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光学相干断层扫描血管成像在全身疾病中的临床应用研究进展

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摘要:全身性疾病是指对全身多个器官影响的系统性疾病,许多全身性疾病对眼部有不同程度的损害,深入研究眼科与全身疾病的关系能提升眼科与全身疾病的综合诊疗水平。光学相干断层扫描血管成像(optical coherence tomography angiography,OCTA)能够以无创的方式提供高分辨率的三维图像,对结膜、虹膜、视网膜和脉络膜血管进行详细观察,已在眼科临床工作中得到广泛应用,对于眼底疾病(如黄斑水肿、脉络膜新生血管、糖尿病性视网膜病变、视网膜分支静脉阻塞等)的诊断和随访具有重要意义。近年来研究发现 OCTA 不仅能早期筛查和诊断神经退行性疾病,而且可以评估危重症和颈动脉狭窄患者严重程度及其治疗效果。此外 OCTA 还被应用于系统性红斑狼疮的活动度评估,并在构建疾病风险预测模型方面展现出重要价值。本文综述了 OCTA 在多种全身性疾病中的最新应用进展,讨论了其潜在的临床价值,为 OCTA 在全身性疾病中的进一步应用提供思路。

关键词:光学相干断层扫描血管成像;全身性疾病;微血管改变;临床应用;研究进展
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Advances in clinical applications of optical coherence tomography angiography in systemic diseases

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Abstract: Systemic diseases refer to conditions that affect multiple organs throughout the body. Many systemic diseases have different degrees of damage to the eye. An in-depth study of the relationship between ophthalmology and systemic diseases can enhance the comprehensive diagnostic and therapeutic level in both fields. Optical coherence tomography angiography (OCTA) provides non-invasive, high-resolution three-dimensional images allowing for detailed observation of the conjunctival, iris, retinal, and choroidal blood vessels. OCTA has been widely used in ophthalmology, which is of great significance in the observation and follow-up of fundus diseases, such as macular edema, choroidal neovascularization, diabetic retinopathy, and retinal branch vein occlusion. Recent studies have shown that OCTA can not only be used for the early screening and diagnosis of neurodegenerative diseases, but also for assessing the severity of critical illnesses and carotid artery stenosis, as well as evaluating the effects of treatment. Furthermore, OCTA has been applied in assessing disease activity in systemic lupus erythematosus and has demonstrated significant value in constructing disease risk prediction models. In this article, we review the latest advances in the application of OCTA in various systemic diseases, discusses its potential clinical value, and provides insights for further application of OCTA in the field of systemic diseases.

Key words: Optical coherence tomography angiography (OCTA); Systemic diseases; Microvascular changes; Clinical application; Recent advances

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光学相干断层扫描血管成像(optical coherence tomography angiography, OCTA)是一种非接触式、非侵入性、重复性高的眼部检查手段,是光学相干断层扫描(optical coherence tomography, OCT)继时域 OCT 和频域 OCT 之后的另一个里程碑,其原理是通过重复的 B-scan 探测视网膜血管内红细胞流速产生对比,提供高质量的视网膜各层和脉络膜血管三维成像[1]。OCTA 已经被越来越广泛地应用于眼科临床,目前已用于多种视网膜疾病的诊断和治疗,包括视网膜血管阻塞性疾病、糖尿病性视网膜病和黄斑病变等[2]。近年来 OCTA 在临床上得到广泛应用,其应用范围已不仅仅局限在眼科,研究发现 OCTA 在阿尔茨海默病[3]、系统性红斑狼疮[4]等全身疾病的诊断、治疗及随访中均显示出巨大的潜力。本文将对 OCTA 在全身性疾病中的应用进展进行综述。

1 OCTA 在危重病中的应用

危重病是指与氧化应激相关的严重疾病,导致器官损伤和全身炎症反应,可导致组织损伤和细胞死亡。常见的病因包括脓毒症(60%)、创伤和围手术期护理。脓毒症是一种由病原体和宿主因子介导的全身炎症反应,其导致的感染性休克是一种与器官功能障碍相关的严重血流动力学改变,毛细血管密度(vessel density, VD)降低和微循环灌注异质性与脓毒患者的预后密切相关,这种微循环的改变是一种动态过程,未灌注的毛细血管几分钟后可能重新恢复血流,选择合适的终末微循环器官进行动态监测是非常有必要的[5-6]。视网膜和大脑都是高代谢器官,通过特殊的血管网进行氧气的输送和物质的交换。两个器官在发育过程中有相似的血管形成模式和相似的血管调节过程[7-8]。在绵羊出血性休克的动物模型中发现 OCTA 可以直观的显示视网膜血管的血流状态,抽取血液诱导绵羊休克后视网膜浅层 VD 从基线的 44.7% 降至 34.5%,液体复苏后恢复至 46.9%,间接提示了脑血流量的恢复[9]。随着眼底成像技术及便携式 OCTA 设备的发展,临床医生可以采用 OCTA 技术测量视网膜血管血流量以间接评估危重症患者的脑血管循环情况,特别是在危重症患者的预后评估方面具有重要意义。

