TESIS DOCTORAL INTERNACIONAL

Physical activity as an adjuvant strategy to pharmacological treatment of glaucoma

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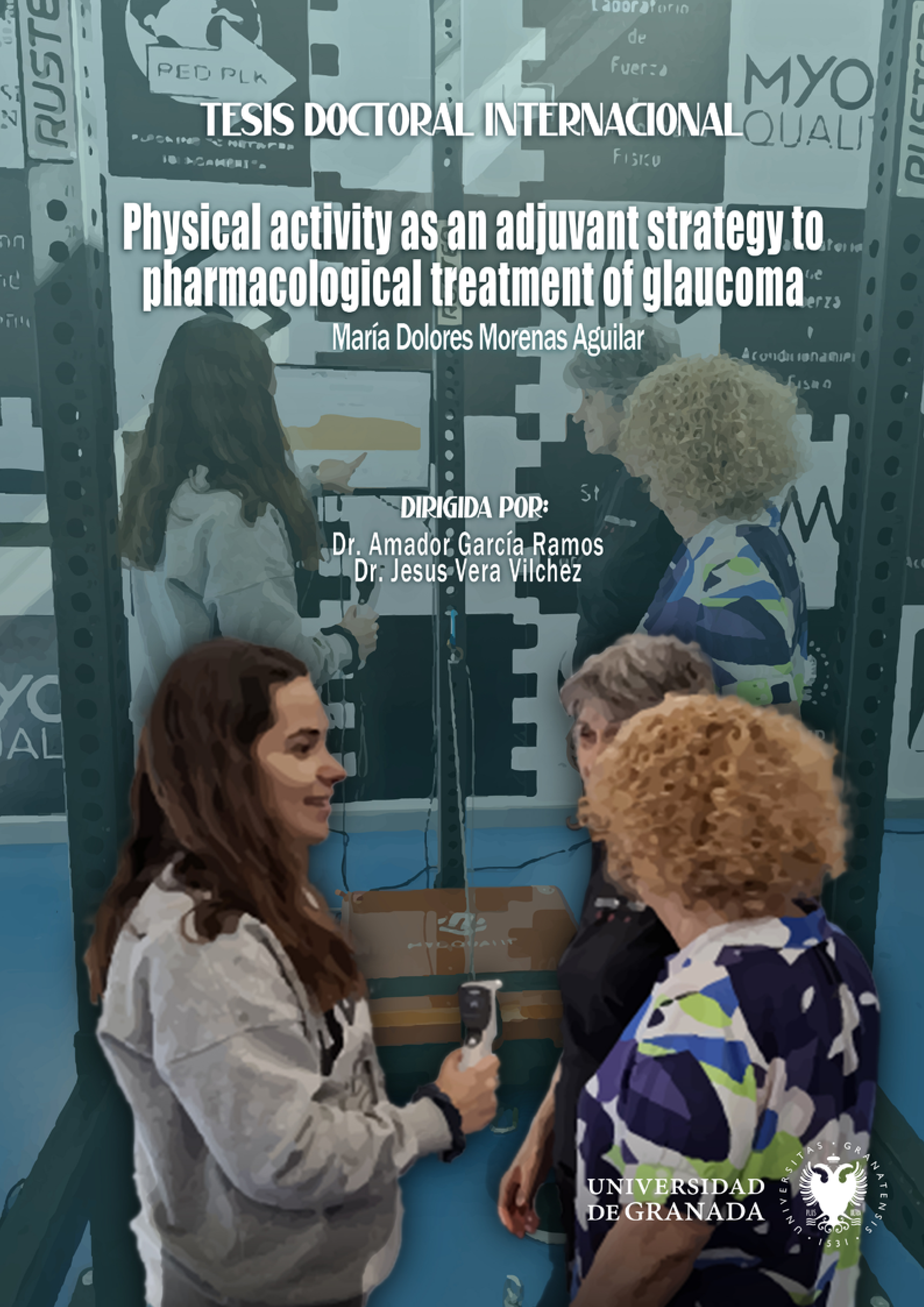

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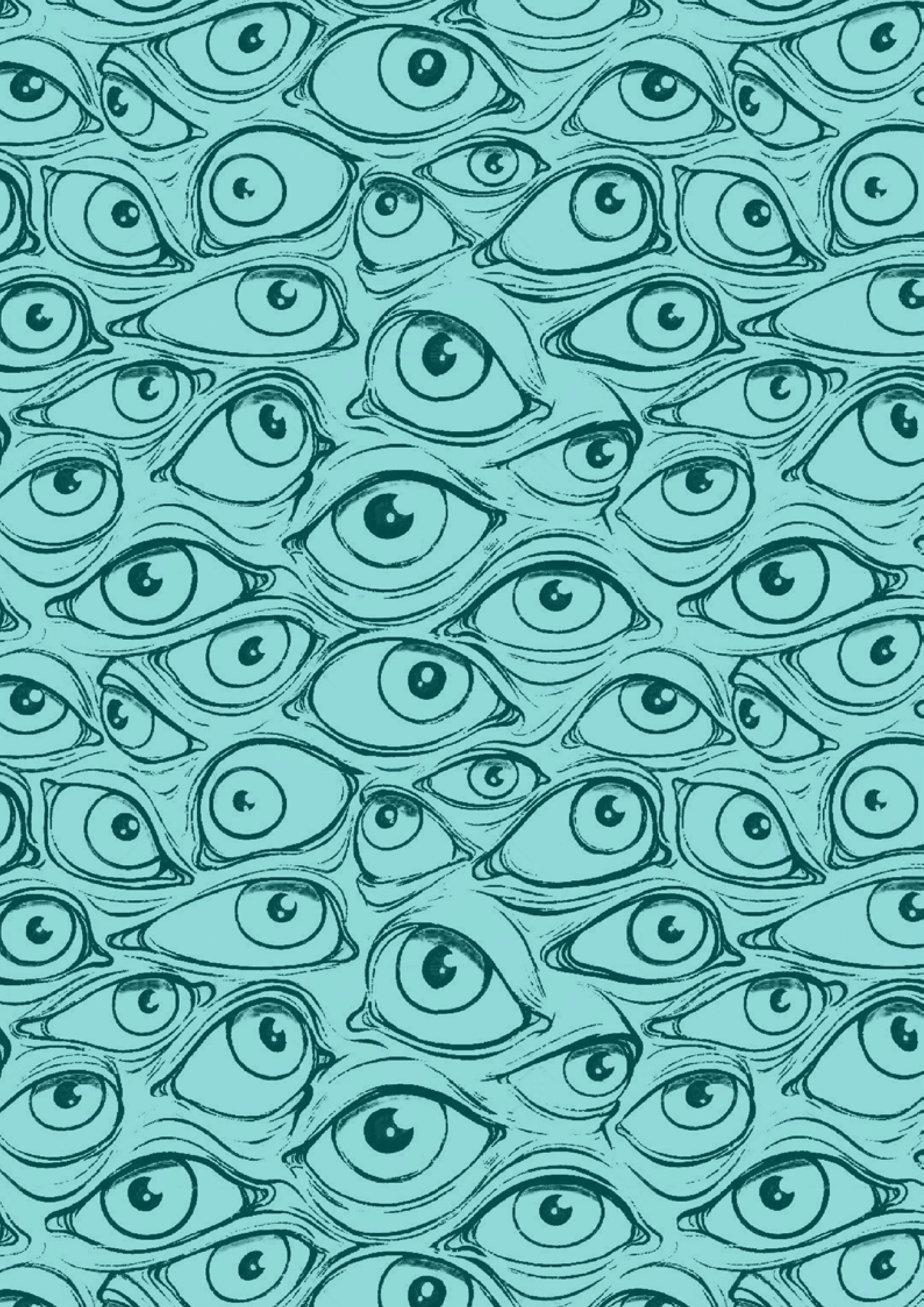

TESIS DOCTORAL INTERNACIONAL

ACTIVIDAD FÍSICA COMO ESTRATEGIA COADYUVANTE AL TRATAMIENTO FARMACOLÓGICO DEL GLAUCOMA

Physical activity as an adjuvant strategy to pharmacological treatment of glaucoma

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A mis padres, cerca o lejos, los promotores de todos mis éxitos.

En los días en que la crítica te picotee y las tormentas oscurezcan tu camino, recuerda al águila: no responde a los cuervos, ni huye del viento, simplemente se eleva. Que tu corazón tenga la fuerza para volar tan alto que ni el ruido ni la tormenta puedan alcanzarte.

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1. LIST OF FIGURES AND TABLES

2. LIST OF STUDIES

The present doctoral thesis is composed of the following studies:

I. Vera, J., **Morenas-Aguilar, M. D.,** & García-Ramos, A. (2025). Evidence-Based Exercise Recommendations for the Reduction and Stabilization of Intraocular Pressure: A Practical Guide for Eye Care and Sport Specialists. Applied Sciences (2076-3417), 15(3). *Status: Published.*

II. **Morenas-Aguilar, M. D.,** González-Hernández, C., Chacón-Ventura, S., Ortiz-Perez, S., Ramos-López, J. F., García-Ramos, A., Vera, J. Intraocular pressure and ocular perfusion pressure responses during low-intensity endurance exercise in primary-open angle glaucoma patients vs. age- and sex-matched controls: Influence of walking pace and external load. Ophthalmic and Physiological Optics. *Status: Accepted.*

III. **Morenas-Aguilar, M. D.,** González-Hernández, C., Marcos-Frutos, D., Miras-Moreno, S., López-Gómez, M. J., García-Ramos, A., Vera, J. Acute intraocular pressure responses changes during dynamic resistance training in primary open-angle glaucoma patients and age-matched controls. Graefe's Archive for Clinical and Experimental Ophthalmology. *Status: Published.*

IV. **Morenas-Aguilar, M. D.,** González-Hernández, C., Marcos-Frutos, D., Koulieris, G., Ramos-López, J. F., García-Ramos, A., Vera, J. Acute intraocular pressure changes during isometric exercise in primary-open angle glaucoma patients: The influence of exercise type and intensity. European Journal of Applied Physiology. *Status: Under review.*

3. LIST OF SCHOLARSHIPS

I. **Research stay** at University of Jyväskylä, Jyväskylä (Finland) supported by the program "Convocatoria de ayudas de movilidad internacional de personal con fines de formación para el curso académico 2023/2024". From 10th to 14th of June, 2024.

II. **Research stay** at Universidad de la Frontera, Temuco (Chile) supported by the program "Ayudas para Realizar Estancias Breves en Centros de Investigación Nacionales y Extranjeros del Plan Propio de Investigación de la Universidad de Granada". The international mention was obtained through this stay. From August to October 2024.

III. **Principal investigator** in the Project "Efecto de la suplementación con cacao con alto contenido en compuestos fenólicos durante la realización de ejercicio físico en pacientes con glaucoma sobre la salud ocular y el estrés oxidativo" supported by "Proyectos de Investigación Precompetitivos para Jóvenes Investigadores – Modalidad B del Plan Propio de Investigación 2024".

IV. **Research stay** at University of Szczecin, Szczecin (Poland) supported by the program "Programa de movilidad Prácticas Erasmus+ para el curso académico 2024/2025". From May to June 2025.

4. ABBREVIATIONS

6-MWT: six-minute walk test.

ANOVA: analysis of variance.

BCAAs: branched-chain amino acids.

BFR: blood flow restriction.

BP: blood pressure.

FEMD: functional electromechanical dynamometer.

HIIT: high-intensity interval training.

IOP: intraocular pressure

IPF: isometric peak force.

mmHg: millimeter of mercury.

OPP: ocular perfusion pressure

η^2_p: partial eta squared.

POAG: primary open-angle glaucoma

RM: repetition maximum.

5. ABSTRACT/RESUMEN

Introduction: Glaucoma is the leading cause of irreversible blindness worldwide, and the only proven effective treatment is the reduction and stabilization of intraocular pressure (IOP). However, modifiable lifestyle factors, such as physical activity, may play a complementary role in its management. Evidence suggests that different types of exercise can modulate both intraocular pressure and ocular perfusion pressure (OPP), although the mechanisms involved and the specific response in patients with primary open-angle glaucoma (POAG) have not been fully clarified. In the absence of evidence-based specific guidelines, this thesis explores the impact of physical exercise as a complementary strategy to pharmacological treatment for glaucoma.

Objective: To provide evidence-based guidelines on the most effective training strategies to improve physical fitness without compromising—and potentially improving—ocular health in patients with primary open-angle glaucoma. Specifically, the aims are: (i) to synthesize existing evidence and generate practical recommendations for exercise and eye care professionals; (ii) to analyze the acute responses of intraocular pressure and ocular perfusion pressure during low-intensity endurance exercise; (iii) to assess the influence of dynamic resistance exercise on intraocular and ocular perfusion pressure; and (iv) to study the response of intraocular and ocular perfusion pressure to isometric resistance exercises considering the intensity of the effort.

Methods: To address these objectives, the thesis comprises four studies: a narrative literature review and three randomized crossover experimental studies. The first phase consisted of a patient-centered clinical review, synthesizing available evidence on the effects of physical exercise on intraocular pressure. In the endurance exercise study, 21 POAG patients and 17 controls performed 400-meter walking trials at different paces (slow/fast), with and without external loads, to assess their impact on IOP and OPP. In the dynamic resistance study, IOP and OPP responses were measured during leg extension and biceps curl exercises performed at low and moderate intensities in 26 POAG patients and 18 controls. The isometric resistance study included 25 POAG patients and 19 controls, analyzing IOP and OPP behavior during isometric contractions of the biceps curl and mid-thigh pull at different intensities.

Results: The review demonstrated that low-to-moderate intensity endurance exercise can acutely reduce IOP, whereas resistance exercises tend to increase it. POAG patients showed stable IOP behavior while walking at both slow and fast paces, while OPP increased after walking, particularly at faster speeds. Our data showed a progressive increase in IOP throughout the sets of leg extension and biceps curl exercises performed at moderate intensity, with POAG patients exhibiting a significantly smaller IOP rise compared to controls, and no significant differences in OPP. Isometric resistance exercises caused a progressive IOP increase that returned rapidly to baseline post-exercise, along with a slight post-exercise increase in OPP. The IOP increase during the mid-thigh pull at moderate intensity was significantly lower in POAG patients compared to the control group.

Conclusion: The findings of this thesis support the use of physical exercise as a safe and potentially beneficial complementary strategy in the management of glaucoma. Low-intensity endurance exercise appears to be particularly safe, while resistance training—especially isometric—should be carefully prescribed based on intensity and individual patient profiles. This thesis provides a valuable scientific foundation for the development of clinical guidelines for exercise prescription in patients with glaucoma.

Introducción: El glaucoma es la principal causa de ceguera irreversible a nivel mundial y su único tratamiento eficaz demostrado consiste en la reducción y estabilización de la presión intraocular. Sin embargo, existen factores modificables del estilo de vida, como la actividad física, que podrían desempeñar un papel coadyuvante en su manejo. La evidencia sugiere que distintos tipos de ejercicio pueden modular la presión intraocular y la presión de perfusión ocular, aunque los mecanismos involucrados y la respuesta específica en pacientes con glaucoma de ángulo abierto primario no han sido completamente aclarados. Ante la falta de guías específicas basadas en evidencia, esta tesis explora el impacto del ejercicio físico como estrategia complementaria al tratamiento farmacológico del glaucoma.

Objetivo: Proporcionar directrices basadas en la evidencia científica sobre las estrategias de entrenamiento más eficaces para aumentar la condición física sin comprometer o incluso mejorando la salud ocular en pacientes con glaucoma primario de ángulo abierto. Específicamente, se pretende: i) sintetizar la evidencia existente y generar recomendaciones prácticas para profesionales del deporte y de la salud visual; ii) analizar las respuestas agudas de la presión intraocular y la presión de perfusión ocular durante el ejercicio aeróbico de baja intensidad; iii) evaluar la influencia del ejercicio de fuerza dinámico sobre la presión intraocular y la presión de perfusión ocular; y iv) estudiar la presión intraocular y la presión de perfusión ocular a ejercicios de fuerza isométricos considerando la intensidad del esfuerzo.

Metodología: Para responder al objetivo, la tesis se compone de cuatro estudios: una revisión narrativa de la literatura y tres estudios experimentales con diseño cruzado y aleatorizado. La primera fase consistió en una revisión clínica centrada en el paciente, sintetizando la evidencia disponible sobre los efectos del ejercicio físico sobre la presión intraocular. En el estudio de ejercicio aeróbico, 21 pacientes con glaucoma primario de ángulo abierto y 17 controles realizaron caminatas de 400 m a diferentes ritmos (lento/rápido), con y sin cargas externas, analizando su efecto en la presión intraocular y la presión de perfusión ocular. En el estudio de fuerza dinámica, se midió la respuesta de la presión intraocular y la presión de perfusión ocular durante ejercicios de extensión de piernas y curl de bíceps realizados a intensidades baja y moderada con 26 pacientes con glaucoma primario de ángulo abierto y 18 controles. El estudio de fuerza isométrica contó con 25 pacientes con glaucoma primario de ángulo abierto y 19 controles, analizando el comportamiento de la presión intraocular y la presión de perfusión ocular durante contracciones isométricas de curl de bíceps y tirón de muslo medio a distintas intensidades.

Resultados: La revisión evidenció que el ejercicio aeróbico a intensidades baja-moderada puede reducir agudamente la presión intraocular, mientras que los ejercicios de fuerza tienden a aumentarla. Los pacientes con glaucoma primario de ángulo abierto muestran un comportamiento estable de la presión intraocular al caminar a velocidades lentas y rápidas, mientras que se observa un aumento de la presión de perfusión ocular después de la caminata, siendo mayor al caminar a un ritmo rápido. Nuestros datos muestran un aumento progresivo de la presión intraocular a lo largo de las series de extensión de piernas y curl de bíceps a intensidad moderada, destacando un incremento menor en los pacientes con glaucoma primario de ángulo abierto en comparación con los controles, mientras que no se encuentran diferencias en la presión de perfusión ocular. Los ejercicios de fuerza isométrica provocaron un aumento progresivo de la presión intraocular volviendo rápidamente a los valores basales tras el ejercicio, mientras que provocaron un leve aumento de la presión de perfusión ocular después del ejercicio. El aumento de la presión intraocular fue significativamente menor en los pacientes con glaucoma primario de ángulo abierto durante el ejercicio de tirón de muslo medio a intensidad moderada en comparación con el grupo control.

Conclusión: Los hallazgos de esta tesis respaldan el uso de ejercicio físico como una estrategia segura y potencialmente beneficiosa en el tratamiento complementario del glaucoma. El ejercicio aeróbico de baja intensidad representa una opción segura, mientras que el ejercicio de fuerza, especialmente el isométrico, debe ser cuidadosamente dosificado en función de la intensidad y el perfil del paciente. Esta tesis ofrece una base científica útil para el desarrollo de guías clínicas de prescripción de ejercicio físico adaptadas a pacientes con glaucoma.

6. INTRODUCTION AND KEY CONCEPTS

In recent years, the evolution of sports science has had a significant impact on contemporary society. An increasing proportion of the population engages in physical activity with objectives ranging from aesthetic enhancement, improved performance and quality of life. Notably, this latter goal generates a great benefit in global public health, and reinforces the relevance of physical activity within the national public health policies (Volf et al. 2022). Research on the role of physical activity and different pathologies focuses the attention of sports scientists, physicians, physiotherapists, and/or nutritionists (Bull 2018). Multidisciplinary research among these professionals is essential to effectively promote physical activity as an adjuvant strategy for both the prevention and management chronic diseases (Hall et al. 2012).

The overwhelming evidence supports the use of physical activity to reduce the risk for premature mortality and chronic disease (Warburton and Bredin 2017). Regular physical exercise is associated with a reduced risk of cardiovascular disease and cancer, as well as improvements in musculoskeletal health brain-related function (neurological condition, mental health and cognitive function). In the cardiovascular domain, exercise improves endothelial function, reduces blood pressure, enhances lipid profiles, and promotes insulin sensitivity (Green et al. 2017). In the context of cancer, physical activity modulates systemic inflammation, boosts immune surveillance, and regulates hormone levels (Pedersen and Saltin 2015). Regarding musculoskeletal health, resistance exercises are effective in preserving bone mineral density and muscle mass, thereby decreasing the risk of osteoporosis and sarcopenia associated with frailty and falls in older adults (Hurley et al. 2011; Indrakumar and Silva 2024). Additionally, regular physical activity has profound benefits for brain health, including enhanced cerebral blood flow, neurogenesis, and synaptic plasticity, reducing the risk of neurodegenerative diseases and improving mood and psychological well-being (Paillard et al. 2015; Gallaway et al. 2017). Therefore, recent guidelines have spread a common message promoting the regular participation in moderate-to-vigorous physical activities (Bull et al. 2020). However, it is important to establish a dose–response relationship between physical activity and health outcomes, which may vary depending on the specific disease (Warburton and Bredin 2017).

Within the broader context of chronic diseases, ocular health may also benefit from regular physical exercise by contributing to the reduction of frailty in affected populations. Glaucoma, as the leading cause of irreversible blindness worldwide and a significant public health concern, warrants particular attention from the scientific community (Weinreb et al. 2014). Accumulated evidence indicates that glaucoma negatively impacts both psychological well-being and participation in daily physical activity (Ramulu et al. 2012; Huang et al. 2020). Notably, certain frailty indices incorporate the presence of glaucoma as a key marker in assessing individual vulnerability (McMonnies 2016). Despite being frequently recommended, physical exercise lacks specific evidence-based guidelines for glaucoma patients, whose vulnerability highlights the need to promote safe and lifelong activity to counteract inactivity (Risner et al. 2009; Loprinzi et al. 2013).

Chasing Glaucoma

Glaucoma is a chronic optic neuropathy characterized by progressive degeneration of retinal ganglion cells, leading to structural and functional damage to the optic nerve and, ultimately, irreversible vision loss. Recent estimates project that, by 2040, the number of people suffering from glaucoma will reach 111.8 million worldwide, highlighting the pressing need for effective strategies for the prevention, early diagnosis, and management of this condition (Tham et al. 2014). While glaucoma encompasses a range of subtypes, including primary open-angle glaucoma (POAG) and angle-closure glaucoma, they share common features such as optic nerve damage and associated visual field defects (Prum et al. 2016). POAG is the most prevalent form of glaucoma and is associated with several high-risk factors, including advanced age, ocular hypertension, myopia, African or Latino ethnicity, and a family history of glaucoma (Prum et al. 2016).

Glaucoma progression is usually slowly, remaining asymptomatic until the disease severity is important, with a huge percentage of patients being unaware of their diagnosis and treatment (Kang and Tanna 2021). Evidence suggests that up to 30–50% of retinal ganglion cells may degenerate before glaucomatous defects become detectable through conventional visual field assessments (Weinreb et al. 2014). When the disease progresses the visual field loss swift from blurred areas to dark or foggy vision to total loss of light perception (Pickett et al. 1985). Topical medications and laser trabeculoplasty constitute the first-line treatment options; nevertheless, in cases of inadequate response, incisional surgical interventions may be considered. Due to the substantial risk of adverse events associated with these procedures, they are generally reserved for patients at high risk of symptomatic disease progression, highlighting the need to explore alternative or complementary therapeutic strategies (Weinreb et al. 2014).

The pathophysiology of glaucoma involves progressive enlargement of the optic cup due to damage to the lamina cribrosa and the loss of retinal ganglion cell axons (**Figures 1 & 2**) (Kang and Tanna 2021). This is provoked by the intraocular pressure (IOP) increase, reducing the metabolic transport of retinal ganglion cells axons, resulting in apoptosis and determining the optic nerve damage. The IOP increase is determined by the accumulation of aqueous humour due to malfunction of aqueous humour outflow (**Figure 3**). Although much attention is focus on IOP control, insufficient optic nerve perfusion has been implicated as a contributing factor in the onset and progression of glaucoma (Leske 2009). A reduction in ocular perfusion pressure (OPP) levels has been identified as a risk factor for glaucoma. For clarity, essential terms and definitions related to glaucoma are summarized in **Table 1**.

Apart from medical treatment, lifestyle habits including caffeine intake, mental stress or physical activity have a significant role in IOP and OPP (Hecht et al. 2017). Specifically, higher levels of physical activity have been shown to contribute to better control of IOP and OPP, potentially reducing the prevalence of glaucoma (Vera et al. 2020a). However, most existing studies have been conducted in healthy individuals, limiting their applicability to clinical populations such as POAG patients. Furthermore, the physiological mechanisms underlying exercise-induced changes in IOP and OPP remain partially understood and appear to be influenced by multiple factors, including exercise type, intensity, and individual fitness level (Gracitelli et al. 2020; Vera et al. 2020f). A review of how IOP and OPP levels could be modified by physical activity will appear throughout the studies of this thesis.

Although exercise is commonly recommended for patients with glaucoma, specific evidence-based guidelines have yet to be established (Risner et al. 2009). Given the vulnerability of these individuals, the promotion of safe and effective forms of physical activity across their lifespan is important to avoid physical inactivity or unfavourable activity-related beliefs (Loprinzi et al. 2013). This doctoral thesis aims to integrate physical activity as an adjuvant to pharmacological treatment, aiming to enhance disease management and patient quality of life through an interdisciplinary approach.

