

有氧运动对原发性开角型青光眼患者眼内压的短期影响：一项Meta分析

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摘要

背景: 多项研究表明, 有氧运动可以降低正常人眼内压(Intraocular Pressure, IOP), 但是原发性开角型青光眼(POAG)患者是否需要有氧运动来降低眼内压(IOP)仍存在争议。目标: 探讨有氧运动是否能降低POAG患者眼内压。方法: 纳入分析的研究来自以下数据库: Embase数据库、PubMed、Web of Science、Cochrane图书馆、中国知网(CNKI), 这些研究均在2023年9月前发表且不受语言限制。本Meta分析使用R 4.1.2 (R; GitHub, 旧金山, 美国)进行, 根据Q检验结果计算平均值和标准差(SD)。为评估结果的稳定性, 本研究进行了敏感性分析, 并通过漏斗图检验发表偏倚。采用纽卡斯尔-渥太华量表(NOS)和Cochrane干预措施系统评价手册来评估每项研究的偏倚风险。结果: 本荟萃分析共纳入5项队列研究和1项随机对照RCT (Randomized Controlled Trial)研究, 共338只眼。汇总数据显示, 这些研究的异质性较高($I^2 = 97, P < 0.01$)。随机效应模型显示, 有氧运动有降低POAG患者眼内压的趋势, 但未达到显著水平($SMD = 0.84, 95\%CI [-1.14, 2.82]$)。结论: 我们的研究显示, 有氧运动可能对POAG患者在短时间内降低IOP的影响有限。然而, 我们发现的机制仍需进一步研究。

关键词

原发性开角型青光眼, 眼内压, 有氧运动, 荟萃分析

Aerobic Exercise Has a Limited Short Time Effect on Reducing IOP in POAG Patients: A Meta-Analysis

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Abstract

Background: Multiple studies have shown that aerobic exercise could reduce the intraocular pressure of normal people. However, whether patients with primary open-angle glaucoma (POAG) need aerobic exercise to decrease their intraocular pressure (IOP) is still controversial. **Objective:** To investigate whether aerobic exercise could reduce the intraocular pressure of patients with POAG. **Methods:** Studies included in this meta-analysis are from the following databases: Embase database, PubMed, Web of Science, Cochrane Library, China National Knowledge Infrastructure (CNKI), which were published before September 2021 without any language restrictions. This meta-analysis was performed by R 4.1.2 (R; GitHub, San Francisco, US), and the means and standard deviation (SD) were calculated based on the results of the Q-test. A sensitivity analysis was performed to determine the stability of the results, and publication bias was evaluated by a funnel plot. The Newcastle-Ottawa Scale (NOS) and Cochrane Handbook for Systematic Reviews of Interventions were used to assess the risk of bias of each study. **Results:** A total of 5 cohort studies and 1 RCT, 338 eyes, were included in this meta-analysis. The pooled data indicated that the high heterogeneity among these studies ($I^2 = 97$, $P < 0.01$). The random effect model showed that aerobic exercise had a tendency to reduce intraocular pressure in POAG patients, but did not reach a significant level (SMD = 0.84, 95%CI [-1.14, 2.82]). **Conclusion:** Our study reveals that aerobic exercise may have a limited effect on decreasing IOP in patients with POAG in a short time. However, the mechanisms of our findings still need further investigation.

Keywords

Primary Open-Angle Glaucoma, Intraocular Pressure, Aerobic Exercise, Meta-Analysis

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1. 介绍

原发性开角型青光眼(POAG),以眼内压升高、视网膜血流障碍和视网膜神经节细胞进行性丧失为特征,导致患者视野缺损和不可逆的视觉损害。在美国,超过 80%的青光眼病例为开角型青光眼,在中国,POAG 占 39% [1][2]。POAG 已成为全球第二大致盲原因,到 2020 年影响 8000 万人[3]。IOP 减少仍然是减缓青光眼疾病进展的主要治疗手段[4]。POAG 的治疗选择包括药物(例如:前列腺素类似物和 β 受体阻滞剂)、激光(例如:氩激光小梁成形术、选择性激光小梁成形术)和手术(例如:小梁切除术、管状手术)[5]。然而,部分患者在多次治疗后仍不能将眼压降至理想水平[6][7]。因此,一些无创和保守的治疗方法变得更为可取。