2 OCTA 在神经退行性疾病中的应用

OCTA 在许多神经退行性疾病的诊断、治疗及随访过程中均体现出巨大的优势。

2.1 多发性硬化

多发性硬化(multiple sclerosis, MS)是一种慢性神经退行性疾病,以炎症性脱髓鞘为特征,超过 50%病人病程中伴随视神经病变。过往报道认为其神经功能损害源自于静脉系统血流改变,但目前研究认为其病程最早涉及微循环系统[10]。OCTA 影像学研究发现,MS 患者的黄斑中心凹及旁中心凹区域视网膜浅层和深层 VD 降低[11]。引起 MS 患者视网膜及视神经的血流减少的原因尚不明确,推测可能与神经节细胞轴突的死亡和视网膜组织变薄、代谢需求减少有关[12]。也有研究认为炎性脱髓鞘过程直接影响视神经和视网膜血管内皮的完整性,从而导致血液减少[13]。Wicklein 等[14]研究发现结合 OCTA 和人工智能技术发现伴发视神经炎或视神经萎缩的 MS 患者其视网膜中型血管的数量(直径 10~20 um)显著减少,推测可能是由于神经节细胞萎缩、视网膜代谢降低所致。总体而言,MS 导致视网膜神经节细胞减少和视神经纤维层厚度变薄,继而导致视网膜代谢活动降低和血管丛减少[15]。因此通过 OCTA 对视网膜血管指标的量化为评估 MS 的严重程度及监控 MS 的进展提供了客观依据。

2.2 阿尔茨海默病

阿尔茨海默病(alzheimer's disease, AD)是一种会导致严重认知障碍的神经退行性疾病,AD 的常见眼科体征和症状包括视野改变和视力下降,以往较少有研究关注视网膜血管变化情况。随着 OCTA 的广泛应用,许多研究者采用 OCTA 技术直观的观察到了 AD 患者视网膜血管情况。Bulut[16]等研究发现 AD 患者视网膜黄斑中心凹无血管区面积扩大,并伴有视网膜 VD 下降,且上述指标与简易精神状态检查(minimum mental state examination, MMSE)评分减少呈线性相关。鉴于视网膜和脑血管网的相似性,研究认为 OCTA 可以作为 AD 患者疾病严重程度和进展的指标。相比于监测已经发生 AD 患者的眼部变化,OCTA 更大的意义在于检测早期 AD 患者的视网膜及脉络膜血流变化。有些横断面研究发现临床前期的 AD 患者一些 OCTA 指标变化,这部分的研究目前仍处于探索阶段,需要论证强度更高的临床研究支持[17]。未来 OCTA 和人工智能相结合将有助于 AD 患者的早期诊断和预后评估[18]。

2.3 帕金森病

帕金森病(parkinson's disease, PD)是一种影响中枢神经系统基底节区的疾病,在 PD 患者中,常见

的视觉障碍包括幻觉和对比敏感度降低[19]。多巴胺受体分布在视网膜的各层,而选择性多巴胺能细胞丢失是 PD 的一个关键病理特征,这种丢失不仅发生在大脑中,也体现在视网膜上[20]。微循环调节障碍和小血管异常也被认为是 PD 的发病机制之一[21]。既往研究者们认为 OCTA 在观察 PD 患者时面临一些挑战,主要是由于不自主的眼球震颤可能会导致运动伪影增加,从而影响了 OCTA 检查的准确性。近年来随着 OCTA 技术的进步,Lauermann 等[22]评估了 PD 患者和健康对照者的 OCTA 图像中的运动伪影,认为 OCTA 可用于治疗后的 PD 患者,而不会显著增加运动伪影。通过 OCTA 技术可观察到 PD 患者脉络膜和视网膜 VD 下降[23-24],这种变化在早期 PD 患者中就能被检测到,明显早于视网膜厚度的减少[25-26]。因此OCTA可以敏锐的发现 PD 患者眼部微循环灌注的变化,未来有望成为 PD 诊断和分期的影像学生物标志物。

3 OCTA 在常见病的应用

3.1 OCTA 在偏头痛的应用

偏头痛是一种常见的神经生物学疾病,以反复发作的头痛和伴随症状为特点。约 1/3 的偏头痛患者在发作前会出现局灶性神经系统障碍,通常是视觉障碍,称为“偏头痛先兆”[27]。Chang 等[28]研究发现,具有临床先兆的偏头痛患者表现为黄斑中心凹无血管区扩大,并且伴有黄斑旁中心凹浅层毛细血管及视盘旁毛细血管灌注密度下降,而在无临床先兆的患者身上也发现了黄斑、视盘区域的灌注密度下降,且与疾病进程密切相关[29]。OCTA 是一种有用的无创筛查工具,可用于检测偏头痛患者的微循环障碍,并可能对具有更高血管事件风险的偏头痛患者进行分层[30]。OCTA 在偏头痛领域的应用尚处探索初期,需更大规模的队列研究来进一步证明其在实际临床中的应用价值。

