic Center, and their families. All participants were between 18- and 65-years old and had clear ocular media, normal visual-field test results, and no history of IOP exceeding 21 mm Hg. Our exclusion criteria were hypertension disease, diabetes mellitus, severe cardiopulmonary insufficiency, use of systemic or topical medications, current ocular disease, previous ocular surgery, high myopia or hyperopia (spherical equivalent [SE] refractive error greater than +3 or –6 diopters [D]), clinically relevant opacities of the optic media, low-quality images due to unstable fixation, severe cataract, or poor patient compliance in performing the VM correctly.

Valsalva Maneuver Training

We first trained the participants upon recruitment into our study to ensure they could perform the VM correctly during the examinations. Because of the limited space between the participants’ faces and the instrument used for examinations, we chose a modified method to perform the VM rather than the classic method developed by Levin.7,8 We asked each participant to take a deep breath and then blow forcefully against his/her hand and the closed glottis, while squeezing his/her nose with his/her index finger and thumb.5 The examiner counted 15 seconds after the participant performed the VM, and then conducted the examinations. The VM was sustained during the examinations by maintaining the expiratory pressure against the hand and the glottis. The participant was given a brief rest between two examinations.

Examinations

All subjects underwent detailed ocular examinations, including best-corrected visual acuity, a slit-lamp examination, a stereoscopic optic disc examination with a 90-D lens, and axial length (AL) measurements by partial optical coherence interferometry (IOL-Master; Carl Zeiss Meditec, La Jolla, CA, USA). The BP (systolic blood pressure [SBP] and diastolic blood pressure [DBP]) was then measured with an electronic sphygmomanometer. IOP was measured by noncontact tonometry, and a refractive error examination was performed using an auto refractometer (KR-8900 version 1.07; Topcon Corp., Tokyo, Japan). Baseline information for BP, IOP, and refractive error was obtained and then, after a brief rest, the VM was performed while repeating the same measurements using the same procedures. The participant maintained a seated position during the examinations.

We performed all examinations following standard operating procedures and all were conducted on the same morning with the participants in a seated position. The influence of cornea contact on the anterior chamber parameters was avoided by ensuring that all examinations performed were noncontact.
Measurements of the choroidal and retinal-layer thicknesses, including internal limiting membrane (ILM) thickness, ganglion cell layer (GCL) thickness, and ganglion cell complex (GCC) thickness, were performed using the SS-OCT segmentation software (9.12.003.04). Automated segmentation was used to create 6 × 6-mm thickness maps of the different layers. The 6 × 6 grid was used for the thickness map (Fig. 2), and the mean regional thicknesses of the layers were calculated for the 36 sectors of the grid.

Statistical Analysis
The minimum required sample size for the study was calculated based on the mean spectral domain of the total sample and the range of continuous variables, including the anterior chamber parameters, determined from a previous study that compared the anterior chamber parameters before and during the VM. The previous study results indicated that 35 participants would be needed to detect a 5% change with the power of a 95% confidence level.

Statistical analyses were performed using SPSS software, Version 17.0 (SPSS, Inc., Chicago, IL, USA). The means and SDs were calculated for all the measured parameters. Paired t-tests were used to detect the differences in the parameters between the baseline status and during the VM. Univariate and multivariate linear regression analysis was used to determine the relationship between the changes in the anterior chamber parameters and the CT. Multivariable-adjusted β coefficients, with 95% confidence intervals (CIs), for the associations between independent and dependent variables were assessed using generalized estimating equations (GEEs), which take into account the correlation between the measurements from two eyes. A P value of less than 0.05 was considered statistically significant.

Results
A total of 63 healthy volunteers (126 eyes) were included in this study. Table 1 lists the demographic and baseline characteristics of the participants. The mean age was 40.1 ± 11.1 years, and there were 17 males and 46 females. The baseline IOP was 13.86 ± 2.33 mm Hg.

The changes in demographic, anterior segment, and posterior segment parameters during the VM are summarized in Table 2. The mean IOP showed a statistically significant increase, from 13.86 ± 2.33 to 14.25 ± 2.56 mm Hg (P = 0.005). The BP also increased during the VM, with SBP increasing from 111.71 ± 12.81 to 116.76 ± 15.06 mm Hg (P < 0.001) and DBP increasing from 70.57 ± 9.36 to 77.06 ± 12.54 mm Hg (P < 0.001). During the VM, no significant changes were observed in ILM thickness, GCL thickness, GCC thickness, retinal thickness, or CT.