多项研究表明,有氧运动(AE, aerobic exercise)可以降低健康眼睛的 IOP。因此,有氧运动可能是一种有益的 POAG 管理生活方式。最近发表的几项研究表明,POAG 患者应该定期进行有氧运动[8]-[10]。然而,以往关于 AE 对 IOP 影响的研究大多是在健康眼睛中进行的,支持 AE 在 POAG 中作用的证据有限。为了确认 AE 与 POAG 的 IOP 之间的关联,我们进行了这项荟萃分析,以提供基于证据的医学管理与治疗 POAG 的依据。

2. 方法

根据系统评价和荟萃分析的首选报告项目(PRISMA)声明进行本项分析[11]。本荟萃分析涉及的研究之前已发表,无需伦理批准和患者同意。

2.1. 检索策略和选择标准

我们从以下数据库中选择了所有与有氧运动和青光眼相关的临床试验：Pubmed、Web of Science、CNKI、Cochrane 图书馆和 Embase，没有语言限制。我们还检索了早期与所选研究相关的荟萃分析的参考文献，以确定更多潜在的研究。

2.2. 研究选择

两名独立且经过培训的评审员筛选了标题/摘要和全文，以确定纳入的文献。若两名评审员之间存在争议，将由另一位经验丰富的医生进行解决。我们的纳入标准如下：1) 研究必须为临床试验。2) 受试者被诊断为 POGA 或其疑似病例，并且未接受任何手术治疗。3) 研究必须包括有氧运动前后测量的眼压(IOP)，并提供相关的标准差(SD)或标准误差(SE)。4) 运动必须为有氧运动。

2.3. 数据提取和结果

两位独立且受过培训的评审员独立地从纳入的研究中提取数据，包括参与者的统计特征、运动方案、接受的抗青光眼药物以及测量设备。对于两位评审员之间的分歧，会与其他有经验的医生进行讨论解决。我们调查了有氧运动对 POAG 患者 IOP 的影响。每项研究的质量评估结果见表 1。

Table 1. Quality assessment of each study
表 1. 各研究的质量评估

NOS score of studies included in this meta-analysis.									
		Selection			Comparability		Exposure		Total
Study	1	2	3	4	2	1	2	3	9
Gracitelli	★	☆	☆	★	★	★	★	★	7
Yuan	★	★	☆	★	★	★	★	★	8
Yang	★	★	☆	★	★	★	★	★	8
Natsis	☆	★	☆	★	★	★	★	★	7
Quruish	☆	☆	☆	★	★	★	★	★	6
Risk of bias of randomized controlled trial									
study	Bias due to randomisation	Bias due to deviations from intended intervention		Bias due to missing data	Bias due to outcome measurement	Bias due to selection of reported result		Overall	
Medina	Some concerns	Low		Low	Low	Low		Low	

2.4. 偏倚风险评估

2 位有经验的评审员使用了纽卡斯尔 - 渥太华量表(NOS)对 5 项队列研究的偏倚风险进行了评价，并使用了 Cochrane 系统评价干预措施手册对 1 项随机对照试验的偏倚风险进行了评估。

2.5. 统计分析

对于连续数据，我们采用标准化均值差(SMD)作为统计分析方法，通过获得 IOP 的均值(SD)和样本量(n)来实现。如果无法获得 SD，则根据研究中报告的其他统计参数进行估算。
Q 统计量和 I² 使用 2 项检验计算所有研究的异质性，当 P 值小于 0.1 或 I² 大于 40%，认为异质性显著，我们使用随机效应模型。相反，当 P 大于 0.1 或 I² 小于 40%，我们使用了固定效应模型。排除几项

低质量研究后，进行敏感性分析以确定结果的稳定性。通过漏斗图评估发表偏倚，以评价不对称性。使用 R 4.1.2 (R; GitHub, 旧金山, 美国)生成森林图图形、漏斗图和敏感性分析结果。所有统计检验均为双侧显著水平：P 值设定为 0.05。