KEY CONCEPTS

Aqueous humor	Produced by the ciliary body. Flows through the pupil from the posterior chamber into the anterior chamber. Plays a vital role in supporting the metabolic functions of the avascular tissues in the anterior segment of the eye.
Aqueous humor outflow	Takes place through the conventional and unconventional outflow, originated in the anterior chamber angle (Figure 3). Conventional outflow includes the trabecular meshwork and Schlemm canal. Unconventional outflow includes the uveal tissues. Increased resistance within the trabecular meshwork leads to elevated IOP despite the absence of visible obstruction.
Intraocular pressure	Pressure of the fluid inside the eye on its solid structures, such as the cornea or crystalline lens. Regulated by the balance of aqueous humor production, aqueous humor outflow, and episcleral venous pressure. Normal values in adults are between 10 and 21 mmHg.
Laser trabeculoplasty	Laser-based intervention targeting the trabecular meshwork to decrease outflow resistance and thereby lower IOP.
Ocular hypertension	IOP greater than 21 mmHg without clinical evidence of optic nerve head damage or visual field defects.
Ocular perfusion pressure	Net pressure gradient representing blood flow to the eye. Estimated by the difference between systemic blood pressure and IOP.
Optic disc	The part of the optic nerve seen at the back of the eye. Where the axons of the retinal ganglion cells leave the eye as the optic nerve. The cup is the depression in the middle of the optic disc. Optic disc cup is enlarge and with visible pores in glaucoma patients (Figures 1 & 2).
Primary open-angle glaucoma	The most common form of glaucoma. Caused by an increase in outflow resistance. Progressive IOP increase. High-risk patients include individuals with ocular hypertension and those presenting an optic nerve appearance indicative of potential glaucomatous damage. Clinical diagnosis is defined by structural damage to the optic disc or retinal nerve fiber layer, and/or functional impairment as evidenced by visual field defects
Tonometer	Used to estimate IOP by measuring the force required to applanate a defined area of the cornea, the degree of corneal indentation, or the deceleration of a probe upon contact with the corneal surface.
Topical medications	Decrease IOP by reducing aqueous humor production or improving outflow. Could be required 2 or more medications to achieve an adequate IOP reduction. Prostaglandin analogues (improve aqueous humor outflow) and β-blocker (reduce aqueous humor production) are the most frequently used medications.

Table 1. Key concepts for glaucoma

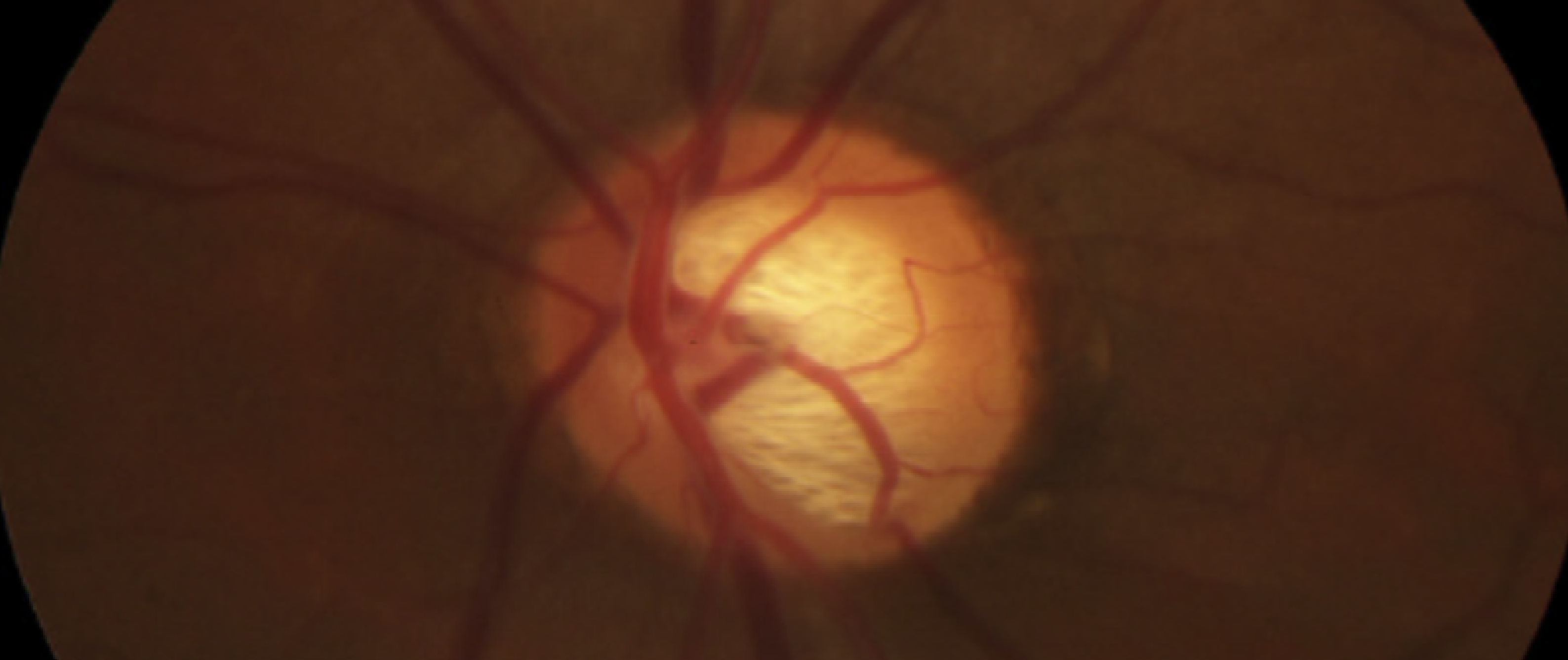


Figure 1. Glaucomatous optic disc cupping. Adapted from Kang and Tanna 2021.

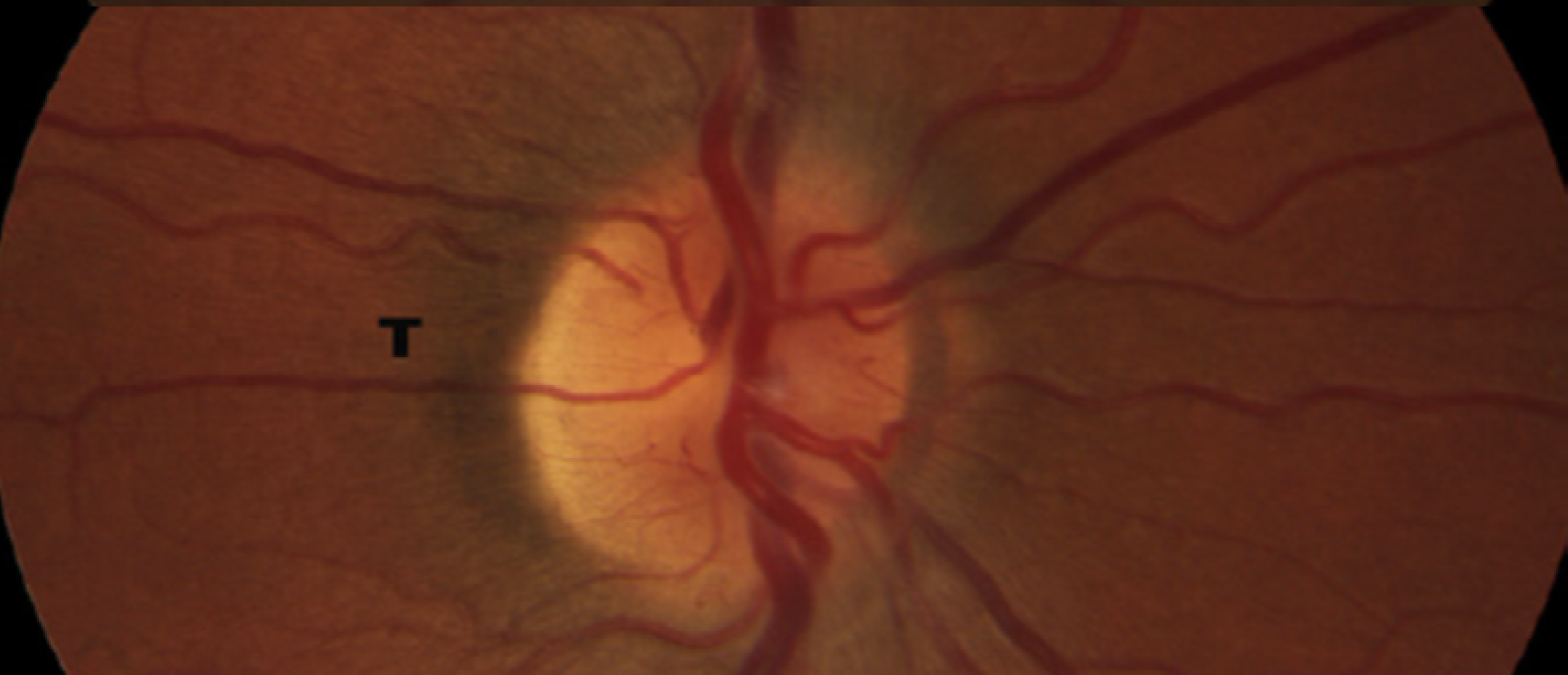


Figure 2. Healthy optic disc. Adapted from Kang and Tanna 2021.

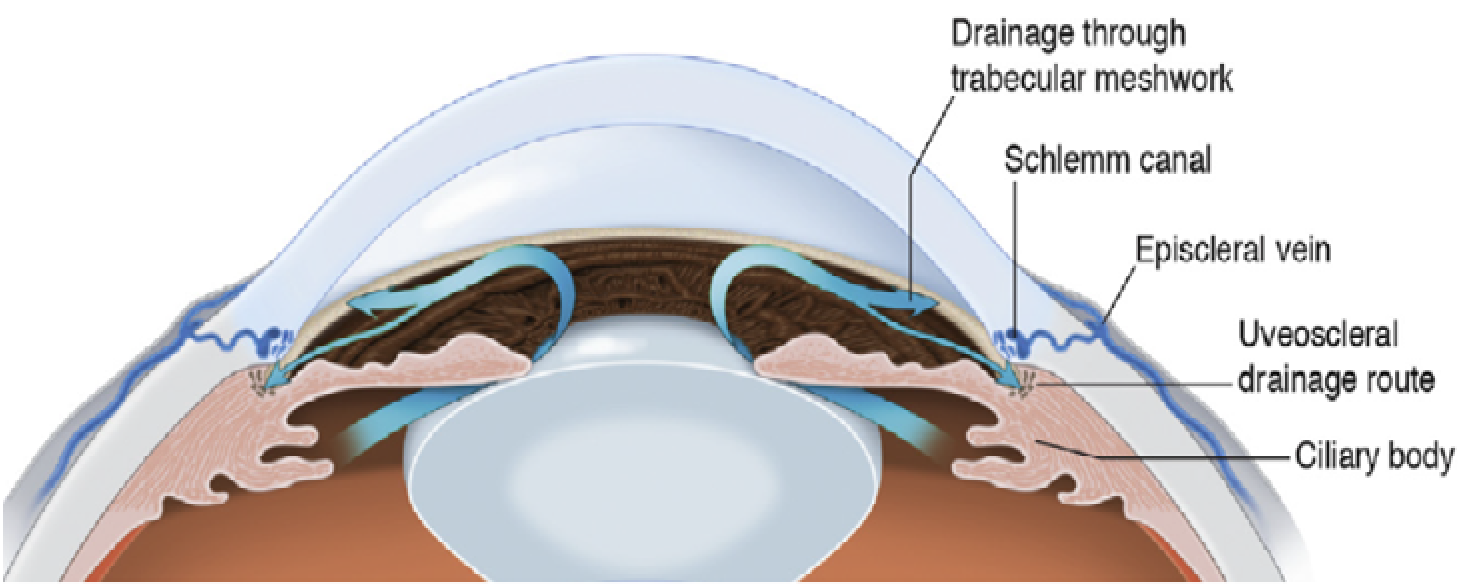


Figure 3. Arqueous humor outflow. Adapted from Kang and Tanna 2021.

7. OBJECTIVES/OBJETIVOS

General objective:

To provide research-based guidelines on the most effective training strategies to increase fitness without compromising or even improving ocular health in POAG patients.

In order to comply with the general objective, this doctoral thesis has been organized into four studies based on the following specific objectives:

Study I: *Evidence-Based Exercise Recommendations for the Reduction and Stabilization of Intraocular Pressure: A Practical Guide for Eye Care and Sport Specialists.*

Objective 1: to synthesize current evidence on the effects of physical exercise on IOP and their implications for glaucoma prevention and management.

Objective 2: to provide research-based guidelines to assist eye care specialists and sports science professionals in designing and implementing exercise strategies tailored to the needs of glaucoma patients or individuals at risk.

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

> ***Objective 3:*** 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 carrying external loads.
>
> ***Objective 4:*** to compare the IOP and OPP acute responses to low-intensity endurance exercise (400-m walking) between POAG patients and age- and sex-matched controls.

Study III: *Acute intraocular pressure responses changes during dynamic resistance training in primary open-angle glaucoma patients and age-matched controls.*

> ***Objective 5:*** to assess the IOP and OPP responses to dynamic lower- and upper-body resistance exercises.
>
> ***Objective 6:*** to compare the IOP and OPP responses between POAG patients and age-matched controls.
>
> ***Objective 7:*** to compare the IOP and OPP responses between lower- and upper-body exercises (leg extension vs. biceps curl).
> ***Objective 8:*** to compare the IOP and OPP responses when leg extension and biceps curl exercises are performed at low and moderate intensities.

Study IV: *Acute intraocular pressure changes during isometric exercise in primary-open angle glaucoma patients: The influence of exercise type and intensity.*

> ***Objective 9:*** to assess the effects of the type of isometric resistance exercise (mid-thigh pull and biceps curl) in POAG patients and age- and sex-matched controls.
>
> ***Objective 10:*** *t*o compare the intensity effects (low vs. moderate) on the IOP and OPP response during exercise and recovery in POAG patients and age- and sex-matched controls.

Objetivo general:

Proporcionar directrices basadas en la evidencia científica sobre las estrategias de entrenamiento más eficaces para aumentar la condición física sin comprometer o incluso mejorando la salud ocular en pacientes con glaucoma primario de ángulo abierto.

Con el propósito de dar cumplimiento al objetivo general, esta tesis doctoral se ha organizado en cuatro estudios basados en los siguientes objetivos específicos:

Estudio I: *Recomendaciones de ejercicio basadas en la evidencia para la reducción y estabilización de la presión intraocular: una guía práctica para especialistas en salud ocular y ciencias del deporte.*

Objectivo 1: Sintetizar la evidencia actual sobre los efectos del ejercicio físico en la presión intraocular y sus implicaciones para la prevención y el manejo del glaucoma.

Objectivo 2: Proporcionar directrices basadas en la investigación que ayuden a los especialistas en salud ocular y a los profesionales de las ciencias del deporte a diseñar e implementar estrategias de ejercicio adaptadas a las necesidades de personas con glaucoma o en riesgo de desarrollarlo.

Estudio II: *Respuestas de la presión intraocular y la presión de perfusión ocular durante ejercicio de resistencia de baja intensidad en pacientes con glaucoma de ángulo abierto primario vs. controles emparejados por edad y sexo: influencia del ritmo de marcha y la carga externa.*

Objectivo 3: Evaluar las respuestas agudas de la presión intraocular y de la presión de perfusión ocular al ejercicio de resistencia de baja intensidad (caminata de 400 m) realizado a dos ritmos de marcha diferentes, con y sin carga externa.

Objectivo 4: Comparar las respuestas agudas de la presión intraocular y la presión de perfusión ocular al ejercicio de resistencia de baja intensidad (caminata de 400 m) entre pacientes con glaucoma primario de ángulo abierto y controles emparejados por edad y sexo.

Estudio III: *Cambios agudos en la presión intraocular durante el entrenamiento de fuerza dinámico en pacientes con glaucoma de ángulo abierto primario y controles emparejados por edad.*

Objectivo 5: Evaluar las respuestas de la presión intraocular y la presión de perfusión ocular a ejercicios dinámicos de fuerza del tren inferior y superior.

Objectivo 6: Comparar las respuestas de la presión intraocular y la presión de perfusión ocular entre pacientes con glaucoma primario de ángulo abierto y controles emparejados por edad.

Objectivo 7: Comparar las respuestas de la presión intraocular y la presión de perfusión ocular entre ejercicios del tren inferior y superior (extensión de piernas vs. curl de bíceps).

Objectivo 8: Comparar las respuestas de la presión intraocular y la presión de perfusión ocular cuando los ejercicios de extensión de piernas y curl de bíceps se realizan a intensidades baja y moderada.

Estudio IV: *Cambios agudos en la presión intraocular durante el ejercicio isométrico en pacientes con glaucoma de ángulo abierto primario: influencia del tipo e intensidad del ejercicio.*

Objectivo 9: Evaluar los efectos del ejercicio de fuerza isométrico (tirón de muslo medio y curl de bíceps) en pacientes con glaucoma primario de ángulo abierto y controles emparejados por edad y sexo.

Objetivo 10: Comparar los efectos de la intensidad (baja vs. moderada) sobre la respuesta de la presión intraocular y la presión de perfusión ocular durante el ejercicio y la recuperación en pacientes con glaucoma primario de ángulo abierto y controles emparejados por edad y sexo.

CHAPTER 1

A PRACTICAL GUIDE FOR EYE CARE AND SPORT SPECIALISTS

Evidence-based exercise recommendations for reduction and stabilization of intraocular pressure: A practical guide for eye care and sport specialists

Jesús Vera, **María Dolores Morenas-Aguilar**, *Amador García-Ramos*

Brief overview

The principal goal of glaucoma management is to reduce and stabilize IOP, as it remains the only proven strategy to slow disease progression and preserve vision (Boland et al. 2013). Advances in pharmacological and surgical interventions, such as topical medications, selective laser trabeculoplasty, and minimally invasive glaucoma surgeries have substantially improved the standard of care for glaucoma patients (Conlon et al. 2017), with topical therapy and selective laser trabeculoplasty considered as the first-line treatment options (Gazzard et al. 2019). However, the increasing prevalence of glaucoma underscores the need for complementary approaches that extend beyond conventional treatments to address modifiable risk factors.

Recent years have witnessed growing interest in the potential influence of environmental and lifestyle factors, such as diet and physical activity, on the pathogenesis and progression of glaucoma (Elhusseiny and Aref 2025). Research suggests that modifiable behaviours may offer an adjunctive therapeutic benefit by providing neuroprotection to retinal ganglion cells and contributing to overall ocular health (Hecht et al. 2017). Among these factors, physical exercise has emerged as a promising area of investigation due to its well-documented systemic health benefits and its potential role in reducing IOP (Zhu et al. 2018; Perez et al. 2019; Fahmideh et al. 2022).

The regular practice of physical exercise is associated with numerous health benefits, including reduced risks of cardiovascular disease, cancer, osteoporosis, and fall-related injuries, as well as enhanced mental and cognitive function (Piercy et al. 2018). These positive effects extend to ocular health, with observational and retrospective studies indicating that individuals who engage in regular physical activity are less likely to develop glaucoma or experience its progression (Williams 2009; Yokota et al. 2016; Meier et al. 2018; Anderson 2019; Lee et al. 2019; Kawakami et al. 2020; Pan et al. 2020). Lee and colleagues (Lee et al. 2019) examined the link between physical activity levels and the rate of visual field loss in 141 patients with suspected or diagnosed glaucoma. They found that increased walking, more time spent in moderate-to-vigorous physical activity, and reduced sedentary behavior were associated with slower rates of visual field loss. This relationship may be mediated by the ability of physical exercise to induce short-term reductions in IOP, improve ocular blood flow, and exert neuroprotective effects on retinal ganglion cells (Zhu et al. 2018).

Despite these promising findings, the clinical application of exercise as an adjunctive strategy for glaucoma management remains underexplored. Notably, exercise prescription for glaucoma patients or at-risk individuals must be tailored to their specific health conditions to maximize benefits and minimize risks (Gildea et al. 2024). Collaboration between sports scientists and eye care professionals is essential to develop evidence-based, individualized exercise regimens that address the unique needs of this population (Pedersen and Saltin 2006). However, no randomized controlled trials have yet systematically evaluated the long-term impact of structured physical exercise programs on glaucoma prevention or disease progression, leaving a significant gap in the literature.

The acute effects of physical exercise on IOP have been extensively studied, with evidence suggesting that various factors, such as exercise intensity, duration, type, and individual fitness levels, mediate the IOP response (Zhu et al. 2018). Understanding these variables is crucial for developing practical guidelines on exercise prescription for glaucoma patients. This clinical review aims to synthesize current evidence on the effects of physical exercise on IOP and their implications for glaucoma prevention and management. The primary objective is to provide research-based guidelines to assist eye care specialists and sports science professionals in designing and implementing exercise strategies tailored to the needs of glaucoma patients or individuals at risk. By bridging the gap between ocular health and exercise science, this review seeks to clarify how physical activity can serve as a complementary approach to conventional glaucoma treatments, ultimately enhancing patient outcomes and quality of life.

The articles included in this review were identified through comprehensive searches of electronic databases, including PubMed, Ebsco-Host (MEDLINE, SportDis-cus, CINAHL Plus), PROQuest, Cochrane Library, and Embase. The search spanned from the inception of each database to September 2024 and was guided by an information specialist with training in systematic reviews. Search strategies were carefully designed to capture relevant studies investigating the relationship between physical exercise and glaucoma, with particular emphasis on IOP modulation and neuroprotection. By critically appraising and synthesizing these studies, this review aims to provide actionable insights for advancing glaucoma care and research.

FACTORS AFFECTING THE IOP RESPONSE TO EXERCISE

Exercise Type and Intensity

Exercises can generally be categorized into endurance-oriented and resistance-oriented types, yet the specific outcomes of these activities can vary significantly based on their implementation (Kenney et al. 2022). Endurance exercises performed at low-to-moderate intensities, which are targeted to enhance the aerobic system, have shown promise for glaucoma prevention and management, with studies linking such activities to acute reductions in IOP (Risner et al. 2009; Roddy et al. 2014). Activities like walking, jogging, or cycling at low intensities typically yield short-term IOP reductions ranging between ~2 to 5 mmHg, with these effects persisting for fewer than 20 min post-exercise (Najmanova et al.

2016; Janicijevic et al. 2022). Longitudinal observations and retrospective studies reinforce these findings, suggesting that regular engagement in such activities reduces the likelihood of glaucoma onset and progression (Williams 2009; Yokota et al. 2016; Meier et al. 2018; Anderson 2019; Lee et al. 2019; Kawakami et al. 2020; Pan et al. 2020). Furthermore, a non-controlled prospective study conducted by Agrawal (2015) demonstrated that open-angle glaucoma patients using topical anti-glaucoma medications experienced greater IOP reductions when advised to perform 30 min of daily low-intensity exercise for a month compared to those who did not exercise (Agrawal 2015). However, due to limitations inherent to observational and retrospective designs, causal relationships remain speculative, underscoring the need for controlled clinical trials to validate these results.

High-intensity endurance exercises, tailored to enhance anaerobic capacity, present a more nuanced picture. For example, studies examining the immediate effects of high-intensity interval training (HIIT) protocols have identified acute reductions in IOP during exercise, with outcomes varying based on the recovery periods between sprints. Less physically demanding HIIT protocols, characterized by longer recovery intervals, demonstrated a progressive IOP decrease, whereas more strenuous protocols exhibited a U-shaped response, negating the beneficial effects (Vera et al. 2019b). Another investigation found that maximal cycling sprints caused IOP reductions when performed against lighter resistances, but heavier loads triggered IOP increases (Vera et al. 2017b). These findings highlight the potential of HIIT as an efficient exercise modality for IOP reduction, provided that protocols are designed to avoid excessive physical strain. Additionally, HIIT offers time-efficient strategies for individuals with busy lifestyles, making it a promising option for integrating physical activity into glaucoma prevention programs. Future studies should explore how variations in intensity, duration, and recovery time influence IOP responses to ensure optimal protocol design.

In contrast, resistance-based exercises, particularly those performed at moderate-to-high intensities, consistently induce acute IOP elevations (Hackett et al. 2024). Research indicates a direct relationship between resistance training intensity — defined by the load lifted — and IOP levels. Additionally, exercises completed closer to failure result in more pronounced IOP increases (Vera et al. 2019a, d, c, 2020a, f). As a result, highly demanding resistance training (e.g., heavy lifting and sets to failure) may be counterproductive for IOP reduction in the short term. Exercises such as bench press and leg press exercises can cause acute IOP increases, with the magnitude of the change being positively correlated with the load used (Vera et al. 2017a; Vaghefi et al. 2021). In addition, larger muscle mass involvement and breath-holding strategies during exercise exacerbates this effect (Vieira et al. 2006). However, most studies found transient IOP decreases after resistance exercises (Hackett et al. 2024).

Nevertheless, resistance-based exercises contribute significantly to the management of chronic conditions and overall health improvement (Hurley et al. 2011). Incorporating multi-component training programs — including endurance, resistance, and balance exercises — could provide comprehensive health benefits while minimizing risks (Bull et al. 2020). The intensity of these programs should remain low to moderate, with careful attention given to maintaining a steady respiratory pattern during exercise to avoid IOP spikes. These programs may also enhance adherence and long-term outcomes for individuals at risk of glaucoma. Further research should investigate whether modifications in resistance training protocols, such as lower resistance levels or fewer repetitions, could mitigate IOP elevations while maintaining overall health benefits.

