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ORIGINAL ARTICLE

Intraocular pressure and ocular perfusion pressure responses during low-intensity endurance exercise in primary-open angle glaucoma patients versus age- and sex-matched controls: Influence of walking pace and external load

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Abstract

This study compared the effects of low-intensity endurance exercise at two different walking paces with/without external loads on intraocular pressure (IOP) and ocular perfusion pressure (OPP) in primary open-angle glaucoma patients (POAG) and matched controls. Twenty-one POAG patients and 17 healthy individuals performed four 400-m walking protocols (slow/fast × with/without loads). IOP was measured before exercise, during the walking test and after 1 and 5 min of recovery. OPP was assessed before exercise and after 1 and 5 min of recovery. IOP was stable in POAG patients during the execution of low-intensity endurance exercise ($p = 0.14$) regardless of the walking pace and the use of external loads (both $p > 0.69$). However, controls showed a moderate IOP rise during the walking test ($p < 0.001$), with this effect being heightened when using external loads ($p < 0.001$). Both groups experienced a transient OPP rise after exercise ($p < 0.001$) and this increase was greater in the fast- than the slow-paced condition ($p = 0.049$). POAG patients showed stable IOP while walking at slow and fast speeds, while OPP increased after walking, particularly at a fast pace. These findings suggest that low-intensity endurance exercise is a safe strategy to improve fitness levels in POAG patients.

KEYWORDS
endurance training, glaucoma, physical activity, POAG patients

INTRODUCTION

Glaucoma, which is the leading cause of irreversible blindness worldwide, is an optic nerve neuropathy caused by progressive degeneration of retinal ganglion cells.[1] The only proven strategy for glaucoma control is the reduction and stabilisation of intraocular pressure (IOP), with eye drops and laser trabeculoplasty being considered as first-line treatment strategies.[2,3] Additionally, modification of certain lifestyle habits (e.g., physical activity, diet, smoking, caffeine intake, psychological stress, etc.) has demonstrated positive effects on IOP in both healthy and clinical populations.[4] Indeed, due to the considerable incidence of glaucoma and its social, economic and health impacts,[5] research is focused on determining valid and feasible strategies for the prevention and management of the condition.

Within the range of modifiable lifestyle interventions, physical exercise has been suggested as a promising adjunct strategy for glaucoma prevention and management.[6] Observational studies have shown lower incidence and progression in physically active individuals, with higher endurance capacity being related to lower IOP and higher ocular perfusion pressure (OPP) values.[7–9] Specifically, the execution of low- to moderate-intensity endurance exercise causes an acute reduction of IOP in both healthy and clinical populations.[10,11] Endurance exercises like walking, jogging and cycling are highly recommended for glaucoma management and prevention.[12–14] However, factors such as intensity and fitness level must be considered carefully when prescribing exercise for glaucoma patients or those deemed at risk, as they can influence IOP and OPP levels.[13,15–17]

To date, most studies regarding the impact of physical exercise on IOP and OPP have been carried out in healthy individuals, and it is generally agreed that the external validity of these results should be confirmed in glaucoma patients.[18,19] It is well known that the outflow facility of the eye is altered in patients with glaucoma, and therapeutic interventions are targeted to regulate this function.[20,21] Indeed, untreated primary open-angle glaucoma (POAG) patients demonstrate elevated outflow resistance to provocative tests, with these findings being associated with the effectiveness of eye drops and surgery on the outflow system.[22,23] Furthermore, comparative studies between POAG and healthy subjects revealed differences in regulatory capacity during the execution of physical activities.[24–26] Therefore, the response of IOP and OPP to exercise seems to be dependent on the outflow resistance in POAG eyes. Accordingly, recommending exercise to reduce IOP levels in glaucoma patients should follow an assessment of outflow function.

Based on the previously mentioned factors known to mediate the IOP response to exercise, a randomised clinical trial was designed with the following objectives: (i) to assess the IOP and OPP acute responses to low-intensity endurance exercise (400-m walking) when performed at two different walking paces with and without external loads and (ii) to compare the results of POAG patients with age- and sex-matched controls. It was hypothesised that low-intensity endurance exercise will cause a moderate reduction in IOP,[13,27] although the use of external loads and faster walking paces could counteract this IOP-lowering effect.[16] No hypothesis regarding comparison between the POAG and control groups, the mediating role of walking pace or the OPP response could be formulated due to the lack of related studies.

