·文献综述·

基于 OCTA 测量黄斑中心凹无血管区形态在眼部疾病中的应用研究进展

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摘要

黄斑中心凹无血管区(FAZ)是视网膜上视觉最敏锐的区域,由视网膜黄斑区毛细血管丛相互连接而成,其形态可以间接反映黄斑区微循环的变化。光学相干断层扫描血管成像(OCTA)技术可以无创的可视化和量化 FAZ 区域,且具有较好的重复性和可靠性, OCTA 展现出的巨大价值使其成为眼科及各个领域重要的辅助检查工具。在高度近视、糖尿病视网膜病变、青光眼等眼科疾病中,FAZ 的面积及周长已被证实具有临床诊断价值,近年来 FAZ 的几何形态也展现出一定的临床意义,圆度指数、非圆指数、轴比等描述 FAZ 几何形态的参数为疾病研究提供了新视角。全方面研究 FAZ 区域的形态特征有助于探索眼部疾病发生和发展机制,或可预测疾病的早期变化及精确病理分期,为监测疾病进展及评估患者的视觉预后提供理论依据。

关键词:黄斑中心凹无血管区;光学相干断层扫描血管成像(OCTA);圆度指数;高度近视;糖尿病视网膜病变

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Research progress on morphology of macular foveal avascular zone in ocular diseases based on optical coherence tomography angiography measurement

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Abstract

• The foveal avascular zone (FAZ) is the most sensitive region of the retina, which is interconnected by the macular capillary plexus. Its morphology can indirectly reflect the alterations of macular microcirculation. With strong repeatability and reliability, optical coherence tomography angiography (OCTA) can non-invasively visualize and quantify the FAZ. The great value of OCTA makes it an important supplemental examination tool in ophthalmology and other professions. The area and perimeter of FAZ have been demonstrated to be an effective clinical diagnostic indicator in high myopia, diabetic retinopathy, glaucoma and other ocular diseases. In recent years, the geometry of FAZ has also proven to have clinical value. The parameters describing the geometry of FAZ, such as circularity index, acircularity index and axial ratio, provide a new perspective for ocular disease research. The comprehensive investigation of the morphological characteristics of the FAZ is helpful to explore the pathological mechanism of the occurrence and development of ocular diseases, predict preclinical changes, make pathological stages of the disease precise, and provide a theoretical basis for monitoring the disease's progression and assessing patients' visual prognosis.

• KEYWORDS: foveal avascular zone; optical coherence tomography angiography (OCTA); circularity index; high myopia; diabetic retinopathy

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0 引言

黄斑中心凹无血管区(foveal avascular zone, FAZ)是视网膜上视觉最敏锐的区域,其由视网膜黄斑区毛细血管

丛相互连接围绕而成,本身不存在毛细血管结构[1]。黄斑中心凹毛细血管脱失是缺血性和血管闭塞性视网膜疾病的显著特征,FAZ 的形态可以反映黄斑微循环的变化[2]。临床上常通过面积、周长和费雷特直径等参数评估 FAZ 的大小,通过圆度指数(circularity index, CI)、非圆指数(acircularity index, AI)、轴比和坚固度等参数评估其形状[3-5]。光学相干断层扫描血管成像(optical coherence tomography angiography, OCTA)技术可以无创的可视化和量化 FAZ 的形态,近几年已广泛应用于眼科疾病的研究,并且不仅局限于视网膜脉络膜相关疾病,也在动物实验及系统性疾病中得到广泛应用[6-8]。本文旨在总结及归纳近期的相关文献,对利用 OCTA 量化 FAZ 形态在眼部疾病中的研究进展作一综述。