The integration of personalized exercise plans, tailored to an individual's physical capacity and health status, could maximize the benefits of physical activity for glaucoma prevention and management (Zhu et al. 2018; Gildea et al. 2024). Collaboration between eye care specialists and exercise professionals is essential to design and implement these programs effectively. Future research should also prioritize longitudinal and randomized controlled trials to better understand the interplay between various exercise modalities and IOP dynamics, ultimately refining exercise recommendations for glaucoma patients.

Body Position

IOP has demonstrated sensitivity to the body position adopted in a variety of non-exercised contexts (i.e., sleeping, reading) (Prata et al. 2010). For instance, a heightened IOP response has been observed when individuals are in a recumbent position with neck flexion compared to when they are seated with their neck in a neutral position (Malihi and Sit 2012). Similarly, reading while lying in a supine position results in a higher IOP than when reading while sitting upright (Vera et al. 2020g). These findings suggest that even minor changes in body position can have a notable impact on IOP.

During exercise, the body frequently adopts various positions depending on the type of activity being performed. For example, in exercises such as yoga or CrossFit, head-down positions are often required to execute specific movements, while some resistance training exercises, such as the bench press, are typically performed in a supine or seated position. These different postures could lead to varying effects on IOP (Prata et al. 2010). Notably, certain exercises that involve head-down positions, such as those commonly practiced in yoga, have been shown to cause significant increases in IOP (Baskaran et al. 2006; Bertschinger et al. 2007; Jasien et al. 2015). For glaucoma patients or those at risk, it is important to avoid some yoga positions (e.g., Adho Mukha Svanasana and Uttanasana) since they cause an acute IOP rise (Jasien et al. 2015). These findings are of particular concern for individuals with glaucoma or those at risk of developing the condition, as sustained or excessive increases in IOP could potentially exacerbate disease progression.

For resistance-based exercises, research from our group has demonstrated that IOP responses can differ based on body position. Specifically, we found that performing the bench press in a supine position leads to greater IOP increases compared to performing the exercise in a seated position (Lara et al. 2023). This difference highlights how even slight changes in body posture during exercise can influence IOP levels, which may have implications for exercise prescription in individuals with or at risk for glaucoma. While the supine position is common for certain resistance exercises, its impact on IOP suggests that adopting alternative positions, such as sitting or standing, may be beneficial in maintaining stable IOP levels.

Taken together, the current evidence indicates that body positions involving head-down or supine postures should be avoided, when possible, by individuals at risk for glaucoma onset or progression. These positions appear to exacerbate

IOP rises, which may increase the risk of damage to the optic nerve in susceptible individuals. However, further research is needed to better understand the long-term effects of these positions on IOP and their potential role in the progression of glaucoma. Future studies should focus on examining the cumulative impact of different body positions across various types of exercise and assessing whether specific postures can be modified or avoided to mitigate the risk of IOP spikes during physical activity. This knowledge will be crucial in developing exercise recommendations tailored to individuals with glaucoma or those at heightened risk of the condition.

Breathing Pattern

The breathing pattern adopted during exercise plays a crucial role in both physical performance and the physiological responses to exercise. Proper breathing techniques are essential for maintaining stability, optimizing energy delivery, and minimizing the strain on the cardiovascular system. For example, the Valsalva maneuver, in which an individual exhales forcefully with a closed airway, is commonly used in high-intensity exercises such as powerlifting. This maneuver enhances trunk stability and allows for greater force production during demanding physical efforts. However, while the Valsalva maneuver can enhance performance, it may also have detrimental effects on hemodynamic function, including significant increases in blood pressure and intrathoracic pressure (Ikeda et al. 2009; Blazek et al. 2019).

Regarding IOP, there has been limited research investigating the specific impact of breathing patterns during exercise. However, recent studies suggest that the pattern of breathing can modulate IOP responses. In particular, restricted breathing or compromised gas exchange during exercise appears to result in higher IOP levels. Two studies, one involving dynamic resistance training and the other examining isometric resistance exercises, demonstrated that, when gas exchange is hindered, such as through the Valsalva maneuver, greater increases in IOP are observed (Vera et al. 2020d, 2021b). This suggests that IOP increases are linked to alterations in breathing that impair normal respiration, potentially contributing to higher IOP during intense exercise.

In addition, the eruption of the COVID-19 pandemic and the use of face masks to reduce its transmission led to assess the effects of wearing face masks on IOP. In this regard, Janicijevic and colleagues (2021) (Janicijevic et al. 2021) investigated the short-term effects of using surgical and FFP2/N95 masks on IOP levels during low-intensity endurance exercise in POAG patients. Although the magnitude of the increase was relatively small, this finding suggests that restricted airflow from wearing masks could influence IOP, particularly during exercise. This highlights the importance of considering breathing dynamics and the potential for mask-induced airflow restriction when assessing exercise safety for individuals with glaucoma or those at risk.

Additionally, research on high-altitude exposure, where oxygen levels are lower and breathing patterns naturally change, has provided further insight into the relationship between breathing and IOP. Numerous studies have investigated the effects of high-altitude exposure on IOP, and, while most agree that high-altitude conditions result in a statistically significant increase in IOP, these changes are generally considered clinically insignificant in healthy individuals (Bayer et al. 2004; Ersanli et al. 2006; Somner et al. 2007; Bosch et al. 2010; Willmann et al. 2017; Najmanová et al.

2019; Yang et al. 2019; Wu et al. 2020). However, this effect may be more pronounced in individuals with glaucoma, where even small increases in IOP could pose a risk to optic nerve health (De Moraes et al. 2011).

In the context of airflow restriction as a performance enhancement tool, certain studies have explored the use of specialized masks designed to limit airflow during exercise, simulating the effects of high-altitude training (Barbieri et al. 2020). These masks are thought to improve physical performance by increasing the body's efficiency in oxygen utilization. However, recent research on the effects of airflow restriction masks has shown that they can counteract the IOP-lowering effects typically observed during low-intensity endurance exercise (Vera et al. 2021a). The study found that the use of airflow restriction masks resulted in higher IOP during exercise, highlighting that any manipulation of normal breathing, whether through masks or other means, may negatively affect IOP regulation.

Taken together, these findings suggest that the manipulation of breathing patterns — whether through the Valsalva maneuver, face masks, or other interventions that restrict airflow — can lead to an increase in IOP during exercise. To minimize the risk of exacerbating IOP in individuals with glaucoma or those at risk, it is important to avoid such alterations in breathing during physical activity. Exercise supervision by qualified sports specialists is highly recommended to ensure that an appropriate breathing pattern is maintained throughout exercise, thereby preventing potential adverse effects on IOP and overall eye health. Further research is needed to investigate the long-term effects of altered breathing patterns on IOP and to develop specific guidelines for managing breathing during exercise, particularly for individuals with glaucoma or those predisposed to elevated IOP. Studies should also explore the potential impact of different types of breathing techniques (e.g., diaphragmatic versus chest breathing) on IOP regulation during exercise to better inform exercise prescriptions and safety recommendations for this population.

Cognitive Requirements

In many settings, physical and cognitive demands occur simultaneously, such as in occupational environments, military operations, and team sports. These activities require individuals to not only perform physically challenging tasks but also to engage in complex cognitive processes like decision making, strategic thinking, and problem solving (Loprinzi et al. 2013; Young et al. 2015). The combined demands of physical and mental exertion can result in an additive or even synergistic effect on IOP. For example, studies have shown that increasing mental demands during physical tasks, such as cycling or basketball free-throw shooting, causes a significant rise in IOP (Vera et al. 2018a; Zaher et al. 2024). These findings suggest that cognitive stress during exercise may exacerbate the IOP response, which could be particularly concerning for individuals with or at risk of glaucoma.

If reducing IOP is a therapeutic goal, mental stress should be minimized during physical activity. This highlights the importance of investigating the role of psychological factors in glaucoma prevention and management. Mental stress has been shown to trigger a range of physiological changes, including elevated IOP, which could undermine the benefits of exercise that typically help to lower IOP (Zaher et al. 2024). For individuals with glaucoma, stress reduction becomes a critical aspect of managing the condition and preventing its progression. Physical activities promoting benefits for physical status and mental well-being should be considered (e.g., yoga, Tai Chi, Pilates, etc.). These practices have been shown to improve both physical and mental health, promoting relaxation, reducing stress, and enhancing overall quality of life (Büssing et al. 2012). Recent studies have also suggested its potential benefits on the management of glaucoma (Dada et al. 2018, 2021, 2022). A recent meta-analysis (Zaher et al. 2024) found that various relaxation techniques (i.e., meditation, yoga, autogenic relaxation exercises, etc.) cause significant IOP reductions in the long term.

One of the major challenges in managing chronic conditions like glaucoma is ensuring long-term adherence to exercise regimens. In the context of exercise prescription, especially for individuals with chronic conditions, maintaining adherence is a key factor in achieving therapeutic benefits. Exercise adherence enables glaucoma patients to meet their physical activity guidelines, which is associated with a lower risk of developing glaucoma (Meier et al. 2018; Lee et al. 2019). Evidence from sports science and psychology has consistently shown that the enjoyment and pleasure derived from physical activity are critical determinants of adherence to exercise programs (Kwan and Bryan 2010; Ekkekakis et al. 2011). If an exercise routine is perceived as enjoyable, individuals are more likely to stick with it, which is essential for improving long-term health outcomes. This is especially important for glaucoma patients, who may need to adopt exercise as a regular part of their lifestyle to manage IOP and reduce disease progression. Eye care providers and fitness professionals can work together to recommend activities that are both beneficial for IOP regulation and enjoyable for the individual, ensuring that the patient remains motivated and committed to long-term exercise participation.

Fitness Level

The IOP responsiveness to physical efforts seems to be mediated by fitness level, with physically fitter individuals showing a more stable IOP behavior during exercise performance. Indeed, this finding has been observed for different physical activities, including maximal treadmill running, all-out cycling sprints, resistance exercises and low-intensity endurance exercises (Vera et al. 2017b, 2018b, 2020b; García-Ramos et al. 2018; Janicijevic et al. 2022). These observations suggest that a higher baseline fitness level may confer a protective effect against exercise-induced IOP fluctuations.

This evidence aligns with the gradual progression models recommended by the American College of Sports Medicine for exercise prescription (Garber et al. 2011; Medicine 2013). These guidelines emphasize the importance of tailoring exercise programs to an individual's initial training status to minimize exercise-related complications, such as significant IOP fluctuations. For example, Vera and colleagues (Vera et al. 2020b) found that less fit individuals (relative maximal oxygen uptake: 43.4 ± 1.2 mL min−1 kg−1) exhibited a greater IOP rise (effect size = 0.95) after completing a treadmill test in comparison to individuals with higher fitness levels (relative maximal oxygen uptake: 57.1 ± 1.7 mL min−1 kg−1). Such fluctuations have been identified as a critical risk factor for glaucoma onset and progression (Gordon et al. 2007; De Moraes et al. 2011). This underscores the necessity of a measured and progressive approach to physical training in glaucoma patients or those at risk of developing the condition.

For individuals with lower baseline fitness levels, initial exercise programs should prioritize low-intensity activities with gradual increments in intensity and duration. This approach can help build endurance and strength without inducing abrupt changes in IOP. For example, unfit individuals might begin with light walking or stretching exercises before progressing to moderate-intensity activities such as brisk walking or cycling. Fitness professionals and healthcare providers should collaborate to ensure that exercise plans for glaucoma patients or at-risk individuals are both safe and effective. Regular assessments of physical fitness and IOP behavior during exercise can provide valuable insights for tailoring these programs. Additionally, promoting adherence to these tailored plans through education and consistent support is crucial for maximizing long-term benefits. Future research should aim to further clarify the relationship between fitness levels, IOP responsiveness, and glaucoma progression. Studies exploring the optimal rate of progression in exercise programs for individuals with varying fitness levels could provide critical insights, enhancing the precision of exercise prescriptions for this population. Moreover, randomized controlled trials could help establish definitive guidelines for integrating fitness considerations into glaucoma prevention and management strategies.

Nutritional Ergogenic Aids

Performance during sporting activities can be significantly influenced by well-chosen nutrition strategies. Adequate nutrition plays a vital role in supporting athletes' physical capacity, recovery, and overall performance. In recent years, dietary supplements have become increasingly popular as a convenient and practical alternative to help athletes meet their nutritional needs, especially when certain nutrients or compounds may be challenging to obtain through food alone (Thomas et al. 2016; Maughan et al. 2018). However, it is important to note that not all supplements are without risks. Some have been associated with harmful health effects, ranging from minor issues like gastrointestinal discomfort to more serious adverse events affecting various organ systems. These adverse effects can occur across all age groups, from amateur athletes to elite competitors, underscoring the need for careful consideration when incorporating supplements into an athlete's regimen (Palmer et al. 2003). For glaucoma patients, certain nutrients have demonstrated benefits, such as lowering IOP or improving optic nerve blood flow (Perez et al. 2019; Fahmideh et al. 2022). In fact, nutritional supplementation can serve as a complementary strategy for managing glaucoma and other eye conditions; however, it is also essential to acknowledge that some supplements may have undesirable effects and should be prescribed by qualified professionals.

Among the most popular and extensively studied dietary supplements is caffeine, widely recognized for its potential to enhance both physical and cognitive performance. Caffeine is known to stimulate the central nervous system, leading to increased alertness, reduced fatigue, and improved focus, all of which are beneficial during exercise and competition (McLellan et al. 2016). Given these performance-enhancing effects, caffeine has been incorporated into various pre-exercise and during-exercise supplementation strategies. The effects of caffeine on IOP have been widely studied in non-sport contexts, with research focusing on its impact on IOP in both healthy individuals and those with conditions like glaucoma (Li et al. 2011; Hecht et al. 2017; Vera et al. 2019e; Fahmideh et al. 2022). In the context of exercise, however, there is a relative paucity of research exploring how caffeine influences IOP during physical activity. One study, for instance, examined the impact of caffeine intake (~4 mg/

kg) on IOP responses during low-intensity endurance exercise, specifically 30 min of cycling. The study found that caffeine intake appeared to counteract the IOP-lowering effects typically observed during low-intensity exercise. While exercise can generally reduce IOP by enhancing ocular perfusion and reducing systemic vascular resistance, caffeine seems to reverse this effect in the short term, leading to an increase in IOP during physical activity (Li et al. 2011). This suggests that caffeine ingestion may disrupt the typical IOP reduction that is often seen with endurance exercise. In the short term, this indicates a potential negative effect on IOP stabilization, particularly for individuals who are susceptible to elevated IOP or those with glaucoma.

Despite these short-term effects, the long-term impact of caffeine consumption on IOP is less clear. Evidence from studies on chronic caffeine consumption suggests that regular intake may lead to a modest increase in baseline IOP levels. However, this increase in IOP is generally not associated with an increased risk of developing glaucoma, especially in individuals without a predisposition to the disease (Rang et al. 2008). Some studies suggest that, over time, the body may adapt to regular caffeine intake, potentially mitigating its acute impact on IOP (Fahmideh et al. 2022). Furthermore, animal models of glaucoma have provided some surprising insights into the potential neuroprotective effects of caffeine. Research has shown that caffeine may reduce neuroinflammation and protect retinal ganglion cells from degeneration, both of which are key factors in glaucoma progression (Madeira et al. 2016). These findings indicate that caffeine may have a protective role in maintaining retinal health and may even reduce the damage caused by elevated IOP in some contexts, though more research is needed to confirm these effects in humans.

Although caffeine is one of the most widely studied ergogenic aids in terms of its impact on physical and cognitive performance, there remains a significant gap in our understanding of its long-term effects on IOP, particularly during exercise. The current body of research, while informative, does not provide conclusive evidence on how regular caffeine consumption influences IOP over extended periods. Additionally, it remains unclear whether the short-term rise in IOP observed after caffeine intake is clinically significant for individuals with glaucoma or those at risk of developing the condition. As the relationship between caffeine and IOP is still not fully understood, further research is necessary to explore both the short- and long-term effects of caffeine and other nutritional supplements on IOP levels, ocular health, and retinal function.

Interestingly, nitric oxide supplements have been proposed to improve muscle performance and training adaptations. Research indicates that dietary nitric oxide supplementation improves peak power during isokinetic resistance training (Gonzalez et al. 2023). Additionally, nitric oxide plays a vital role in maintaining IOP homeostasis, with disruptions in its signalling linked to glaucoma and related conditions (Reina-Torres et al. 2021). This compound has also been identified as a promising strategy for reducing IOP in glaucoma patients by enhancing outflow through the conventional outflow pathway (Cavet et al. 2014; Aliancy et al. 2017). Furthermore, nitric oxide supports ocular blood flow and regulates vascular tension, potentially offering protection for the optic nerve (Erdinest et al. 2021). These findings suggest that nitric oxide supplementation could be a valuable adjunct in glaucoma treatment, particularly by targeting the conventional outflow pathway (Han et al. 2021).

In addition to caffeine and nitric oxide, other nutritional ergogenic aids, such as creatine, beta-alanine, and branched-chain amino acids (BCAAs), are commonly used to improve athletic performance. However, their effects on IOP and ocular health remain largely unexplored. For the rest of the substances, future studies should aim to investigate the impact of these supplements on IOP during different types of exercise, particularly those that may increase IOP levels, such as resistance training and HIIT. By expanding our understanding of how various dietary supplements influence IOP and retinal function, we can provide evidence-based recommendations for athletes, particularly those with eye conditions like glaucoma, ensuring that supplementation strategies support both performance and long-term eye health.

Specific Training Devices

Swimming and aquatic exercise have shown to offer numerous health benefits (Omar et al. 2021; Kwok et al. 2022). The resistance of water reduces the stress on joints and muscles, which makes swimming an accessible and effective form of exercise for older adults (Reichert et al. 2020; Chen et al. 2024). Therefore, this physical activity is a very interesting for glaucoma patients or those at risk. However, one factor that requires consideration when swimming is the use of swimming goggles. Studies have shown that wearing swimming goggles can lead to a small, but statistically significant, rise in IOP (Morgan et al. 2008; Paula et al. 2016; Jiménez et al. 2020; Zhang et al. 2022). While the increase in IOP is modest, it may still be relevant for individuals with glaucoma or those seeking to maintain stable IOP levels. However, the frequent use of swimming goggles was not associated with an increased risk of glaucoma over time in adults (Franchina et al. 2015).

Interestingly, the rise in IOP associated with swimming goggles may be linked to the design of the goggles and how they fit on the face. The pressure exerted by the goggles on the eyes and surrounding tissues, particularly the ocular and periocular areas, can cause temporary changes in IOP (Morgan et al. 2008). This effect is thought to be due to the compression of the ocular structures, which might impede normal ocular drainage and increase the pressure within the eye (Paula et al. 2016). It is hypothesized that the anatomical characteristics of the face and head, as well as the specific design of the goggles, may influence how much pressure is applied to the eye. As shown by Zhang and colleagues (Zhang et al. 2022), the use of wider frames in swimming goggles causes smaller IOP elevation in comparison to smaller frames.

In response to these concerns, researchers have proposed that redesigning swimming goggles to reduce the compressive forces on the eyes and surrounding tissues could be a valuable alternative. Innovations in goggle design, such as using softer materials or incorporating adjustable pressure mechanisms, could help minimize the potential IOP increases associated with their use (Jiménez et al. 2020). While there is no definitive consensus on the optimal design, advancements in goggle technology could provide a solution for individuals with glaucoma who wish to engage in swimming without negatively affecting their IOP.

Blood flow restriction (BFR) training, which involves the application of cuffs or wraps to limit blood flow to the working muscles during exercise, has gained attention in recent years for its potential to enhance athletic performance and improve muscle strength in a more efficient manner (Patterson et al. 2019). This approach allows individuals to achieve similar gains in muscle mass and strength as traditional high-load resistance training, but with the added benefit of using lower weights, which can reduce the strain on joints and tissues. BFR is also seen as a promising strategy for individuals in fragile populations, such as older adults or those with joint issues, as it minimizes the risk of injury associated with heavy lifting (Loenneke et al. 2012; Centner et al. 2019).

However, the effects of BFR on IOP have not been extensively studied. To address this gap in knowledge, our research group has conducted two studies to investigate the impact of BFR on IOP levels. In our first study, we found that applying bilateral blood flow restriction to the upper and lower extremities at 60% and 40% of the participants' predicted arterial occlusion pressure did not result in significant changes in IOP during rest (Vera et al. 2020c). This suggests that, at least under resting conditions, BFR may not significantly affect IOP levels, offering some reassurance for individuals concerned about the potential impact of this training method on ocular health.

In a follow-up study published in 2023, we further explored the acute effects of combining resistance training with blood flow restriction on IOP. We observed that applying BFR at 40% pressure during resistance exercises led to similar IOP responses compared to exercises performed without blood flow restriction (Gene et al. 2023). This indicates that low-intensity BFR combined with light-load resistance training may be a safe and effective approach for inducing muscle adaptations typically associated with high-load exercises, without causing harmful changes in IOP.

These findings are particularly important for individuals with glaucoma, as they suggest that BFR could be a viable alternative to traditional high-load resistance training. By combining BFR with light resistance training, individuals may achieve similar strength and muscle endurance benefits, while avoiding the potentially harmful effects of heavy lifting on IOP. Given the limited research on the subject, further studies are needed to explore the long-term effects of BFR on IOP, especially in individuals with glaucoma or those at risk. Nevertheless, current evidence suggests that BFR could be incorporated into exercise regimens for glaucoma patients as a means of improving physical performance without negatively impacting ocular health.

LIMITATIONS AND FUTURE RESEARCH

The available scientific evidence about the association between physical activity and IOP is mainly based on results from non-clinical populations. While these studies provide insights into the general effects of exercise on IOP, the unique pathophysiology of glaucoma means that findings from non-glaucoma individuals should be interpreted cautiously (Weinreb et al. 2014). Glaucoma patients are particularly vulnerable to IOP fluctuations, which may lead to optic nerve damage and retinal ganglion cell loss (De Moraes et al. 2011). Therefore, it is crucial to prioritize research that specifically involves glaucoma patients to better understand how different types of exercise impact IOP and glaucoma progression.

When possible, researchers should prioritize the inclusion of glaucoma patients for their studies. Also, the primary goal of an exercise intervention is to promote long-term benefits on the underlying condition (i.e., glaucoma). Thus, more longitudinal studies are required to shed light on the link between exercise practice and glaucoma prevention and management (Meier et al. 2018). The design of well-powered randomized controlled trials with a sufficient period of follow-up aiming to test the effects of physical exercise interventions on glaucoma prevention and management would be very relevant (Lee et al. 2019). The main goal of this report is to provide an evidence-based guide for exercise prescription in subjects who need to maintain IOP levels as low as possible. Nevertheless, exercise prescription should be individualized considering risk factors, medical history, musculoskeletal limitations, functional ability, tolerance, and personal preferences (Izquierdo et al. 2021).

While the focus of this report is on exercise interventions, it is important to acknowledge that glaucoma management extends beyond physical activity. Modifiable lifestyle factors such as diet, mental stress, sleep hygiene, and smoking cessation all influence IOP and overall eye health (Hecht et al. 2017; Fahmideh et al. 2022). Healthcare providers should consider these factors when developing comprehensive treatment plans for glaucoma patients. For example, dietary changes could improve ocular blood flow, while stress reduction techniques, such as meditation and yoga, may help mitigate IOP increases associated with mental stress.

Given the multifactorial nature of glaucoma management, future research should explore the potential of multi-component lifestyle interventions that combine exercise with other behavioral modifications (Fahmideh et al. 2022). This approach could offer a more holistic solution for preventing glaucoma progression and improving patient outcomes. By investigating the combined effects of exercise, diet, and mental health strategies, researchers may identify synergistic benefits that enhance the management of IOP and protect against optic nerve damage. In addition, glaucoma types such as pigmentary glaucoma should be carefully considered. There is evidence that dynamic exercise may cause significant IOP elevation in these cases due to exercise-induced iris concavity, which enhances mechanical rubbing of the iris against the zonular bundles and results in pigment release (Jensen et al. 1995; Haargaard et al. 2001).

In summary, while the existing evidence on exercise and IOP is promising, further research is needed to understand the long-term effects of exercise in glaucoma patients. Future studies should prioritize the inclusion of glaucoma patients, investigate the effectiveness of different exercise modalities, and consider other modifiable lifestyle factors that contribute to IOP management. Such research will be vital in developing individualized, evidence-based recommendations for glaucoma prevention and management, ultimately improving the quality of life and visual outcomes for patients with this condition.

A PRACTICAL GUIDE FOR EXERCISE PRESCRIPTION IN GLAUCOMA PATIENTS OR THOSE AT RISK

There is robust and irrefutable evidence supporting the regular practice of physical exercise as an essential component in reducing premature mortality and the prevalence of numerous chronic conditions, including cardiovascular diseases, diabetes, and obesity (Pedersen and Saltin 2015; Warburton and Bredin 2017). Regular physical activity has been widely recognized for its broad spectrum of health benefits, both for general well-being and the management of specific medical conditions. As a result, various international organizations, such as the World Health Organization and the American Heart Association, have proposed general physical activity guidelines to promote public health. These recommendations typically suggest a threshold of 150 min per week of moderate to vigorous physical activity or

10,000 steps per day for both healthy individuals and those with clinical conditions (Piercy et al. 2018; Bull et al. 2020).

