European Journal of Sport Science

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/tejs20

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To cite this article: Jesús Vera PhD , Beatriz Redondo PhD , Alejandro Perez-Castilla PhD , George-Alex Koulieris PhD , Raimundo Jiménez PhD & Amador Garcia-Ramos PhD (2020): The intraocular pressure response to lower-body and upper-body isometric exercises is affected by the breathing pattern, European Journal of Sport Science, DOI: 10.1080/17461391.2020.1790670

To link to this article: https://doi.org/10.1080/17461391.2020.1790670

Accepted author version posted online: 30 Jun 2020.

Publisher: Taylor & Francis & European College of Sport Science

Journal: *European Journal of Sport Science*

DOI: 10.1080/17461391.2020.1790670

Title: The intraocular pressure response to lower-body and upper-body isometric exercises is affected by the breathing pattern

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Disclosure: The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

Acknowledgments: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors**.** The authors thank all the participants who selflessly collaborated in this research.

Abstract

We assessed the mediating role of the breathing pattern adopted during isometric exercise on the intraocular pressure (IOP) response in the back squat and biceps curl exercises. Twenty physically active young adults performed sets of 1-minute isometric effort against a load corresponding to 80% of the maximum load while adopting three different breathing patterns: (i) *Constant breathing*: 10 cycles consisting of 3 seconds of inhalation and 3 seconds of exhalation, (ii) *10-sec Valsalva*: 3 cycles consisting of 10 seconds holding the breath and 10 seconds of normal breathing, and (iii) *25-sec Valsalva*: 2 cycles consisting of 25 seconds of the Valsalva maneuver and 5 seconds of normal breathing. A rebound tonometer was used to semi-continuously assesses IOP during the six sets of 1-minute isometric effort (2 exercises × 3 breathing patterns). We found a progressive IOP rise during isometric effort ($P < 0.001$, $\eta_p^2 = 0.83$), with these increases being greater when the breath was held longer ($P < 0.001$, $\eta_p^2 = 0.58$; 25-sec Valsalva > 10-sec Valsalva = constant breathing). There was a trend towards higher IOP values for the back squat in comparison to the biceps curl, although these differences did not reach statistical significance for any breathing pattern (corrected P-value ≥ 0.146, $d \leq 0.69$). These findings reveal that glaucoma patients or those at risk should avoid activities in which the breath is held, especially when combined with physical exercise modalities that also promote an increment in IOP values (e.g., isometric contractions).

Keywords: resistance training; ocular health; glaucoma; rebound tonometry.

Introduction

Glaucoma is the leading cause of global irreversible blindness [1]. An elevated intraocular pressure (IOP) is an important risk factor for the onset and progression of glaucoma [2, 3]. The only medical strategy that has been shown to be effective for the prevention and management of glaucoma is the reduction and stabilization of IOP values [4]. Eye care specialists generally use pharmacological, laser or surgical interventions for reducing IOP values to desirable levels [5]. However, multiple daily life activities have been demonstrated to play a significant role in the management of IOP, including food and caffeine intake, sleeping position, playing wind instruments, mental stress or physical exercise [6, 7].

The immediate and long-term effects of physical exercise on the prevention and management of glaucoma have been thoroughly examined in recent years [8]. Endurance training at a low intensity (e.g., cycling or jogging) facilitates a reduction in IOP values [9, 10], whereas resistance training (i.e., weightlifting) against heavy loads promotes an immediate IOP rise [11, 12]. Importantly, the IOP response to resistance training is modulated by different factors such as the exercise modality (dynamic vs. isometric), exercise type (i.e., squat, bench press, biceps curl, military press), exercise intensity, or participants´ fitness level [12–16]. Specifically, greater changes in IOP values have been observed during isometric compared to dynamic exercises, while increases in IOP values have been positively associated with the size of the muscle mass involved in the exercise and the load used [12, 14, 16]. In addition, high-fit individuals have shown a more stable IOP response to exercise than low-fit individuals [13]. Therefore, it seems reasonable to discourage the execution of highly demanding isometric efforts for glaucoma patients or individuals at high risk of glaucoma onset, especially if they have a low fitness level.