3.2 OCTA 在鞍区占位性疾病中的应用

由于解剖位置,鞍区占位性病变常压迫视交叉造成视神经损伤,导致视野缺损和视力下降。Lee 等[31]纳入了 36 名视交叉受压患者,通过 OCTA 技术发现视交叉受压导致明显的视网膜血管丛密度下降,并且鼻侧视网膜 VD 与视野缺损密切相关;Lee 等[32]进一步应用 OCTA 评估减压手术后视交叉受压患者视网膜 VD 的变化,发现术前视网膜浅层毛细血管丛的 VD 与术后视野变化密切相关,这意味着可以在术前通过 OCTA 评估视网膜血流情况以预测术后患者的视功能恢复情况;Cennamo 等[33]分析了 14 例垂体瘤病人,进一步证实了 OCTA 在视交叉受压患者视功能恢复中的作用。Wang 等[34]通过对无功能的垂体腺瘤分析,也证实了视交叉压迫导致视网膜 VD 下降,并且还发现视盘旁 VD 与压迫视交叉的肿块大小相关,提示 OCTA 有潜力评估此类病人的病情严重程度。OCTA 具有无创、快速、直观和可重复的特性,可以有效为神经外科医生和眼科医生提供有关视网膜血流信息,为患者远期视功能恢复提供重要参考。

3.3 OCTA 在系统性红斑狼疮中的应用

系统性红斑狼疮(systemic lupus erythematosus,SLE)是一种慢性全身性自身免疫性疾病,临床表现极为复杂,发病机制尚不明确。几乎所有器官系统都会受到影响,包括眼睛。1/3 的 SLE 患者伴有眼部病变,早期发现并干预 SLE 患者眼部病变十分必要。角结膜干燥综合征是 SLE 患者最常见的眼部表现,但视网膜微血管病变是 SLE 患者视觉损害的主要原因,并被认为是 SLE 病情进展的重要标志[35]。相关研究发现 SLE 患者视力损害主要与毛细血管灌注损失有关,SLE 患者毛细血管灌注异常主要发生在视网膜深毛细血管丛[36]。研究已证实 SLE 患者黄斑区深层 VD 明显低于正常健康人[37]。另外 Meng 等[38]研究发现在无眼部病变的 SLE 患者中,视网膜浅层 VD 与 SLE 疾病活动度密切相关。综上所述,OCTA 不仅能有效检测 SLE 患者的眼部损害,而且可能是 SLE 病情评估及进展预测的理想工具。

3.4 OCTA 在糖尿病肾病中的应用

糖尿病视网膜病变(diabetic retinopathy, DR)和糖尿病肾病(diabetic nephropathy, DN)都是糖尿病的微血管并发症,这两种疾病有着密切的联系,Zhuang 等[39]在调整混杂因素后发现 DR 分期和糖尿病性黄斑水肿(Diabetic macular edema, DME)与 DN 分期呈正相关。研究发现 DN 患者黄斑区 VD 明显下降,且浅层 VD 降低较深层 VD 降低更快[40-41];终末期肾病患者血液透析后外层视网膜 VD 显著降低,且伴有黄斑区 VD 减少或黄斑厚度增加的患者发生严重肾脏疾病的风险更高[42]。OCTA 有望成评估 DN 疾病进展及治疗效果的重要手段。

3.5 OCTA 在高血压中的应用

高血压和视网膜脉管系统的关系已有许多研究报道,高血压会引起一些典型的视网膜体征,如动静脉压迹、小动脉狭窄、微动脉瘤、视网膜内出血和棉絮斑,这些体征被证明会增加心脑血管事件[43-44]。

高血压主要并发症之一是微血管损伤,研究发现高血压患者黄斑区 VD 显著降低,伴有浅层黄斑中心凹无血管区扩大[45]。与血压控制良好的患者相比,血压控制不良的患者的视网膜深层 VD 降低更加明显[46],进一步凸显了 OCTA 在监测高血压引起的早期微血管变化中的潜在作用[47]。OCTA 是评估高血压脑血管疾病患者视网膜结构和微血管改变的有效手段,可用于预测心脑血管风险事件。

3.6 OCTA 在心脏病中的应用

冠心病(coronary heart disease, CHD)是全球死亡的主要原因之一,动脉粥样硬化、血管痉挛和动脉壁增厚或狭窄均是冠心病的危险因素,冠状动脉与人体的许多外周血管(眼、脑、肾)之间存在潜在关联。OCTA 能发现 CHD 患者在任何眼底体征出现在之前观察到视网膜 VD 下降,Wang 等[48]证明了 OCTA 是有效且无创检测 CHD 的方法,可以有效提高早期 CHD 的诊断率,并降低晚期 CHD 患者心肌梗死的发生率。另外,研究该发现心房颤动(Atrial fibrillation, AF)患者视网膜视乳头周围毛细血管丛和浅毛细血管丛灌注密度明显减少,而行肺静脉隔离治疗后眼灌注明显改善,因此研究者认为 OCTA 可用于评估 AF 患者接受肺静脉隔离治疗后的预后情况[49]。