Key points

- This study is the first to evaluate the acute effects of low-intensity endurance exercise on intraocular pressure and ocular perfusion pressure in individuals with primary open-angle glaucoma.
- The findings suggest that low-intensity endurance exercise is associated with a stable intraocular pressure in individuals with primary open-angle glaucoma, potentially supporting glaucoma management.
- The study underscores the potential of physical exercise as a non-pharmacological strategy for glaucoma management, with possible benefits for ocular blood flow.

METHODS

Experimental design

A cross-sectional study was designed to determine the impact of endurance exercise (400-m walking) on the IOP and OPP responses (see Figure 1 for a schematic illustration of the study design). Participants completed four walking conditions at two different paces (slow and fast), both with and without external loads. The four conditions were performed in random order during a single session, with conditions separated by 10 min of passive rest.[27]

Subjects

Thirty-eight participants were recruited, including 21 POAG patients (9 men, 12 women: [mean age = 71.1 ± 6.5 years, mean body mass = 73.8 ± 12.0 kg, mean height = 167.8 ± 12.0 cm]) from the Glaucoma Unit at Virgen de las Nieves University Hospital (Granada, Spain) and 17 age- and sex-matched healthy controls (7 men, 10 women: [mean age = 69.2 ± 5.9 years, mean body mass = 73.7 ± 13.7 kg, mean height = 163.8 ± 9.6 cm]). The sample size was determined by an a priori power