3. 结果

3.1. 研究选择

文献检索策略和排除标准：在 PUBMED 数据库中，检索策略如下：首先，使用 MeSH 词汇进行“exercise”相关的检索(#1)，并进一步通过多种运动形式(如 aerobic exercise, acute exercise, isometric exercise 等)进行扩展(#2)。接着，检索与“Glaucoma”相关的文献(#3)，并加入“Glaucomas”作为关键词进行补充(#4)。然后，将#1 和#2 的结果合并(#5)，将#3 和#4 的结果合并(#6)。最后，通过交集筛选#5 和#6 的结果，得到最终的检索文献(#7)；文献筛选过程首先通过标题和摘要进行初步筛选，排除与研究主题无关的文献。随后，对通过初步筛选的文献进行全文阅读，进一步排除数据不完整或无法获取原始数据、研究对象不符合标准、研究设计质量不合格以及与研究目的不符的文献。最终，保留符合条件的文献用于进一步分析。经过仔细和谨慎评价，最终纳入 6 项研究进行本荟萃分析[12]-[17]。

3.2. 研究特征

本荟萃分析共纳入 212 名被诊断为 POAG 的患者。纳入研究的基本特征见表 2。受试者进行了步行、慢跑或自行车测功仪有氧运动，持续时间从 5 到 60 分钟不等。有氧运动后，参与者立即接受 Goldmann 压平眼压计测量 IOP 值。来自两项研究的患者[13] [15]同时接受了抗青光眼药物治疗。

Table 2. Systematic review of included studies

表 2. 系统综述纳入研究

Study	Region	Age, years	Eyes	Male/Female	Diagnosed type	Exercise Protocol	IOP Measurement Device	Medication
Gracitelli 2019	Brazil	62.9 ± 1.7	30	16/14	POAG	Cycloergometry, 40 min	Goldman	-
Medina 2007	Brazil	-	32	14/24	POAG	Cycloergometry, 15 minutes, 60~70 HR	Goldman	Antiglaucoma treatment
Yang 2014	China	53.35 ± 11.20	100	21/29	POAG	Cycloergometry, 10 minutes of 20% Wmax or 5 minutes of 60% Wmax	Goldman	-
Yuan 2020	China	36.09 ± 10.53	59	31/4	POAG	Treadmill 30 min	Goldman	-
Natsis 2009	Greece	62.5	90	20/25	POAG	Cycloergometry, 10 minutes, 60~80 w	Goldman	Antiglaucoma treatment
Quruish 1995	Pakistan	46.14 ± 3.23	28	-	POAG	Walking, 1 h or jogging 1 h	Goldman	-

这项 Meta 分析包含的 6 项试验均为随机对照试验(RCT)。试验数据概述包括受试者的国家、性别分布和年龄。数据以均值和标准差(SD)形式报告。

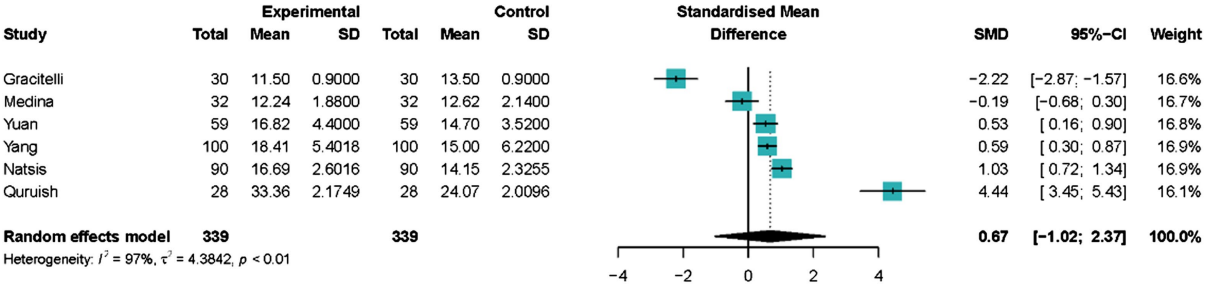
3.3. 文献质量评价

采用纽卡斯尔 - 渥太华量表(NOS)对 5 项队列研究的质量进行评估，6 分或以上视为高质量文献。1 项随机对照试验的偏倚风险通过《Cochrane 系统评价手册》进行评估。质量评估详情见表 1。