The Valsalva maneuver is commonly used during resistance training when lifting heavy loads (≥ 80% of the one-repetition maximum) to facilitate force production through the stabilization of the spine and trunk [17]. Previous studies have shown that the increase in intra-thoracic and intra-abdominal pressures caused by the Valsalva maneuver alters the cardiovascular hemodynamic [18, 19]. The use of the Valsalva maneuver during resistance training influences the cardiovascular response, with these effects being more evident during isometric compared to dynamic exercises [20, 21]. The execution of the Valsalva maneuver also induces an acute IOP rise both at baseline [22] and during dynamic resistance training [14]. However, no study has examined the influence of the breathing pattern adopted during isometric resistance training on IOP.

In order to fill gaps in existing knowledge, we aimed (i) to determine the influence of the breathing pattern adopted during isometric resistance training on IOP, and (ii) to compare the IOP changes between the back squat and biceps curl exercises. Based on the accumulated evidence, we hypothesized that (i) greater IOP values would be observed when performing the Valsalva maneuver compared to the use of a constant breathing as it has been reported for dynamic resistance training [14], and (ii) the back squat would promote a higher IOP rise in comparison to the biceps curl due to the larger amount of muscle mass involved in the back squat exercise [14].

Methods

Participants

The required sample size was based upon an a-priori power analysis for a repeated measures analysis of variance using the GPower 3.1 software [23]. For this analysis, an effect size of 0.25, at power of 0.80 and alpha of 0.05 were assumed. This calculation projected a necessary sample size of 18 participants. As such, 20 physically active young adults (12 women; age = 22.4 ± 2.1 years [average ± standard deviation]) were recruited to participate in this study. All participants were free of any systemic or ocular condition and had at least one year of resistance training experience. They were asked to refrain from strenuous exercise 48 h preceding each visit to the laboratory, and also to avoid alcohol or caffeine consumption 12 h prior to each testing session. The present study was conducted in conformity with the Declaration of Helsinki and was approved by the Institutional Review Board (438/CEIH/207). Written informed consent was obtained from each participant before the commencement of the study.

Experimental design

A cross-sectional study was performed to assess the impact of the breathing pattern adopted during isometric training on IOP. The first session was used to determine the heaviest load that each participant could hold for 1 minute during the back squat and biceps curl exercises. The second session was the main experimental session and consisted of 6 sets (2 exercises × 3 breathing patterns) of 1-min isometric effort performed in a randomized order. IOP was measured just before each training set, during the 1-min isometric effort (semi-continuous IOP assessment: 14 measurements), immediately after exercise cessation, and after 1-min of passive recovery. Participants were asked to refrain from eating or drinking during the course of the second testing sessions. Both experimental sessions were performed under similar environmental conditions (~22°C and ~60% humidity), and were scheduled at the same time slot (± 1 h) in order to control the effects of circadian variations on physical performance [24].

Testing procedures

The isometric back squat exercise was performed at a 90º knee angle with a free-weight barbell over the participants' shoulders (Figure 1, panel A). The standing EZ-bar isometric biceps curl exercise was also performed at a 90º elbow angle (Figure 1, panel B). The maximum load with which the participants could hold the described isometric position for 1 min was determined in session 1, and 80% of this load was applied on the main experimental session (i.e., session 2) to ensure that all participants could complete 1-min isometric effort without reaching muscular failure. The average load used was 23.3 ± 3.4 kg for the back squat and 13.3 ± 3.0 kg for the biceps curl. Participants randomly performed 6 sets (2 exercises × 3 breathing patterns) during the main experimental session. Two consecutive sets were separated by 10 min of passive recovery. A metronome was used to guide the participants during the 3 breathing patterns used in this study:

- *Constant breathing*: Participants completed a total of 10 cycles consisting of 3 seconds of inhalation followed by 3 seconds of exhalation.
- *10-sec Valsalva*: Participants completed a total of 3 cycles consisting of 10 seconds of the Valsalva maneuver (i.e., holding the breath) followed by 10 seconds of normal breathing (i.e., inhaling and exhaling).
- *25-sec Valsalva*: Participants completed a total of 2 cycles consisting of 25 seconds of the Valsalva maneuver (i.e., holding the breath) followed by 5 seconds of normal breathing (i.e., inhaling and exhaling).

