

玻璃体切除术相关视神经病变

林铁柱, 沈丽君

引用:林铁柱,沈丽君. 玻璃体切除术相关视神经病变. 国际眼科杂志, 2024,24(10):1620-1623.

基金项目:沈阳市中青年科技创新人才支持计划项目(No. RC210267);沈阳市卫健委科研课题计划(No. 2022103)

作者单位:(310014)中国浙江省杭州市,浙江省人民医院眼科中心

作者简介:林铁柱,毕业于温州医科大学,博士,副主任医师,硕士研究生导师,研究方向:玻璃体及视网膜疾病。

通讯作者:沈丽君,博士,主任医师,博士研究生导师,研究方向:黄斑界面疾病、眼科手术机器人。slj@mail.eye.ac.cn

收稿日期:2023-12-27 修回日期:2024-08-19

摘要

玻璃体切除术发明至今已经有 50 余年的历史,目前在眼科的应用指征涵盖了大部分玻璃体视网膜疾病。尽管随着设备的革新和技术的进步,玻璃体切除术的手术风险已经降至很低,但仍有一些并发症难以避免,意外或原因不明的视功能下降时有发生。玻璃体切除术后视神经病变的发生率较高,可发生于术后即刻或数周至数月,会引起不可逆的视觉损伤。致病原因大致可分为术中视神经损伤和术后继发损伤。术中视神经损伤包括机械性损伤、染料毒性及眼内压影响,术后继发损伤包括眼内压升高、硅油毒性及氧化应激等微环境改变对视神经的损伤。文章将对玻璃体切除术相关视神经病变的临床表现、常见原因及相关管理做一综述,以期引起眼科医生们对于此类疾病的关注。

关键词:玻璃体切除术;视神经病变;眼内压;硅油;氧化应激;染料毒性

DOI:10.3980/j.issn.1672-5123.2024.10.18

Vitrectomy associated optic neuropathy

Lin Tiezhu, Shen Lijun

Foundation items: Middle-aged Science and Technology Innovation Talents Support Program of Shenyang (No. RC210267); Scientific Research Program of Shenyang Health Commission (No.2022103)
Department of Ophthalmology, Zhejiang Provincial People's Hospital, Hangzhou 310014, Zhejiang Province, China

Correspondence to: Shen Lijun. Department of Ophthalmology, Zhejiang Provincial People's Hospital, Hangzhou 310014, Zhejiang Province, China. slj@mail.eye.ac.cn

Received:2023-12-27 Accepted:2024-08-19

Abstract

• Over half a century has passed since the inception of vitrectomy, and the indications for its utilization in ophthalmology encompass the majority of vitreoretinal disorders. Technological advancements and equipment innovation have drastically reduced the surgical risk of vitrectomy, but some complications remain unavoidable. Occasionally, unexpected or unexplained visual impairments can manifest. Vitrectomy is associated with a high incidence of optic neuropathy, which can manifest weeks to months following the procedure and result in permanent visual impairment. An intraoperative optic nerve injury and a postoperative secondary injury comprise the causes. Intraocular pressure, dye toxicity, or mechanical damage can cause intraoperative optic nerve injury. Secondary injuries that occur after surgery include an increase in intraocular pressure, toxicity to silicone oil, oxidative stress, and other alterations in the microenvironment. This review will discuss the common causes, clinical manifestations, and related management of optic neuropathy connected to vitrectomy in order to attract the interest of ophthalmologists.

• **KEYWORDS:** vitrectomy; optic neuropathy; intraocular pressure; silicone oil; oxidative stress; toxicity of dyes

Citation: Lin TZ, Shen LJ. Vitrectomy associated optic neuropathy. *Guoji Yanke Zazhi (Int Eye Sci)*, 2024,24(10):1620-1623.