However, while these threshold-centered recommendations have been widely adopted, there is growing recognition that they may not fully capture the nuanced relationship between physical activity and health outcomes, especially for individuals with specific health conditions like glaucoma. Specifically, there is a well-established dose–response relationship between physical activity and health status, where incremental increases in physical activity can lead to progressive improvements in health, particularly for those who are least active (Warburton and Bredin 2017; Stens et al. 2023). For example, individuals who are sedentary or engage in low levels of physical activity tend to experience the greatest health benefits from even small increments in physical activity, such as moving from no exercise to engaging in light physical activity.

Exercise prescription must be tailored to the individual's specific health needs and condition. For patients with glaucoma, for instance, the primary focus of exercise-based interventions should be on managing IOP, as it is a critical factor in the prevention and management of the disease. Exercise recommendations for glaucoma patients should consider the effects of different types of physical activity on IOP and how they can be optimally leveraged to achieve the best possible outcomes for disease control. **Figure 4** provides an evidence-based summary of key exercise-related factors that eye care providers and sports specialists should consider when prescribing exercise for individuals with glaucoma. These factors include the type, intensity, duration, and frequency of exercise, all of which can influence IOP levels. By using this approach, clinicians can ensure that their exercise prescriptions are not only safe but also effective in managing IOP and preventing glaucoma progression.

Furthermore, while the general public can benefit from a one-size-fits-all approach to physical activity, individuals with chronic conditions like glaucoma may require more individualized exercise recommendations. These recommendations should be based on factors such as the patient's current IOP levels, physical fitness, and any other comorbidities they may have. An individualized approach would help maximize the benefits of exercise for glaucoma management while minimizing any potential risks or adverse effects. Ultimately, a well-tailored exercise prescription, when combined with other therapeutic strategies, can significantly enhance the quality of life for individuals with glaucoma and improve long-term outcomes.

CONCLUSIONS

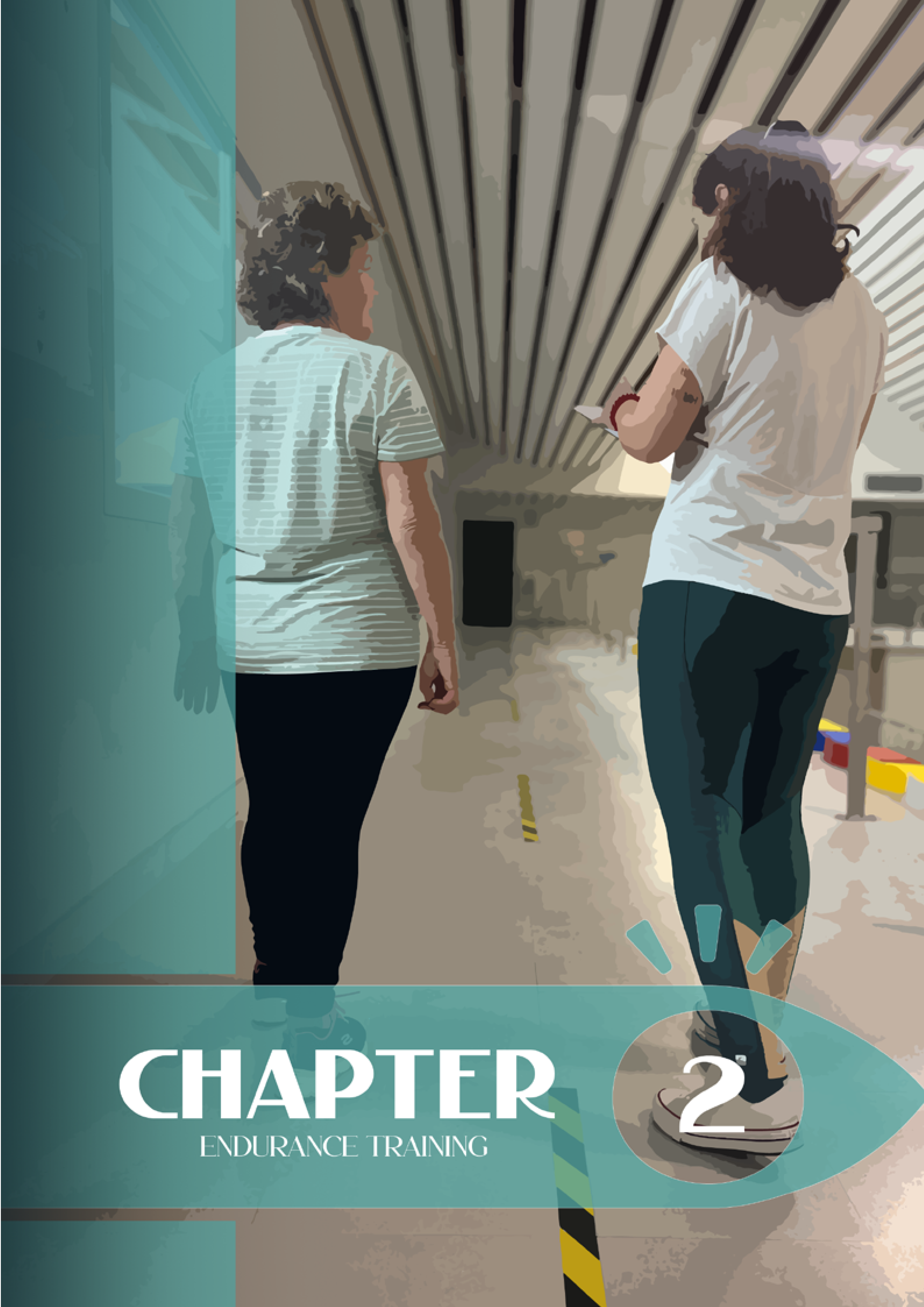
Physical exercise is one of the most important modifiable glaucoma risk factors, and exercise prescription must be considered by eye care providers and sport specialists when providing guidance and counselling for this population. There is a dose–response relationship between exercise practice and health status, highlighting that small increases in exercise practice provide significant health benefits (i.e., every step counts). A progressive involvement with physical activities that promote participation and adherence seems to be a good strategy for older adults with chronic conditions.

Exercise should be considered as medicine, and the prescription of physical activity should therefore be based on the subject's characteristics (i.e., medical history, musculoskeletal limitations, personal preferences, etc.) and controlled like any other medical treatment. We encourage the research community to design randomized controlled trials to assess the long-term effects of exercise and multicomponent interventions on glaucoma prevention and management.

FACTORS FOR EXERCISE PRESCRIPTION IN GLAUCOMA MANAGEMENT AND PREVENTION

	DO'S	DON'TS
Exercise type and intensity	Endurance exercise at low to moderate intensities (i.e., jogging, cycling, swimming)	Training close to maximum aerobic power (i.e., running/cycling to volitional exhaustion)
	Resistance training with moderate loads not reaching muscular failure	Resistance traingin with heavy relative loads (i.e., ≥ 80% 1-RM) and leading to failure.
Fitness level	Enhance fitness level by a progressive involvement in physical training	Perform highly demanding physical efforts by unfit individuals
Body position	Adopt standing or sitting positions for exercise execution	Adopt head-down or surprise positions for exercise execution
Breathing pattern	Follow a regular and controlled breathing pattern during exercise	Limit the interchange of gases (i.e., Valsalva maneuver or airflow restriction mask)
Nutritional ergogenic		Ingest a high caffeine dose before performing aerobic exercise
Cognitive requirements	Physical activities that reduce stress and maximize enjoyment	Cognitively stressful and unpleasant physical activities
Swimming goggles	Swimming at low- to moderate-intensity with appropriate goggles for head/facial anatomy	Using very tight swimming goggles that compress the ocular and periocular tissues
Blood flow restriction	Include blood flow restriction to reduce the relative load used for resistance training	Combine blood flow restriction and resistance training without adjusting intensity

Figure 4. Schematic illustration of the experimental design of study 2. 6-MWT = six-minute walk test, NLC = non-load carriage, LC = load carriage



CHAPTER 2

ENDURANCE TRAINING

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

María Dolores Morenas-Aguilar, *Cristina González Hernández, Sara Chacón-Ventura, Santiago Ortiz-Perez, Juan Francisco Ramos-López, Amador García-Ramos, Jesús Vera*

Brief overview

Within the range of modifiable lifestyle interventions, physical exercise has been suggested as a promising adjuvant strategy for glaucoma prevention and management (Zhu et al. 2018). Observational studies have shown a lower glaucoma incidence and progression in physically active individuals with higher endurance capacity being related to lower IOP and higher OPP values (Yip et al. 2011; Meier et al. 2018; Lee et al. 2019). Specifically, the execution of low to moderate intensity endurance exercise causes an acute reduction of IOP levels in healthy and clinical populations (Najmanova et al. 2016; Vera et al. 2020e). Endurance exercises like walking, jogging, and cycling are highly recommended for glaucoma management and prevention (Hamilton-Maxwell and Feeney 2012; Najmanová et al. 2019; Janicijevic et al. 2022). However, factors such as intensity and fitness level must be carefully considered when prescribing exercise for glaucoma patients or those at risk, as they can influence IOP and OPP levels (Vera et al. 2019f, 2020b; Vaghefi et al. 2021; Janicijevic et al. 2022).

To date, most studies about the impact of physical exercise on IOP and OPP have been carried out in healthy individuals, and the scientific community agrees that the external validity of these results in glaucoma patients should be confirmed (Tribble et al. 2021; Fahmideh et al. 2022). It is well-known that the outflow facility of the eye is altered in glaucoma patients, and therapeutic interventions are targeted to regulate this function (Brubaker 2003; Stamer and Acott 2012). In fact, untreated POAG patients have demonstrated an elevated outflow resistance to provocative tests, with these tests being associated with the effectiveness of eye drops and surgeries on the outflow system (Susanna et al. 2017; Lele et al. 2024). Also, comparative studies between POAG and healthy subjects have revealed that there are some differences in their regulatory capacity during the execution of physical activities (Portmann et al. 2011; Jasien et al. 2015; Yuan et al. 2021). Therefore, the IOP and OPP responses to exercise seem to be dependent on the outflow resistance in POAG eyes, and exercise prescription aiming to reduce IOP levels should be based on results from glaucoma patients who might have an altered outflow function.

Based on the previously mentioned factors that are known to mediate on the IOP response to exercise, we considered of interest to design a randomized clinical trial 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 carrying external loads, and (ii) to compare these results between POAG patients and age- and sex-matched controls. We hypothesized that low-intensity endurance exercise will cause a moderate IOP reduction (Janicijevic et al. 2021, 2022), although the use of external loads and faster walking paces could counteract the IOP-lowering effect (Vera et al. 2019f). The hypothesis about the comparison between the POAG and control groups, the mediating role of walking pace and the OPP response cannot be formulated due to the lack of related studies.

METHODS

Experimental design

A cross-sectional study was designed to determine the impact of endurance exercise (i.e., 400-m walking) on the IOP and OPP responses (see **Figure 5** for a schematic illustration of the study design). Participants completed four walking conditions, combining two different paces (slow and fast) with and two loading conditions (with and without external loads). The four conditions were randomly performed in a single session, with two subsequent conditions separated by 10 minutes of passive rest (Janicijevic et al. 2021).

Participants

Thirty-eight participants were recruited, including 21 POAG patients (9 men, 12 women: [age = 71.1 ± 6.5 years, body mass = 73.8 ± 12.0 kg, 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: [age = 69.2 ± 5.9 years, body mass = 73.7 ± 13.7 kg, height = 163.8 ± 9.6 cm]). The sample size was determined by an a-priori power analysis using the G*Power 3.1 software (Faul et al. 2007) 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 (Janicijevic et al. 2021), the required sample size was determined to be 34 participants (17 POAG, 17 controls). POAG patients were screened according to 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) have a sufficient level of mobility to perform low to moderate physical activity, c) be free of other injuries or diseases that prevent exercise performance, d) receive medical treatment with prostaglandin analogs or a combination of prostaglandin analog and beta-blockers, and e) have no history of any surgical intervention for the treatment of glaucoma. Inclusion criteria for control group was as follows: (a) be free of any systemic or ocular disease, (b) have a 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) be between 60 and 80 years old. 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 (IRB approval: 1961-N-22).

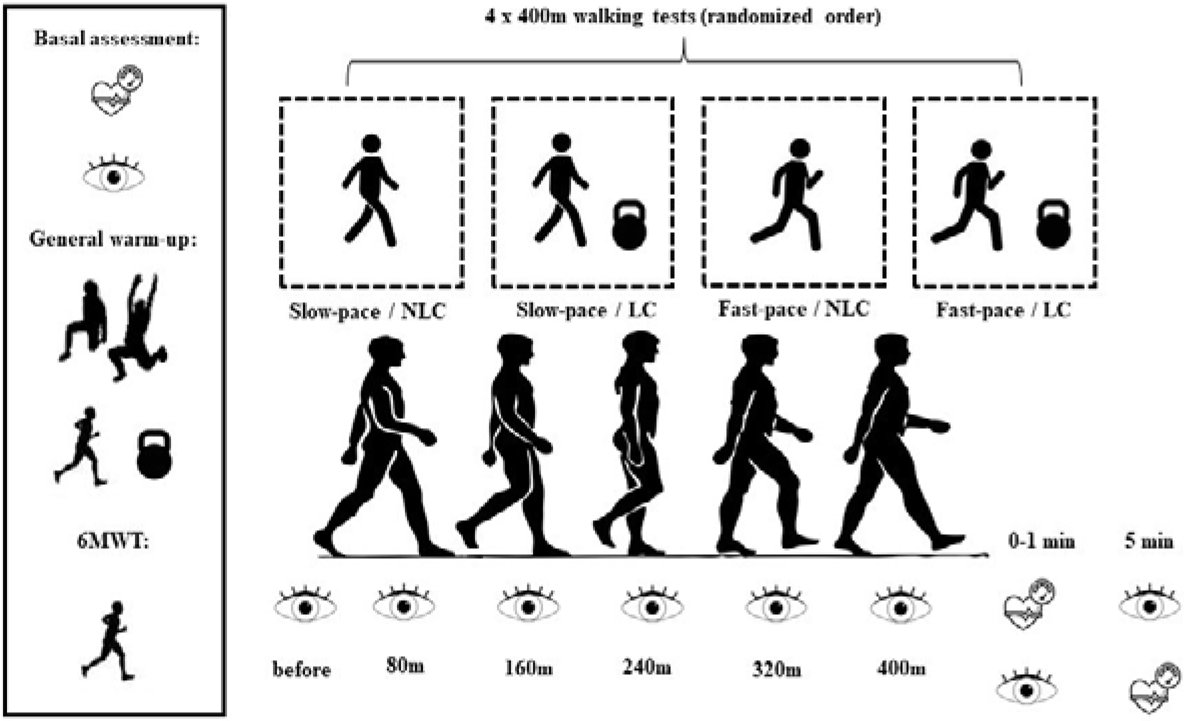


Figure 5. Schematic illustration of the experimental design of study 2. 6-MWT= six-minute walk test, NLC= non-load carriage, LC= load carriage

Procedures

Upon arrival, participants were informed about the experimental procedures and signed the consent form to participate in the study. After 5 minutes of passive rest, IOP and blood pressure were measured. Afterwards, a standardized warm-up, consisting of 5 minutes of joint mobility and dynamic stretching, along with 5 minutes of comfortable-paced load carriage walking (the pace they usually use to walk down the street). The external load was subjectively determined during warm-up to ensure a low-to-moderate effort level for the 400-m walk. Participants tested different weights during 4 laps of 40 m. If they felt unable to complete 10 laps, the weight was reduced; otherwise, it was maintained or increased. After 3 minutes of rest, a six-minute 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 (Kervio et al. 2003). 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 x 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 minutes before the start of the 400-m walking protocols. The 400-m walking protocol was performed completing 10 laps of 40 m, walking 20 m in a straight line, turning around 180º, and comeback 20 m to the starting line (Janicijevic et al. 2021). Participants were accompanied always 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 seconds) was made every 2 laps (80 m) to measure IOP while participants remained in a standing position (holding the weight in the load carriage conditions) (Janicijevic et al. 2021). For load carriage conditions, participants were carrying an identical kettlebell in each hand weighing 2.5, 4, 5 or 8 kg (POAG [men: 5.7 ± 1.9 kg; women: 3.3 ± 0.8 kg], controls [men: 6.1 ± 1.8 kg; women: 3.7 ± 0.6 kg]).

IOP measurements were performed in the affected eye for POAG patients and in a randomly chosen eye for controls. When POAG patients had both eyes 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 (80 m, 160 m, 240, 320 m, 400 m), and after 1 and 5 minutes of passive recovery from each walking test by the same experienced researcher. A portable rebound tonometer (Icare ic200, ICare Finland Oy, Helsinki, Finland) was used to measure IOP (Salim et al. 2013). The mean of six rapid consecutive IOP measurements taken against the central cornea while the participants fixated on a distant target was considered. Blood pressure was measured with an automatic digital wrist blood pressure monitor (M3 Intellisense, Omron, Hoofddorp, The Netherlands) (Hoffmann et al. 2019) before-exercise, and after 1 and 5 minutes of passive recovery. OPP was calculated from the IOP and BP values using the following equation: OPP = 2/3 of the mean arterial BP – IOP; where mean arterial pressure = diastolic BP + 1/3 (systolic BP – diastolic BP) (Costa et al. 2014).

Statistical analysis

Descriptive data are presented as means ± standard deviation. The normal distribution of the data was checked with the Shapiro-Wilk test, and the homogeneity of variances with the 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 1and 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^2_p) for T and F tests, respectively. All statistical analyses were performed using the JASP package (version 0.18.3).

RESULTS

First, we checked the between-group differences for baseline IOP and OPP assessments, and fitness level (i.e., 6-MWT). No statistically significant differences were found for baseline IOP ($t = -1.32$, $p = 0.197$, $d = -0.43$), OPP ($t = -1.53$, $p = 0.135$, $d = -0.52$), or fitness level ($t = 0.83$, $p = 0.414$, $d = 0.27$) between the POAG and control groups.

The 4-way ANOVA applied for the analysis of IOP changes revealed statistical significance for the main effects of *load* ($F = 9.70$, $p = 0.004$, $\eta^2_p = 0.21$) and *point of measure* ($F = 7.69$, $p < 0.001$, $\eta^2_p = 0.17$). However, the main effect of *walking pace* ($F = 0.20$, $p = 0.658$, $\eta^2_p = 0.01$) and *group* ($F = 0.98$, $p = 0.330$, $\eta^2_p = 0.03$) did not reach statistical significance. The interaction effects *load* × *group* ($F = 6.13$, $p = 0.018$, $\eta^2_p = 0.14$) and *load* × *point of measure* ($F = 9.90$, $p < 0.001$, $\eta^2_p = 0.21$) 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 not statistically significant differences for any of the three main effects (*walking pace*: $F = 0.01$, $p = 0.953$; *load*: $F = 0.16$, $p = 0.690$; and *point of measure*: $F = 1.96$, $p = 0.136$), and statistical significance was only reached for the interaction *load* × *point of measure* ($F = 4.36$, $p < 0.001$, $\eta^2_p = 0.18$). Regarding the control group, we obtained statistically significant differences for the main effects of *load* ($F = 24.62$, $p < 0.001$, $\eta^2_p = 0.59$) and *point of measure* ($F = 7.65$, $p < 0.001$, $\eta^2_p = 0.31$), and the interaction *load* × *point of measure* ($F = 6.25$, $p < 0.001$, $\eta^2_p = 0.27$). The main effect of *walking pace* ($F = 0.20$, $p = 0.658$) and the rest of 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 160m (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, $d = 0.89$), 320m (mean difference = 1.9 ± 2.9; corrected p-value = 0.007, $d = 0.87$) and 400m (mean difference = 1.8 ± 3.2; corrected p-value = 0.026, $d = 0.78$) in comparison to the before-exercise IOP measurement (**Figure 6**).

The analysis of OPP changes revealed statistically significant differences for the main effects of *walking pace* ($F = 4.15$, $p = 0.049$, $\eta^2_p = 0.11$) and *point of measure* ($F = 13.50$, $p < 0.001$, $\eta^2_p = 0.28$), whereas the factors *external load* ($F = 0.04$, $p = 0.863$) and *group* ($F = 1.27$, $p = 0.268$) did not reach statistical significance. For its part, any of the interactions showed statistical significance (all p-values > 0.152). As shown in **Figure 7**, 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 pre-exercise levels after 5 min of passive recovery (before-exercise comparison: mean difference = 0.2 ± 5.4; $p = 0.741$; 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 in comparison to the 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 IOP and OPP acute responses to low-intensity endurance exercise at two different walking paces with and without carrying external loads in POAG patients and age- and sex-matched controls. We found a stable IOP behavior during the execution of low-intensity endurance exercise in POAG patients whereas a moderate IOP increase was found in the control group. IOP levels were higher when holding external loads during the walking test, but the walking pace used did not significantly affect the IOP behavior. Regarding OPP, both groups experienced an OPP increase after exercise, although these changes returned to pre-exercise levels within 5 minutes of passive recovery. Taken together, this study supports the use of low-intensity endurance exercise, preferably limiting the use of external loads, as a safe training strategy for POAG patients.

In agreement with recent findings, we found a stable IOP behaviour during the execution of low-intensity endurance exercise in POAG patients (Janicijevic et al. 2021). This finding supports the idea that endurance exercise could be a desirable choice to improve fitness level in POAG patients, since fitness level has been negatively associated with glaucoma progression (Lee et al. 2019). Remarkably, physical exercise is known to promote numerous health benefits, but exercise must be carefully prescribed to maximize its positive effects (Warburton and Bredin 2016). Regarding walking pace, it has been negatively associated with the risk of a wide range of important health conditions, with a brisk walking pace promoting the better health outcomes (Celis-Morales et al. 2019). Our results show that IOP levels in POAG patients are stable regardless of the walking pace. Specifically, POAG patients exhibited a very similar IOP behaviour during the 400-m walking test in the slow- and fast-pace conditions performed without the use of external loads (i.e., mean difference of 0.12 mmHg). Thus, POAG patients should be advised to walk at fast velocities to maximize its protective effect on glaucoma progression and other health conditions.

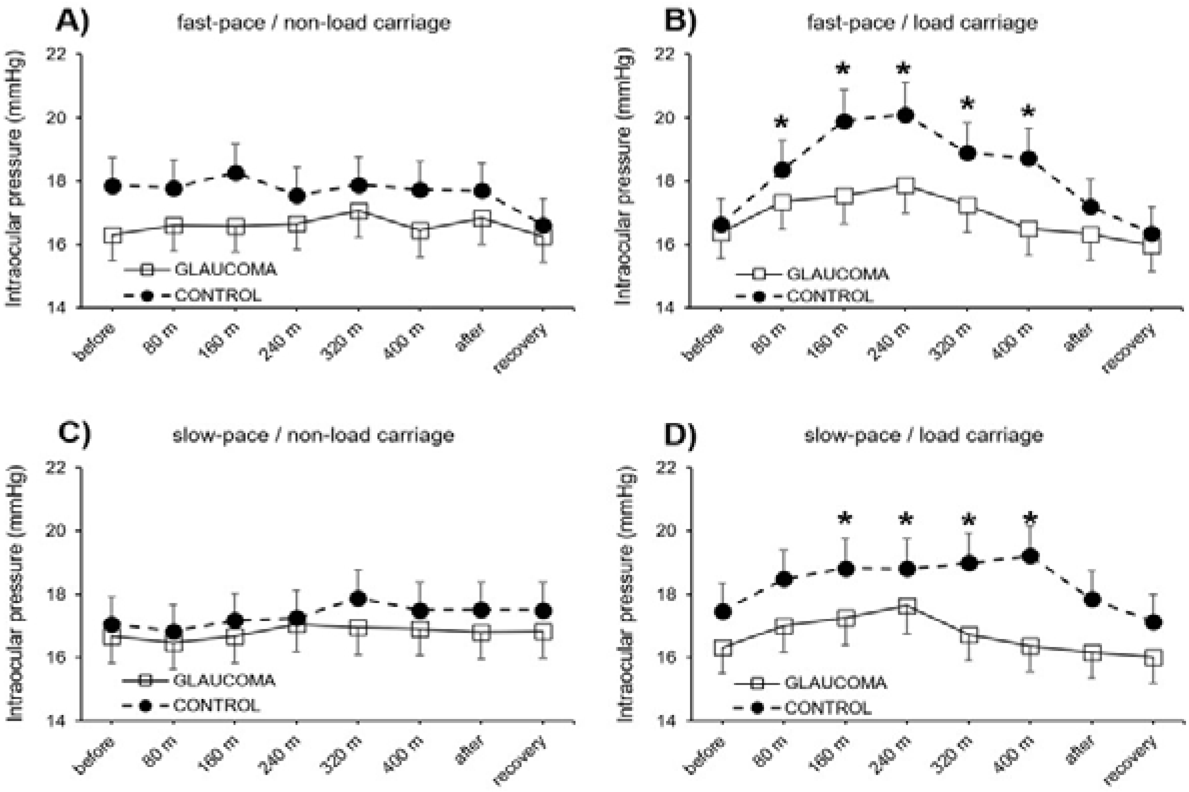


Figure 6. Effects of walking at two different paces with and without carrying external loads on intraocular pressure. The specific experimental condition is depicted above each panel. Error bars represent the 95% confidence intervals. * denotes statistically significant differences ($p < 0.05$) in comparison to the pre-exercise measurement for the control group

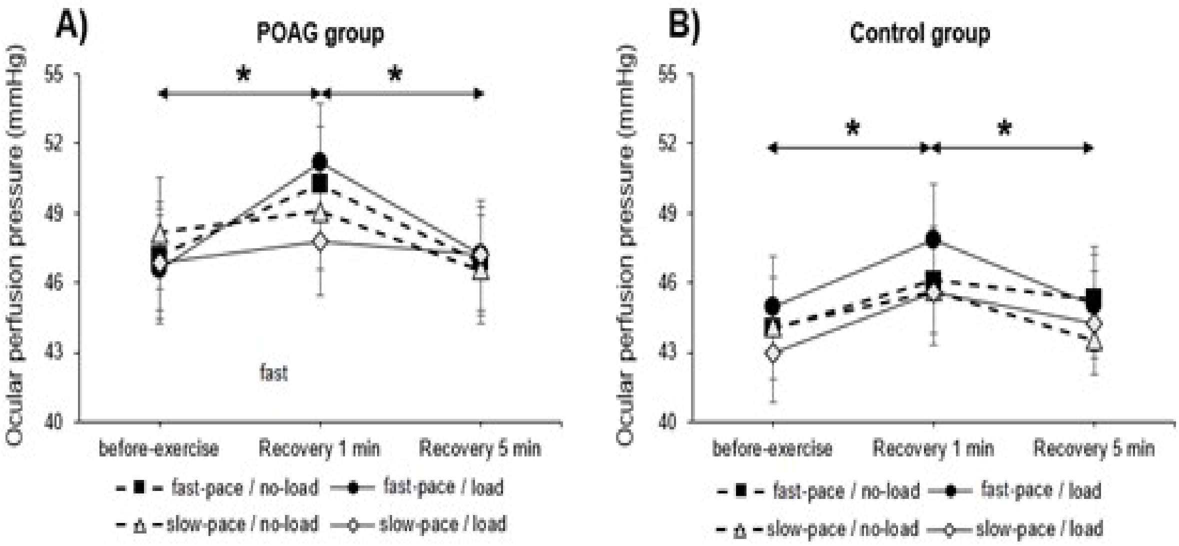


Figure 7. Effects of walking at two different paces with and without carrying external loads on ocular perfusion pressure in the primary open-angle glaucoma (POAG; Panel A) and control (Panel B) groups. Error bars represent the 95% confidence intervals. *denotes statistically significant differences ($p < 0.05$) between two points of measure

We found a heightened IOP response with the use of external loads during the walking test in both groups. Although these differences were higher for the control (i.e., 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. This set of findings are in accordance with Vera et al. (2019) and Baser et al. (2018), who found a significant IOP rise when holding weights (Baser et al. 2018; Vera et al. 2019f), and these effects have been linked to the increase in intraabdominal and intracranial pressure (Dickerman et al. 1999; Ece et al. 2015). As depicted in **Figure 3**, the 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 (i.e., an average 19% higher variability [17% and 21% for the POAG and control groups, respectively] in the load-carriage in comparison to the non-load carriage conditions). The scientific evidence agrees that IOP increments and fluctuations should be avoided as much as possible for the optimal prevention and management of glaucoma (De Moraes et al. 2011). Therefore, the use of external loads during low-intensity endurance exercise seems to have a detrimental effect on IOP levels, and when possible, it should be discouraged in glaucoma patients or those at risk.