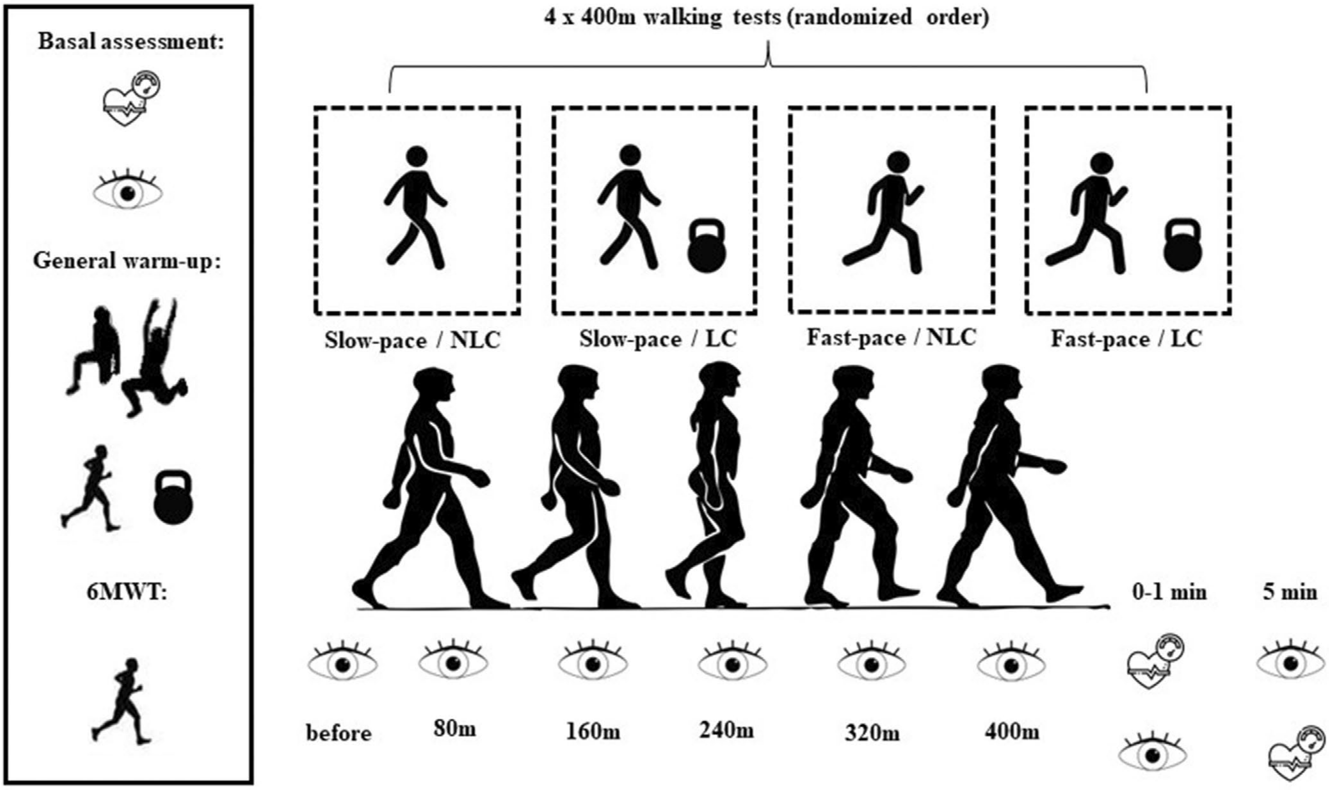

FIGURE 1 Schematic illustration of the experimental design. LC, load carriage; 6MWT, 6-min walk test; NLC, non-load carriage.

analysis using G*Power 3.1 software (psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower),[28] based on an analysis of variance (ANOVA) with within- and between-participant factors. Assuming an effect size (f) of 0.2, an α-level of 0.05 and a power of 0.90,[27] the required sample size was 34 participants (17 POAG, 17 controls). POAG patients were screened using the following inclusion criteria: (a) POAG diagnosis based on objective criteria such as glaucomatous alterations of the optic nerve head and visual field defects compatible with glaucoma, (b) having a sufficient level of mobility to perform low to moderate physical activity, (c) be free of other injuries or diseases that might prevent exercise performance, (d) receiving medical treatment with prostaglandin analogues or a combination of a prostaglandin analogue and a beta-blocker and (e) no history of surgical intervention for the treatment of glaucoma. Inclusion criteria for the control group were: (a) be free of any systemic or ocular disease, (b) have sufficient level of mobility to perform low to moderate physical activity, (c) be free of other injuries or diseases that discourage exercise performance and (d) between 60 and 80 years of age. Participants were instructed to refrain from caffeine intake and strenuous exercise before testing. This study followed the tenets of the Declaration of Helsinki and was approved by the local Ethical Committee of Biomedical Research.

Procedures

Upon arrival, participants were informed about the experimental procedures and signed the consent form to participate in the study. After 5 min of passive rest, IOP and blood pressure were measured. Subsequently, a standardised warm-up comprising 5 min of joint mobility and dynamic stretching, along with 5 min of comfortable-paced load carriage walking (the pace they usually use to walk down the street). The external load was determined subjectively during the warm-up to ensure a low to moderate effort level for the 400-m walk. Participants tested different weights during four laps of 40 m each. If they felt unable to complete 10 laps, the weight was reduced; otherwise, it was maintained or increased. After 3 min of rest, a 6-min walk test (6-MWT) was carried out in a 20-m-long corridor, walking back and forth at maximal effort to cover the greatest distance possible.[29] A researcher accompanied participants to ensure maximal effort and safety. The researcher simply followed the participant's pace and encouraged them to complete the maximum possible distance. The distance covered during the 6-MWT was recorded. Subsequently, the following equation was used to determine the duration of each 40-m lap during the fast-walking pace protocols: Lap duration (s) = 360 s × 400 m/6-MWT distance/10. This lap duration was multiplied by 0.6 to determine the duration of each 40-m lap to be completed during the slow-walking pace protocols.

Afterwards, participants rested for 5 min before the start of the 400-m walking protocol. This required completing 10 laps of 40 m, namely walking 20 m in a straight line, turning around 180° and coming 20 m back to the starting line.[27] Participants were always accompanied by the same researcher to set the pace of 100% or 60% of the 6-MWT, while another researcher remained at the starting line to conduct IOP and blood pressure measurements. A brief pause (5–7 s) was made every two laps (80 m) to measure IOP while participants remained in a standing position (holding the weight in the load carriage conditions).[27] For load carriage conditions, participants were carrying an identical kettlebell in each hand weighing 2.5, 4, 5 or 8 kg. The mean weights for the POAG and control groups were men: 5.7 ± 1.9 kg; women: 3.3 ± 0.8 kg and men: 6.1 ± 1.8 kg; women: 3.7 ± 0.6 kg, respectively.