The anterior ocular parameters measured by AS-OCT showed a consistently significant narrowing of the anterior chamber (Table 2). The anterior chamber parameters sharply decreased from the baseline values as follows: AOD500 (from 0.35–0.20 mm, P < 0.001) and AOD750 (from 0.44–0.24 mm, P = 0.007), TISA500 (from 0.14–0.08 mm, P = 0.12), TISA750 (from 0.25–0.12 mm, P = 0.45), IT750 (from 0.48–0.57 mm, P = 0.45), IAREA (from 1.42–1.65 mm², P = 0.73), ICURV (from −0.14–0.07 mm, P = 0.49), AOD500 (from 0.35–0.20 mm, P < 0.001), and AOD750 (from 0.44–0.24 mm, P = 0.007), TISA500 (from 0.14–0.08 mm, P = 0.12), TISA750 (from 0.25–0.12 mm, P = 0.45), and ACV (from 143.09–27.94 mm³, P = 0.056). No significant changes were noted in IT750, iris thickness at 2000 µm from the scleral spur (IT2000), IAREA, ICURV, ACD, ACW, ACA, IV, or PD.

Table 3 summarizes the linear regression analyses of the associations between the change in IOP and ocular biometric parameters. After adjusting for eye, age, sex, SE, AL, IOP, SBP, and DBP, the ΔIOP was only associated with the baseline IOP (β = 0.26 [0.15, 0.37], P < 0.001) and ΔACW (β = −5.24 [−5.65, −0.83], P = 0.008).

The predictors of changes in anterior angle (ΔAOD750) were determined by univariate and multivariate linear regression analyses. After adjusting for eye, age, sex, SE, AL, IOP, SBP, and DBP, an association was found between the ΔAOD750 and ΔAOD500 (β = 0.73 [0.51, 0.95], P < 0.001), ΔACV (β = 0.01 [0.00, 0.01], P = 0.001), and ΔACA (β = −0.04 [−0.08, −0.01], P = 0.019); Table 4), whereas AL, SE, IOP, and ΔCT were not correlated with ΔAOD750.
Dada et al. used UBM to investigate the changes in anterior segment parameters during the VM. The anterior ocular structure changed significantly in healthy subjects and patients with narrow angles and reported no significant changes in ACW, IT1000, or IT1500 during the VM and was the reason for the narrowing angle; however, they did not measure CT or changes in the IOP. In our study, we did not detect any significant decrease in ACW in our cohort; this result was similar to that of Dada et al., but inconsistent with the result of Wang et al. This discrepancy may have arisen due to the use of different inclusion criteria for the subjects, nonstandardized pressure and duration of the VM, the use of different instruments for measuring ocular parameters, or time variations in the measurements. The advantages of our study lie in the noncontact nature of the examination, the high resolution of the inspection equipment used, and the simultaneous measurement of the anterior and posterior parameters.

Several physiological responses were evident during the VM, including a reduction in venous flow and increases in BP and peripheral venous pressure. An elevation of IOP during the VM was widely recorded, with ΔIOP ranging from 2 to 26 mm Hg. The extent of the IOP increase was correlated with the volume of air expiration and the duration of the VM.

To the best of our knowledge, this study is the first to evaluate the effects of the VM on IOP, BP, and anterior and posterior ocular parameters simultaneously using AS-OCT and SS-OCT. The anterior ocular structure changed significantly in this cohort. Dada et al. used UBM to investigate the changes in anterior segment parameters and ciliary parameters in 76 patients with primary-angle closure (PAC) before and during the VM. They found a significant increase in IOP, a narrowing of the anterior chamber angle recess, a disappearance of the ACA, and an increase in the iris thickness and ciliary body thickness. No significant changes occurred in the angle opening distance, ACD, or pupillary diameter. The authors reported that the narrowing of the angle during the VM was significantly associated with the baseline ciliary body thickness and angle recess ($R^2 = 96.1\%$). Wang et al. used UBM to study healthy subjects and patients with narrow angles and reported a reduction in the ACD and ACA and a thickening of IT500, but no significant changes in ACW, IT1000, or IT1500 during the VM. The percentage reduction in ΔACD was more pronounced in narrow angle eyes than in healthy eyes (1.307% vs. 0.692%, $P = 0.048$), indicating that the iridolenticular diaphragm has a greater forward displacement in narrow angle eyes. The authors hypothesized that the choroid expands during the VM and was the reason for the narrowing angle; however, they did not measure CT or changes in IOP. In our study, we did not detect any significant decrease in ACW in our cohort; this result was similar to that of Dada et al., but inconsistent with the result of Wang et al. This discrepancy may have arisen due to the use of different inclusion criteria for the subjects, nonstandardized pressure and duration of the VM, the use of different instruments for measuring ocular parameters, or time variations in the measurements. The advantages of our study lie in the noncontact nature of the examination, the high resolution of the inspection equipment used, and the simultaneous measurement of the anterior and posterior parameters.