Studies conducted in healthy young individuals have consistently reported an IOP-lowering effect of low-intensity endurance exercise (Hamilton-Maxwell and Feeney 2012; Najmanova et al. 2016; Vera et al. 2020e, 2021a; Janicijevic et al. 2022). Here, we found that controls experienced a moderate IOP increase during the 400-m walking test, whereas POAG patients maintained stable IOP levels during the execution of the exercise protocol. For controls, these discrepancies between our experimental sample (elderly subjects: age = 69.2 ± 5.9 years) and healthy young adults can be explained by the differences in fitness level, which has demonstrated to be an important modulator of the IOP behaviour during exercise (Janicijevic et al. 2022). Also, aqueous humour outflow facility is reduced with ageing (Tan et al. 2006), and thus, the regulatory IOP functioning between young and elderly people cannot be compared. Somewhat surprisingly, POAG patients showed a more stable IOP behaviour performing the walking protocol than age- and sex-matched controls, who also have 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 (i.e., all POAG patients included in this study were under treatment with prostaglandin analogs or a combination of prostaglandin analog and beta-blockers), modulating the effects of physical activity on IOP. It is well-known that all active first-line drugs are effective in reducing and stabilizing IOP levels, with prostaglandins being the most efficacious drugs (Stewart et al. 2008; Li et al. 2016). Future studies are required to investigate the IOP behavior during low-intensity endurance exercise in untreated POAG patients or those with a different treatment option (e.g., laser or incisional surgical procedures).

Although the elevation of IOP is recognized as the main risk factor for glaucoma development, vascular factors also play a key role on glaucoma pathogenesis (Cherecheanu et al. 2013). Remarkably, individuals with lower OPP levels seem to have a higher risk to develop glaucoma and a faster disease progression (Zhu et al. 2018). We found that low-intensity endurance exercise induced an OPP increment in POAG patients and healthy controls (average increment for POAG = 2.39 mmHg and controls = 2.29 mmHg) with this increment being heightened in the fast pace (average increment = 3.17 mmHg) in comparison to the slow-pace condition (average increment = 1.51 mmHg). In line with these findings, recent investigations have found an acute increase in ocular blood flow after performing endurance exercise in POAG patients (Gracitelli et al. 2020; Ma et al. 2022). In addition, evidence from a correlational study revealed that physically active individuals have a lower risk of having low OPP, suggesting the potential benefits of physical exercise for reducing the risk of POAG (Yip et al. 2011). Summing up, endurance exercise causes a transient OPP increase in elderly subjects, including POAG patients and healthy controls, which support the positive effect of physical exercise on glaucoma prevention and management. Therefore, eye care providers (i.e., optometrists and ophthalmologists) and sport science specialists should encourage their glaucoma patients or those at risk to perform endurance exercises such as walking, and preferably using a fast-walking pace, due to its 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 POAG patients. However, these results must be interpreted taking into account the following limitations. First, we chose a low-intensity endurance exercise (i.e., 400-m walking task) and our findings cannot be extrapolated to other types of exercises. Numerous investigations indicate that resistance training promotes important health benefits (Ashton et al. 2020; Maestroni et al. 2020), and thus, its effects on glaucoma prevention and management are worthy of further investigation. Second, fitness level has demonstrated to be an important modulator of the IOP and OPP response to exercise (Janicijevic et al. 2022). Future studies with larger samples should assess the mediating effect of fitness level on the current findings. Third, as previously discussed, our experimental sample was formed by pharmacologically treated POAG patients, and it is known that the functioning of aqueous humour outflow system is dependent on the type of medication and glaucoma type (Brubaker 2003; Stamer and Acott 2012). Therefore, the external validity of the current outcomes in other types of glaucoma or different treatment options should be investigated. Fourth, the individual loading percentage and blood pressure measurements lacked precision, as the weight for load carriage conditions was determined based on their subjective performance capacity. Lastly, this study examines only the acute effects of exercise on IOP and OPP. The development of randomized clinical trials is needed to determine the long-term effects of different supervised exercise programs on glaucoma prevention and management.

CONCLUSION

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

CHAPTER 3

DYNAMIC RESISTANCE TRAINING

Acute intraocular pressure responses changes during dynamic resistance training in primary open-angle glaucoma patients and age-matched controls

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Brief overview

Resistance training provides a range of performance and health benefits for both athletes and clinical populations. Athletes typically engage in resistance training to enhance performance or prevent injuries, while healthy adults and those with medical conditions use it to improve functional capacity (Hackett et al. 2024). Regular resistance training has been shown to effectively manage and prevent various chronic conditions (e.g., arthritis, diabetes, and heart disease) by slowing disease progression and enhancing quality of life through the maintenance of muscle quality (Hurley et al. 2011; Lizama-Pérez et al. 2023). Additionally, resistance training reduces the risk of fall-related injuries and neurodegenerative disorders, while also promoting bone, cardiovascular, and mental health (Piercy et al. 2018). Resistance training may help reduce the risk of frailty commonly observed in older adults with hypertension, glaucoma, or diabetes. Additionally, it may slow physical and cognitive decline, reduce disability, and lower mortality risk (McMonnies 2016). However, an individualized exercise prescription is essential, tailored to the patient's condition and underlying medical issues.

Concerns about eye health have grown significantly in recent years, especially in relation to lifestyle habits (Vera et al. 2020h). Indeed, due to the considerable incidence of glaucoma and its social, economic and health impact (Tham et al. 2014), the research community is focused on determining the most valid and feasible strategies for the prevention and management of glaucoma. Regular physical exercise has been shown to positively affect ocular health, reducing the risk of various eye diseases (Meier et al. 2018). Observational studies have reported lower IOP and higher OPP values in individuals with greater fitness levels (Yip et al. 2011; Meier et al. 2018; Lee et al. 2019).

Overall, physical exercise has been proposed as a feasible strategy for preventing and managing glaucoma alongside medical treatment (Zhu et al. 2018). Among the various factors influencing the IOP responsiveness to physical exercise, the type of exercise performed is particularly relevant (Vera et al. 2019d). While low to moderate intensity endurance exercises tend to reduce IOP (Najmanova et al. 2016; Vera et al. 2019e), resistance exercises, particularly when executed with high levels of effort (e.g., heavy loads and close proximity to failure) cause an acute rise in IOP (Vera et al. 2017a, 2019d, 2020h). This increase is further exacerbated by breath-holding and the Valsalva maneuver during high-intensity resistance exercises (Vera et al. 2019f). Additionally, exercises involving larger muscle groups (e.g., squats) result in greater IOP changes than those targeting smaller muscle groups (e.g., biceps curls) (Vera et al. 2020h; Hackett et al. 2024). Of the few studies comparing upper- and lower-body exercises, two found squats produced greater IOP fluctuations compared to biceps curl and military press (Vera et al. 2019c, 2020h). To date, most studies have been conducted on healthy individuals, but glaucoma patients, who have an impaired outflow facility (Portmann et al. 2011; Yuan et al. 2021), may experience different IOP responses (Brubaker 2003; Stamer and Acott 2012). Further studies are needed to explore IOP changes during resistance exercises in glaucoma patients.

Elevated IOP is the primary risk factor for glaucoma, but vascular factors also play a crucial role in its pathogenesis (Cherecheanu et al. 2013). Higher OPP has been associated with a lower incidence of glaucoma and slower disease progression (Yip et al. 2011). While endurance and resistance exercises generally increase OPP (Zhu et al. 2018), resistance exercise sets performed to failure have demonstrated to reduce OPP in healthy individuals (Vera et al. 2019c). The relationship between physical exercise and OPP is complex, influenced by the autoregulatory mechanisms that regulate blood flow (Zhang et al. 2012). In glaucoma patients, the altered outflow facility may contribute to differences in blood flow regulation during certain resistance exercises compared to healthy individuals (Portmann et al. 2011). Although few studies have investigated blood flow responses to isometric exercise in POAG patients (Gugleta et al. 2003; Pournaras et al. 2004; Portmann et al. 2011), dynamic resistance exercises remain unexplored. Thus, further research on resistance exercise prescriptions to improve OPP in POAG patients with impaired outflow resistance is warranted.

The primary objective of this study was to assess the IOP and OPP responses to dynamic lower- and upper-body resistance exercises. To ensure participant safety and proper technical execution while minimizing the risk of injury, we selected monoarticular exercises, such as leg extensions and biceps curls, instead of compound exercises like squats. Additionally, the secondary objectives included: (i) comparing IOP and OPP responses between POAG patients and age-matched controls, (ii) comparing IOP and OPP responses between lower- and upper-body exercises (leg extension vs. biceps curl) and (iii) comparing IOP and OPP responses when the exercises are performed at low and moderate intensities. We hypothesized that moderate-intensity dynamic resistance exercise would result in a moderate increase in IOP (Hackett et al. 2024). While the results of the comparison between the POAG and control groups are uncertain due to the lack of related studies, however, the altered mechanism of regulation of aqueous humor in POAG patients may lead to a greater increase compared to control individuals (Stamer and Acott 2012).

METHODS

Experimental design

A cross-sectional design was used to investigate the influence of dynamic biceps curl and leg extension exercises on IOP behaviour at low and moderate intensities in POAG patients and sex-matched controls. Participants attended two days to the laboratory, with both sessions being separated by at least 48 hours. In order to avoid circadian fluctuations, participants were tested at the same time of the day (± 2h). In the first session, the 15 repetitions maximum (RM) load in the biceps curl and leg extension exercises was determined. In the second session, participants randomly performed 1 set of 10 repetitions of each exercise at low intensity (0.5 kg bar for biceps curl and 5 kg for leg extension) and moderate intensity (15RM). IOP was measured at baseline (upon arrival), after each of the 10 repetitions, and after 1 and 5 minutes of passive recovery. Additionally, blood pressure was measured at baseline, immediately after exercise cessation, and after 5 minutes of passive recovery. All participants were tested under similar environmental conditions (approximately 22°C and 60% humidity) and were not allowed to drink or eat during the assessment.

Participants

The required sample size was determined by an a-priori power analysis using the G*Power 3.1 software (Faul et al. 2007), considering an ANOVA with within- and between-participant factors. For this analysis, we have considered an effect size (Cohen´s f) of 0.2, which corresponds to approximately 40% of the magnitude of the change found for IOP levels during aerobic exercise in POAG patients (Janicijevic et al. 2021), an α-level of 0.05 and a power of 0.80. This calculation projected that the required number of participants to ensure the detection of significant differences was 36 subjects (18 POAG and 18 controls). For this study, 26 POAG patients (age = 68.9 ± 8.1 years, body mass = 71.9 ± 12.2 kg, height = 165.7 ± 10.4 cm) and 18 healthy older adults (age = 69.6 ± 5.9 years, body mass = 73.3 ± 12.9 kg, height = 162.9 ± 9.4 cm) were recruited. The POAG group was formed by 13 men and 13 women recruited from the Unit of Glaucoma at Virgen de las Nieves University Hospital (Granada, Spain), whereas the control group was formed by 6 men and 12 women. All participants were of Caucasian race. For POAG patients' recruitment, the disease diagnosis was based on objective criteria such as glaucomatous optic nerve head changes and visual field defects consistent with glaucoma, and all patients were medically treated with prostaglandin analogues or a combination of prostaglandin analogue and beta-blockers. In addition, the inclusion criteria for all participants were as follows: (a) have a sufficient level of mobility to perform low to moderate intensity physical activity; (b) be free of other underlying diseases that could be negatively affected by exercise; (c) absence of any surgical intervention for glaucoma treatment; and (d) be between 60 and 80 years old. Participants were instructed to avoid caffeine, alcohol, and strenuous exercise before testing. This study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and was approved by the Institutional Review Board (IRB approval: 1961-N-22).

Procedures

A schematic overview of the study protocol is depicted in **Figure 8**. The first session (familiarization session) was used to determine the 15RM (i.e., the load at which participants can perform a maximum of 15 repetitions) for the biceps curl (free weights) and leg extension (leg extension machine) exercises. At the beginning of the session, participants' age, body mass, and height were obtained. After that, participants performed a general warm-up of full-body mobility and practiced the exercises with elastic bands, a light bar and the leg extension machine. The 15RM load for biceps curls and leg extension was determined through an incremental loading test. The weight in the sets of each exercise was progressively incremented until the 15RM load was reached. The set was stopped when an experienced strength and conditioning coach identified that participants could perform more than 15 repetitions. Three minutes of passive rest were implemented between sets. The order of the exercises was randomized.

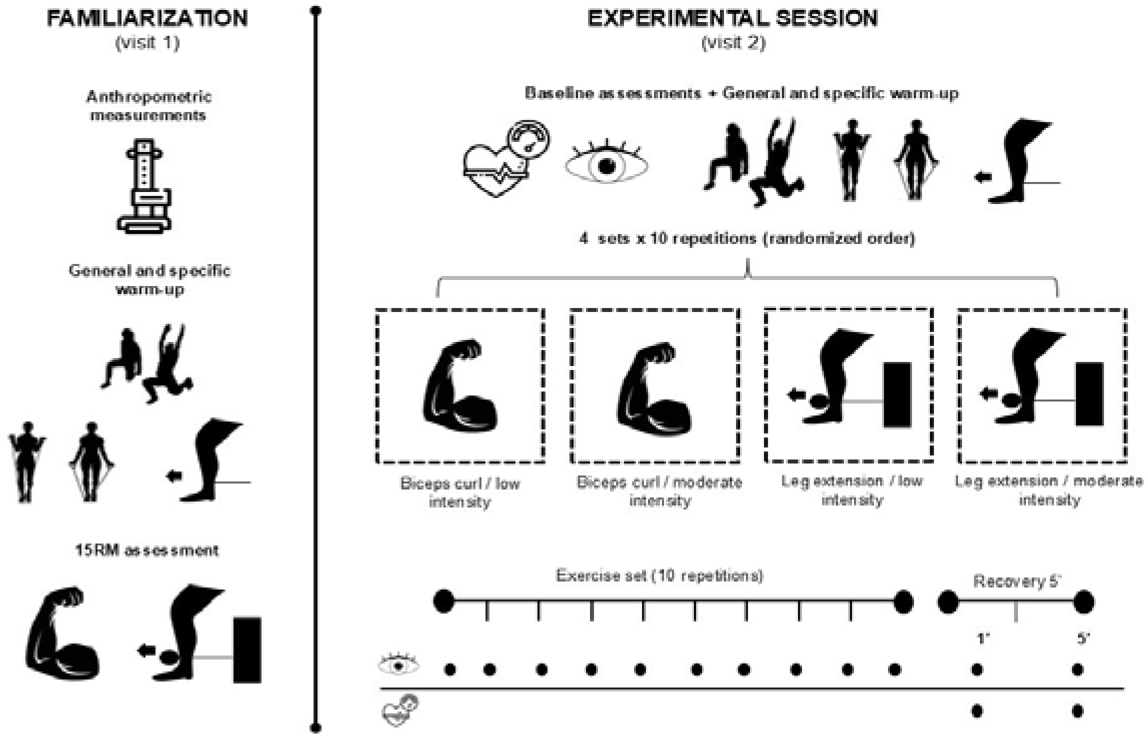


Figure 8. A schematic illustration of the study 3 procedures in both experimental sessions.

In the second session (experimental session), IOP was assessed at baseline and then participants conducted the same warm-up as the described for the first session. After that, participants performed one set of 10 repetitions against the 15RM load and one set of 10 repetitions with a light bar (0.5 kg) for biceps curl and leg extension with 10 minutes of rest between exercises. The IOP was measured immediately after each repetition at the resting position to avoid the influence of active effort as Vera et al. previously reported (Vera et al. 2020h). Participants were asked to maintain a normal breathing pattern during both exercises.

IOP was measured using a portable rebound tonometer (Icare IC200, Tiolat Oy, Helsinki, Finland). Participants were instructed to fixate on a distant target while six consecutive measurements were taken against the central cornea. The average of these six measurements was used for further analysis. Blood pressure was measured using a wrist digital automatic monitor (RS6 HEM-6221, Omron, Kyoto, Japan), which has been validated for blood pressure assessment (Takahashi et al. 2013). OPP was estimated from the assessment of IOP and blood pressure (OPP = [95/140 × mean arterial pressure] – IOP).

STATISTICAL ANALYSIS

Descriptive data are presented as means ± standard deviation. The normal distribution of the data was checked with the Shapiro-Wilk test, and the homogeneity of variances with the Levene's test ($p > 0.05$). For the analysis of IOP changes, a repeated measures analysis of variance was carried out with the *intensity* (low, moderate), *exercise* (biceps curl, leg extension) and *point of measure* (baseline, after each repetition, 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 changes, data were submitted to another repeated measures analysis of variance with the *intensity* (low, moderate), *exercise* (biceps curl, leg extension) and *point of measure* (baseline, immediately after exercise cessation and after 5 min of passive recovery) as the within-participant factors, and the *group* (POAG, control) as the only between-participant factor. 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 by the Cohen's d effect size (d) and partial eta squared (η^2_p) for T and F tests, respectively. All statistical analyses were performed using the JASP statistics package (version 0.18.3).

RESULTS

First, we checked the between-group differences for baseline IOP and OPP assessments and fitness level (i.e., biceps curl and leg extension 15RM). There were not statistically significance differences for baseline IOP (POAG = 17.3 ± 4.4 mmHg, control = 16.6 ± 3.2 mmHg; t = -0.625, p = 0.535, d = 0.19), OPP (POAG = 53.8 ± 9.8 mmHg, control = 49.9 ± 8.0 mmHg; t = -1.41, p = 0.165, d = 0.43), biceps curl 15RM (POAG = 11.7 ± 4.6 kg control = 10.1 ± 2.8 kg; t = -1.290, p = 0.204, d = 0.395) and leg extension 15RM (POAG = 21.1 ± 12.9 kg, control = 21.7 ± 11.9 kg; t = 0.157, p = 0.876, d = 0.048) between the POAG and control groups.

The 4-way ANOVA applied for the IOP changes revealed statistical significance for the main effects of *intensity* ($F = 49.1$, $p < 0.001$, $\eta^2_p = 0.54$), *point of measure* ($F = 23.3$, $p < 0.001$, $\eta^2_p = 0.36$), and *group* ($F = 4.2$, $p = 0.048$, $\eta^2_p = 0.09$). However, the main effect of *exercise* did not reach statistical significance ($F = 0.9$, $p = 0.339$, $\eta^2_p = 0.02$). The interaction effects *point of measure* × *group* ($F = 4.9$, $p < 0.001$, $\eta^2_p = 0.11$), *exercise* × *intensity* ($F = 39.8$, $p < 0.001$, $\eta^2_p = 0.49$), *intensity* × *point of measure* ($F = 10.8$, $p < 0.001$, $\eta^2_p = 0.20$), and *exercise* × *intensity* × *point of measure* ($F = 4.7$, $p < 0.001$, $\eta^2_p = 0.10$) showed statistical significance, whereas the rest of interactions did not reach statistically significant differences ($p > 0.184$ in all cases). Post-hoc analyses revealed higher IOP increments in the moderate- in comparison to the low-intensity condition (corrected p-value < 0.001, Cohen's d = 0.38), and POAG patients experienced a lower IOP increase when compared with the control group (corrected p-value = 0.048, Cohen's d = 0.52). Also, there was a linear IOP rise during exercise execution, with IOP returning to baseline levels immediately after completing the exercise (**Figure 9**).

Complementarily, four separate ANOVAs for both exercises (leg extension and biceps curl) and intensities (low and moderate) were carried out to explore the differences between the POAG and control groups (see **Figure 9**). For the biceps curl exercise, POAG patients tended towards showing a more stable IOP response than controls in the moderate-intensity condition ($F = 4.0$, $p = 0.052$, $\eta^2_p = 0.09$), but the differences in the low-intensity condition were statistically and clinically insignificant ($F = 2.0$, $p = 0.162$, $\eta^2_p = 0.05$). When considering the leg extension exercise, controls showed greater IOP increments than POAG patients during the execution of the 10 exercise repetitions in both exercise intensities (low-intensity: $F = 4.6$, $p = 0.038$, $\eta^2_p = 0.10$; and moderate-intensity: $F = 4.6$, $p = 0.037$, $\eta^2_p = 0.10$). However, these differences were only evident during the execution of the training set, with IOP levels rapidly returning to baseline levels after exercise cessation (see **Figure 9**).

Regarding OPP, there were not statistically significant differences for the main effects of *exercise* ($F = 0.6$, $p = 0.431$), *intensity* ($F = 2.1$, $p = 0.152$), *point of measure* ($F = 0.2$, $p = 0.700$), and *group* ($F = 0.1$, $p = 0.722$). Also, all interactions were far from reaching statistical significance (all p-values > 0.195).

DISCUSSION

This study aimed to assess the IOP and OPP responses to dynamic resistance exercise (leg extension and biceps curl) in POAG patients and age-matched controls. We found a progressive IOP increase throughout the sets of leg extension and biceps curl exercises when performed at moderate intensity. However, IOP returned to baseline levels immediately after exercise cessation. Remarkably, POAG patients showed a smaller IOP increase compared to the control group. The magnitude of these differences between groups was higher in the more physically demanding conditions, observing a heightened IOP increment for the control group in comparison to the POAG patients during the 10 exercise repetitions in the moderate-intensity conditions of the leg extension (POAG = 0.3 ± 0.6 mmHg vs. control = 2.3 ± 0.7 mmHg) and biceps curl (POAG = 1.4 ± 0.6 mmHg vs. control = 3.4 ± 0.8 mmHg) exercises. No changes in OPP were observed across any exercise or intensity in either group. Taken together, this study supports the use of low- to moderate-intensity leg extension and biceps curl exercises as a safe training strategy for POAG patients undergoing eye drops treatment.