IOP measurements were performed in the affected eye for POAG patients and in a randomly chosen eye for the controls. When both eyes of POAG patients were affected, the more severely affected eye, as indicated in clinical reports, was selected for measurements. IOP measurements were taken before exercise, during the 400-m walking test (after 80 m, 160 m, 240 m, 320 m and 400 m) and following 1 and 5 min of passive recovery after each walking test by the same experienced researcher. A portable rebound tonometer (Icare ic200, icare-world.com/) was used to measure IOP.[30] Six rapid consecutive IOP measurements were taken against the central cornea while the participants fixated on a distant target and subsequently averaged. Blood pressure (BP) was measured using an automatic digital wrist blood pressure monitor (M3 Intellisense, omronhealthcare.nl/) both before exercise and after 1 and 5 min of passive recovery.[31] OPP was calculated from the IOP and BP values using the following formula: OPP = 2/3 mean arterial BP – IOP; where mean arterial pressure = diastolic BP + 1/3 (systolic BP – diastolic BP).[32]

Statistical analysis

Descriptive data are presented as mean ± standard deviation. The normal distribution of the data was checked with the Shapiro–Wilk test and the homogeneity of variances with Levene's test ($p > 0.05$). For the analysis of IOP changes, a repeated measures analysis of variance was carried out with the *walking pace* (fast, slow), *load* (load carriage, non-load carriage) and *point of measure* (pre-exercise, after 80, 160, 240, 320 and 400 m of walking and after 1 and 5 min of passive recovery) as the within-participant factors, whereas the *group* (POAG, control) was considered as the only between-participant factor. For the analysis of OPP, data were submitted to a repeated measures analysis of variance with the *walking pace* (fast, slow), *external load* (load carriage, non-load carriage) and *point of measure* (pre-exercise and after 1 and 5 min of passive recovery) as the within-participant factors and the *group* (POAG, control) as the only between-participant factor. The Greenhouse–Geisser correction was used when sphericity was violated and the Holm–Bonferroni procedure was applied when performing pairwise comparisons. Statistical significance was set at $p \leq 0.05$. The magnitude of the differences was reported by the Cohen's *d* effect size (*d*) and partial eta squared (η_p^2) for *T*- and *F*-tests, respectively. All statistical analyses were performed using the JASP statistics package (jasp-stats.org, version 0.18.3).

RESULTS

First, the between-group differences for baseline IOP and OPP assessments and fitness levels (i.e., 6-min walking test) were checked. No significant differences were found for baseline IOP ($t = -1.32$, $p = 0.20$, $d = -0.43$), OPP ($t = -1.53$, $p = 0.14$, $d = -0.52$) or fitness level ($t = 0.83$, $p = 0.41$, $d = 0.27$) between the POAG and control groups.

The four-way ANOVA applied for the analysis of IOP changes revealed statistical significance for the main effects of *load* ($F = 9.70$, $p = 0.004$, $\eta_p^2 = 0.21$) and *point of measure* ($F = 7.69$, $p < 0.001$, $\eta_p^2 = 0.17$). However, the main effect of *walking pace* ($F = 0.20$, $p = 0.66$, $\eta_p^2 = 0.01$) and *group* ($F = 0.98$, $p = 0.33$, $\eta_p^2 = 0.03$) did not reach statistical significance. The interaction effects *load × group* ($F = 6.13$, $p = 0.02$, $\eta_p^2 = 0.14$) and *load × point of measure* ($F = 9.90$, $p < 0.001$, $\eta_p^2 = 0.21$) showed statistical significance, whereas the rest of the interactions did not reach statistically significant differences ($p > 0.05$).