0 引言

玻璃体切除术是眼科手术领域的伟大创新。1971年, Machemer 等首次提出 17G 经睫状体平坦部闭合式玻璃体切除术 (pars plana vitrectomy, PPV); 1974 年, O'Malley 和 Heitz 将手术系统分离为切除、灌注和照明三通道,同时设计了 20G 手术器械,成为接下来 30 a PPV 的标准术式;本世纪,PPV 手术进入微切口和精准时代,23G/25G/27G 器械可以经结膜免缝合^[1];眼科手术机器人、多模式影像及微视野等精准手术操作和精细视觉评估也逐渐被应用于眼科临床中^[2-4]。

目前,PPV 已经被广泛应用于各种玻璃体视网膜疾病,包括视网膜脱离、增生性糖尿病视网膜病变、玻璃体视网膜界面疾病和葡萄膜炎等,大幅度提高了此类患者视功能的救治率。医生们一方面惊叹于其取得的卓越成就,另一方面也越来越关注到其可能引起的相关并发症,如白内障、青光眼、视网膜光/化学损伤以及视神经病变等。

PPV 术后视神经病变的发生率较高,可发生于术后

即刻或数周至数月,会引起不可逆的视功能损伤。但其具体机制目前尚不完全清楚,本文将就 PPV 术后视神经病变的临床表现、可能因素及相关治疗作一综述,以期引起玻璃体视网膜手术医生的重视。

1 临床表现

视神经是由视网膜神经节细胞 (retinal ganglion cell, RGC) 轴突的神经纤维束汇聚形成,属于中枢神经系统,对于缺血、缺氧和代谢紊乱异常敏感。PPV 可以直接/间接影响或损伤视神经。早期可能只表现为色觉异常及对对比敏感度下降;在光学相干断层扫描 (optical coherence tomography, OCT) 上表现为黄斑区视网膜神经节细胞-内丛状层变薄,盘周视网膜神经纤维层 (retinal nerve fiber layer, RNFL) 变薄^[5-6];在 OCT 血流成像上表现为视盘旁的毛细血管网血流密度降低^[7];在激光散斑血流成像上,可以表现为视盘的血管变细、血流减少^[8-9]。严重的视神经损伤会导致患者视力下降和视野缺损,甚至无光感。

2 致病原因及预防

PPV 相关视神经病变的致病原因大致可分为术中视神经损伤和术后继发损伤。术中视神经损伤包括机械性损伤、染料毒性及眼内压影响,术后继发损伤包括眼内压升高、硅油毒性及氧化应激等微环境改变对视神经的损伤。

2.1 机械性损伤 PPV 术中导致的视神经直接损伤可能是术后不明原因视野缺损的原因。这种损伤可发生在 PPV 的多个步骤中,如制作玻璃体后脱离 (posterior vitreous detachment, PVD) 时对视神经的牵拉导致轴突或毛细血管损伤,其中因素可能包括器械的直接损伤或高压吸引形成的剪切力^[10]。曾有研究观察自发 PVD 组和手术诱发 PVD 组 PPV 术后的 RNFL 变化,发现自发 PVD 组术后 6 mo 的 RNFL 平均厚度无明显变化,而手术诱发 PVD 组的 RNFL 平均厚度降低^[11]。在糖尿病视网膜病变中,切除残留于视盘表面的增殖膜茎也可能导致视神经的直接损伤。在这些膜茎的组织学研究中,33% 的标本中含有轴突成分^[12]。在制作 PVD 或切除视盘前新生血管膜时,避免高压吸引牵拉可能会减少一定程度的视神经损伤。在黄斑前膜或黄斑裂孔中,行黄斑前膜/视网膜内界膜 (internal limiting membrane, ILM) 剥除导致的 RNFL 直接损伤是术后微视野缺损和视力下降的一个潜在原因^[13]。手术医生需要思考 ILM 剥除对于疾病康复的必要性以及 ILM 的剥除范围,以避免不必要的副损伤。

2.2 染料毒性 ILM 几乎不可见,对其剥除通常需借助染色剂完成。吲哚菁绿 (indocyanine green, ICG) 可选择性地染色 ILM,是国内最常用的染色剂^[14]。一些研究发现,ICG 染色对视力预后有着不良影响。Engelbrecht 等^[15]回顾了 21 例 ICG 染色辅助 ILM 剥除的黄斑裂孔患者,尽管术后裂孔闭合,但最佳矫正视力中位数下降,黄斑裂孔和 ICG 直接接触的 RPE 细胞发生萎缩样改变。Haritoglou 等^[16]报道了 20 例行 ICG 染色辅助 ILM 剥除治疗的黄斑裂孔患者,术后视力无明显改善,7 只眼 (35%) 出现明显的视野缺损。Gass 等^[17]根据是否行 ICG 染色将黄斑裂孔