先天性心脏病(congenital heart disease, CHD)是最常见的先天性缺陷,可分为紫绀和非紫绀型,紫绀型通常缺氧更严重、死亡率更高和生活质量更差[50]。Li 等[51]纳入先天性心脏病患者和对照组,应用 OCTA 定量分析 VD,与对照组相比,紫绀型先天性心脏病患者视盘周围毛细血管、浅层毛细血管丛和深毛细血管丛的 VD 显著降低,与非紫绀型先天性心脏病患者相比,紫绀型先天性心脏病患者视盘周围毛细血管和深毛细血管丛的 VD 显著降低,研究认为视网膜 VD 可以作为评估先天性心脏病患者缺氧程度的有效指标,可能反映了慢性全身性低氧血症对这些患者的影响。

3.7 OCTA 在颈动脉狭窄的应用

颈动脉狭窄是一种常见疾病,是公认的缺血性卒中的危险因素[52],颈动脉狭窄导致眼底血流量减少,部分患者会出现一过性黑朦或眼缺血综合征[53]。在 Cao 等[54]的研究队列中,利用 OCTA 和血管造影发现视网膜 VD 降低的程度主要与颈动脉狭窄的长度相关,而与狭窄程度无关。OCTA 不仅有潜力成为颈动脉狭窄的无创筛查手段[54-56],还能有效评估颈动脉狭窄患者接受颈动脉内膜切除术的疗效[57-58]。

3.8 OCTA 在 COVID-19 的应用

2019 冠状病毒病(COVID-19)由严重急性呼吸系统综合症冠状病毒 2(SARS-CoV-2)引起。大多数 COVID - 19 患者最初表现为呼吸综合征;然而,越来越多的证据表明存在眼部表现。视网膜病变,如棉毛斑(CWS)、视网膜微出血、血管扭曲、黄斑病变和神经视网膜病变均有报道[59-60],可能是由于 SARS-CoV-2 感染引起的炎症和血栓前期并发症。多项研究证明了 SARS-CoV-2 感染患者视网膜 VD 下降[61-63],Chiosi 等[62]纳入了 152 名 SARS-CoV-2 感染者和 60 名健康人作为对照组,发现服用洛匹那韦和利托那韦治疗的患者脉络膜毛细血管损伤更为严重,而抗血小板治疗对视网膜脉络膜 VD 无明显影响。利用 OCTA 评估视网膜、脉络膜的损害,并及早进行干预,将显著降低 COVID-19 患者发生严重视功能损害的风险。

4 OCTA 在罕见遗传疾病中的应用

视网膜作为独特微循环窗口,使 OCTA 也可以应用在某些罕见遗传病的诊断或随访过程中。法布里病(fabry disease, FD)是一种由位于 X 染色体上的 GLA 基因突变引起的罕见遗传病,主要累及心脏、肾脏和中枢神经系统。多项研究发现 FD 患者的浅、深层 VD 均显著降低,且与肾脏的受累程度密切相关[64-65]。OCTA 可以作为 FD 患者肾脏是否受累的可靠指标,并可以协助评估患者预后。

Wolfram 综合征(wolfram syndrome, WS)是一种罕见的常染色体隐性遗传进行性疾病,视神经萎缩是 WS 的一个持续特征,患者通常表现为视力逐渐丧失、色觉缺陷和视野缺损[66]。Battista 等[67]采用 OCTA 技术发现 WS 患者伴有明显的黄斑区和视盘周围浅表微血管损害。因此,OCTA 有望为 WS 的病理生理学研究提供新的影像学依据。

5 小 结

综上所述,OCTA 是一种可重复性高、无创检测视网膜血流的工具,除了已广泛应用在各种视网膜血管疾病及黄斑病变的诊断、治疗外,OCTA 亦在全身疾病的诊疗过程中得到了越来越广的临床应用。此外人工智能技术近年来发展迅速,在 OCTA 领域应用也越来越广,在图像的处理和分析(去除伪影、减少噪声以及自动分割视网膜脉络膜等重要结构)具有独特的优势。结合人工智能和 OCTA 技术有望显著提高各类全身疾病的早期诊断比率[68-69]。总之 OCTA 不止是一项对眼科具有突破性意义的

技术,同样对于各类全身疾病的早期诊断、治疗以及随访均具有重要的参考价值。

参考文献:

[1] Spaide RF, Fujimoto JG, Waheed NK, et al. Optical coherence tomography angiography[J]. Prog Retin Eye Res, 2018, 64: 1-55. doi: 10.1016/j.preteyeres.2017.11.003

[2] Kashani AH, Chen CL, Gahm JK, et al. Optical coherence tomography angiography: a comprehensive review of current methods and clinical applications[J]. Prog Retin Eye Res, 2017, 60: 66-100. doi: 10.1016/j.preteyeres.2017.07.002

[3] Gupta VB, Chitranshi N, den Haan J, et al. Retinal changes in Alzheimer's disease- integrated prospects of imaging, functional and molecular advances[J]. Prog Retin Eye Res, 2021, 82: 100899. doi: 10.1016/j.preteyeres.2020.100899