3.4. 统计结果

该荟萃分析显示，有氧运动可降低 POAG 患者的房内压，但不达到显著水平(SMD = 0.84, 95%CI [-1.14, 2.82]; 图 1)。异质性检验结果表明 $I^2 = 97\%$, $P < 0.01$ ，表明 6 项研究存在显著异质性。为了探讨异质性的可能来源，我们进行了亚组分析。亚组分析结果显示，在中国(SMD = 0.56, 95%CI [0.34, 0.79])、希腊和巴基斯坦，IOP 水平显著降低；而巴西的数据表明，有氧运动对 POAG 患者的 IOP 没有影响(SMD

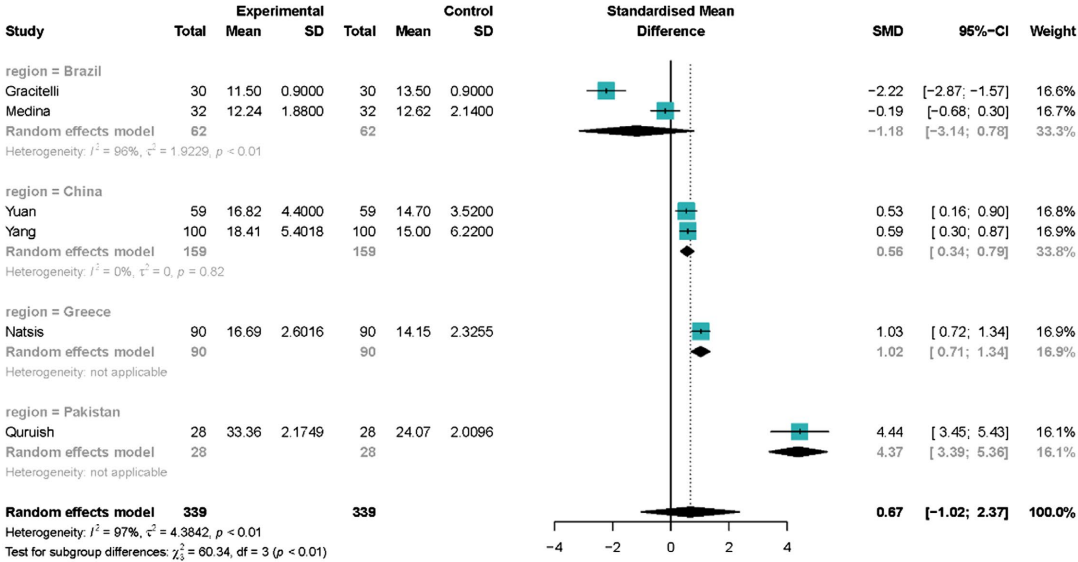
= -1.18, 95%CI [-3.14, 0.78])。此外, 亚组内异质性减少, 提示纳入研究的区域可能是异质性的来源(巴西: $I^2 = 96\%$, $P < 0.01$; 中国: $I^2 = 0\%$, $P = 0.82$; 图 2)。为了确认研究的稳定性, 我们进行了敏感性分析, 在该分析中, 删除一项研究对总体结果没有显著影响(图 3), 表明我们的结果具有良好的稳定性。



在荟萃分析中, 灰色方块的大小与权重成正比, 黑色线条表示置信区间, 虚线代表合并效应值。

Figure 1. Forest plot demonstrates mild or moderate Aerobic exercise has a limited short time effect on reducing IOP in POAG patients