患者进行分组,发现 ICG 染色组患者的视功能结局显著较低,视野缺损的发生率达 50%,而未用 ICG 染色患者未见视野缺损。Uemura 等^[18]回顾了 16 例因特发性黄斑前膜行 PPV 治疗的患者,在 7 例行 ICG 染色的患者中有 4 例 (57.1%) 术后出现鼻侧或广泛的视野缺损,而 9 例未行 ICG 染色的患者未出现上述不良结果。在 Ando 等^[19]研究中,行 ICG 辅助 ILM 剥除术后,46.7% 眼出现视神经萎缩。动物模型和体外实验的数据表明,玻璃体腔注射 ICG 会造成视网膜形态和功能的损伤^[20-21]。Gandorfer 等^[22]认为,玻璃体视网膜界面的染料积累可能会升高视网膜中 ICG 的浓度和渗透压,超过玻璃体腔值和临界界限。因此,ICG 对神经视网膜和视神经有潜在的毒性损伤^[23]。选择神经毒性小的 ILM 染色剂是一种有效的预防方法,如台盼蓝^[14];另一方面,可以考虑稀释染色剂的浓度,用高糖或黏弹剂配药以减少视网膜染色范围,和及时吸除以减少染色剂的眼内存留时间。

2.3 眼内压升高 PPV 可通过多种机制导致眼内压升高^[24]。术中有时眼内灌注压的设置 (如气液交换/诱发 PVD 时) 会高于眼内压正常值上限,建议手术过程中应尽量将灌注压维持在正常眼内压范围内。

术后早期眼内压升高最可能的原因是眼内填充过度、房水迷流、晶状体虹膜隔移位、前房炎症、气体膨胀和特殊体位。术后需对眼内压进行密切监测,若眼内填充过度,需排放部分填充物;若考虑炎症致眼内压升高,需积极局部抗炎治疗;若房水迷流和晶状体虹膜隔前移,需考虑恶性青光眼可能并积极应对。

后期的眼内压升高可能是由于房角黏连、硅油填充、使用类固醇滴眼液、房角后退、新生血管性青光眼或原有青光眼恶化^[25]。一些研究表明,PPV 眼最终发展为开角型青光眼的风险较非 PPV 眼增加 15% - 20%^[26],PPV 眼需要抗青光眼手术治疗的几率高于对侧眼^[27]。与有晶状体眼相比,人工晶状体眼在 PPV 术后更容易发生开角型青光眼,这是由于 PPV 术后玻璃体腔内的氧含量增加会导致氧化应激,导致小梁网的损伤和功能降低^[25]。硅油填充是 PPV 术后眼内压升高的另一个重要原因,可能的机制包括瞳孔阻滞、炎症、前房硅油和硅油乳化等^[28-29]。长期的高眼压可对视神经产生直接损伤,导致 RGC 和 RNFL 厚度降低,视乳头血流降低^[8-9]。所以,PPV 术后需长期随访并监测眼内压,若眼内压升高可给予降眼内压药物;若考虑长期应用激素导致眼内压升高需及时停药;可根据眼底状态考虑取出硅油,必要时可能需行抗青光眼手术治疗。

2.4 硅油毒性 硅油 (聚二甲基硅氧烷) 是由硅氧烷和氧键重复单元组成的液态疏水双聚合物,比重略小于水,具有惰性、稳定和透明的特性,折射率与玻璃体相似,具有较高的表面张力和黏度^[30]。硅油作为 PPV 术后玻璃体的长期替代物已被眼科医生广泛接受,但其相关并发症仍不容忽视,主要包括:眼内压升高、视力下降、玻璃体视网膜增殖、黄斑前膜、角膜失代偿、硅油乳化和白内障等^[29-32]。有一些研究报道了硅油的视网膜毒性,在 OCT 中可以观