Uveal engorgement and expansion (iris and choroid) are dynamic phenomena and are risk factors for the development of primary-angle closure glaucoma (PACG). Zheng et al. found that angle closure eyes have a smaller acceleration of iris stretch and a larger acceleration of pupil block in response to physiological pupil dilation. Aptel et al. assessed the dynamic changes of iris volumes after pupil dilation using AS-OCT and reported a sharp decrease in iris volume in eyes with POAG but an increase in eyes with acute primary-angle closure (APAC). These authors subsequently found that the responses of iris volume to illumination differed among the fellow eyes of APAC.
eyes, PAC suspect eyes, and POAG eyes. Regression analysis suggested that the changes in iris volumes were significantly correlated with ΔAOD500. Ganeshrao et al.21 also reported that the iris area and volume decreased less in angle closed eyes than in healthy eyes during pupil dilation in a South Indian cohort. However, we did not find any significant changes in iris parameters during VM: iris thickness, iris area, iris curve, and PD did not differ from baseline. Two reasons could explain this discrepancy: (1) VM may not change the iris thickness, area, curve, and PD, or (2) healthy people might have better iris adaptability to withstand changes caused by VM, whereas patients with shallow anterior chambers would have significant increases in iris thickness and volume. Therefore, we might hypothesize that the adaptability of the iris could be involved in the occurrence of angle closure; this possibility requires further study.

Schuman et al.17 found that the VM caused by playing wind instruments led to an elevation of the IOP of up to 40 mm Hg, whereas SD-OCT measurements indicated a thickening of the uvea near the pars plana of 20%. The degree of IOP elevation was associated with uveal thickening and those researchers hypothesized that this uveal thickening was widespread among the eyeballs of subjects who played wind instruments. The increased pressure in the chest and abdomen while playing these instruments led to an increase in venous pressure in the head and neck. That pressure was then transferred to the choroid through the jugular, orbital, and vortex veins, causing engorgement of the choroid. The expansion of choroidal volume could then push the lens and iris to the anterior chamber and lead to anterior angle narrowing. Expansion of the choroidal volume by 20% would result in a loss of two-thirds of the anterior chamber space. The CT increased from 371 to 440 μm (ΔCT = 70 μm), which caused IOP elevation of up to 26 mm Hg.

Schuman et al.17 proposed an estimation equation whereby a CT increase of 69 μm would induce a 26 mm Hg elevation of IOP. However, Schuman’s study only measured the uveal thickness around the pars plana; the CT in the posterior pole was not studied due to the limitations of UBM. They used UBM for measurement, but they failed to define the location of the pars plana choroid in their UBM figures. Distinguishing the boundary between the pars plana choroid and the ciliary body in UBM figures is well recognized as a difficult challenge. The uveal thickness reported in the study by Schuman et al.17 was probably the pars plana thickness of ciliary body, which might be anatomically different from the choroid.

We did not observe any significant changes in the posterior CT during the VM, which was consistent with the findings of a previous study with a small sample size. Falco et al.5 used EDI SD-OCT to evaluate the changes in CT within 3000 μm of the posterior pole before and after the VM and observed no significant changes in the CT during the VM. However, this study had several disadvantages, as it enrolled only nine healthy volunteers, measured CT manually using time-consuming EDI SD-OCT, and lacked IOP measurements. Our present study confirmed the observations that the anterior angle becomes shallow, but the CT in the macular region did not change significantly in our cohort when measured using newer instruments with high resolution and quick acquisition speed.

The asymmetrical response of the anterior and posterior segments may be correlated with the different response to the VM observed in different locations of the uvea, which is segmented and asymmetric. Our observations suggested that the IOP elevation and anterior angle narrowing noted in healthy persons were not caused by posterior pole choroid.