1 FAZ 与 OCTA

眼底荧光素血管造影(fundus fluorescein angiography, FFA)在很长一段时间一直是量化 FAZ 的金标准[9],然而 FFA 有着不可忽视的缺点,向血管内注射荧光素是有创操作,且可能出现潜在的不良反应,例如从轻微的恶心呕吐到过敏性皮疹,甚至造成休克危及生命,此外 FFA 需要 7-8 min的循环时间,导致其学习曲线长、操作性差、持续时间长,不能频繁重复应用。Mendis 等[10]研究表明,FFA 提供的浅层毛细血管网络形态学信息不完全,而深层毛细血管网络的形态学信息更少,在利用 FFA 评估微血管病理变化时应谨慎。因此,寻找一种简单无创的能够对 FAZ 进行可视化的方法,已成为眼科领域的研究热点。近几年 OCTA 的出现弥补了 FAZ 测量技术上的空缺,可避免 FFA 侵入性操作造成的潜在风险及造影剂聚集和渗漏造成的干扰。OCTA 基于连续的 B-扫描,利用运动对比度提供视网膜和脉络膜血管结构的三维影像,从而获取任意层次的血管结构试图[11],使 FAZ 结构立体化和可视化,从而进行量化分析。OCTA 可以生成视网膜各层 FAZ 图像,通过内置软件矫正眼轴长度带来的眼底放大效应[12],自动生成 FAZ 的面积、周长和 CI 等参数。

作为描述 FAZ 几何形态的参数,CI 和 AI 在数学上表示 FAZ 与标准圆形的相似程度。CI 越小,AI 越大,表示形状越偏离标准圆形。计算公式为:$CI=4\pi\times$面积/周长^2;AI=FAZ 周长/FAZ 等面积圆的周长。轴比是通过 FAZ 最佳拟合椭圆确定的参数,计算公式为:轴比=FAZ 最长轴/最短轴[3]。这几个参数与面积、周长等不同,不需要考虑眼轴长度产生的放大作用。FAZ 几何形态已广泛应用于多种眼科疾病,包括高度近视、青光眼、糖尿病视网膜病变(diabetic retinopathy, DR)等,具有重要临床意义[3-5,13]。

作为一种新兴的影像学技术,众多研究组一直在探究 OCTA 测量 FAZ 参数的可信度和精确度。研究表明,使用 OCTA 自动测量血管密度和 FAZ 形态在正常人群中展现了极好的重复性和可靠性[14-15]。FAZ 可以通过 OCTA 内部软件自动计算,也可以通过外部程序手动测量,如 Image J[3,16]。Linderman 等[17]研究发现,无论是自动计算还是手动测量,FAZ 形态参数的可信度都较高。这使得 OCTA 成为了一个有潜力的疾病诊断工具,对监测疾病进展及治疗效果有很大的价值[4,18]。

2 FAZ 与高度近视

近视作为世界主要致盲性眼病之一,近几十年来发病率显著上升。预计到 2050 年,全球近视和高度近视的患病人群将达到 50 亿和 10 亿[19]。高度近视的定义为当眼睛调节放松时,眼睛的等效球镜度≤-6.00 D 或眼轴长度≥26~26.5 mm[20]。高度近视可造成包括漆裂纹、视网膜劈裂、视网膜脱离、黄斑裂孔、脉络膜新生血管等眼底病变。近视性黄斑病变是高度近视的一种复杂并发症,Ruiz-Medrano 等[21]通过新分级分期系统(ATN)将近视性黄斑病变分为 3 类:近视萎缩性黄斑病变,近视牵拉性黄斑病变,近视新生血管性黄斑病变。近来多项研究表明,在高度近视的发展过程中,FAZ 发生扩大和变形,FAZ 可能成为一种监测高度近视黄斑病变进展的有效指标[3,22-26]。

与非高度近视眼相比,高度近视眼的 FAZ 扩大,并伴随黄斑区血流密度的降低[22-24]。Cheng 等[22]研究发现,高度近视患者浅层和深层 FAZ 面积增大,浅层和深层视网膜血流密度降低,且与眼轴长度显著相关,FAZ 面积和血流密度的改变在深层更加明显。深层 FAZ 更易受到高度近视眼眼轴伸长的影响,可能与浅层和深层毛细血管丛的血供来源不同有关,视网膜浅层的氧气和营养需求主要由视网膜中央动脉满足,而视网膜深层的氧气和营养需求主要由脉络膜血管系统满足[25-27]。He 等[23]研究表明,高度近视眼视乳头旁和黄斑区毛细血管密度降低,FAZ 面积增大,这与 Sung 等[24]研究类似,他们认为除了视乳头周围血管密度外,FAZ 还受视盘倾斜程度的影响,由于眼轴伸长的拉伸作用,视盘水平倾斜程度不同,高度近视眼视网膜微血管结构也有显著差异。这些研究有利于我们探讨高度近视眼中 FAZ 形态扩大的发生机制:(1)眼轴的伸长对视网膜血管产生牵引力,可能导致终末毛细血管变形,从而 FAZ 面积增大;(2)眼轴的伸长导致黄斑区视网膜脉络膜变薄,供氧量降低,从而造成血管密度降低、FAZ 面积增大[25]。以上研究均表明高度近视眼 FAZ 的异常扩大往往伴随着视网膜血流密度的降低,提示 FAZ 的形态大小可以间接反映高度近视眼视网膜微循环灌注的变化。