察到硅油填充眼的内层视网膜较对侧眼变薄,包括RNFL、RGC和内丛状层,分别代表RGC的轴突、胞体和树突^[33-34]。早在1983年,Ni等首次在摘除眼球中观察到硅油向筛板后移位^[35]。在既往硅油填充眼的组织学检查中,13%-24%的病例在视神经中观察到硅油滴,后续又有多个病例陆续报道了硅油可进一步迁移到视交叉甚至脑室^[31,35]。因为玻璃体与蛛网膜下腔正常没有解剖沟通,其发生机制目前尚不明确,先天性视盘解剖异常、长期高眼压导致视神经海绵样变性,或巨噬细胞对乳化硅油的吞噬作用在其中可能起到一定作用^[35]。此外,硅油具有很强的亲脂性,可以溶解眼内细胞膜的脂质^[36],有个别研究在硅油填充眼中发现了硅油抗体^[37]。因此,硅油有潜在的长期神经毒性作用。有研究发现,硅油中的低分子量成分可诱导视网膜细胞凋亡,认为低分子量成分可能是硅油长期毒性的主要原因^[38-39]。目前,临床上一般不推荐硅油长期眼内保留,若术后视网膜解剖复位,一般建议在3-6 mo内进行硅油取出。

2.5 氧化应激 玻璃体凝胶对于氧的调节和分布十分重要。玻璃体凝胶中的氧呈阶梯样分布:在视网膜表面最高,向晶状体方向逐渐降低^[40]。玻璃体凝胶中含有较高浓度的抗坏血酸(2 mmol/L)^[41],具有抗氧化损伤的作用。既往研究已经证实,PPV术后玻璃体腔中的氧浓度会升高约3倍^[40]。过度的氧化应激除了可以促使核性白内障形成和小梁网变性,还可以通过直接损伤和激活凋亡蛋白酶间接损伤导致RGC凋亡^[42]。此外,氧化应激还会损伤视神经血流的自动调节功能,引起缺血损伤^[43-44]。虽然一些眼科学者已经关注到了眼氧化损伤,但目前尚缺乏有效的药物,需要进一步的基础及临床研究。

3 PPV 相关视神经病变的治疗

目前,对于PPV相关的视神经病变尚缺乏特效药物,可以考虑给予营养神经(维生素B族、甲钴胺、胞磷胆碱钠和鼠神经生长因子等)、改善微循环(复方樟柳碱、银杏叶提取物、前列腺素类药物和活血化瘀中成药)及抗氧化损伤(α -硫辛酸等)药物。

4 小结和展望

PPV相关视神经病变在临床中常见却容易被患者和临床医生忽视,影响患者的视功能预后。医生进行手术操作时应该重视视神经的保护,术后加强视神经的监测,以期早发现、早治疗,尽量避免视神经的意外损伤和延迟治疗。此外,国内外对于PPV相关的视神经病变认识尚不充分,基础研究和临床研究都很匮乏,需引起广大科研工作者的重视。

参考文献

[1] Bansal R, Dogra M, Chawla R, et al. Pars Plana vitrectomy in uveitis in the era of microincision vitreous surgery. *Indian J Ophthalmol*, 2020,68(9):1844-1851.
[2] Ramamurthy SR, Dave VP. Robotics in vitreo-retinal surgery. *Semin Ophthalmol*, 2022,37(7-8):795-800.
[3] Cheng D, Tao JW, Yu XT, et al. Characteristics of macular microvasculature before and after idiopathic macular hole surgery. *Int J Ophthalmol*, 2022,15(1):98-105.