### Table 3. Associations Between the Change of IOP and Ocular Biometric Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate β [95% CI]</th>
<th>Univariate P* Value</th>
<th>Multivariate β [95% CI]</th>
<th>Multivariate P† Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP, mm Hg</td>
<td>0.24 [0.15, 0.35]</td>
<td>0.001*</td>
<td>0.26 [0.15, 0.37]</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>0.00 [0.00, 0.02]</td>
<td>0.836</td>
<td>0.00 [0.00, 0.03]</td>
<td>0.954</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>0.00 [0.00, 0.03]</td>
<td>0.850</td>
<td>0.018 [0.00, 0.02]</td>
<td>0.401</td>
</tr>
<tr>
<td>PD, mm</td>
<td>0.15 [0.04, 0.33]</td>
<td>0.127</td>
<td>0.05 [0.013, 0.23]</td>
<td>0.594</td>
</tr>
<tr>
<td>AOD750, mm</td>
<td>-0.32 [1.17, 0.74]</td>
<td>0.556</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TISA750, mm²</td>
<td>-0.82 [3.02, 1.58]</td>
<td>0.467</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IT750, mm</td>
<td>0.51 [0.15, 0.87]</td>
<td>0.005*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ACV, mm³</td>
<td>0.007 [0.00, 0.02]</td>
<td>0.154</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LV, μm</td>
<td>0.00 [0.00, 0.00]</td>
<td>0.549</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔAOD750, mm</td>
<td>-0.37 [1.46, 0.75]</td>
<td>0.511</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔTISA750, mm²</td>
<td>0.11 [3.59, 3.81]</td>
<td>0.954</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔACV, mm³</td>
<td>0.00 [0.01, 0.02]</td>
<td>0.641</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔACW, mm</td>
<td>-3.18 [-5.73, -0.64]</td>
<td>0.014*</td>
<td>-3.24 [-5.65, -0.83]</td>
<td>0.008†</td>
</tr>
<tr>
<td>ΔLV, μm</td>
<td>0.00 [0.00, 0.00]</td>
<td>0.926</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔIT750, mm</td>
<td>0.89 [0.31, 1.48]</td>
<td>0.003*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔIT2000, mm</td>
<td>0.30 [-0.18, 0.78]</td>
<td>0.219</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔAREA, mm²</td>
<td>0.22 [0.09, 0.36]</td>
<td>0.001*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔCURV, mm</td>
<td>-0.09 [-0.51, 0.52]</td>
<td>0.655</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ΔCT, μm</td>
<td>-0.00 [-0.02, 0.02]</td>
<td>0.884</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* β/P value: regression coefficient and P value of the independent variables in the univariate linear regression model.

† β/P value: regression coefficient and P value of the independent variables in the generalized estimating equations. Insignificant variables were not present in multivariate regressions. The influence factors as eye, age, sex, SE, AL, PD, IOP, SBP and DBP have been adjusted.
expansion. One possible explanation is that the expansion of the ciliary body and anterior choroids caused an increase in post-iris pressure, followed by the elevated IOP. Future studies should focus on the ciliary body and anterior choroids near the pars plana.

The present study recruited only healthy people for the analysis of the correlations between the parameters and the changes caused by the VM. Our previous studies identified thicker choroids in eyes with APAC, PAC, and PACG than in healthy eyes. These findings may support the hypotheses that choroidal expansion is a contributing factor to the development of angle closure disease. Sihota et al.22 found no protective efficacy of a laser iridotomy on the significant anterior segment angle shallowing produced by the VM in eyes with PAC. The VM decreased the anterior chamber depth, but the pressure of choroid expansion to the posterior chamber was not caused by iris bombe and pupillary blocking; instead, the ciliary body expansion directly pushed the iris forward and the angle closed. This was additional evidence indicating how the VM might improve IOP primarily by means of ciliary body and anterior choroid expansion as one cause of angle closure.

One strength of this study is the inclusion of simultaneous measurements of anterior and posterior ocular structures using AS-OCT and SS-OCT. However, the study also has some limitations. First, all subjects were enrolled from a university-based hospital, which may introduce selection bias. The subjects were all open angle, so the results cannot be applied directly to patients with narrow angle. Second, the thickness of the choriocapillaris, Satter’s layer, and Haller’s layer were not measured due to the limited resolution of SS-OCT.23,24 Third, the choroidal flow was not determined in this study. The relationship between choroidal flow and CT remains controversial. The latest introduced OCT angiography provides the opportunity to qualify macular and peripapillary blood flow, and we concentrated on clarifying the ocular flow response to the VM.25,26 Last, in order to control the sample size of participants, we included both eyes of one participant in our study. We adjusted the intereye correlation using GEEs to assess the associations between independent and dependent variables.

**Conclusions**

To the best of our knowledge, this is the first study to use AS-OCT and SS-OCT to provide simultaneous measurements of the anterior and posterior ocular structures before and during the Valsalva maneuver. We found that the VM could cause a significant IOP increase and narrowing of the angles in healthy subjects. However, the VM did not change the CT at the macular region. The elevation of IOP caused by the VM cannot be explained by choroidal expansion, according to the present study findings. More studies with larger sample sizes and various ethnicities are required before a general conclusion can be made.

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