FAZ 几何形态学改变在多种眼底缺血性疾病中得到证实[3],而在高度近视中的研究较少。Piao 等[3]研究发现,在高度近视组和非高度近视组中,浅层和深层 FAZ 的最长轴和最短轴体现出显著差异,高度近视组最长轴和最短轴的较长,线性回归分析显示,高度近视组 FAZ 的 CI 和 AI 与 FAZ 面积显著相关。这说明随着近视的加深和眼轴的伸长,FAZ 变得更大且更不趋近于圆形。一项前瞻性观察研究表明,在眼轴伸长过程中,视盘筛板的中央血管干向鼻侧牵引[26]。或许视网膜血管干的牵拉可导致黄斑区视网膜血流灌注的不规则减少,进而黄斑区 FAZ 向视盘扭曲,导致 FAZ 变形。因此,FAZ 的几何形态变化或可成为近视进展的新型监测指标。

3 FAZ 与 DR

DR 是糖尿病常见的微血管并发症之一,可导致视网膜微血管渗漏和阻塞,从而引起一系列眼底病变,如非增殖期的微血管瘤、硬性渗出、棉絮斑,增殖期新生血管、玻璃体增殖,甚至视网膜脱离。DR 是成年糖尿病患者失明的主要原因[28],大多数 DR 患者直到疾病的晚期才会出现明显的视觉症状,及时采取干预措施可能会延缓视力进一步下降,因此 DR 的早期诊断和准确分期是治疗的关键[29]。在 20 a 前,Conrath 等[30]利用 FFA 发现随着 DR 的进展,FAZ 表现出明显的不规则性,周长、面积及周围毛细血管间区增大,且周长改变更明显。Alipour 等[31]将 FFA 和彩色眼底照相结合,发现 FAZ 大小和形态轮廓的测量

对DR等眼底缺血性疾病的临床分期有指导作用。随着近年来影像技术的发展,OCTA成为了评估DR临床分期和监测DR进展的有力工具,其自动化算法可以快速获取FAZ数据,从而使临床医生将FAZ的形态学信息应用到临床实践中[32]。

多项研究显示[32-35],OCTA是一种有潜力的无创性DR早期筛查工具。Takase等[33]研究发现,与健康眼相比,无论是否患有DR,糖尿病患者的FAZ有显著增大,且深层FAZ面积增大更明显。Samara等[29]将患者分为轻度非增殖型DR、中度至重度非增殖型DR和增殖型DR三组,与健康眼相比,三组患者FAZ面积增大,且随着DR严重程度增加,FAZ呈现出扩大的趋势。这与纪风涛等[34]研究一致。FAZ面积和周长增大、黄斑区视网膜血流密度减少,是DR前期或早期视网膜缺血的证据[35]。有类似研究认为,DR患者具有较大的FAZ,且具有较大FAZ的眼睛更容易出现视力障碍[32],这可能与黄斑中心凹的神经胶质密度和血管密度有关,FAZ大小和黄斑区的血流密度可能是预估糖尿病患者远期视力的敏感指标。