[4] Fekrazad S, Hassanzadeh G, Salehi MA, et al. Optical coherence tomography angiography measurements in systemic lupus erythematosus: a systematic review and meta-analysis[J]. Surv Ophthalmol, 2024, 69(5): 743-755. doi: 10.1016/j.survophthal.2024.04.007

[5] De Backer D, Orbegozo Cortes D, Donadello K, et al. Pathophysiology of microcirculatory dysfunction and the pathogenesis of septic shock[J]. Virulence, 2014, 5(1): 73-79. doi: 10.4161/viru.26482

[6] Taccone FS, Su FH, Pierrakos C, et al. Cerebral microcirculation is impaired during sepsis: an experimental study[J]. Crit Care, 2010, 14(4): R140. doi: 10.1186/cc9205

[7] Zadeh JK, Ruemmler R, Hartmann EK, et al. Responses of retinal arterioles and ciliary arteries in pigs with acute respiratory distress syndrome (ARDS)[J]. Exp Eye Res, 2019, 184: 152-161. doi: 10.1016/j.exer.2019.04.021

[8] Simkiene J, Pranskuniene Z, Patasius M, et al. Alterations of retinal vessels in patients with sepsis[J]. J Clin Monit Comput, 2020, 34(5): 937-942. doi: 10.1007/s10877-019-00401-0

[9] Alnawaiseh M, Ertmer C, Seidel L, et al. Feasibility of optical coherence tomography angiography to assess changes in retinal microcirculation in ovine haemorrhagic shock[J]. Crit Care, 2018, 22(1): 138. doi: 10.1186/s13054-018-2056-3

[10] Franceschi C. The unsolved puzzle of multiple sclerosis and venous function[J]. J Neurol Neurosurg Psychiatry, 2009, 80(4): 358. doi: 10.1136/jnnp.2008.168179

[11] Kılınç Hekimsoy H, ekeroğlu MA, Koçer AM, et al. Analysis of retinal and choroidal microvasculature in systemic sclerosis: an optical coherence tomography angiography study[J]. Eye (Lond), 2020, 34(4): 763-770. doi: 10.1038/s41433-019-0591-z

[12] Saidha S, Al-Louzi O, Ratchford JN, et al. Optical coherence tomography reflects brain atrophy in multiple sclerosis: a four-year study[J]. Ann Neurol, 2015, 78(5): 801-813. doi: 10.1002/ana.24487

[13] Doche E, Lecocq A, Maarouf A, et al. Hypoperfusion of the thalamus is associated with disability in relapsing remitting multiple sclerosis[J]. J Neuroradiol, 2017, 44(2): 158-164. doi: 10.1016/j.neurad.2016.10.001

[14] Wicklein R, Kreitner L, Wild A, et al. Retinal small vessel pathology is associated with disease burden in multiple sclerosis[J]. Mult Scler, 2024, 30(7): 812-819. doi: 10.1177/13524585241247775

[15] Wylęgała A. Principles of OCTA and applications in clinical neurology[J]. Curr Neurol Neurosci Rep, 2018, 18(12): 96. doi: 10.1007/s11910-018-0911-x

[16] Bulut M, Kurtulu F, Gözkaya O, et al. Evaluation of optical coherence tomography angiographic findings in Alzheimer's type dementia[J]. Br J Ophthalmol, 2018, 102(2): 233-237. doi: 10.1136/bjophthalmol-2017-310476

[17] López-Cuenca I, Salobrar-García E, Elvira-Hurtado L, et al. The value of OCT and OCTA as potential biomarkers for preclinical Alzheimer's disease: a review study[J]. Life (Basel), 2021, 11(7): 712. doi: 10.3390/life11070712

[18] Wisely CE, Wang D, Henao R, et al. Convolutional neural network to identify symptomatic Alzheimer's disease using multimodal retinal imaging[J]. Br J Ophthalmol, 2022, 106(3): 388-395. doi: 10.1136/bjophthalmol-2020-317659

[19] Chaudhuri KR, Healy DG, Schapira AHV, et al. Non-motor symptoms of Parkinson's disease: diagnosis and management[J]. Lancet Neurol, 2006, 5(3): 235-245. doi: 10.1016/S1474-4422(06)70373-8[PubMed]

[20] Archibald NK, Clarke MP, Mosimann UP, et al. The retina in Parkinson's disease[J]. Brain, 2009, 132(Pt 5): 1128-1145. doi: 10.1093/brain/awp068

[21] Schwartz RS, Halliday GM, Cordato DJ, et al. Small-vessel disease in patients with Parkinson's disease: a clinicopathological study[J]. Mov Disord, 2012, 27(12): 1506-1512. doi: 10.1002/mds.25112

[22] Lauermann JL, Sochurek JAM, Plöttner P, et al. Applicability of optical coherence tomography angiography (OCTA) imaging in Parkinson's disease[J]. Sci Rep, 2021, 11(1): 5520. doi: 10.1038/s41598-021-84862-x

[23] Robbins CB, Thompson AC, Bhullar PK, et al. Characterization of retinal microvascular and choroidal structural

changes in parkinson disease[J]. JAMA Ophthalmol, 2021, 139(2): 182-188. doi: 10.1001/jamaophthalmol.2020.5730