Figure 1. Photographs of the study procedure during the isometric back squat (Panel A) and biceps curl (Panel B) exercises.

IOP assessment and processing

The Icare PRO portable rebound tonometer (ICare, Tiolat Oy, Inc. Helsinki, Finland) was used for IOP assessment. This apparatus has been clinically validated and has shown to be a reproducible method for determining IOP in humans [25]. The Icare PRO tonometer is handheld, allows to rapidly acquire IOP measurements without using topical anesthesia, and is more comfortable than Goldmann applanation tonometry [26]. Due to these advantages, the rebound tonometer is commonly used in applied situations, allowing the assessment of IOP during the execution of isometric exercises [16, 27]. Following the manufacturer instructions and similar to previous studies [16, 27], an experienced examiner acquired IOP measurements with participants being instructed to fixate on a target placed at 6 m.

The Icare PRO tonometer acquires IOP measurements at irregular intervals without providing exact timestamps. In order to obtain a set of equally distributed IOP measurements at exact regular intervals, we used a technique based on polynomial interpolation, developed previously by Vera et al., (2019) [27]. The IOP signal was re-sampled at 14 discrete intervals for the 1-minute period.

Statistical analysis

First, we confirmed the normal distribution of the data (Shapiro-Wilk test) and the homogeneity of variances (Levene's test) ($P > 0.05$). A two-way repeated measures ANOVA (exercise [back squat and biceps curl] and breathing pattern [constant, 10-sec Valsalva, and 25-sec Valsalva]) was applied to the baseline IOP values to determine if they were comparable.

For the main analysis, we performed a repeated measures ANOVA for IOP considering the type of exercise (back-squat and biceps-curl), breathing pattern (constant, 10-sec Valsalva, and 25-sec Valsalva), and point of measure (baseline, 1 to 14, after exercise, and recovery [a total of 17 measurements]). Linear regressions analyses were applied to the 14 IOP measurements collected during the isometric effort in each of the six sets (2 exercise × 3 breathing patterns). In addition, we explored whether baseline IOP levels were associated with the IOP change occurring during isometric effort in the six experimental conditions by linear regression analyses.

The magnitude of the differences was reported as partial eta squared (η_p^2) and Cohen's *d* effect size (*d*) for F and T tests, respectively. Multiple comparisons were corrected with the Holm-Bonferroni procedure, and the level of statistical significance was set at 0.05.

Results

The ANOVA did not detect significant differences on baseline IOP values: exercise ($F_{1, 19} = 0.37$, $P = 0.548$), breathing pattern ($F_{2, 38} = 0.45$, $P = 0.640$), and exercise × breathing pattern ($F_{2, 38} = 0.16$, $P = 0.855$).

The main ANOVA applied on IOP values revealed a statistically significant effect for the breathing pattern ($F_{2, 38} = 25.79$, $P < 0.001$, $\eta_p^2 = 0.58$) and the point of measure ($F_{2, 38} = 95.29$, $P < 0.001$, $\eta_p^2 = 0.83$), but not for the exercise ($F_{1, 19} = 1.83$, $P = 0.192$). There were also statistically significant differences for the interactions exercise × point of measure ($F_{16, 304} = 1.93$, $P = 0.017$, $\eta_p^2 = 0.09$) and breathing pattern × point of measure ($F_{32, 608} = 6.36$, $P < 0.001$, $\eta_p^2 = 0.25$), whereas no differences were observed for the interactions exercise × breathing pattern ($F_{2, 38} = 0.26$, $P = 0.773$) and exercise × breathing pattern × point of measure ($F_{32, 608} = 0.91$, $P = 0.616$). Post-hoc analyses showed that there were greater IOP values during the 25-sec Valsalva condition in comparison to the constant (corrected P-value < 0.001, $d = 1.24$) and 10-sec Valsalva conditions (corrected P-value < 0.001, $d = 1.92$) conditions. However, the comparison between the constant and 10-sec Valsalva conditions did not reach statistical significance (corrected P-value $= 0.399$) **(Figure 2)**. As previously indicated, the main effect of exercise did not reach statistical significance ($F_{1, 19} = 1.83$, $P = 0.192$), although pairwise comparisons performed separately for each breathing pattern showed a trend towards higher IOP values for the back squat compared to the biceps curl (corrected P-value ≥ 0.146, $d \geq 0.38$) **(Figure 3).**

