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白内障手术对视网膜静脉阻塞黄斑水肿影响研究进展

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摘　要

视网膜静脉阻塞(RVO)是仅次于糖尿病视网膜病变的第二大致盲性视网膜血管疾病，其并发症黄斑水肿是视力下降的重要原因。白内障术后黄斑水肿仍然是当代白内障手术中术后视力受损的重要原因。但对接受白内障手术的视网膜静脉阻塞患者的结局文献研究较少，本文旨在总结国内外学者目前对白内障术后黄斑水肿的分子机制的认识，阐述近年来白内障手术对视网膜静脉阻塞继发黄斑水肿影响研究进展。

关键词

视网膜静脉阻塞，黄斑水肿，白内障术后

Research Progress of the Effect of Cataract Surgery on Macular Edema Caused by Retinal Vein Occlusion

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Abstract

Retinal vein occlusion (RVO) is the second leading cause of retinal vascular disease after diabetic retinopathy, and its complication macular edema is an important cause of vision loss. Macular edema after cataract surgery is still an important cause of postoperative visual impairment in contemporary cataract surgery. However, there are few literatures on the outcomes of patients with

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retinal vein occlusion who underwent cataract surgery. This article aims to summarize the current understanding of the molecular mechanism of macular edema after cataract surgery by domestic and foreign scholars, and to elaborate the research progress of the effect of cataract surgery on macular edema secondary to retinal vein occlusion in recent years.

Keywords

Retinal Vein Occlusion, Macularedema, Postoperative Cataract Surgery

1. 引言

视网膜静脉阻塞是临床上常见的一类视网膜血管疾病，该病多发于中、老年患者。全球流行病学研究显示该病的平均患病率约 0.77%，RVO 全球发病率为 0.86%至 1.63%，近几年该病的发病率仍在上升，尤其是 65~74 岁之间的患者的视网膜静脉阻塞发生率持续增加[1]。传统上，视网膜静脉阻塞患者视力丧失的主要原因是黄斑水肿[2]，当患者发生视网膜静脉血栓时，该部位血管压力、渗透性随之增加，渗出液体易积聚在黄斑区，从而出现黄斑水肿等情况，另静脉血栓形成会导致视网膜缺血、缺氧，促进血管内皮生长因子释放，进一步破坏血视网膜屏障，增加血管通透性，加重了黄斑水肿的症状，严重影响患者视力[3]。

随着玻璃体内抗血管内皮生长因子(VEGF)注射以及玻璃体内类固醇治疗视网膜静脉阻塞的使用，视网膜静脉阻塞引起的黄斑水肿得到了更好的控制[4]。重要的是，接受抗 VEGF 治疗的患者认识到尽管需要频繁注射，但视力可以保持或者恢复。

考虑到与年龄的显著关系，视网膜静脉阻塞患者受到白内障的影响并不罕见。更重要的是，随着目前对视网膜静脉阻塞患者的治疗不断进步，白内障可能比视网膜疾病更可能限制视力。白内障手术是最常进行的外科手术之一，可有效恢复视功能[5]。虽然白内障手术技术的最新进展已显著降低了术后并发症的发生率，但黄斑水肿仍然是视力不佳的重要原因，其发病机制尚不明确，炎症反应是黄斑水肿形成的重要原因[6]。

有许多研究评价了糖尿病性黄斑水肿患者白内障手术的结局，糖尿病是常见的独立危险因素且患病风险与术前糖尿病严重程度密切相关，有人提出，白内障手术后眼内压升高的眼睛，包括那些用前列腺素类似物滴眼液治疗的眼睛，发生黄斑水肿的风险可能更高[7]。众所周知，有视网膜静脉阻塞病史的眼睛发生白内障术后黄斑水肿的风险增加，我们总结了国内外学者目前对白内障术后黄斑水肿的分子机制的认识，综述了近年来白内障手术对视网膜静脉阻塞继发黄斑水肿影响研究进展的文献。

2. 病理生理

白内障术后黄斑水肿(PCME)被认为是术后炎症反应的结果。大多数关于白内障术后黄斑水肿发病机制的研究都集中在肾上腺素的作用上，但其他炎症介质，如血管内皮生长因子(VEGF)等细胞因子也是术后炎症反应重要的炎症因子[8]。白内障手术期间的手术操作被认为刺激前段葡萄膜组织产生炎症介质，导致血－房水屏障和血－视网膜屏障(BRB)破坏。随后，漏出液在视网膜的外丛状层和内核层中积累，加快了白内障术后黄斑水肿发展[9]。