[24] Kwapong WR, Ye H, Peng CL, et al. Retinal microvascular impairment in the early stages of Parkinson's disease[J]. Invest Ophthalmol Vis Sci, 2018, 59(10): 4115-4122. doi: 10.1167/iovs.17-23230

[25] Zhang YF, Zhang D, Gao YZ, et al. Retinal flow density changes in early-stage Parkinson's disease investigated by swept-source optical coherence tomography angiography[J]. Curr Eye Res, 2021, 46(12): 1886-1891. doi: 10.1080/02713683.2021.1933054

[26] Zhang YF, Yang L, Gao YZ, et al. Choroid and choriocapillaris changes in early-stage Parkinson's disease: a swept-source optical coherence tomography angiography-based cross-sectional study[J]. Alzheimers Res Ther, 2022, 14(1): 116. doi: 10.1186/s13195-022-01054-z

[27] Rasmussen BK, Olesen J. Migraine with aura and migraine without aura: an epidemiological study[J]. Cephalalgia, 1992, 12(4): 221-228;discussion186. doi: 10.1046/j.1468-2982.1992.1204221.x

[28] Chang MY, Phasukkijwatana N, Garrity S, et al. Foveal and peripapillary vascular decrement in migraine with aura demonstrated by optical coherence tomography angiography[J]. Invest Ophthalmol Vis Sci, 2017, 58(12): 5477-5484. doi: 10.1167/iovs.17-22477

[29] Ulusoy MO, Horasanlı B, Kal A. Retinal vascular density evaluation of migraine patients with and without aura and association with white matter hyperintensities[J]. Acta Neurol Belg, 2019, 119(3): 411-417. doi: 10.1007/s13760-019-01094-7

[30] Romozzi M, Cuffaro G, Rollo E, et al. Microvascular involvement in migraine: an optical coherence tomography angiography study[J]. J Neurol, 2023, 270(8): 4024-4030. doi: 10.1007/s00415-023-11697-z

[31] Lee GI, Park KA, Oh SY, et al. Parafoveal and peripapillary perfusion predict visual field recovery in chiasmal compression due to pituitary tumors[J]. J Clin Med, 2020, 9(3): 697. doi: 10.3390/jcm9030697

[32] Lee GI, Park KA, Oh SY, et al. Changes in parafoveal and peripapillary perfusion after decompression surgery in chiasmal compression due to pituitary tumors[J]. Sci Rep, 2021, 11(1): 3464. doi: 10.1038/s41598-021-82151-1

[33] Cennamo G, Solari D, Montorio D, et al. Early vascular modifications after endoscopic endonasal pituitary surgery: The role of OCT-angiography[J]. PLoS One, 2020, 15(10): e0241295. doi: 10.1371/journal.pone.0241295

[34] Wang XQ, Chou YY, Zhu HJ, et al. Retinal microvascular alterations detected by optical coherence tomography angiography in nonfunctioning pituitary adenomas[J]. Transl Vis Sci Technol, 2022, 11(1): 5. doi: 10.1167/tvst.11.1.5

[35] Conigliaro P, Triggianese P, Draghessi G, et al. Evidence for the detection of subclinical retinal involvement in systemic lupus erythematosus and sjögren syndrome: a potential association with therapies[J]. Int Arch Allergy Immunol, 2018, 177(1): 45-56. doi: 10.1159/000488950

[36] Sultan W, Asanad S, Karanjia R, et al. Long-term attenuation of the deep capillary plexus in SLE utilizing OCTA[J]. Can J Ophthalmol, 2019, 54(4): e207-e212. doi: 10.1016/j.jcjo.2018.10.013

[37] Arfeen SA, Bahgat N, Adel N, et al. Assessment of superficial and deep retinal vessel density in systemic lupus erythematosus patients using optical coherence tomography angiography[J]. Graefes Arch Clin Exp Ophthalmol, 2020, 258(6): 1261-1268. doi: 10.1007/s00417-020-04626-7

[38] Meng LH, Chen LL, Zhang CX, et al. Quantitative assessment of retinal vasculature changes in systemic lupus erythematosus using wide-field OCTA and the correlation with disease activity[J]. Front Immunol, 2024, 15: 1340224. doi: 10.3389/fimmu.2024.1340224

[39] Zhuang XN, Cao D, Yang DW, et al. Association of diabetic retinopathy and diabetic macular oedema with renal function in southern Chinese patients with type 2 diabetes mellitus: a single-centre observational study[J]. BMJ Open, 2019, 9(9): e031194. doi: 10.1136/bmjopen-2019-031194

[40] Zhuang XN, Cao D, Zeng YK, et al. Associations between retinal microvasculature/microstructure and renal function in type 2 diabetes patients with early chronic kidney disease[J]. Diabetes Res Clin Pract, 2020, 168: 108373. doi: 10.1016/j.diabres.2020.108373

[41] Man REK, Fenwick EK, Gan ATL, et al. Association between perceived barriers to diabetes self-management and diabetic retinopathy in Asian patients with type 2 diabetes[J]. JAMA Ophthalmol, 2017, 135(12): 1387-1393. doi: 10.1001/jamaophthalmol.2017.4888