Linear regression analyses showed a progressive IOP rise during the isometric effort (all P-values < 0.001). The coefficients of determination in the back-squat exercise were 0.94 , 0.90 and 0.86 for the constant, 10-sec Valsalva and 25-sec Valsalva conditions, respectively, whereas in the biceps curl exercise were 0.92, 0.89 and 0.85 for the constant, 10-sec Valsalva and 25-sec Valsalva conditions, respectively. The analysis of the possible association between baseline IOP levels and the mean IOP rise observed during isometric effort revealed that the IOP rise caused by isometric effort is not associated with the baseline IOP levels (coefficients of correlation ranged between -0.38 and 0.16, all P-values ≥ 0.099).

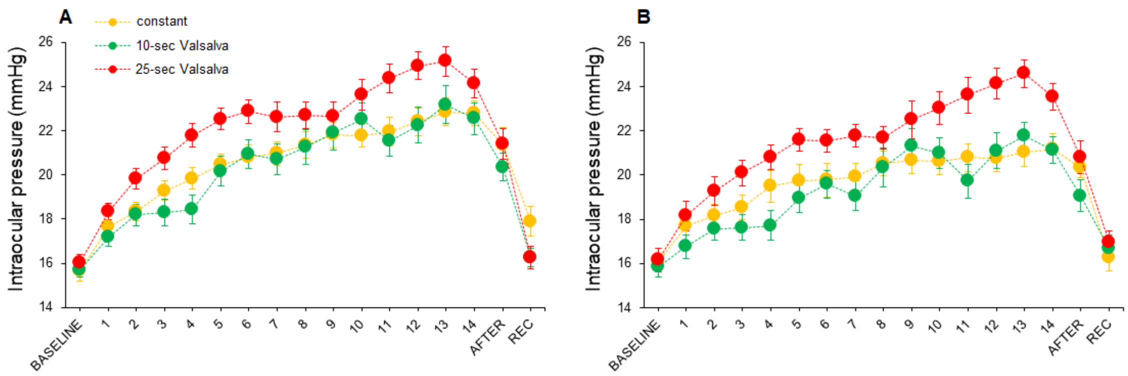

Figure 2. Comparison of intraocular pressure values between isometric efforts of 1-min following three different breathing patterns during the back squat (panel A) and biceps curl (panel B) exercises. Error bars show the standard error. After: measurement taken immediately after exercise cessation, Rec: measurement taken after 1-min of passive recovery.