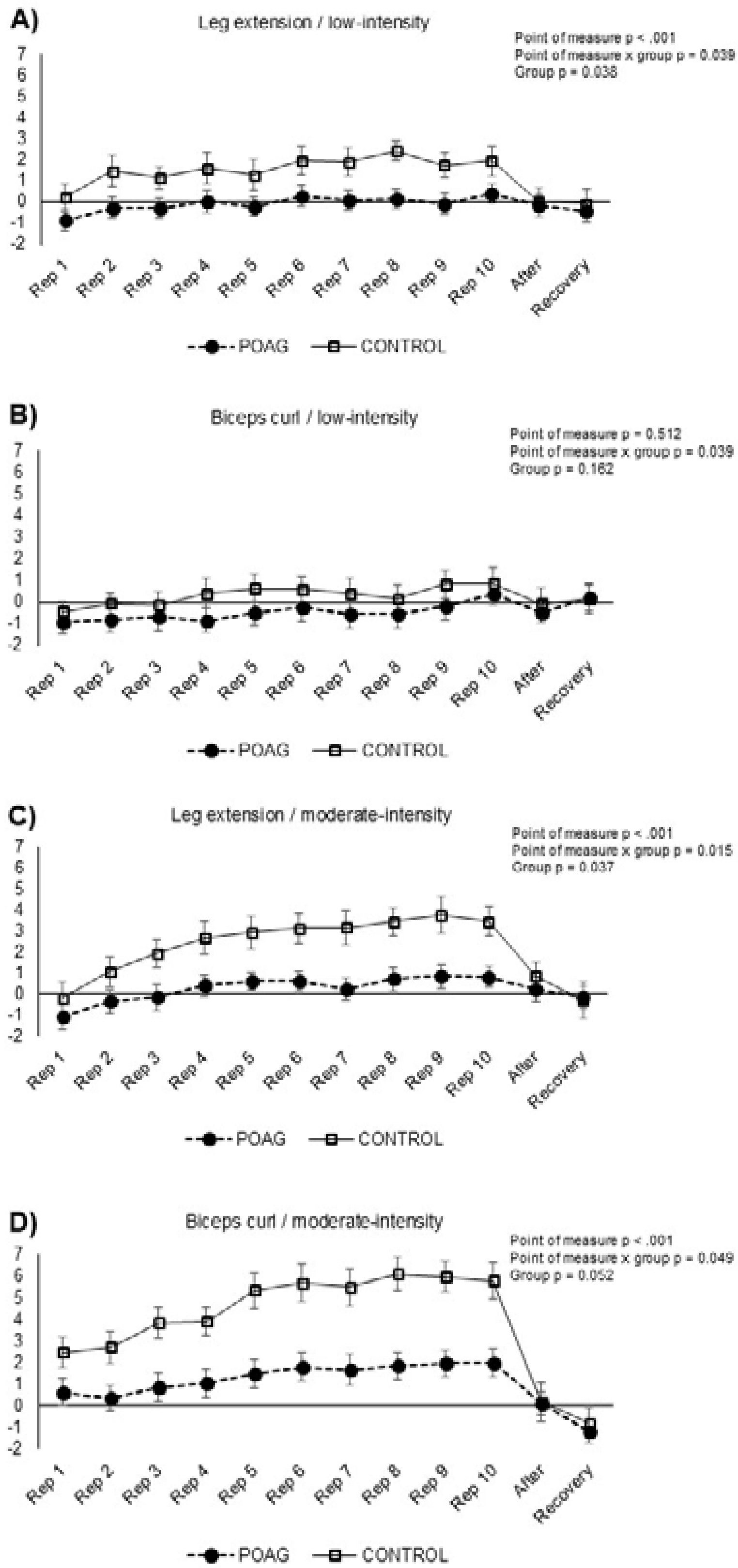


Figure 9. Effects of leg extension and biceps curl exercises at two intensities on intraocular pressure in the primary open-angle glaucoma (POAG) and control groups. The specific experimental condition is depicted above each panel (panel A = leg extension exercise at low-intensity, panel B = biceps curl exercise at low intensity, panel C = leg extension exercise at moderate intensity, and panel D = biceps curl exercise at moderate intensity). Error bars represent the 95% confidence intervals. Bold font has been used to highlight statistically significant effects ($p<0.05$). IOP = intraocular pressure; Rep = repetition; After = measurement taken after completing the set (within 1 minute); Recovery = measurement taken after 5 minutes of completing the set

In line with previous studies, we found an acute increase in IOP levels during the execution of dynamic resistance exercises (Hackett et al. 2024). Although repeated IOP increases could potentially harm retinal function, the rise observed in this study was clinically modest, reaching 0.8 ± 0.6 mmHg for POAG patients and 2.8 ± 0.7 mmHg for the control group at moderate intensity and, -0.3 ± 0.4 mmHg for POAG patients and 1.2 ± 0.3 mmHg for the control group at low intensity. However, other studies have found a greater IOP elevation (up to 28 mmHg) during dynamic and isometric resistance exercises (Vera et al. 2021b; Hackett et al. 2024). This may be explained by the different physiological responses associated with the exercise intensity (i.e., breathing pattern). In fact, performing high intensity resistance exercises (i.e., near to failure) tends to alter the normal breathing pattern, leading to the Valsalva manoeuvre or breath-holding strategies, which can exacerbate IOP changes (McCARTNEY 1999; Vera et al. 2019c). In contrast, low- to moderate-intensity exercises tend to promote a steady breathing pattern, allowing to maintain an stable IOP behaviour (Vera et al. 2021b). In the present study, participants were advised to avoid the Valsalva manoeuvre; however, it was not objectively monitored, and the possibility of unintentional breath-holding cannot be ruled out. Nonetheless, we hypothesized that performing leg extensions and biceps curls at higher intensities would require greater physical effort, resulting in a more pronounced increase in IOP. Therefore, exercise intensity and the associated breathing pattern should be carefully considered by trainers and eye care specialists in the prevention and management of glaucoma. While high-intensity resistance exercises result in significant IOP increments (Vera et al. 2019c, 2020a), moderate-intensity exercise appear to be effective for improving fitness level without compromising eye health. Future studies using the biceps curl and leg extension exercises at higher intensities should be performed to explore its impact on IOP levels.

Additionally, previous results have shown that accumulated repetitions lead to greater IOP levels (corrected p-value < 0.001, Cohen's d = 0.43) (Vera et al. 2020h). Beyond exercise intensity, longer set durations increase effort, resulting in a pronounced impact on IOP (Hackett et al. 2024). To minimize undesirable IOP alterations, performing only half of the maximum possible repetitions (medium level of effort) should be recommended for POAG patients or those at risk. In the present study, a brief rest period (1 minute) was sufficient for IOP to return to baseline levels. Recent research has also indicated that even significant IOP elevations from resistance training are transient, with recovery occurring in a short time (Vera et al. 2019d). Thus, incorporating intra-set rests may be an alternative to prevent continuous IOP elevation. Moreover, unlike previous studies comparing various resistance exercises, we did not observe significant differences between leg extension and biceps curl exercises. In general, exercises that recruit larger muscle masses (e.g., squat) lead to greater IOP increases compared to those involving smaller muscle groups (e.g., biceps curl) (Vera et al. 2019c, 2020h; Hackett et al. 2024). However, when comparing exercises with similar muscle mass recruitment (e.g., biceps curl vs. calf raise), upper-body exercises tend to provoke a higher IOP increase (Vera et al. 2019c). In this study, we found a greater IOP increase during biceps curl compared to leg extension at moderate intensity (2.2% for POAG patients and 9.3% for controls).

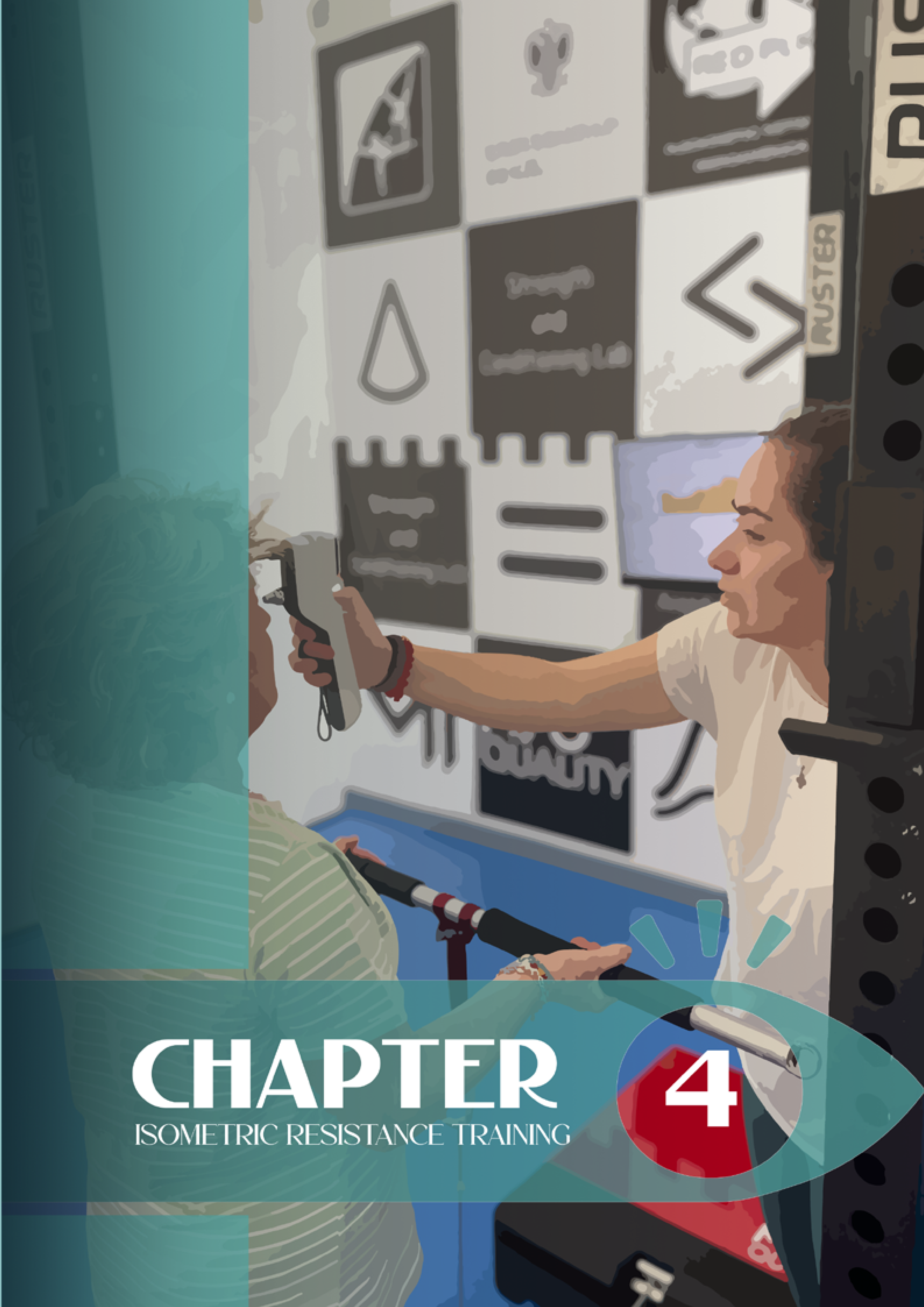
Overall, during resistance exercise in healthy adults, IOP acutely rises, with varying degrees of fluctuation (Hackett et al. 2024). In line with these findings, the present results showed an IOP elevation with low- to moderate-intensity dynamic exercises in POAG patients and age-matched controls. Contrary to our hypothesis, a lower IOP increase was found in POAG patients in comparison to the control group. Also, greater differences between groups appear in the more physically demanding conditions when IOP tends to increase sharply (Vera et al. 2019c). This result may be attributed to the effectiveness of eye drops used to regulate the altered outflow facility in this cohort, as all POAG patients in the study were treated with prostaglandin analogues or a combination of prostaglandin analogues and beta-blockers. The IOP increase in POAG patients at both intensities was minimal (< 1 mmHg), supporting the combined use of medication and physical training (Vera et al. 2021b). Moreover, although the sample size of the POAG group was relatively small, we explored the potential effect of eye drop treatment (prostaglandin analogues vs. a combination of prostaglandin analogues and beta-blockers) on the IOP response to dynamic resistance training. This analysis revealed that the IOP changes in POAG patients were independent of the eye drop treatment ($p = 0.902$). Therefore, it appears that glaucoma patients treated with eye drops could benefit from a higher training intensity without suffering from instability of IOP values.

Regarding vascular factors, physical exercise has been linked with higher OPP values (Zhu et al. 2018), which may reduce the risk of glaucoma development and progression (Yip et al. 2011). Isometric exercises have shown increased blood flow and OPP levels in glaucoma patients (Gugleta et al. 2003; Portmann et al. 2011). However, we found no significant differences in OPP levels after low- to moderate-intensity dynamic resistance exercises. High-effort exercises, in contrast, have been shown to cause an acute OPP reduction (Vera et al. 2019c), highlighting the complex relationship between physical exercise and OPP regulation. The medication regimen of the POAG patients in this study may have influenced their altered outflow facility response, permitting them an effective regulation of OPP levels during exercise.

This study provides new exercise strategies for managing glaucoma, showing that low- to moderate-intensity dynamic resistance exercise could be a feasible option for enhancing muscle strength in POAG patients with controlled IOP levels. However, these results should be interpreted cautiously due to the following limitations. Although leg extension and biceps curl are commonly included in resistance training programs, our findings should not be generalized to other types of exercises, as IOP and OPP responses could vary. Additionally, while participants were instructed to maintain steady breathing, breathing patterns are known to be important modulators of the IOP response to resistance exercises (Vera et al. 2020d, 2021b). Furthermore, the use of eye drops appears to influence the IOP response to exercise in POAG patients; therefore, other types of glaucoma or different medications may affect the functioning of the aqueous humour outflow system (Stamer and Acott 2012). Thus, the external validity of these findings should be explored in other types of glaucoma or with different treatment regimens. Also, some studies have observed that IOP and OPP responses to exercise are influenced by sex and fitness level (Vera et al. 2019d; Janicijevic et al. 2022). Future studies with a larger sample size should further explore these relationships in the context of the current findings. Lastly, randomized clinical trials are needed to assess the long-term effects of dynamic resistance training on glaucoma management.

CONCLUSION

IOP shows a slight (clinically irrelevant) increase during dynamic sets of leg extension and biceps curl exercises executed at low to moderate intensities in POAG patients. However, age-matched controls experienced a heightened IOP rise during resistance exercise. This finding could be associated with the effectiveness of the eye drop treatment (prostaglandin analogues or a combination of prostaglandin analogues and beta-blockers) for regulating the IOP behaviour in POAG patients. Additionally, OPP remains stable after dynamic resistance exercises in both groups. Moderate-intensity dynamic resistance training seems to be a safe training strategy, and thus it should be considered for trainers and eye care specialists working with POAG patients treated with eye drops.



CHAPTER 4

ISOMETRIC RESISTANCE TRAINING

Acute intraocular pressure changes during isometric exercise in primary-open angle glaucoma patients: The influence of exercise type and intensity

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Brief overview

Regular physical exercise promotes different health benefits, including enhanced functional capacity in clinical populations (Izquierdo et al. 2021). In this regard, observational and retrospective studies suggest that individuals who engage in regular physical activity have a lower risk of developing glaucoma or experiencing its progression (Yip et al. 2011; Meier et al. 2018; Lee et al. 2019). Specifically, resistance training appears to influence ocular physiology, with these effects depending on both individual and exercise-specific characteristics (Wylęgała 2016).

While research highlights exercise's potential benefits for glaucoma, detailed guidelines remain lacking. Different exercise parameters influence IOP, with resistance training performed against relative heavy loads causing acute IOP rises (Vieira et al. 2006; Rüfer et al. 2014; Vera et al. 2019c, 2020a), and isometric exercises causing greater IOP spikes than dynamic exercises (Bakke et al. 2009; Vera et al. 2019a, 2020f, 2023). Remarkably, isometric training is widely used in older adults to manage musculoskeletal conditions and hypertension with lower fatigue levels (Inder et al. 2016; Lum and Barbosa 2019; Hansford et al. 2021).

The multiple mechanisms contributing to IOP elevation during resistance exercise include vascular, mechanical, and neural factors. Several studies have reported that acute increases in systemic arterial and venous pressures during exertion can cause vascular engorgement and choroidal volume expansion, elevating IOP (Bakke et al. 2009; Vaghefi et al. 2021)six repetitions using 75% of maximal load (6RM. Increased episcleral venous pressure reduces aqueous humor outflow, further contributing to IOP elevation (Vaghefi et al. 2021)six repetitions using 75% of maximal load (6RM. Mechanical factors, such as the Valsalva maneuver and sustained muscle contraction, increase intrathoracic and intra-abdominal pressures, transmitting pressure to the orbital vasculature and impeding venous return, which results in transient IOP spikes (Vera et al. 2019c). Changes in the Schlemm's canal have also been linked to alterations in autonomic nervous system activity (Sun et al. 2020). Specifically, isometric exertion, such as holding a weight, can reduce the anterior chamber angle, thereby increasing resistance to aqueous humor outflow and leading to elevated IOP (Vera et al. 2019f). These findings highlight the complex interplay between vascular, mechanical, and neural factors during resistance exercise, underscoring the multifactorial mechanisms underlying exercise-induced IOP changes.

Vascular factors also play a role in glaucoma, as compromised optic nerve blood flow regulation increases disease risk (McMonnies 2016). Based on the observed effects of isometric efforts on IOP and blood pressure (Bakke et al. 2009; Inder et al. 2016; Vera et al. 2019a, 2020f, 2023; Hansford et al. 2021), elevated IOP combined with reduced blood pressure can lower OPP, accelerating disease progression (Yip et al. 2011). However, glaucoma patients have demonstrated to have an altered mechanism of IOP regulation (Galambos et al. 2006; Stamer and Acott 2012), and thus, the effects observed on healthy subjects may not be generalizable to glaucoma patients. POAG patients often exhibit impaired IOP homeostasis due to trabecular meshwork dysfunction and abnormal episcleral venous responses (Stamer and Acott 2012; Acott et al. 2014). Furthermore, optic nerve head susceptibility to vascular dysregulation increases the risk of damage during IOP fluctuations (McMonnies 2016). Anti-glaucoma medications may attenuate exercise-induced IOP increases by reducing aqueous humor production (e.g., beta-blockers, alpha-agonists, carbonic anhydrase inhibitors) or enhancing outflow (e.g., prostaglandin analogs, rho-kinase inhibitors) (Casson 2022). Despite this, no study has directly assessed whether these medications modify the IOP or OPP response to resistance exercise in glaucoma patients. Understanding the interplay between exercise-induced IOP changes, glaucoma pathophysiology, and medication effects remains a critical gap in the current literature.

Most studies focus on healthy individuals, leaving gaps in understanding glaucoma patients' responses. The exercises selected to explore these gaps were mid-thigh pull and biceps curl as used in previous studies (Vera et al. 2019d, 2020f). This study aims to assess (i) the effects of the type of isometric resistance exercise (mid-thigh pull and biceps curl), and (ii) the intensity effects (low vs. moderate) on the IOP and OPP response during exercise and recovery in POAG patients and age- and sex-matched controls. We hypothesize that isometric resistance exercise will cause an increase in IOP and OPP values, with greater effects in exercises engaging larger muscle groups and performed at higher intensities, and in POAG patients.

METHODS

Experimental design

A cross-sectional study design was used to examine the influence of isometric mid-thigh pull and biceps curl exercises on IOP and OPP behaviour at two intensities in POAG patients and sex- and age- match controls (**Figure 10**). Participants visited the laboratory twice, 48 hours apart, for familiarization with the procedures and assessment sessions. Isometric peak force (IPF) for the mid-thigh pull and biceps curl was measured using a functional electromechanical dynamometer (FEMD) (MyoQuality, Model Research, Granada, Spain) to objectively estimate exercise intensity (Table 1). Participants performed one set of each exercise at low (light bar) and high intensity (50% of IPF). IOP was assessed at baseline (upon arrival), during exercise, and after 1 and 5 minutes of passive recovery. Additionally, blood pressure was measured at baseline, and after 1 and 5 minutes of passive recovery. The order of exercises and intensity levels was randomized using an Excel spreadsheet. All assessments were conducted under standardized environmental conditions (~22°C, 60% humidity), and participants were instructed to refrain from eating or drinking during the session.

Participants

The required sample size was determined through an a-priori power analysis using the G*Power 3.1 software based on an analysis of variance (ANOVA) with both within- and between-participant factors. The analysis assumed an effect size (f) of 0.2, an α-level of 0.05 and a power of 0.80 (Janicijevic et al. 2021). This calculation indicated that 36 participants (18 POAG and 18 controls) were needed to detect significant differences. A total of 25 POAG patients and 19 age-matched Caucasian controls participated in this study (**Table 2**). The POAG group (14 men, 11 women) included patients with a confirmed diagnosis based on glaucomatous optic nerve head changes and visual field defects consistent with glaucoma. All were undergoing treatment with eye drops, either prostaglandin analogs alone or in combination with beta-blockers. Participants were recruited from the Glaucoma Unit at Virgen de las Nieves University Hospital (Granada, Spain). The control group consisted of 7 healthy men and 12 healthy women. Inclusion criteria for all participants were: (a) sufficient mobility to engage in low to moderate physical activity; (b) absence of underlying conditions that could be adversely affected by exercise; (c) no history of surgical intervention for glaucoma; and (d) age between 60 and 80 years. This study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and was approved by the Institutional Review Board (1961-N-22).

Procedures

The familiarization session focused on learning the proper execution of the mid-thigh pull and biceps curl using the FEMD. At the start, participants' age, body mass, and height were recorded. They then completed a general warm-up consisting of full-body mobility exercises and practiced the movements using elastic bands and light bars. Next, participants performed a progressive warm-up, consisting of three 6-second sets at 40%, 60%, and 80% of their self-perceived maximum effort for both exercises, with 1-minute rest intervals between sets. This was followed by two 6-second sets at maximal effort, with a 3-minute rest between attempts. The highest peak force of each exercise was recorded as IPF. Participants were encouraged to exert maximum effort from the start to the end of each 6-second trial.

The second visit (assessment session) began with baseline measurements of IOP and blood pressure. Participants then completed a general warm-up followed by a specific warm-up, consisting of three 6-second sets at 40%, 60%, and 80% of their IPF for both the mid-thigh pull and biceps curl exercises, with 1-minute rest intervals between sets. After a 5-minute rest, participants performed one 30-second set of each exercise (mid-thigh pull and biceps curl) using a light bar (0.1 kg), followed by one set at 50% of their IPF. IOP was measured before exercise, during the 30-second exertion period of each exercise, and at 1- and 5-minutes post-exercise. Blood pressure was recorded before exercise, and again at 1- and 5-minutes post-exercise. A 10-minute rest period was maintained between conditions.

Sample characteristics	POAG	Control	p-value (ES [b])
Sample size	25	19	
Age (years)	70.4 ± 6.8	69.2 ± 6.0	0.541 (0.19)
Weight (kg)	74.3 ± 13.3	74.7 ± 13.9	0.914 (0.03)
Height (cm)	165.9 ± 10.5	163.9 ± 10.1	0.532 (0.19)
Baseline IOP (mmHg)	16.9 ± 4.2	16.4 ± 3.2	0.681 (0.13)
Baseline OPP (mmHg)	53.7 ± 9.3	50.3 ± 8.0	0.897 (0.04)
MTP [a] 100% IPF (kg)	77.1 ± 32.7	75.2 ± 29.0	0.844 (0.06)
Biceps curl 100% IPF (kg)	23.9 ± 10.1	22.0 ± 9.5	0.547 (0.19)

[a] MTP: mid-thigh pull, [b] ES = effect size.

Table 2. Descriptive (mean ± standard deviation) and statistical (p-value and effect size) of anthropometrical and isometric exercise characteristics of all participants included in this study.

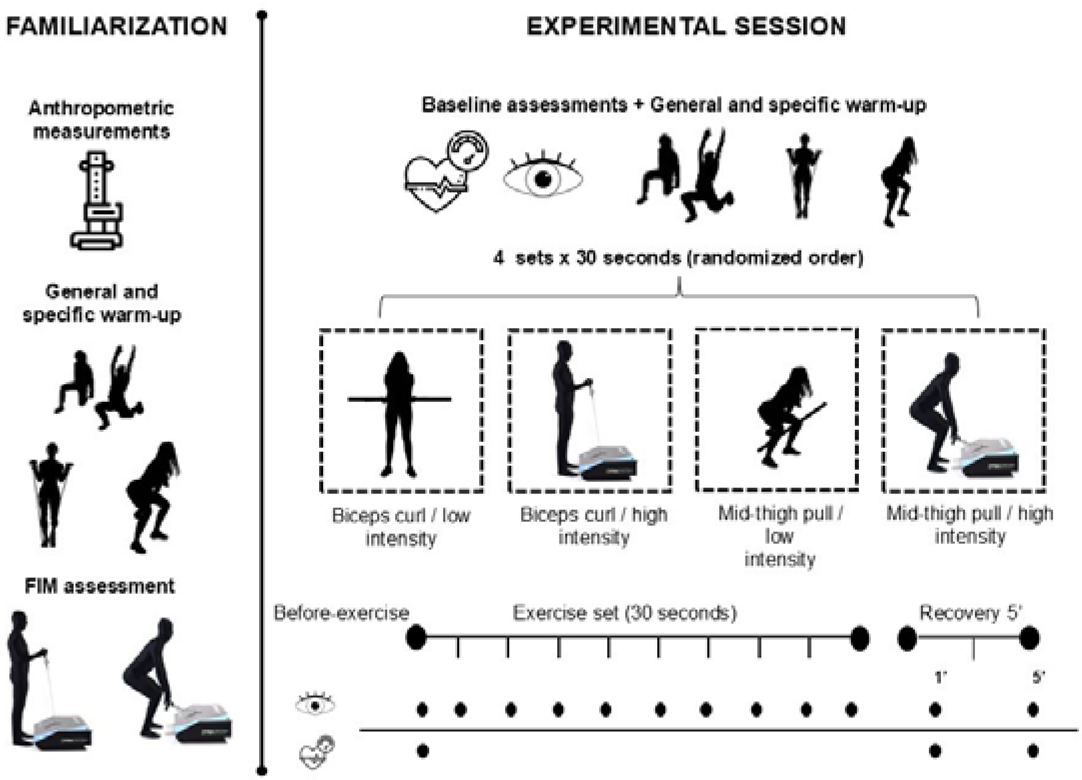

Figure 10. A schematic illustration of the study 4 procedures.