[42] Sng CCA, Sabanayagam C, Lamoureux EL, et al. Fractal analysis of the retinal vasculature and chronic kidney disease[J]. Nephrol Dial Transplant, 2010, 25(7): 2252-2258. doi: 10.1093/ndt/gfq007

[43] Ong YT, Wong TY, Klein R, et al. Hypertensive retinopathy and risk of stroke[J]. Hypertension, 2013, 62(4): 706-711. doi: 10.1161/HYPERTENSIONAHA.113.01414

[44] Wong TY, McIntosh R. Hypertensive retinopathy signs as risk indicators of cardiovascular morbidity and mortality

[J]. Br Med Bull, 2005, 73/74: 57-70. doi: 10.1093/bmb/ldh050

[45] Sun C, Ladores C, Hong J, et al. Systemic hypertension associated retinal microvascular changes can be detected with optical coherence tomography angiography[J]. Sci Rep, 2020, 10(1): 9580. doi: 10.1038/s41598-020-66736-w

[46] Chua J, Chin CWL, Hong J, et al. Impact of hypertension on retinal capillary microvasculature using optical coherence tomographic angiography[J]. J Hypertens, 2019, 37(3): 572-580. doi: 10.1097/HJH.0000000000001916

[47] Chua J, Le TT, Sim YC, et al. Relationship of quantitative retinal capillary network and myocardial remodeling in systemic hypertension[J]. J Am Heart Assoc, 2022, 11(6): e024226. doi: 10.1161/JAHA.121.024226

[48] Wang J, Jiang J, Zhang Y, et al. Retinal and choroidal vascular changes in coronary heart disease: an optical coherence tomography angiography study[J]. Biomed Opt Express, 2019, 10(4): 1532-1544. doi: 10.1364/BOE.10.001532

[49] Lange PS, Mihailovic N, Esser E, et al. Improvement of retinal microcirculation after pulmonary vein isolation in patients with atrial fibrillation-an optical coherence tomography angiography study[J]. Diagnostics (Basel), 2021, 12(1): 38. doi: 10.3390/diagnostics12010038

[50] Ross FJ, Arakaki LSL, Ciesielski WA, et al. Assessment of muscle oxygenation in children with congenital heart disease[J]. Paediatr Anaesth, 2019, 29(8): 850-857. doi: 10.1111/pan.13668

[51] Li C, Zhong PT, Yuan HY, et al. Retinal microvasculature impairment in patients with congenital heart disease investigated by optical coherence tomography angiography[J]. Clin Exp Ophthalmol, 2020, 48(9): 1219-1228. doi: 10.1111/ceo.13846

[52] Morales-Valero SF, Lanzino G. Asymptomatic carotid artery stenosis: time to rethink our therapeutic options? [J]. Neurosurg Focus, 2014, 36(1): E2. doi: 10.3171/2013.10.FOCUS13389

[53] McCullough HK, Reinert CG, Hynan LS, et al. Ocular findings as predictors of carotid artery occlusive disease: is carotid imaging justified? [J]. J Vasc Surg, 2004, 40(2): 279-286. doi: 10.1016/j.jvs.2004.05.004

[54] Cao L, Wang H, Kwapong WR, et al. Length of carotid plaque impacts retinal microvascular densities of carotid artery stenosis patients[J]. Transl Vis Sci Technol, 2023, 12(9): 3. doi: 10.1167/tvst.12.9.3

[55] Xu Q, Sun HY, Yi Q. Association between retinal microvascular metrics using optical coherence tomography angiography and carotid artery stenosis in a Chinese cohort[J]. Front Physiol, 2022, 13: 824646. doi: 10.3389/fphys.2022.824646

[56] Li SQ, Zhao WJ, Jian TZ, et al. Quantitative assessment of retinochoroidal microvasculature in patients with carotid artery stenosis using OCT angiography[J]. Photodiagnosis Photodyn Ther, 2024, 46: 104082. doi: 10.1016/j.pdpdt.2024.104082

[57] Lahme L, Marchiori E, Panuccio G, et al. Changes in retinal flow density measured by optical coherence tomography angiography in patients with carotid artery stenosis after carotid endarterectomy[J]. Sci Rep, 2018, 8(1): 17161. doi: 10.1038/s41598-018-35556-4

[58] Pierro L, Arrigo A, De Crescenzo M, et al. Quantitative optical coherence tomography angiography detects retinal perfusion changes in carotid artery stenosis[J]. Front Neurosci, 2021, 15: 640666. doi: 10.3389/fnins.2021.640666

[59] Virgo J, Mohamed M. Paracentral acute middle maculopathy and acute macular neuroretinopathy following SARS-CoV-2 infection[J]. Eye (Lond), 2020, 34(12): 2352-2353. doi: 10.1038/s41433-020-1069-8

[60] Marinho PM, Marcos AAA, Romano AC, et al. Retinal findings in patients with COVID-19[J]. Lancet, 2020, 395(10237): 1610. doi: 10.1016/S0140-6736(20)31014-X