Two separate ANOVAs for each experimental group (i.e., POAG and controls) were carried out. For POAG patients, there were no statistically significant differences for any of the three main effects (*walking pace*: $F = 0.01$, $p = 0.95$; *load*: $F = 0.16$, $p = 0.69$ and *point of measure*: $F = 1.96$, $p = 0.14$) and significance was only reached for the interaction *load × point of measure* ($F = 4.36$, $p < 0.001$, $\eta_p^2 = 0.18$). Regarding the control group, statistically significant differences were obtained for the main effects of *load* ($F = 24.62$, $p < 0.001$, $\eta_p^2 = 0.59$) and *point of measure* ($F = 7.65$, $p < 0.001$, $\eta_p^2 = 0.31$) and the interaction *load × point of measure* ($F = 6.25$, $p < 0.001$, $\eta_p^2 = 0.27$). The main effect of *walking pace* ($F = 0.20$, $p = 0.66$) and the rest of the interactions (all *p*-values >0.05) did not reach statistical significance. Post hoc analyses showed a significant IOP rise during the execution of the walking test in the control group, with higher IOP values obtained in the measurements taken at 160 m (mean difference = 2.1 ± 2.7; corrected *p*-value = 0.002, $d = 0.97$), 240 m (mean difference = 1.9 ± 3.2; corrected *p*-value = 0.006, $d = 0.89$), 320 m (mean difference = 1.9 ± 2.9; corrected *p*-value = 0.007, $d = 0.87$) and 400 m (mean difference = 1.8 ± 3.2; corrected *p*-value = 0.03, $d = 0.78$) in comparison with the before exercise IOP measurement (Figure 2).