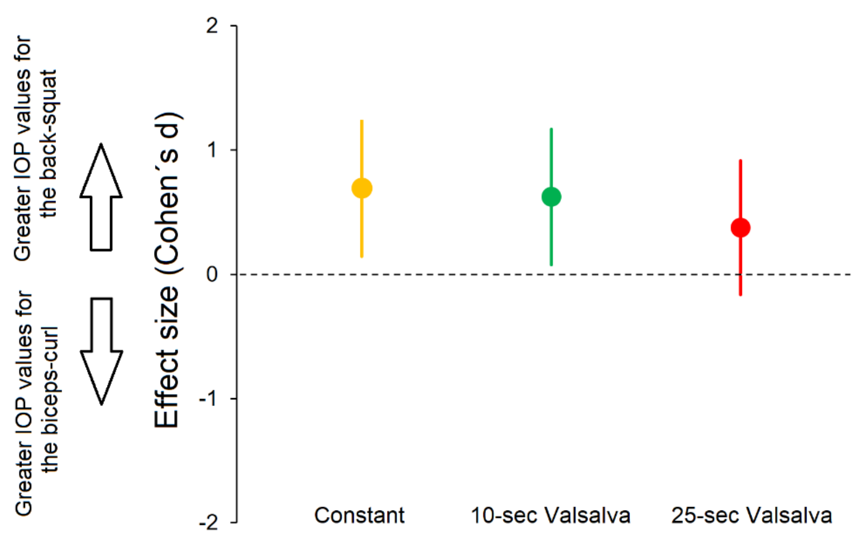

Figure 3. Standardized differences (Cohen´s d effect size) for the average intraocular pressure values between the back squat and biceps curl exercises during the 1-min isometric effort for the three breathing patterns. Error bars show the 90% confidence intervals. IOP: intraocular pressure.

Discussion

The current study aimed to assess the influence of the breathing pattern adopted during lower-body and upper-body isometric training on IOP. We found that the IOP response to both the back squat and biceps curl exercises depended on the breathing pattern, exhibiting the greatest IOP values when the breath was held for a longer period (25-sec Valsalva condition). There was also a trend towards greater IOP values for the back squat compared to the biceps curl exercise, being this result consistent across the three breathing patterns. Regardless of the exercise type and breathing pattern, a linear increase in IOP was observed from the beginning to the end of the isometric effort (coefficients of determination ranged from 0.85 to 0.94). The present outcomes evidence that different factors are able to modulate the IOP response to physical exercise and, specifically, our data highlight that the breathing pattern used during exercise is an important aspect to consider when prescribing exercise for glaucoma patients or those at risk.

The manipulation of the breathing pattern adopted during isometric exercise allowed us to corroborate our first hypothesis. Namely, compromising the interchange of gases during isometric effort yielded a more abrupt IOP rise (25-sec Valsalva > 10-sec Valsalva = constant). This finding is in line with previous investigations that have demonstrated higher IOP values when performing the Valsalva maneuver during dynamic resistance training [11, 28]. Vieira and colleagues (2006) observed that holding the breath during the last repetition of the bench press exercise induced an IOP rise of 4.3 ± 4.2 mmHg, whereas an IOP rise of 2.2 ± 3.0 mmHg was obtained when participants were asked not to hold the breath during the last repetition. Also, a recent study of Vera et al., (2019) reported higher IOP values when participants were instructed to hold their breath during the entire repetition of the dynamic back squat and biceps curl compared to performing the same exercises holding the breath during the first phase of the exercise and exhaling in the second phase of the exercise (IOP was 2.9 ± 2.7 and 1.9 ± 2.0 mmHg higher for the back squat and biceps curl exercise, respectively). Here, participants experienced IOP rises of 8.1 ± 3.3 and 7.4 ± 3.1 mmHg when performing the Valsalva maneuver during 25 seconds in the back squat and biceps curl exercises, whereas the IOP rise using a constant breathing pattern (inhaling and exhaling every 3 seconds) was 7.1 ± 2.7 mmHg for the back squat and 5.1 ± 3.1 mmHg for the biceps curl. Therefore, the magnitude of the change induced by performing the Valsalva maneuver seems to be similar for dynamic and isometric resistance training exercises (~ 2 - 3 mmHg). The findings of this study may be applicable to other everyday life situations in which the breath is held (e.g., playing wind-instruments) [7, 30]. Therefore, glaucoma patients or those at risk should avoid activities in which the breath is held, especially when combined with physical exercise modalities that also promote an increment in IOP values (e.g., isometric contractions).