图 1. 森林图显示轻度或中度有氧运动对原发性开角型青光眼(POAG)患者眼压(IOP)的短期降低效果有限



该图展示了不同地理区域类别下效应量的分布特征。

Figure 2. Result of subgroup analysis categorized in regions

图 2. 基于区域的亚组分析结果

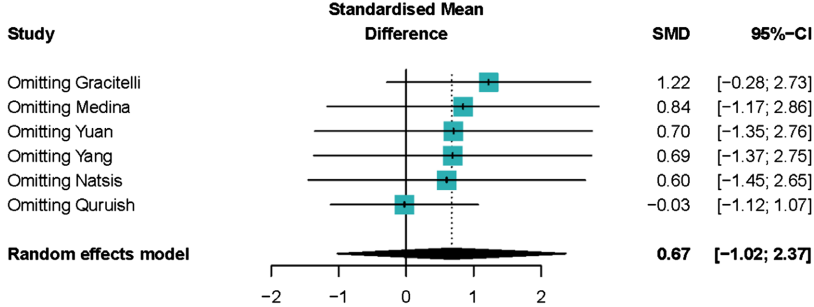
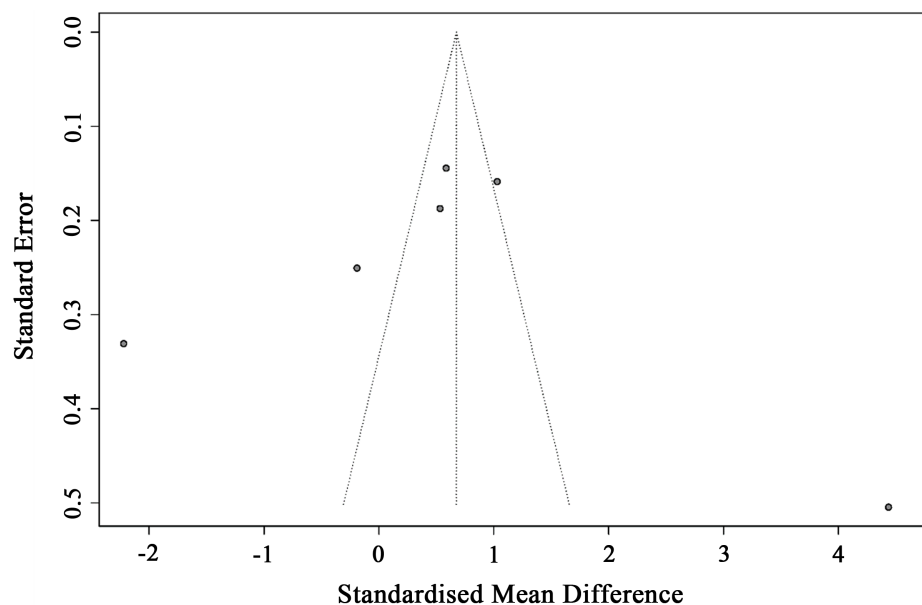


Figure 3. The result of sensitivity analysis. Omitting one study has no significant effect on our overall outcome

图 3. 敏感性分析结果。剔除任意一项研究均未对综合效应量产生统计学显著影响

3.5. 偏倚检验

通过漏斗图对纳入研究的发表偏倚进行评价,如图4所示,漏斗图似乎对称,但由于本次荟萃分析中仅纳入6项研究,漏斗图对发表偏倚的评价可能有限。



采用随机效应模型对效应量进行汇总,本漏斗图展示了标准化均数差(SMD)及其标准误(SE)。黑色圆圈代表已发表文献,两侧由虚线围成的锥形区域表示95%置信区间。

Figure 4. Publication bias of overall outcome

图4. 综合效应量的发表偏倚分析

4. 讨论

尽管多项研究表明,有氧运动可以降低健康眼睛的IOP值,增加眼部血流量[14][18],这项荟萃分析显示,有氧运动可能对降低POAG患者的IOP有有限的影响。

运动对青光眼患病率的影响是一个长期争论和有争议的领域。一项基于韩国人群的横断面研究表明,每天进行剧烈运动与较高的青光眼患病率有关[19]。无氧运动,如抗阻训练可以增加IOP[20]-[24]。在动态阻力训练过程中,不可避免地会出现短暂的瓦尔萨尔瓦动作(整个过程中屏住呼吸)。瓦尔萨尔瓦动作可减少通过上、下腔静脉的静脉回流,导致远端静脉系统的扩张和IOP升高[25]。然而,一项多中心横断面研究显示,运动强度的增加与青光眼发病率的降低有关[26]。一项前瞻性流行病学队列研究报道,男性跑步者跑步速度每米/秒的增量越高,青光眼发病率越低[27]。美国眼科学会也建议进行高强度运动以降低青光眼发病风险[28]。