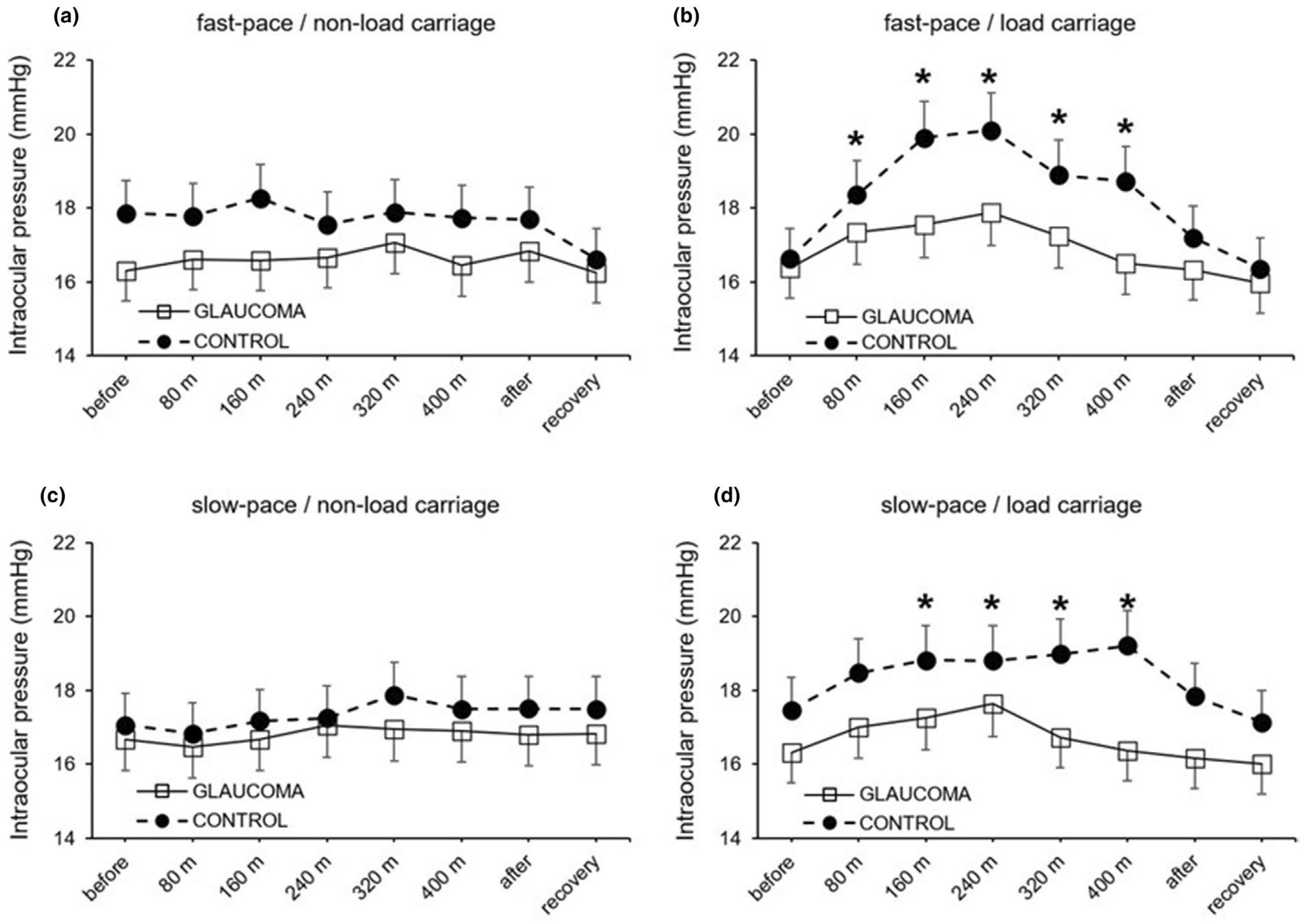

FIGURE 2 Effect of walking at two different paces on intraocular pressure, with and without carrying external loads. Error bars represent the 95% confidence intervals. * Statistically significant differences ($p<0.05$) in comparison with the pre-exercise measurement for the control group.

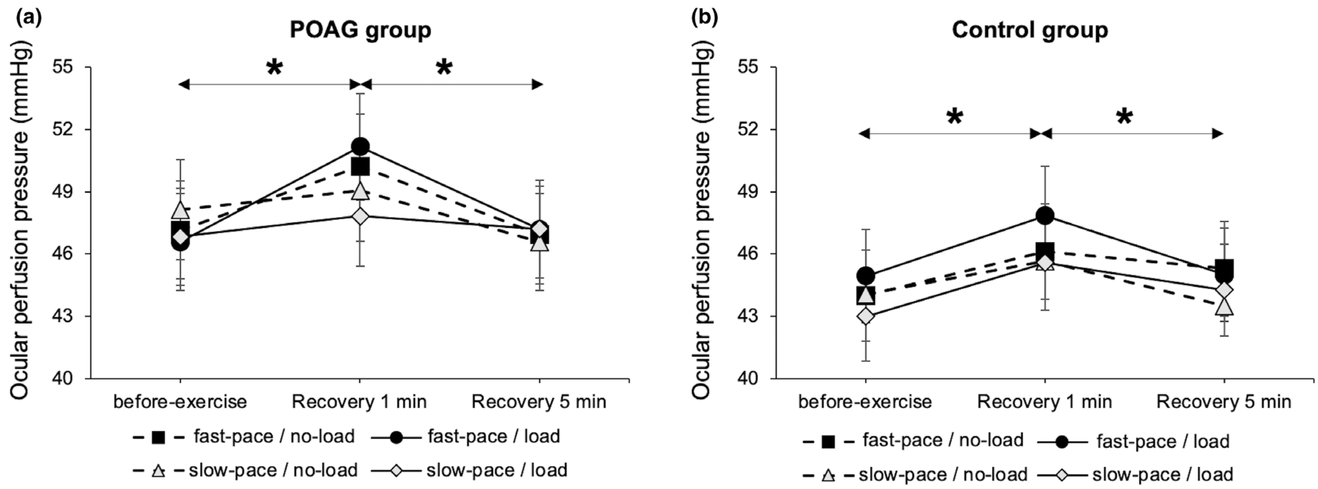

FIGURE 3 Effects of walking at two different paces on ocular perfusion pressure, with and without carrying external loads in the primary open-angle glaucoma (POAG; Panel a) and control (Panel b) groups. Error bars represent the 95% confidence intervals. *Statistically significant differences ($p<0.05$) between two points of measurement.