Our second hypothesis regarding the comparison of IOP values between the back squat and biceps curl exercises was rejected because no significant differences in IOP values were observed between both exercises. However, the analysis of the magnitude of the differences suggested a trend towards higher IOP values for the back squat compared to the biceps-curl exercise (ES ranged from 0.38 to 0.69). This finding agrees with previous evidence suggesting that the size of the muscle mass involved in the exercise is positively associated with the increase in IOP values [14, 29]. Indeed, a recent study found higher IOP increases during the execution of a training set of 10 repetitions to muscular failure in the back squat in comparison to the biceps curl exercise [14]. Nevertheless, the IOP differences observed between exercises seem to be reduced during the 25-sec Valsalva condition. This may suggest that IOP values are already very high during a Valsalva maneuver, and that performing a physical effort simultaneously only induces a minor additional increases in IOP values. Taken together, the present outcomes indicate that, whenever possible, the use of the Valsalva maneuver and the execution of isometric resistance exercises involving large muscles should be discouraged for individuals who need to avoid IOP peaks (i.e., glaucoma patients or those at risk).

From a clinical point of view, further investigation is needed to determine the possible glaucomatous damage associated with the acute increase in IOP that inevitably occurs during isometric effort. Of note, the average IOP rise observed in this study was ~ 20% (range = 19.5% to 22.6%). Remarkably, an IOP rise of 1 mmHg has been associated with a 10% higher risk of glaucoma progression [2] and, thus, the acute IOP increases induced by isometric effort should be considered by eye care specialists. Also, our results suggest that baseline IOP levels are not associated with the

IOP rise caused by isometric effort, which may indicate that individualized recommendations cannot be based on baseline IOP levels. The current outcomes should be also taken into account when recommending the most pertinent strategies for exercise prescription in glaucoma patients. For example, the International Glaucoma Association (https://www.glaucoma-association.com/) should consider suggesting that isometric resistance exercise leads to abrupt IOP rises, with these IOP increases being substantially higher than those associated with the execution of dynamic resistance exercises. Future studies are required to explore the risk of developing glaucoma by individuals who routinely perform isometric efforts and, consequently, suffer significant IOP rises.

Our findings confirm that isometric effort leads to meaningful IOP rises, with these increases in IOP being greater when the interchange of gases is compromised. However, this study has limitations and they must be acknowledged. As stated in the introduction section, the IOP response to exercise is dependent on different factors including exercise intensity and participants´ fitness level [13, 27], which have not been manipulated in the current study. Future studies should compare the influence of the breathing pattern during isometric exercises performed at different intensities, as well as whether the IOP behavior differs between high-fit and low-fit individuals. Also, inclusion only of healthy subjects limits the external validity of our results. In this regard, the IOP response to different stress tests have demonstrated to be heightened in glaucoma patients [31] and, thus, the IOP responses to isometric exercises should be explored in glaucoma patients. A metronome was used in this study to help participants to accomplish the different breathing patterns and an examiner supervised that participants followed these instructions. However, a potential limitation was that we did not monitor the breathing pattern and, therefore, it is plausible that participants were not able to fully comply with the breathing instructions given to them. Lastly, both exercises were performed in a standing position, and the body posture has demonstrated to affect IOP with a supine position leading to greater IOP values in comparison to sitting or upright positions [32]. Due to the fact that numerous resistance training exercises are performed in a supine position (e.g., bench press), it would be relevant to compare the influence of the body posture adopted during exercise on IOP.

Conclusions

The execution of isometric resistance training with the back squat and biceps curl exercises induces an immediate and progressive IOP rise, being the increase in IOP more accentuated when the interchange of gases is compromised during the isometric effort (Valsalva manoeuver). Our data also indicated a trend towards greater IOP rises in the back squat compared to the biceps curl exercise, which may be expected due to the larger amount of muscle mass involved in the back squat exercise. The increase in IOP observed during isometric resistance training in the present study is higher than those previously reported for dynamic resistance training. However, the increase in IOP promoted by the Valsalva manoeuver was comparable for both exercise modalities (~ 2 - 3 mmHg higher in comparison to a normal breathing pattern). Therefore, the performance of isometric resistance training, especially using the Valsalva maneuver that compromises the interchange of gases, should be discouraged for individuals who need to avoid IOP fluctuations. The generalizability of the current findings to glaucoma patients or those at risk should be addressed in future studies.

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