[61] Abrishami M, Emamverdian Z, Shoeibi N, et al. Optical coherence tomography angiography analysis of the retina in patients recovered from COVID-19: a case-control study[J]. Can J Ophthalmol, 2021, 56(1): 24-30. doi: 10.1016/j.jcjo.2020.11.006

[62] Chiosi F, Campagna G, Rinaldi M, et al. Optical coherence tomography angiography analysis of vessel density indices in early post-COVID-19 patients[J]. Front Med (Lausanne), 2022, 9: 927121. doi: 10.3389/fmed.2022.927121

[63] Gao YZ, Zhang YF, Mou KF, et al. Assessment of alterations in the retina and vitreous in pre- and post-COVID-19 patients using swept-source optical coherence tomography and angiography: a comparative study[J]. J Med Virol, 2023, 95(10): e29168. doi: 10.1002/jmv.29168

[64] Dogan C, Gonen B, Dincer MT, et al. Evaluation of the reasons for the microvascular changes in patients with Fabry disease using optic coherence tomography angiography[J]. Eur J Ophthalmol, 2021, 31(6): 3231-3237. doi: 10.1177/1120672120974288

[65] Cennamo G, Di Maio LG, Montorio D, et al. Optical coherence tomography angiography findings in fabry disease[J]. J Clin Med, 2019, 8(4): 528. doi: 10.3390/jcm8040528

[66] Ustaoglu M, Onder F, Karapapak M, et al. Ophthalmic, systemic, and genetic characteristics of patients with Wolfram syndrome[J]. Eur J Ophthalmol, 2020, 30(5): 1099-1105. doi: 10.1177/1120672119842489

[67] Battista M, Cascavilla ML, Grosso D, et al. Retinal vascular impairment in wolfram syndrome: an optical coherence tomography angiography study[J]. Sci Rep, 2022, 12(1): 2103. doi: 10.1038/s41598-022-06150-6

[68] Sampson DM, Dubis AM, Chen FK, et al. Towards standardizing retinal optical coherence tomography angiography: a review[J]. Light Sci Appl, 2022, 11(1): 63. doi: 10.1038/s41377-022-00740-9

[69] Hormel TT, Hwang TS, Bailey ST, et al. Artificial intelligence in OCT angiography[J]. Prog Retin Eye Res, 2021, 85: 100965. doi: 10. 1016/j. preteyeres. 2021. 100965

(编辑:李纬)

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[49] Smarr CB, Yap WT, Neef TP, et al. Biodegradable antigen-associated PLG nanoparticles tolerize Th2-mediated allergic airway inflammation pre- and postsensitization [J]. Proc Natl Acad Sci U S A, 2016, 113(18): 5059-5064. doi:10.1073/pnas.1505782113

[50] Krieg AM. CpG motifs in bacterial DNA and their immune effects[J]. Annu Rev Immunol, 2002, 20: 709-760. doi:10.1146/annurev.immunol.20.100301.064842

[51] Hanagata N. CpG oligodeoxynucleotide nanomedicines for the prophylaxis or treatment of cancers, infectious diseases, and allergies[J]. Int J Nanomedicine, 2017, 12: 515-531. doi: 10.2147/IJN.S114477

[52] Yang X, Su B, Liu J, et al. A CpG-oligodeoxynucleotide suppresses Th2/Th17 inflammation by inhibiting IL-33/ST2 signaling in mice from a model of adoptive dendritic cell transfer of smoke-induced asthma[J]. Int J Mol Sci, 2023, 24(4): 3130. doi: 10.3390/ijms24043130

[53] Zhou J, Deng GM. The role of bacterial DNA containing CpG motifs in diseases[J]. J Leukoc Biol, 2021, 109(5): 991-998. doi: 10.1002/JLB.3MR1220-748RRRRR

[54] Liu W, Ota M, Tabushi M, et al. Development of allergic rhinitis immunotherapy using antigen-loaded small extracellular vesicles[J]. J Control Release, 2022, 345: 433-442. doi:10.1016/j.jconrel.2022.03.016

[55] Sun SC. The non-canonical NF-κB pathway in immunity and inflammation[J]. Nat Rev Immunol, 2017, 17: 545-558. doi:10.1038/nri.2017.52

[56] Karri U, Harasimowicz M, Carpio Tumba M, et al. The complexity of Being A20: from biological functions to genetic associations[J]. J Clin Immunol, 2024, 44(3): 76. doi: 10.1007/s10875-024-01681-1

[57] Hu WH, Ma L, Yang G, et al. Der p2-A20 DNA vaccine attenuates allergic inflammation in mice with allergic rhinitis[J]. Mol Med Rep, 2019, 20(6): 4925-4932. doi:10.3892/mmr.2019.10760

[58] Jewell CM, Bustamante López SC, Irvine DJ. In situ engineering of the lymph node microenvironment via intranodal injection of adjuvant-releasing polymer particles [J]. Proc Natl Acad Sci USA, 2011, 108(38): 15745-15750. doi:10.1073/pnas.1105200108

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