一般来说，白内障术后黄斑水肿被认为与眼部炎症有关。糖尿病、视网膜静脉阻塞、视网膜前膜、黄斑裂孔、葡萄膜炎和对侧眼发生白内障术后黄斑水肿是白内障术后发生黄斑水肿的重要危险因素[10]。在对患者(包括具有白内障术后黄斑水肿风险因素的患者)进行术后 4 个月评估的研究中，白内障手术后临床黄斑水肿的发生率报告为 0.1%~7.0%。与患者出现视力主诉后报告的发生率相比，使用荧光素血管造影(FFA)或光学相干断层扫描(OCT)对眼睛进行评估时观察到的白内障术后黄斑水肿发生率要高得多[11]。这表明有许多临床未识别的白内障术后黄斑水肿病例。

3. 自身危险因素

最近的文献报告称，在白内障手术前有视网膜静脉阻塞相关黄斑水肿治疗史的患者中，白内障术后黄斑水肿的发生率增加至35.4%。与现代超声乳化技术相关的白内障术后黄斑水肿发生率在0.2%至2.35%之间。尽管无法与其他研究进行直接比较，但结果显示，与之前的报告相比，白内障术后黄斑水肿的发生率更高[12]。白内障术后黄斑水肿被认为是由炎症介质(包括白内障)诱导的血管通透性增加引起的。现代超声乳化技术可能会触发花生四烯酸从细胞膜释放，导致通过脂氧合酶途径产生白三烯或通过环氧合酶途径产生洋地黄素。也有报道称，炎症可导致血管通透性增加，增加视网膜静脉阻塞患者炎症因子的释放[13]。此外，据报道，视网膜静脉阻塞患者的毛细血管网异常，包括浅表和深部毛细血管丛的破裂或扩张，在视网膜静脉阻塞患者中很常见。这些发现提示视网膜静脉阻塞患者的血视网膜屏障功能障碍[14]。因此，与没有视网膜静脉阻塞的患者相比，视网膜静脉阻塞患者更容易因白内障手术后的炎症而发生黄斑水肿。这项研究的结果表明，白内障手术前黄斑水肿的治疗史是白内障术后黄斑水肿的一个重要危险因素。我们还发现，手术后发生白内障术后黄斑水肿的风险随着术前黄斑水肿玻璃体内注射次数的增加而增加。在接受三次以上此类注射的 34 只眼睛中，白内障术后黄斑水肿的发生率达到 61.8%，尽管其在白内障手术前至少 6 个月黄斑的 OCT 结果稳定[15]。

其他需要考虑的基线因素包括视网膜静脉阻塞亚型，如视网膜分支静脉阻塞或视网膜中央静脉阻塞、FFA 结果(灌注或缺血)和视网膜静脉阻塞持续时间[16] [17]。据报道，视网膜中央静脉阻塞患者白内障术后的黄斑水肿往往比视网膜分支静脉阻塞患者更频繁发生，并且表现更难治[18]。在既往文献研究中，视网膜中央静脉阻塞患者的白内障术后黄斑水肿发生率略高于视网膜分支静脉阻塞患者。这些结果可能是由于视网膜中央静脉阻塞患者术前 6 个月黄斑水肿的频率较高，导致黄斑受损[19]。在既往研究中，大多数患者在白内障手术后视力得到改善。术后 3 个月，有白内障术后黄斑水肿的眼的平均视力明显低于无白内障术后黄斑水肿的眼，但在术后 6 个月，两组之间没有显著差异，这可能是由于白内障术后黄斑水肿的自然史或治疗诱导的疾病消退[20]。据报道，白内障术后黄斑水肿在许多情况下是自限性的，视力下降发病率相对较低。

4. 其他危险因素

(一) 术前危险因素

发生白内障术后黄斑水肿的眼睛更有可能是男性，年龄较大，并显示出危险因素。合并玻璃体切除、有视网膜前膜病史、葡萄膜炎、视网膜脱离手术的患者，其相对危险度增加[21]。

研究指出，即使在无糖尿病性视网膜病变的情况下，糖尿病患者在白内障手术后发生新发黄斑水肿的可能性也高出 1.8 倍。在存在任何术前糖尿病性视网膜病变的情况下，风险显著增加至 6.23 倍，并且随着糖尿病性视网膜病变严重程度的增加而成比例增加。既往行全视网膜光凝不能降低白内障术后黄斑水肿的风险，既往有糖尿病黄斑水肿病史的患者术后发生黄斑水肿的风险更大[22]。