POAG患者从AE中获益的潜在机制可能多种多样。AE通过短期内增加收缩压来提高眼内血流量[29][30],降低视网膜氧化应激,减缓视网膜神经节细胞凋亡[31],降低健康眼睛的IOP。因此,AE是否能降低POAG患者的IOP受到了越来越多的关注。库雷希发表了首项研究,探讨AE与POAG患者IOP之间的关系。他得出结论,AE可以显著降低POAG患者的IOP,且重度AE的IOP减少幅度高于轻度或中度AE[13]。Whatmore、Yuan等报告称,在跑步机运动30分钟后,POAG患者的IOP显著降低($P < 0.001$)[17]。AE可通过改变前房结构降低健康眼睛的IOP,从而增强房水流出[32]。此外,有氧运动导致晶状体向后移位,引起小梁网和Schlemm管的扩张[33]。另一种可能的机制是血浆胶体渗透压(COP)的变

化。运动在短时间内使身体脱水,增加胶体渗透压,导致 IOP 降低[34]。此外,运动引起的高血乳酸和 β 肾上腺素受体阻断的低血压效应可能参与健康受试者 IOP 的短期降低[35]。

然而,后者的研究结果各不相同。巴西的一项研究报告称,在 AE 之后,POAG 患者的 IOP 略有升高。为了确认运动诱发的衰弱(AE)与 POAG 的 IOP 之间的关联,我们进行了这项荟萃分析,以提供基于证据的 POAG 管理和治疗指南。我们发现,在短时间内,有氧运动可能对减少 POAG 患者的 IOP 效果有限。运动过程中,交感神经系统被激活,这可能会扩大瞳孔直径,促进房水的产生[36][37]。此外,在 POAG 患者中,小梁网的僵硬导致房水流出减少,IOP 升高[38][39]。

几项研究调查了有氧运动对青光眼患者 IOP 的长期影响。Passo 等人报告称,在进行 3 个月的规律有氧运动训练后,POAG 组受试者的 IOP 显著下降,停训三周后眼压恢复到升高的水平[40],这种“训练效应”可能与长期运动诱导的 SC 内皮细胞紧密连接蛋白重构有关,通过增加孔隙率和降低流出阻力实现。Fujiwara 等人进行了一项为期 5 年的队列研究,得出结论认为频率水平的增加和运动时间的增加与健康眼睛 IOP 的降低有关[41]。AE 对 POAG 患者 IOP 的长期影响的潜在机制尚不清楚,运动通过激活 AMPK-PGC1 α 通路增强小梁网细胞线粒体功能,改善其细胞骨架重构能力[42]。

5. 限制

本研究仍存在一些局限性:1) 本研究仅纳入了 6 项研究,需要更多的临床试验;2) 研究来自不同国家,6 项研究中观察到的高度异质性,这一结果提示,不同研究之间可能存在诸多差异,导致总体效果的不一致。虽然我们进行了基于区域的亚组分析,但仅按地理区域划分的子组分析未能充分揭示异质性的具体来源。为了更好地理解这些差异,未来的研究应考虑更多的潜在异质性来源;3) 研究对象在运动方案、IOP 测量时间、初始 IOP 水平方面存在一定的差异,可能影响结果;4) 本文结论不能推广到有氧运动对 IOP 的长期影响,需要更多的临床试验来探讨有氧运动的长期效果。

6. 结论

我们的研究显示,有氧运动可能对 POAG 患者在短时间内降低 IOP 的影响有限。然而,我们发现的机制仍需进一步研究。

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