The analysis of OPP changes revealed statistically significant differences for the main effects of *walking pace* ($F=4.15$, $p=0.049$, $\eta_p^2=0.11$) and *point of measure* ($F=13.50$, $p<0.001$, $\eta_p^2=0.28$), whereas the factors *external load* ($F=0.04$, $p=0.86$) and *group* ($F=1.27$, $p=0.27$) did not reach statistical significance. For its part, none of the interactions showed statistical significance (all p-values >0.15). As shown in Figure 3, there was an OPP increase after exercise (before exercise vs. 1 min of passive recovery: mean difference = 2.3 ± 5.5; $p < 0.001$, $d = 0.78$), with OPP values recovering to pre-exercise levels after 5 min of passive recovery (before-exercise comparison: mean difference = 0.2 ± 5.4; $p = 0.74$; 1 min of passive recovery: mean difference = −2.1 ± 5.1; $p < 0.001$, $d = 0.72$). Also, higher OPP values were obtained in the fast- versus slow-walking pace; however, OPP was independent of the external load used or the group (i.e., POAG vs. controls).

DISCUSSION

This study aimed to assess the acute IOP and OPP responses to low-intensity endurance exercise at two different walking paces, both with and without carrying external loads in POAG patients and age- and sex-matched controls. A stable IOP was observed during the execution of low-intensity endurance exercise in POAG patients whereas a moderate IOP increase was noted in the control group. IOP levels were higher when carrying external loads during the walking test, but the walking pace used did not affect the IOP significantly. Regarding OPP, both groups experienced an OPP increase after exercise, although these changes returned to pre-exercise levels within 5 min of passive recovery. Taken together, this study supports the use of low-intensity endurance exercise, while limiting the use of external loads, as a safe training strategy for POAG patients.

In agreement with recent findings, stable IOP was recorded during the execution of low-intensity endurance exercise in POAG patients.[27] This supports the notion that endurance exercise could be a desirable choice to improve fitness level in POAG patients, since fitness levels have been negatively associated with glaucoma progression.[8] While physical exercise is known to promote numerous health benefits, it must be prescribed carefully to maximise its positive effects.[33] Indeed, a brisk walking pace has been shown to promote better health outcomes.[34] The present results show that IOP levels in POAG patients are stable regardless of walking pace. Specifically, POAG patients exhibited very similar IOP behaviour during the 400-m walking test in the slow- and fast-paced conditions performed without the use of external loads (mean difference of 0.12 mmHg). Thus, POAG patients should be advised to walk at fast velocities to maximise their protective effect on glaucoma progression and other health conditions.

A heightened IOP response was found with the use of external loads during the walking test in both groups. Although these differences were higher for the control (mean difference of 1.44 mmHg) than the POAG (i.e., mean difference of 0.41 mmHg) group, the rise observed in this study is clinically modest. These findings are in accordance with Vera et al.[16] and Baser et al.,[35] who found a significant rise in IOP when holding weights, and these effects have been linked to an increase in intraabdominal and intracranial pressure.[36,37] As depicted in Figure 2, IOP behaviour during the walking protocols with load carriage was less stable than in the non-load carriage conditions for the POAG and control groups, with an average of 19% higher variability (17% and 21% for the POAG and control groups, respectively). Previous work has indicated that IOP fluctuations should be avoided as much as possible for the optimal prevention and management of glaucoma.[38] Therefore, the use of external loads during low-intensity endurance exercise appeared to have a detrimental effect on IOP levels and should be discouraged in glaucoma patients or those deemed at risk.

Studies conducted in healthy young individuals have consistently reported that low-intensity endurance exercise lowers IOP.[10,11,13,14,39] The results of the present study showed that the controls experienced a moderate increase in IOP during the 400-m walking test, whereas the POAG patients maintained stable IOP levels during the execution of the exercise protocol. For the control group, the discrepancy between the experimental sample (elderly subjects: age = 69.2 ± 5.9 years) and healthy young adults can be explained by differences in fitness level, which have demonstrated to be an important modulator of IOP behaviour during exercise.[13] In addition, aqueous humour outflow facility is reduced with ageing,[40] and thus, regulatory IOP functioning in younger and older people cannot be compared. Somewhat surprisingly, POAG patients showed a more stable IOP when performing the walking protocol than the age- and sex-matched controls, who had a similar fitness level. However, this result could be attributed to the effectiveness of the eye drops used to regulate the altered outflow facility in this cohort (all of the POAG patients included here were undergoing treatment with prostaglandin analogues or a combination of a prostaglandin analogue and beta-blockers), thus modulating the effects of physical activity on IOP. It is well known that active first-line drugs are effective in reducing and stabilising IOP levels, with prostaglandins being the most efficacious agents.[41,42] Future studies are required to investigate IOP behaviour during low-intensity endurance exercise in untreated POAG patients or those receiving a different treatment option (e.g., laser or incisional surgery).