[4] Shen Y, Ye X, Tao J, et al. Quantitative assessment of retinal microvascular remodeling in eyes that underwent idiopathic epiretinal membrane surgery. *Front Cell Dev Biol*, 2023,11:1164529.
[5] Pollreisz A, Desissaire S, Sedova A, et al. Early identification of retinal neuropathy in subclinical diabetic eyes by reduced birefringence of the peripapillary retinal nerve fiber layer. *Invest Ophthalmol Vis Sci*, 2021,62(4):24.
[6] Zeng Y, Cao D, Yu H, et al. Early retinal neurovascular impairment in patients with diabetes without clinically detectable retinopathy. *Br J Ophthalmol*, 2019,103(12):1747-1752.
[7] Pujari A, Bhaskaran K, Sharma P, et al. Optical coherence tomography angiography in neuro-ophthalmology: Current clinical role and future perspectives. *Surv Ophthalmol*, 2021,66(3):471-481.
[8] Hashimoto R, Sugiyama T, Maeno T. Comparison of optic nerve head blood flow autoregulation among quadrants induced by decreased ocular perfusion pressure during vitrectomy. *Biomed Res Int*, 2017,2017:6041590.
[9] Hashimoto R, Sugiyama T, Masahara H, et al. Impaired autoregulation of blood flow at the optic nerve head during vitrectomy in patients with type 2 diabetes. *Am J Ophthalmol*, 2017,181:125-133.
[10] Bonfiglio V, Orisi E, Nebbioso M, et al. Optical coherence tomography angiography evaluation of peripapillary microvascular changes after rhegmatogenous retinal detachment repair. *Retina*, 2021,41(12):2540-2548.
[11] Mariotti C, Nicolai M, Longo A, et al. Peripapillary retinal nerve fiber thickness changes after vitrectomy for epiretinal membrane in eyes with and without vitreous detachment. *Retina*, 2017,37(12):2304-2309.
[12] Pendergast SD, Martin DF, Proia AD, et al. Removal of optic disc stalks during diabetic vitrectomy. *Retina*, 1995,15(1):25-28.
[13] Tao J, Yang J, Wu Y, et al. Internal limiting membrane peeling distorts the retinal layers and induces scotoma formation in the perifoveal temporal macula. *Retina*, 2022,42(12):2276-2283.
[14] Wang XW, Long Y, Gu YS, et al. Outcomes of 4 surgical adjuvants used for internal limiting membrane peeling in macular hole surgery: a systematic review and network Meta-analysis. *Int J Ophthalmol*, 2020,13(3):481-487.
[15] Engelbrecht NE, Freeman J, Sternberg P, et al. Retinal pigment epithelial changes after macular hole surgery with indocyanine green-assisted internal limiting membrane peeling. *Am J Ophthalmol*, 2002,133(1):89-94.
[16] Haritoglou C, Gandorfer A, Gass CA, et al. Indocyanine green-assisted peeling of the internal limiting membrane in macular hole surgery affects visual outcome: a clinicopathologic correlation. *Am J Ophthalmol*, 2002,134(6):836-841.
[17] Gass CA, Haritoglou C, Schaumberger M, et al. Functional outcome of macular hole surgery with and without indocyanine green-assisted peeling of the internal limiting membrane. *Graefes Arch Clin Exp Ophthalmol*, 2003,241(9):716-720.
[18] Uemura A, Kanda S, Sakamoto Y, et al. Visual field defects after uneventful vitrectomy for epiretinal membrane with indocyanine green-assisted internal limiting membrane peeling. *Am J Ophthalmol*, 2003,136(2):252-257.
[19] Ando F, Yasui O, Hirose H, et al. Optic nerve atrophy after vitrectomy with indocyanine green-assisted internal limiting membrane peeling in diffuse diabetic macular edema. Adverse effect of ICG-assisted ILM peeling. *Graefes Arch Clin Exp Ophthalmol*, 2004,242(12):995-999.
[20] Enaida H, Sakamoto T, Hisatomi T, et al. Morphological and

functional damage of the retina caused by intravitreal indocyanine green in rat eyes. *Graefes Arch Clin Exp Ophthalmol*, 2002, 240(3):209-213.

[21] Sippy BD, Engelbrecht NE, Hubbard GB, et al. Indocyanine green effect on cultured human retinal pigment epithelial cells: implication for macular hole surgery. *Am J Ophthalmol*, 2001, 132(3):433-435.

[22] Gandorfer A, Haritoglou C, Gandorfer A, et al. Retinal damage from indocyanine green in experimental macular surgery. *Invest Ophthalmol Vis Sci*, 2003, 44(1):316-323.

[23] Ejstrup R, la Cour M, Heegaard S, et al. Toxicity profiles of subretinal indocyanine green, Brilliant Blue G, and triamcinolone acetate: a comparative study. *Graefes Arch Clin Exp Ophthalmol*, 2012, 250(5):669-677.