IOP was measured using a portable rebound tonometer (Icare IC200, Tiolat Oy, Helsinki, Finland), which has demonstrated to provide valid and reliable results (Pakrou et al. 2008). Participants were instructed to fixate on a distant target while six measurements were taken against the central cornea during baseline and post exercise assessments. The average of six measurements was used for further analysis. During the isometric exercise IOP was continuously measured during the 30-second exertion period. The evaluator vocalized the measurements for a research assistant to record the data. The Icare tonometer does not acquire IOP measurements at perfectly regular intervals, and manual logging introduces uncertainty in the exact time stamps. To overcome these limitations, we devised a data processing approach to generate a set of equally spaced IOP values with precise time stamps. Specifically, we re-sample the manually obtained IOP values over a 30-second period using polynomial interpolation. Given the recorded IOP measurements, we fit a polynomial function that passes through the available data points. This function is then evaluated at regular intervals to estimate missing values, ensuring a uniform time distribution over a 30-second interval. The polynomial degree is chosen to balance accuracy and stability, minimising potential overfitting or oscillations, enhancing temporal resolution while preserving the trend of IOP fluctuations. A similar approach has been conducted in previous investigations assessing IOP changes during isometric efforts (Vera et al. 2019a, 2020f, 2021b). Blood pressure was measured using a wrist digital automatic monitor (RS6 HEM-6221, Omron, Kyoto, Japan). OPP was estimated from the assessment of IOP and blood pressure (OPP = [95/140 × mean arterial pressure] – IOP).

STATISTICAL ANALYSIS

Descriptive data are presented as means ± standard deviation. The normal distribution of the data was checked with the Shapiro-Wilk test, and the homogeneity of variances with the Levene's test ($p > 0.05$). For the analysis of IOP changes, a repeated measures analysis of variance was carried out with the *exercise intensity* (high, low), *exercise* (mid-thigh pull, biceps curl) and *point of measure* (before-exercise, 10 points during the effort, 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 changes, data were submitted to another repeated measures analysis of variance with the *exercise intensity* (high, low), amount of *exercise* (mid-thigh pull, biceps curl) and *point of measure* (before-exercise, 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 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^2_p) for T and F tests, respectively. All statistical analyses were performed using the JASP statistics package (version 0.18.3).

RESULTS

First, we found no significant between-group differences for baseline IOP and OPP assessments and fitness level (i.e., biceps curl and mid-thigh pull IPF) (**Table 2**).

The 4-way ANOVA applied for the IOP changes revealed statistical significance for the main effects of *intensity* ($F = 103.6$, $p < 0.001$, $\eta^2_p = 0.71$) and *point of measure* ($F = 65.2$, $p < 0.001$, $\eta^2_p = 0.61$). However, the main effect of *exercise* ($F = 0.6$, $p = 0.455$, $\eta^2_p = 0.01$) and group ($F = 1.4$, $p = 0.238$, $\eta^2_p = 0.03$) did not reach statistical significance. The interaction effect *intensity* × *point of measure* ($F = 32.0$, $p < 0.001$, $\eta^2_p = 0.43$), showed statistical significance, whereas the rest of interactions did not reach statistically significant differences ($p > 0.060$ in all cases). Post-hoc analyses revealed higher IOP increments in the high- in comparison to the low-intensity condition (corrected p-value < 0.001, Cohen's $d = 0.52$). Also, there was a linear IOP rise during exercise execution, with IOP returning to baseline levels immediately after completing the exercise (**Figure 11**).

Complementarily, four separate ANOVAs for both exercises (mid-thigh pull and biceps curl) and intensities (low and high) were carried out to explore the differences between the POAG and control groups (see **Figure 11**). For the low-intensity conditions, both groups tended to show a stable IOP response during exercise execution. For high-intensity, both groups experienced a linear increase during the effort, reaching higher IOP levels in control group in comparison to POAG patients in the mid-thigh pull exercise (*point of measure* × *group*: $F = 2.5$, $p = 0.048$, $\eta^2_p = 0.06$). Independent sample t-tests were performed to explore point of *measure* × *group* interaction, however no differences were found between groups in any point of measure (all p-values > 0.052).

Regarding OPP, statistically significant differences were found for the main effect of point of measure ($F = 3.3$, $p = 0.048$, $\eta^2_p = 0.07$), whereas the rest of main effects did not reach statistically significant differences (all p-values > 0.181). Also, all interactions did not reach statistically significant differences (all p-values > 0.063). Post-hoc analyses revealed a slight increase in OPP after the exercise (corrected p-value < 0.095, Cohen's $d = -0.11$), returning to baseline levels after 5 minutes of recovery (**Figure 12**).

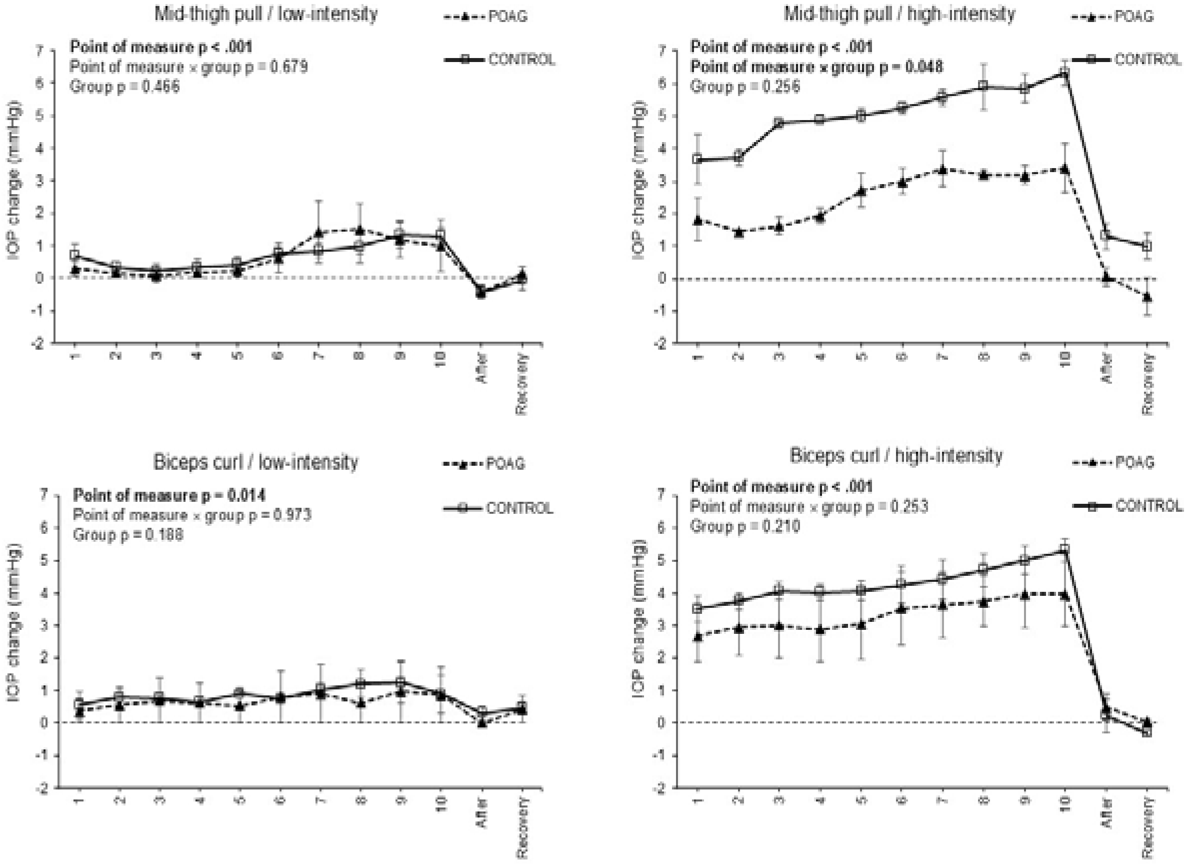

Figure 11. Effects of mid-thigh pull and biceps curl exercises at two intensities on intraocular pressure in the primary open-angle glaucoma (POAG) and control groups. Error bars represent the 95% confidence intervals. Bold font has been used to highlight statistically significant effects ($p<0.05$). IOP= intraocular pressure; After= measurement taken after completing the set (within 1 minute); Recovery= measuresment taken after 5 minutes of completing the set.

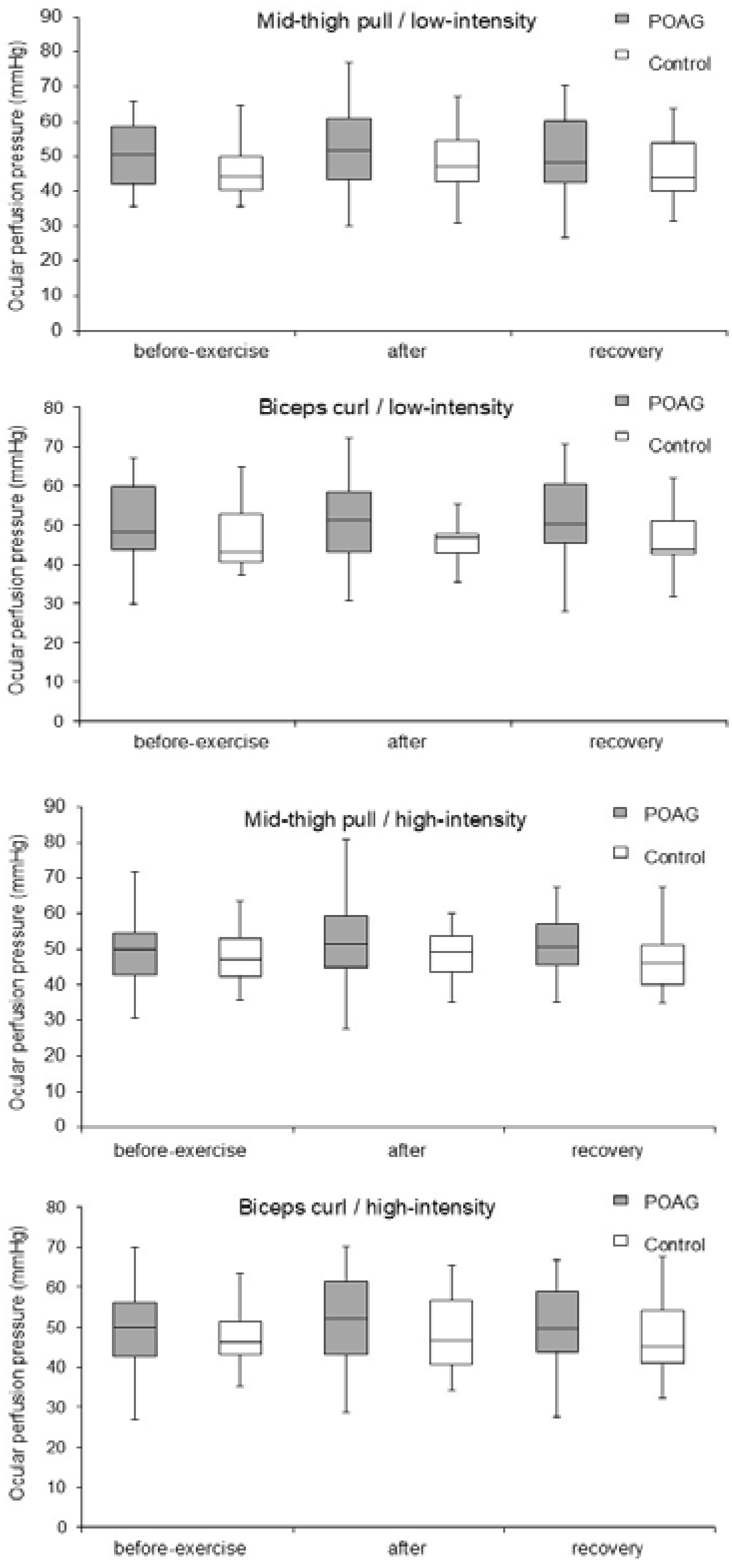

Figure 12. Effects of mid-thigh pull and biceps curl exercises at two intensities on ocular perfusion pressure in the primary open-angle glaucoma (POAG) and control groups. After = measurement taken after completing the set (within 1 minute); Recovery = measurement taken after 5 minutes of completing the set

DISCUSSION

This study aimed to evaluate IOP and OPP responses to isometric resistance exercises (mid-thigh pull and biceps curl) in POAG patients and age-matched controls. We observed a progressive increase in IOP throughout both exercises, with greater increments at high intensity. However, IOP quickly returned to baseline after exercise cessation. Notably, POAG patients exhibited a smaller IOP increase during the mid-thigh pull at high intensity compared to controls (POAG: 2.6 ± 0.8 mmHg vs. control: 5.1 ± 0.9 mmHg). There was a slight OPP increase post-exercise, but no differences were observed after 5 minutes of recovery. Overall, these exercises could be cautiously incorporated into training programs for POAG patients, ensuring IOP levels are carefully monitored to prevent undesirable IOP fluctuations.

Consistent with previous reports, our findings indicate an acute increase in IOP during isometric resistance exercises (Hackett et al. 2024). At high intensity, the IOP rise was notable, reaching 3.0 ± 0.6 mmHg for POAG patients and 4.7 ± 0.7 mmHg in the control group. The results support the notion that isometric effort provokes transient IOP elevations, particularly at high intensities and toward the end of each set, likely due to mechanical strain (e.g., Valsalva-like maneuvers), vascular engorgement, and potential reductions in anterior chamber angle width (Vera et al. 2019f, a). Additionally, prior studies have reported IOP elevations of 7–9 mmHg with longer effort durations (1–2 minutes) and higher intensities (80% 1RM), with even greater increases when the Valsalva maneuver was performed (Vera et al. 2019d, 2021b). It is well established that high-intensity exercises can lead to altered breathing patterns, resulting in acute IOP spikes, whereas low- to moderate-intensity exercises tend to promote steady breathing, helping maintain stable IOP levels (Vera et al. 2019c, 2021b). However, an unintentional Valsalva maneuver may have occurred during the execution of the mid-thigh pull and biceps curl at high intensity, likely due to the challenge of maintaining trunk stability (Ikeda et al. 2009). Therefore, trainers and eye care specialists should carefully assess exercise intensity and associated breathing patterns when considering physical activity for glaucoma prevention and management.

Additionally, IOP levels peaked toward the end of the set, as previously observed with longer set durations and accumulated repetitions (Hackett et al. 2024). It appears advisable to reduce exercise duration during isometric efforts to avoid undesirable IOP elevations in POAG patients or those at risk. Moreover, the significant rise in IOP during exercise seems to be temporary, returning to baseline levels within 1 minute of passive rest. This finding aligns with previous studies that show a rapid decrease in IOP immediately after exercise cessation (8-10 seconds of rest) (Vera et al. 2019d, 2020f). Mechanistically, this drop likely reflects a release of intrathoracic and intra-abdominal pressure (via Valsalva release), normalization of episcleral venous pressure, and autonomic regulation favouring parasympathetic tone. As suggested by Vaghefi et al. (2021)six repetitions using 75% of maximal load (6RM, stimulation of the sympathetic-parasympathetic axis during and after exertion may transiently enhance trabecular meshwork outflow, facilitating a rapid drop in IOP. This recovery dynamic suggests that the eye's fluid regulation system is highly reactive to acute hemodynamic and autonomic changes, even in the context of glaucoma, particularly when pharmacologically supported. Furthermore, exercises involving larger muscle groups tend to provoke higher IOP levels compared to those involving smaller muscle groups (Hackett et al. 2024). Contrary to our hypothesis, we found no significant differences between mid-thigh pull and biceps curl exercises. Similar results, showing no significant difference in IOP based on muscle mass recruitment during isometric efforts, have been reported in previous research (Vera et al. 2020f). However, during dynamic resistance exercises, higher IOP values were observed with squats compared to biceps curl (Vera et al. 2020d). It is plausible that the amount of muscle mass recruited is more relevant when dynamic exercises are performed.

Overall, most studies conducted with healthy adults have shown a significant increase in IOP during resistance training exercises (Hackett et al. 2024). In line with this, both POAG patients and the control group experienced comparable IOP elevations across both intensities and exercises. However, a slight difference was observed during the mid-thigh pull exercise at high intensity, with the control group reaching higher IOP levels than the POAG patients. A novel contribution of this study is the attenuated IOP rise observed in POAG patients, especially during the mid-thigh pull at high intensity, compared to healthy controls. This suggests a potential protective effect of anti-glaucoma medications during physical exertion. The most plausible mechanism involves the modulation of aqueous humor dynamics. Specifically, medications such as prostaglandin analogs increase uveoscleral outflow, while beta-blockers and carbonic anhydrase inhibitors reduce aqueous production (Casson 2022). When combined with sympathetic activation during exercise, these medications may buffer the transient rise in IOP by maintaining outflow facility or suppressing production at a time when venous return and episcleral pressure are elevated. Although the sample size of the POAG group was relatively small, we examined whether the anti-glaucoma medications influenced the IOP response. The analysis showed that IOP changes in POAG patients were not affected by the treatment type ($p = 0.957$). In either case, the IOP increase in both groups exceeded 2 mmHg, which could be considered of relevance for preventing ocular damage (Vera et al. 2021b). Therefore, it would be advisable to adjust exercise intensity and selection based on individual responses. Additionally, evidence suggests that a gradual approach to resistance training may help mitigate potential ocular risks associated with acute IOP increases caused by intense physical exertion (Vera et al. 2018b).

In addition to IOP values, ocular perfusion and blood flow play an important role on glaucoma pathogenesis (Cherecheanu et al. 2013). In line with previous research using isometric exercises with glaucoma patients (Gugleta et al. 2003; Portmann et al. 2011), we found a slight increase in OPP after the exercise regardless of the experimental group. Portmann and colleagues (Portmann et al. 2011) suggested that glaucoma patients have a less active regulatory capacity, but our results do not support this statement due to the similar OPP behavior found in POAG patients and healthy controls. Based on the current findings, the positive effects of increased OPP levels can be achieved through low- to high-intensity isometric resistance training in both healthy and clinical populations. Therefore, eye care and sports professionals should consider these exercises and intensities as safe and effective alternatives when recommending physical activity for glaucoma patients or individuals at risk.

This study has certain limitations that should be acknowledged. First, our experimental sample included only POAG patients treated with eye drops, and thus, the applicability of these findings to other types of glaucoma or treatments requires further exploration (Stamer and Acott 2012). Second, while we tested two isometric exercises commonly used in resistance training, additional exercises should be evaluated to strengthen the current findings (Vera et al. 2020f). Third, breathing patterns were not objectively monitored, which may have introduced undesirable variations (Vera et al. 2021b). Fourth, the influence of physical fitness on IOP changes induced by isometric exercises should be investigated (Vera et al. 2017b, 2020b). Finally, randomized clinical trials are necessary to assess the long-term impact of isometric exercises on glaucoma progression.

CONCLUSION

IOP shows a significant increase during isometric sets of mid-thigh pull and biceps curl exercises at high intensity in both POAG patients and age-matched controls. Also, a slight increase has been found at low intensity for both groups. To prevent uncontrolled IOP elevation, it is advisable to adjust the intensity and exercise selection based on individual responses. Additionally, moderate increases in OPP are observed after isometric resistance exercises in both groups. These findings suggest that isometric exercise can be considered a viable option to improve fitness levels in POAG patients, if exercise intensity is individually adjusted according to individual responses.

CONCLUSIONS

9. CONCLUSIONS/CONCLUSIONES

This doctoral thesis has been organized into four studies, and the following conclusions can be derived from them:

Study I: *Evidence-Based Exercise Recommendations for the Reduction and Stabilization of Intraocular Pressure: A Practical Guide for Eye Care and Sport Specialists.*

Conclusion 1: physical exercise is an important modifiable factor in glaucoma management that should be considered by healthcare providers. Exercise should be prescribed and monitored like any other medical treatment, with consideration for the individual's unique characteristics and preferences.

Conclusion 2: small increases in physical activity can provide significant health benefits, and a gradual progressive approach is recommended to minimize exercise-induced IOP fluctuations. Endurance exercises at low-to-moderate intensities can acutely reduce IOP and HIIT response depends on the specific protocol parameters, while resistance exercises at moderate-to-high intensities consistently increase IOP.

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

Conclusion 3: the IOP behaviour is mostly stable when walking at slow and fast velocities.

However, the incorporation of carrying external loads during walking was associated with higher IOP levels, and although the rise is clinically modest, it should be discouraged in POAG patients. There is a moderate OPP rise after walking for POAG patients and control group, and interestingly, this effect was heightened when using a fast-walking pace.

Conclusion 4: POAG patients had a better IOP regulation during walking compared to the control group, with greater differences with the incorporation of carrying external loads. OPP showed a similar behaviour for POAG patients and control group. These findings suggest that low-intensity endurance exercise is a safe exercise strategy that can be used to improve fitness level in POAG patients, avoiding the use of external loads.

Study III: *Acute intraocular pressure responses changes during dynamic resistance training in primary open-angle glaucoma patients and age-matched controls.*

Conclusion 5: the dynamic sets of leg extension and biceps curl reveals an increase in IOP levels returning to baseline levels immediately after exercise cessation whereas OPP remains stable.

Conclusion 6: IOP shows a slight (clinically irrelevant) increase during dynamic sets of leg extension and biceps curl exercises in POAG patients, whereas age-matched controls experienced a higher IOP rise. Additionally, OPP remains stable after dynamic resistance exercises in both groups.

Conclusion 7: the choice of exercises between upper and lower body seems not to be relevant comparing leg extension and biceps curl.

Conclusion 8: the magnitude of IOP increase was higher in the more physically demanding conditions, however, the use of low- to moderate-intensity leg extension and biceps curl exercises seems to be a safe training strategy for POAG patients undergoing eye drops treatment.

Study IV: *Acute intraocular pressure changes during isometric exercise in primary-open angle glaucoma patients: The influence of exercise type and intensity.*

Conclusion 9: isometric sets of mid-thigh pull and biceps curl exercises reveals an increase in IOP levels, returning to baseline levels immediately after completing the exercise for both groups. Additionally, moderate increases in OPP are observed after isometric resistance exercises in both groups. The choice of exercises between upper and lower body seems not to be relevant.

Conclusion 10: IOP shows a significant increase during isometric sets of mid-thigh pull and biceps curl exercises at moderate intensity while a slight increase has been found at low intensity for both groups. An OPP elevation response occurs regardless of the intensity. These findings suggest that isometric exercise can be considered a viable option to improve fitness levels in POAG patients, if exercise intensity is individually adjusted according to individual responses.

Esta tesis doctoral se ha organizado en cuatro estudios y se han extraído las siguientes conclusiones:

Estudio I: *Recomendaciones de ejercicio basadas en la evidencia para la reducción y estabilización de la presión intraocular: una guía práctica para especialistas en salud ocular y ciencias del deporte.*

Conclusión 1: el ejercicio físico es un factor modificable importante en el manejo del glaucoma que debe ser considerado por los profesionales de la salud. El ejercicio debe prescribirse y monitorearse como cualquier otro tratamiento médico, teniendo en cuenta las características y preferencias individuales.

Conclusión 2: pequeños aumentos en la actividad física pueden proporcionar beneficios significativos para la salud, se recomienda un enfoque progresivo y gradual para minimizar las fluctuaciones de la presión intraocular inducidas por el ejercicio. Los ejercicios de resistencia a intensidades bajas y moderadas pueden reducir agudamente la presión intraocular, mientras que la respuesta a los HIIT depende de los parámetros específicos del protocolo. En contraste, los ejercicios de fuerza a intensidades moderadas y altas aumentan la presión intraocular de manera consistente.

Estudio II: *Respuestas de la presión intraocular y la presión de perfusión ocular durante ejercicio de resistencia de baja intensidad en pacientes con glaucoma primario de ángulo abierto vs. controles emparejados por edad y sexo: influencia del ritmo de marcha y la carga externa.*

Conclusión 3: el comportamiento de la presión intraocular se mantiene mayormente estable al caminar a velocidades lentas y rápidas. Sin embargo, la incorporación de carga externa durante la caminata se asoció con niveles más altos de presión intraocular y, aunque el aumento es clínicamente modesto, debería desaconsejarse en pacientes con glaucoma primario de ángulo abierto. Se observó un aumento moderado en la presión de perfusión ocular después de caminar tanto en pacientes con glaucoma primario de ángulo abierto como en el grupo control, y, de manera interesante, este efecto fue más pronunciado al caminar a un ritmo rápido.

Conclusión 4: los pacientes con glaucoma primario de ángulo abierto mostraron una mejor regulación de la presión intraocular durante la caminata en comparación con el grupo control, con diferencias más notables cuando se incorporó carga externa. La presión de perfusión ocular mostró un comportamiento similar en ambos grupos. Estos hallazgos sugieren que el ejercicio de resistencia de baja intensidad es una estrategia segura para mejorar el nivel de condición física en pacientes con glaucoma primario de ángulo abierto, siempre que se evite el uso de cargas externas.