Although the elevation of IOP is recognised as the main risk factor for glaucoma development, vascular factors also play a key role in glaucoma pathogenesis.[43] Remarkably, individuals with lower OPP levels seem to have a higher risk of developing glaucoma and a faster disease progression.[6] In this study, low-intensity endurance exercise induced an increase in OPP in both POAG patients and healthy controls (average increment for the POAG and control groups was 2.39 mmHg and 2.29 mmHg, respectively) with this change being heightened in the fast-paced (average increment = 3.17 mmHg) compared with the slow-paced condition (average increment = 1.51 mmHg). In line with these findings, recent investigations have found an acute increase in ocular blood flow after endurance exercise in

POAG patients.[44,45] Additionally, evidence from a correlational study revealed that physically active individuals have a reduced risk of low OPP, suggesting the potential benefits of physical exercise for reducing the risk of POAG.[9] In summary, endurance exercise caused a transient increase in OPP in elderly subjects, including POAG patients and healthy controls, which supports the positive effect of physical exercise on glaucoma prevention and management. Therefore, both eye care providers and sport science specialists should encourage glaucoma patients or those at risk of the disease to perform endurance exercise such as walking, preferably using a fast pace, due to the positive effects on ocular blood flow.

The current study provides valuable insights into the most appropriate exercise-based strategies for glaucoma management, showing that low-intensity endurance exercise is a safe and desirable option to improve fitness level in patients with POAG. However, the following limitations must be considered. First, a low-intensity endurance exercise (400-m walking task) was chosen, and the findings cannot necessarily be extrapolated to other types of exercise. Numerous investigations have indicated that resistance training promotes important health benefits,[46,47] and the effects of this form of exercise on glaucoma prevention and management are worthy of further investigation. Second, fitness level is an important modulator of the IOP and OPP response to exercise.[13] Future studies with larger samples should assess the mediating effect of fitness level on the current findings. Third, as discussed previously, the experimental sample was formed of pharmacologically treated POAG patients, and it is known that the functioning of the aqueous humour outflow system varies with the type of medication and glaucoma.[20,21] Therefore, the external validity of the current outcomes in other types of glaucoma or in individuals using different treatment options should be investigated. Fourth, the weight for the load carriage condition was determined based on the subject's subjective performance capacity. Lastly, this study only examined the acute effects of exercise on IOP and OPP. The development of randomised clinical trials to determine the long-term effects of different supervised exercise programmes on glaucoma prevention and management would be valuable.

CONCLUSION

When walking at slow and fast velocities, IOP was mostly stable in patients with POAG. However, carrying external loads during walking was associated with higher IOP levels, and although the rise was clinically modest, it should be discouraged in POAG patients. Additionally, there was a moderate rise in OPP after walking, and interestingly, this effect was heightened when adopting a fast-walking pace. These findings suggest that low-intensity endurance exercise is a safe strategy to improve fitness level in patients with POAG.

AUTHOR CONTRIBUTIONS

María Dolores Morenas-Aguilar: Data curation (lead); formal analysis (supporting); methodology (equal); writing – original draft (lead). **Cristina González Hernández:** Data curation (supporting). **Sara Chacón-Ventura:** Data curation (supporting). **Santiago Ortiz-Perez:** Conceptualization (equal); investigation (supporting). **Juan Francisco Ramos-López:** Conceptualization (equal); methodology (equal); project administration (equal); supervision (lead). **Amador García-Ramos:** Funding acquisition (equal); methodology (equal); supervision (lead); writing – review and editing (equal). **Jesús Vera:** Conceptualization (lead); formal analysis (lead); funding acquisition (equal); methodology (equal); project administration (equal); supervision (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

All data are available upon request from the author.

CONSENT

All patients signed the informed consent form.

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