[24] 蔡雅群, 张旭. 玻璃体视网膜手术后继发性青光眼的病因及治疗. *国际眼科杂志*, 2020, 20(5):806-809.

[25] Rossi T, Ripandelli G. Pars Plana vitrectomy and the risk of ocular hypertension and glaucoma: where are we? *J Clin Med*, 2020, 9(12):3994.

[26] Chang S. LXII Edward Jackson lecture: open angle glaucoma after vitrectomy. *Am J Ophthalmol*, 2006, 141(6):1033-1043.

[27] Kovacic H, Wolfs RCW, Kılıç E, et al. The effect of multiple vitrectomies and its indications on intraocular pressure. *BMC Ophthalmol*, 2019, 19(1):175.

[28] Wang L, Liu J, Lu T. Clinical analysis of early and mid-late elevated intraocular pressure after silicone oil injection. *Eye Sci*, 2014, 29(2):85-89.

[29] Miller JB, Papakostas TD, Vavvas DG. Complications of emulsified silicone oil after retinal detachment repair. *Semin Ophthalmol*, 2014, 29(5-6):312-318.

[30] Ni Y, Fang H, Zhang X, et al. Analysis of the causative factors related to earlier emulsification of silicone oil. *Int J Ophthalmol*, 2019, 12(3):517-519.

[31] Valentín-Bravo FJ, García-Onrubia L, Andrés-Iglesias C, et al. Complications associated with the use of silicone oil in vitreoretinal surgery: a systemic review and meta-analysis. *Acta Ophthalmol*, 2022, 100(4):e864-e880.

[32] 许菁, 王方. 硅油对视神经的毒性作用. *国际眼科杂志*, 2019, 19(5):787-790.

[33] Pichi F, Hay S, Abboud EB. Inner retinal toxicity due to silicone oil: a case series and review of the literature. *Int Ophthalmol*, 2020, 40(9):2413-2422.

[34] Ma Y, Zhu XQ, Peng XY. Macular perfusion changes and ganglion cell complex loss in patients with silicone oil-related visual loss. *Biomed Environ Sci*, 2020, 33(3):151-157.

[35] Grzybowski A, Pieczynski J, Ascaso FJ. Neuronal complications of intravitreal silicone oil: an updated review. *Acta Ophthalmol*, 2014, 92(3):201-204.

[36] PastorJimeno JC, de la Rúa ER, Fernández Martínez I, et al. Lipophilic substances in intraocular silicone oil. *Am J Ophthalmol*, 2007, 143(4):707-709.

[37] Pastor JC, Puente B, Telleria J, et al. Antisilicone antibodies in patients with silicone implants for retinal detachment surgery. *Ophthalmic Res*, 2001, 33(2):87-90.

[38] Chen Y, Lam Ip Y, Zhou L, et al. What is the cause of toxicity of silicone oil? *Materials (Basel)*, 2021, 15(1):269.

[39] Romano MR, Ferrara M, Gatto C, et al. Safety of silicone oils as intraocular medical device: an in vitro cytotoxicity study. *Exp Eye Res*, 2020, 194:108018.

[40] Zong Y, Gao QY, Hui YN. Vitreous function and intervention of it with vitrectomy and other modalities. *Int J Ophthalmol*, 2021, 14(10):1610-1618.

[41] Ankamah E, Sebag J, Ng E, et al. Vitreous Antioxidants, Degeneration, and Vitreo - Retinopathy: Exploring the Links. *Antioxidants (Basel)*, 2019, 9(1):7.

[42] Shestopalov VI, Spurlock M, Gramlich OW, et al. Immune responses in the glaucomatous retina: regulation and dynamics. *Cells*, 2021, 10(8):1973.

[43] Feilchenfeld Z, Yücel YH, Gupta N. Oxidative injury to blood vessels and glia of the pre-laminar optic nerve head in human glaucoma. *Exp Eye Res*, 2008, 87(5):409-414.

[44] Nakazawa T. Ocular Blood Flow and Influencing Factors for Glaucoma. *Asia Pac J Ophthalmol (Phila)*, 2016, 5(1):38-44.