葡萄膜炎通常是白内障术后黄斑水肿发生的一个众所周知的危险因素。既往诊断为葡萄膜炎的眼睛

发生白内障术后黄斑水肿的可能性是无风险因素的眼睛的 2.88 倍[23]。另一项研究发现，手术前 3 个月内有活动性炎症的眼睛发生白内障术后黄斑水肿的风险是没有炎症的眼睛的 6.19 倍。然而，在葡萄膜炎控制良好的眼睛中，术后 3 个月可以达到与健康眼睛相似的结果[23]。

其他与白内障术后黄斑水肿风险增加相关的风险因素包括视网膜前膜和既往视网膜脱离修复。虽然青光眼本身并不被认为是白内障手术后发生黄斑水肿的危险因素，但未经治疗的眼内压升高伴青光眼性视神经或视网膜神经纤维层损伤和相关青光眼性视野缺损已被证明可增加白内障术后黄斑水肿的风险[24]。迄今为止，研究显示术前使用前列腺素类似物后发生白内障术后黄斑水肿风险的结果不一。

(二) 术中因素

白内障手术中后囊破裂是一种潜在的严重术中并发症，与白内障术后黄斑水肿风险增加密切相关[25]。与未发生临床白内障术后黄斑水肿的患者相比，发生临床白内障术后黄斑水肿的患者的后囊膜破裂或术中需要玻璃体切除术的发生率在统计学上更高，比值比为 3.35 [26]。

(三) 术后因素

术后局部使用前列腺素和 β 受体阻滞剂均与白内障术后黄斑水肿发生率增加相关[27]。一项研究报告称，使用前列腺素类似物的急性闭角型青光眼组发生白内障术后黄斑水肿的风险最大。相反，一项包括 3394 只使用前列腺素类似物的眼睛的大型回顾性研究报告局部前列腺素类似物未显著增加白内障术后黄斑水肿的风险[28]。

5. 术后预防

使用局部非类固醇抗炎药(NSAID)加/或代替局部皮质类固醇(CS)可显著降低白内障手术后发生黄斑水肿的风险。理想情况下，预防性治疗应在手术前几天开始，对于高危患者，应在术后至少持续 3 个月[29]。急性黄斑水肿在大多数情况下会自发消退，但及时诊断和充分治疗是必要的，以防止视网膜损伤和持续的视力损害。局部非甾体类抗炎和皮质类固醇是白内障手术后急性黄斑水肿的有效治疗方法，而口服乙酰唑胺或玻璃体内地塞米松植入剂可用于难治性病例[30]。

有文献研究了各种非类固醇抗炎药和皮质类固醇及其联合治疗预防术后黄斑水肿的有效性。非类固醇抗炎药包括酮咯酸、溴芬酸、奈帕芬酸、双氯芬酸和吲哚美辛，皮质类固醇包括泼尼松龙、倍他米松、氟米龙和地塞米松[31]。研究发现，非类固醇抗炎药与皮质类固醇的组合比单药可显著降低发生白内障黄斑水肿术后的风险。非类固醇抗炎药与皮质类固醇的组合比单独皮质类固醇更不可能发生不良事件。在排序特征中，联合治疗显示出比单一药物显著的优势，在预防白内障术后黄斑水肿方面，非类固醇抗炎药比单独使用皮质类固醇有益处，有文献比较了各种非类固醇抗炎药和皮质类固醇预防术后黄斑水肿的效果，发现双氯芬酸在预防白内障术后黄斑水肿方面优于其他非类固醇抗炎药和皮质类固醇[32]。目前的一项系统评价也表明，双氯芬酸在治疗白内障手术后前房炎症方面比其他非类固醇抗炎药更有效。地塞米松可降低血管通透性和白细胞聚集性，预防白内障术后黄斑水肿的疗效上级优于倍他米松和氟米龙[33]。

6. 小结

白内障术后黄斑水肿是一个潜在的公共卫生保健负担，因为有黄斑水肿治疗史的患者更有可能在未来需要额外的白内障术后黄斑水肿治疗[34] [35]。例如，美国的一项调查报告称，涉及白内障术后黄斑水肿的病例的相关费用比不涉及白内障术后黄斑水肿的病例高 41%。在既往研究中，绝大多数患者均接受了白内障术后黄斑水肿的额外治疗，包括使用非类固醇抗炎药、玻璃体内抗血管内皮生长因子、曲安奈德、地塞米松植入注射或这些治疗的组合[36]。

临床医生在考虑患者进行白内障手术时应注意视网膜静脉阻塞病史，并尽量减少术后白内障术后黄斑水肿的风险[4] [37]。在这方面，有黄斑水肿治疗史的患者值得特别注意。临床医生可以考虑使用预防性药物，如非类固醇抗炎药，以解决视网膜静脉阻塞患者的白内障术后黄斑水肿风险[38] [39]。

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