Estudio III: *Cambios agudos en la presión intraocular durante el entrenamiento de fuerza dinámico en pacientes con glaucoma primario de ángulo abierto y controles emparejados por edad.*

Conclusión 5: la realización de series dinámicas de extensión de piernas y curl de bíceps provoca un aumento en los niveles de presión intraocular, que regresa a los valores basales inmediatamente después de la finalización del ejercicio, mientras que la presión de perfusión ocular se mantiene estable.

Conclusión 6: la presión intraocular muestra un leve aumento (clínicamente irrelevante) durante las series dinámicas de extensión de piernas y curl de bíceps en pacientes con glaucoma primario de ángulo abierto, mientras que el grupo control experimentó un aumento mayor de la presión intraocular. Además, la presión de perfusión ocular se mantiene estable después del ejercicio de fuerza dinámica en ambos grupos.

Conclusión 7: la elección entre ejercicios del tren superior e inferior parece no ser relevante al comparar la extensión de piernas y el curl de bíceps.

Conclusión 8: la magnitud del aumento de la presión intraocular fue mayor en las condiciones más exigentes físicamente; sin embargo, el uso de ejercicios de extensión de piernas y curl de bíceps a intensidades bajas y moderadas parece ser una estrategia de entrenamiento segura para pacientes con glaucoma primario de ángulo abierto que están en tratamiento con colirio.

Estudio IV: *Cambios agudos en la presión intraocular durante el ejercicio isométrico en pacientes con glaucoma primario de ángulo abierto: influencia del tipo e intensidad del ejercicio.*

Conclusión 9: la realización de series isométricas de tirón de muslo medio y curl de bíceps provoca un aumento en los niveles de presión intraocular, que regresa a los valores basales inmediatamente después de completar el ejercicio en ambos grupos. Además, se observaron aumentos moderados en la presión de perfusión ocular después de los ejercicios de fuerza isométricos en ambos grupos. La elección entre ejercicios del tren superior e inferior parece no ser relevante.

Conclusión 10: l a presión intraocular muestra un aumento significativo durante las series isométricas de tirón de muslo medio y curl de bíceps a intensidad moderada, mientras que a intensidad baja se observó un aumento leve en ambos grupos. La respuesta de elevación de la presión de perfusión ocular ocurre independientemente de la intensidad del ejercicio. Estos hallazgos sugieren que el ejercicio isométrico puede considerarse una opción viable para mejorar el nivel de condición física en pacientes con glaucoma primario de ángulo abierto, siempre que la intensidad del ejercicio se ajuste de manera individual según las respuestas de cada persona.

10. FUTURE RESEARCH

The findings of this doctoral thesis support physical exercise as an adjuvant strategy to pharmacological treatment of glaucoma. Endurance and resistance exercises performed at low to moderate intensities seems to be a feasible training option for glaucoma patients. However, longitudinal studies need to be addresses to explore long-term adaptations on ocular health parameters. In addition, these longitudinal studies could analyse the effect of improved physical fitness on IOP and OPP responses since some studies have shown positive results in more physically active individuals.

In order to address these gaps, a clinical trial has been registered to conduct a structured physical training program to assess the impact on glaucoma progression. The clinical trial will be used to determine the chronic effects of a concurrent training program in comparison to no training prescribed (control group). The participants will be pharmacological treated POAG patients. There will be 4 pre-intervention sessions and 4 post-intervention sessions (3 physical assessment and 1 clinical assessment). The study protocol for experimental group will consist of 48 training sessions performed during a 24-week period. The concurrent training sessions will consist of 30 minutes of lower and upper-body endurance low-intensity exercise (arm and leg cycling) and 30 minutes of lower and upper-body resistance exercises (i.e. leg extension, inclined bench press and seated row) at a moderate level of effort.

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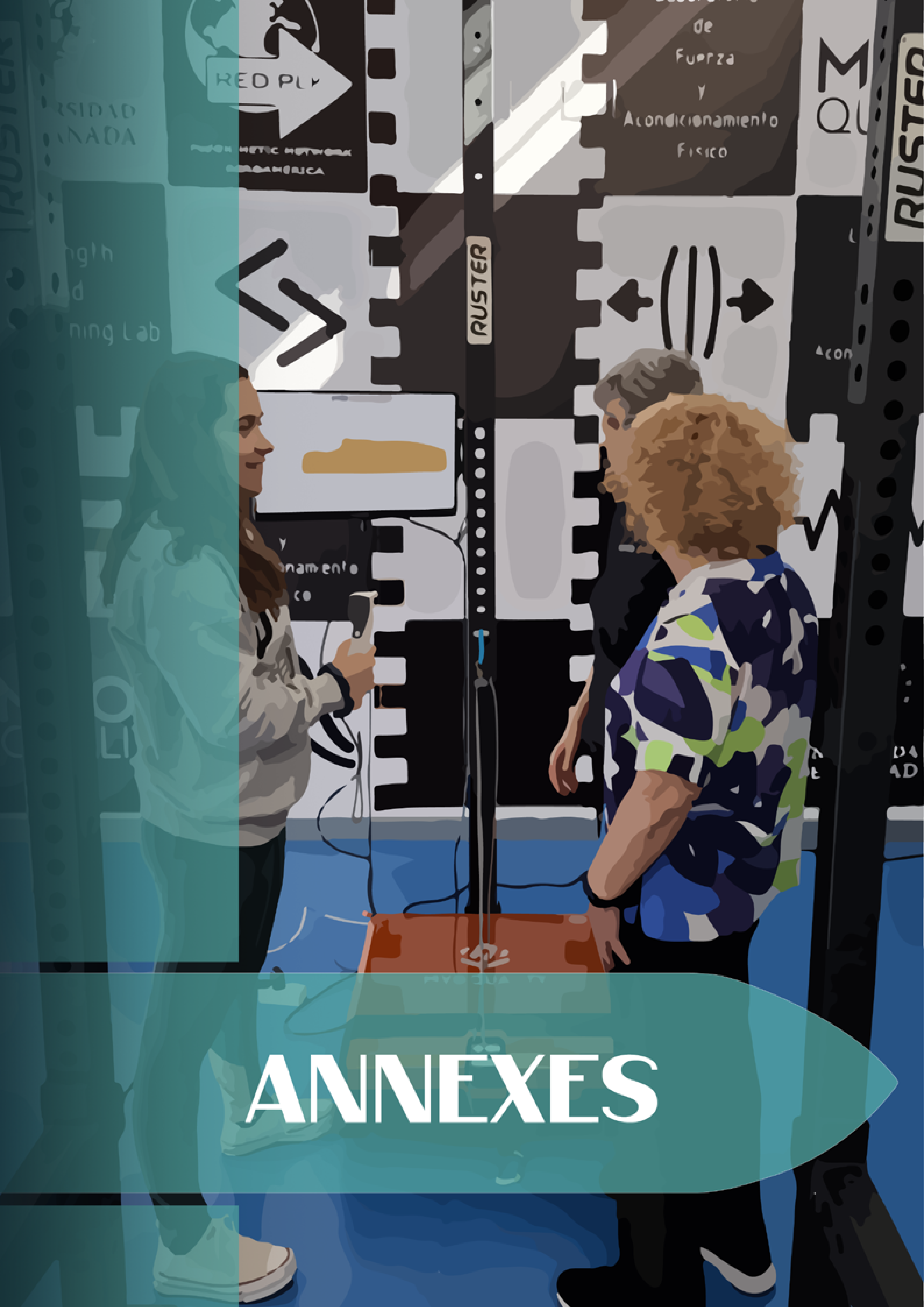

ANNEXES

ANNEXE 2

Junta de Andalucía
Consejería de Salud y Consumo
Servicio Andaluz de Salud

DICTAMEN ÚNICO EN LA COMUNIDAD AUTÓNOMA DE ANDALUCÍA

D. ANTONIO SALMERÓN GARCÍA, EN CALIDAD DE SECRETARIO DEL COMITÉ DE ÉTICA DE LA INVESTIGACIÓN BIOMÉDICA DE LA PROVINCIA DE GRANADA (CEI/CEIM GRANADA)

C E R T I F I C A:

Que este Comité ha evaluado la propuesta del promotor/investigador: Amador García Ramos, para realizar el estudio titulado:

TÍTULO DEL ESTUDIO: *EFECTOS DE UN PROGRAMA DE ENTRENAMIENTO FÍSICO DE 24 SEMANAS EN EL MANEJO DEL GLAUCOMA PRIMARIO DE ÁNGULO ABIERTO*
Código protocolo: *PID2021-127505NA-I00*
Código Portal de Ética: *1961-N-22*
Investigador Principal: *Amador García Ramos*
Centro: *Universidad de Granada*

Versión de los documentos:

Protocolo	*Versión: 2 de fecha 13/12/2022*
HIP	*Versión: 1 de fecha 08/11/2022*
CI	*Versión: 1 de fecha 08/11/2022*

Y considera que:

- Se cumplen los requisitos necesarios de idoneidad del protocolo en relación con los objetivos del estudio y se ajusta a los principios éticos aplicables a este tipo de estudios.
- La capacidad del investigador y los medios disponibles son apropiados para llevar a cabo el proyecto.
- El protocolo del estudio contempla de forma adecuada toda la legislación aplicable.
- Que los aspectos económicos involucrados en el proyecto no interfieren con respecto a los postulados éticos.

Por lo que este Comité ha acordado emitir **DICTAMEN FAVORABLE** para la realización de dicho estudio, para lo cual corresponde a la Dirección del Centro/os correspondiente/s determinar si la capacidad y los medios disponibles son apropiados para llevarlo a cabo.

En el caso de que su estudio requiera acceso y uso de la información santiaria contenida en los sitemas de información del sSstema Sanitario Público de Andalucia, tendran que estar a lo establecido en la Resolución Conjunta 1/2021 de fecha 04/12/2021, de la Secretaría General de Investigación, Desarrollo e Innovación en Salud de la Consejería de Salud y Familias y de la Dirección Gerencia del SAS, por la que se aprueban las Instrucciones para la ordenación de acceso y uso de la información sanitaria contenida en los sitemas de información del Sistema Sanitario Público de Andalucía con fines de investigación e innovación por la entidades dependientes de la Consejería de Salud y Familias.

Lo que firmo en Granada

Es responsabilidad del Investigador Principal garantizar que todos los investigadores asociados con este proyecto, conozcan las condiciones de aprobación y los documentos aprobados.

El Investigador Principal debe informar a la Secretaría del CEIm, mediante una enmienda, informe anual de seguimiento o notificación, de:

- Cualquier cambio significativo en el proyecto y la razón de ese cambio, incluida una indicación de las implicaciones éticas (si las hubiera)
- Cualquier evento imprevisto o inesperado, como desviaciones de protocolo
- El cambio de Investigador Principal
- Informe anual de seguimiento
- La fecha de finalización del estudio
- Informe final del estudio y/o publicación de resultados

ANEXO I COMPOSICIÓN DEL CEI/CEIM DE GRANADA

El Comité, tanto en su composición como en los PNTs, cumple con las normas de BPC (CPMP/ICH/135/95)

En dicha reunión del Comité se cumplió el quórum preceptivo legalmente.

En caso de que se evalúe algún proyecto del que un miembro sea investigador/colaborador o se detecte conflicto de interés, este se ausentará de la reunión durante la discusión del proyecto.

Que a dicha sesión asistieron los siguientes integrantes del Comité:

PRESIDENTA: Dª Aurora Bueno Cavanillas	Catedrática M. Preventiva y S. Pública (UGR)
VICEPRESIDENTA: Dª Paloma Muñoz de Rueda	Doctora en Ciencias Biológicas - Unidad de Apoyo Investig – HUCSC
SECRETARIO: D. Antonio Salmerón García	F.E.A Farmacia Hospitalaria.- HUCSC
VOCALES:	
Álvarez López, Miguel	F.E.A Cardiología HUVN
Arias Santiago, Salvador	F.E.A. Dermatología UGR (Vinculado HUVN)
Cardona Contreras, Jesús	F.E.A. Obstetricia y Ginecología HUCSC
Cobos Vargas, Angel	Enfermero HUCSC. Responsable Seguridad del Paciente
Cuadros Celorrrio, Marta Eugenia	Doctora en Farmacia UGR
Delgado Pérez, Juan Ramón	F.E.A. HUVN (Jefe Sección Oncología)
Del Pozo Gavilán, Esperanza	Catedrática Farmacología Clínica UGR

Domenech Gil, Luis Miguel	Enfermero HUCSC
Domínguez Almendros, Sonia	Metodóloga/Estadística HUCSC
Espínola García, Esther	Distrito Granada-Metropolitano (Farmacéutica AP)
Gálvez Martín, Patricia	Doctora en Farmacia.- BIOIBERICA S.A.U
García Lirola, Mª. Ángeles	Distrito Granada-Metropolitano (Farmacéutica A.P)
García Valverde, Mª. Dolores	Profesora Facultad Derecho.-Doctora en Derecho
Gorlat Sánchez, Berta	Enfermera/Supervisora HUVN
Guijosa Campos, Pilar	Distrito Granada-Metropolitano (Epidemiología)
Jiménez Pacheco, Antonio	F.E.A Urología.- HUCSC
López Guadalupe, Miguel	Miembro LEGO – Prof. titular Hª UGR
Luque Martínez, Francisco M.	Técnico Función Adtva.- HUVN
Manzano Manzano, Fco. Luis	F.E.A. Medicina Intensiva (HUVN)
Marín Jiménez, Rafael	Técnico Oficina Delegado Protección de datos del SSPA
Martin Díaz, Manuel	F.E.A. Cirugía General HOSP. Santa Ana Motril
Martínez Galán, Joaquina	F.E.A. Oncología Médica HUVN
Martínez García, Encarnación	Matrona.- Hospital Alta Resolución Guadix
Martínez González, Luis Javier	Doctor en Ciencias Biológicas.Investigador GENYO
Molina Rivas, Esther	Porfesora Facultad Ciencias Salud (Enfermera)
Morales Romero, Antonio	Enfermero .- Distrito Granada-Metropolitano
Morón Romero, Rocío	F.E.A Farmacia Hospitalaria HUCSC
Mozas Moreno, Juan	F.E.A. Obstetricia y Ginecología UGR Vinculado HUVN
O`Valle Ravassa, Francisco Javier	Vicerrectorado de Investigación UGR
Pérez Fernández , Antonio Juan	C. Ética Asistencial AGS Sur
Sánchez López, José Darío	F.E.A Cirugía Oral y Maxilofacial.- HUVN

Que dicho Comité está constituido y actúa de acuerdo con la normativa vigente y las directrices de la Conferencia Internacional de Buena Práctica Clínica.

Lo que firmo en Granada a

ANNEXE 3

Fecha del CVA	09/05/2025

Parte A. DATOS PERSONALES

Nombre	Maria Dolores		
Apellidos	Morenas Aguilar		
Sexo	Mujer	Fecha de Nacimiento	08/12/1995
DNI/NIE/Pasaporte			
URL Web			
Dirección Email	mdmorenas@ugr.es		
Open Researcher and Contributor ID (ORCID)	0000-0003-0924-3255		

A.2. Situación profesional anterior (incluye interrupciones en la carrera investigadora - indicar meses totales, según texto convocatoria-)

Periodo	Puesto / Institución / País
2023 - 2024	Personal Investigador / Universidad de Granada / España
2023 - 2023	Personal Investigador / Universidad de Granada / España
2022 - 2023	Personal Investigador / Universidad de Granada / España

A.3. Formación académica

Grado/Master/Tesis	Universidad / País	Año
Máster Universitario en Investigación en Actividad física y deporte	Universidad de Granada	2020
Optimización del Entrenamiento y Readaptación Físico-Deportiva	Instituto de posgrado Fundación San Pablo Andalucía y ESYDE / España	2018
Graduado o Graduada en Ciencias de la Actividad Física y Deporte	Universidad de Granada	2017

Parte C. LISTADO DE APORTACIONES MÁS RELEVANTES

C.1. Publicaciones más importantes en libros y revistas con "peer review" y conferencias

AC: Autor de correspondencia; (nº x / nº y): posición firma solicitante / total autores. Si aplica, indique el número de citaciones

1 **Artículo científico**. (1/7) Morenas-Aguilar; González-Hernández; Marcos-Frutos; Miras-Moreno; López-Gómez; García-Ramos; Vera. 2025. Acute intraocular pressure responses changes during dynamic resistance training in primary open-angle glaucoma patients and age-matched controls. Graefe's Archive for Clinical and Experimental Ophthalmology. Springer.

2 **Artículo científico**. (1/9) Morenas-Aguilar (AC); Miras-Moreno; Chacón-Ventura; et al; García-Ramos. 2025. Highly branched cyclic dextrin supplementation and resistance training: A randomized double-blinded crossover trial examining mechanical, metabolic, and perceptual responses. Clinical Nutrition ESPEN. Elsevier. 65, pp.305-314.

3 **Artículo científico**. Vera; (2/3) Morenas-Aguilar; García-Ramos. 2025. Evidence-Based Exercise Recommendations for the Reduction and Stabilization of Intraocular Pressure: A Practical Guide for Eye Care and Sport Specialists. Applied sciences. MDPI. 15-1396.

4 **Artículo científico**. Zwierko; Tapia; Vera; Redondo; (5/6) Morenas-Aguilar; García-Ramos. 2024. Enhancing reactive agility in soccer: The impact of stroboscopic eyewear during warm-up across fatigued and non-fatigued conditions. European Journal of Sport Science. Wiley. 24-12, pp.1798-1808.

5 **Artículo científico**. (1/6) Morenas-Aguilar; Ruiz-Alias; Blanco; Lago-Fuentes; García-Pinillos; Pérez-Castilla. 2023. Does the Menstrual Cycle Impact the Maximal Neuromuscular Capacities of Women? An Analysis Before and After a Graded Treadmill Test to Exhaustion. The Journal of Strength and Conditioning Research. Wolters Kluwer. 37-11, pp.2185-2191.

6 **Artículo científico**. (1/8) Morenas-Aguilar; Chirosa Rios; Rodriguez-Perea; Vázquez; Chirosa Rios; Vera; Ruiz-Orellana; Jerez-Mayorga. 2023. Test–Retest Reliability of 3 Specific Strength Tests in Professional Handball Players. Journal of Sport Rehabilitation. Human Kinetics. 1, pp.1-10.

7 **Artículo científico**. Rodriguez-Perea; (2/5) Morenas-Aguilar (AC); Martinez-Garcia; Chirosa-Rios; Garcia-Buendia. 2023. Influence of trunk rotator strength on rotational medicine ball throwing performance. The Journal of Sports Medicine and Physical Fitness. EDIZIONI MINERVA MEDICA. 63.

8 **Artículo científico**. (1/5) Morenas-Aguilar; Cupeiro; Fernandes; Janicijevic; Garcia-Ramos. 2022. The menstrual cycle does not influence vertical jump performance or throwing velocity in amateur team handball players. Science and Sports. Elsevier. 38-2, pp.211-215.

9 **Capítulo de libro**. Rodríguez-Perea; (2/6) Morenas-Aguilar; Soto-García; Chirosa-Ríos; Serrano-Gómez; Vila-Suarez. 2024. THROWING VELOCITY AMONG FEMALE YOUNG HANDBALL PLAYERS: INFLUENCE OF TRUNK STRENGTH AND ANTHROPOMETRIC MEASUREMENT. 7th EHF Scientific Conference. pp.95-102. ISBN 978-3-9503311-8-9.

10 **Capítulo de libro**. (1/1) Morenas-Aguilar. CICLO MENSTRUAL Y PREPARACIÓN FÍSICA EN BALONMANO. Nuevas perspectivas en entrenamiento para el balonmano del futuro. Universidad de Extremadura. Servicio de Publicaciones. ISBN 978-84-9127-258-8.

C.2. Congresos

1 Morenas-Aguilar; García-Ramos; Vera. Efectos del ejercicio isométrico sobre los niveles de presión intraocular. II Congreso Pleokinetic Functional Dynamometric in Sports Sciences. Universidad de la Frontera. 2024. Participativo - Ponencia oral (comunicación oral). Congreso.

2 Morenas-Aguilar; García-Ramos; Vera. Respuesta de la presión intraocular durante el ejercicio de resistencia de baja intensidad en pacientes con glaucoma primario de ángulo abierto frente a controles emparejados por edad y sexo. II Congreso Pleokinetic Functional Dynamometric in Sports Sciences. Universidad de la Frontera. 2024. Participativo - Póster. Congreso.

3 IV Congreso Internacional de Balonmano 2023. Escuela Nacional de Entrenadores. 2023. Organizativo - Comité científico y organizador. Congreso.

4 Morenas-Aguilar; Delgado-Floody; Jerez-Mayorga. Upper muscle quality index in women with morbid obesity candidates for obesity surgery: A pilot study. VIII Simposio EXERNET. Red Española de Investigación en Ejercicio Físico y Salud. 2023. Participativo - Póster. Congreso.

5 Morenas-Aguilar; Miras-Moreno; Chacón-Ventura; Martín-Olmedo; Jiménez-Martínez; Alix-Fages; Janicijevic; García-Ramos. Cyclodextrin Supplementation during Resistance Training: A Randomized, Double- Blinded Crossover Trial Examining Mechanical, Metabolic, and Perceptual Responses. II CONGRESO INTERNACIONAL SOBRE OPTIMIZACIÓN DEL ENTRENAMIENTO DE FUERZA Y RENDIMIENTO NEUROMUSCULAR. Red de Entrenamiento de Fuerza y Rendimiento. 2023. Participativo - Póster. Congreso.

6 Morenas-Aguilar; Delgado-Floody; Martínez-Salazar; Liempi; Balboa. Reliability of an upper-body isometric strength in severe/morbid obesity patients: a pilot study. I Congreso Pleokinetic Functional Dynamometric in Sports Sciences. Red Internacional de Conocimiento Pleokinetic. 2022. España. Participativo - Póster. Congreso.

7 Morenas-Aguilar; Jerez-Mayorga; Chirosa-Ríos; Soto. Reliability of specific strength tests in young handball players with the use of a functional electromechanical dynamometer (FEMD). I Congreso Pleokinetic Functional Dynamometric in Sports Sciences. Red Internacional de Conocimiento Pleokinetic.. 2022. España. Participativo - Póster. Congreso.

8 Marcos-Blanco; Pérez-Castilla; García-Pinillos; Ruiz-Alias; Fernández-Navarrete; Moreno-Ortega; Morenas-Aguilar. “Influence of menstrual cycle phase on lower-body neuromuscular fatigue”. "I Congreso Internacional sobre Optimización del Entrenamiento de Fuerza y Rendimiento Neuromuscular”. Red de Entrenamiento de Fuerza y Rendimiento Neuromuscular. 2022. España. Participativo - Ponencia oral (comunicación oral). Congreso.

9 Morenas-Aguilar; Pérez-Castilla; García-Pinillos; Ruiz-Alias; Fernández-Navarrete; Moreno-Ortega; Marcos-Blanco. “The influence of menstrual cycle phase on maximal neuromuscular capacities of lower-body muscles: a pilot study”. "I Congreso Internacional sobre Optimización del Entrenamiento de Fuerza y Rendimiento Neuromuscular”. Red de Entrenamiento de Fuerza y Rendimiento Neuromuscular. 2022. España. Participativo - Póster. Congreso.

10 I CONGRESO INTERNACIONAL SOBRE OPTIMIZACIÓN DEL ENTRENAMIENTO DE FUERZA Y RENDIMIENTO NEUROMUSCULAR. Red de Entrenamiento de Fuerza y Rendimiento. 2022. Organizativo - Comité científico y organizador. Congreso.

C.3. Proyectos o líneas de investigación

1 **Proyecto**. PPJIB-2024-15, Efecto de la suplementación con cacao con alto contenido en compuestos fenólicos durante la realización de ejercicio físico en pacientes con glaucoma sobre la salud ocular y el estrés oxidativo.. “Proyectos de Investigación Precompetitivos para Jóvenes Investigadores – Modalidad B” del Plan Propio de Investigación de la Universidad de Granada. María Dolores Morenas Aguilar. (Universidad de Granada). 01/01/2025-31/12/2025. 1.000 €. Investigador principal.

2 **Proyecto**. PID2021-127505NA-I00, ACTIVIDAD FISICA COMO ESTRATEGIA COADYUVANTE AL TRATAMIENTO FARMACOLOGICO DEL GLAUCOMA: UN ENSAYO CLINICO ALEATORIZADO EN PACIENTES CON GLAUCOMA PRIMARIO DE ANGULO ABIERTO. PROYECTOS DE INVESTIGACION DEL PLAN NACIONAL, CONVOCATORIA 2021. Amador García Ramos. (Universidad de Granada). 01/05/2023-31/08/2025. 89.540 €. Miembro de equipo.

3 **Proyecto**. PPJIB2023-079, THE IBOW-TRAINING PROJECT: ENTRENAMIENTO DE FUERZA EN PACIENTES CON ENFERMENDAD INFLAMATORIA INTESTINAL (EEII): EFECTOS EN BIOMARCADORES INFLAMATORIOS E INMUNITARIOS.. AYUDAS DEL PLAN PROPIO UGR 2023. Sergio Miras Moreno. (Universidad de Granada). 01/01/2024-31/12/2024. 1.000 €. Miembro de equipo.