OCTA可以清晰的显示DR患者发生病变的毛细血管。微动脉瘤在OCTA图像中表现为梭状、囊状或卷曲的毛细血管,在OCT图像中表现为环形、圆形或椭圆形的高反射病变,与健康眼相比,DR的FAZ区域和轮廓更易识别[36],因此出现了大量针对DR患者FAZ几何形态的研究[4,37-40]。Krawitz等[4]针对糖尿病患者的AI和轴比进行了研究,他们将糖尿病患者分为非DR、非增殖型DR和增殖型DR三组,研究发现,除了对照组与非DR外,其余组间的AI和轴比均具有差异性,DR严重程度和AI、轴比成正相关。Tang等[37]发现DR的病程进展伴随着FAZ面积增加和CI降低,且FAZ的CI降低与视觉功能下降相关。同样的,Kim等[38]研究显示,NDR和NPDR患者的CI均小于健康对照组。Bates等[39]研究细化了NPDR的分组,并分析了不同严重程度NPDR患者的FAZ结构,结果发现中度NPDR患者的FAZ面积、周长增大,不规则度明显增高。与高度近视不同的是,造成DR患者FAZ形态改变的并非是眼轴伸长对黄斑区血管的牵拉作用,而是糖尿病本身毛细血管的损伤。糖尿病视网膜的机械特性存在潜在的各向异性,会触发FAZ在任一方向上的延伸,导致FAZ形态发生不规则改变,这与血管收缩和毛细血管缺失有关[40]。以上研究均显示,利用OCTA测量CI、AI、轴比等FAZ几何形态参数可以用于评估DR严重程度并明确DR分期。量化FAZ的不规则性和重塑视网膜微结构依然是未来的研究重点,深入了解这些病理改变之间的相互关系对于理解DR及其进展至关重要。

Krawitz等[4]还利用OCTA对2例糖尿病患者进行了随访。随着病程进展,第1例患者FAZ的AI和轴比均有增大。第2例患者注射抗VEGF药物和激光治疗后,在1 mo和4 mo分别对AI和轴比进行了测量,结果显示,随着黄斑水肿的消退,AI和轴比均呈现减小的趋势。这提示了FAZ几何形态学指标在纵向跟踪疾病变化方面的潜力。然而该研究样本量较小,FAZ几何形态在监测DR进展及评估疗效上的作用仍需大样本的纵向研究来证明。

4 FAZ与青光眼

青光眼是一组以视乳头萎缩、凹陷、视野缺损及视力下降为共同特征的疾病。由于青光眼患者眼压较高,进行需散瞳的眼底检查有一定风险,而OCTA可以在小瞳下采集眼底图像和数据,能够对青光眼的眼底进行更细致全面的检查和诊断[41]。尽管视神经乳头是青光眼的主要观察指标,但近年来大量研究显示FAZ的扩大和变形对青光眼的诊断起重要作用[5,13,42-44]。

Choi等[5]对开角型青光眼(open angle glaucoma, OAG)患者进行OCTA检查,结果显示OAG患者黄斑血流密度减少,FAZ周长增加,CI降低。CI可能是一种表征青光眼中心凹旁毛细血管网破坏程度的新型指标。与周边视野缺损的OAG患者相比,中央视野缺损的OAG患者FAZ面积更大,CI更小,且与黄斑区神经节内丛状层厚度有关[13]。有研究分别对闭角型青光眼急性发作期和间歇期的患者进行了分析,各组的FAZ面积和周长无差异,而急性发作期的CI比间歇期小,且均小于健康眼,CI可以监测闭角型青光眼进展变化并进行早期诊断[42]。在正常眼压青光眼(normal tension glaucoma, NTG)中针对FAZ的研究存在争议。Zivkovic等[43]发现NTG人群的FAZ面积、水平径、垂直径和最长径增大,黄斑区血管密度减小。而Wang等[44]研究显示,NTG与健康人群相比,FAZ面积、CI和黄斑区视网膜血流密度没有显著差异。通过OCTA可以监测青光眼患者的FAZ和视网膜血流灌注情况,然而在某些青光眼类型中,研究结果尚未达成一致。由此可见,FAZ的形态学指标可对青光眼的诊断提供一定参考价值,但其特异性仍需更多的理论支持。

5 FAZ与其他眼科疾病

视网膜静脉阻塞(retinal vein occlusion, RVO)是中老年人群常见的视网膜血管疾病,其并发的黄斑水肿是影响视力的重要原因[45]。OCTA全面展示了RVO患者FAZ区域的结构及形态,对临床患者的视力评估和改善具有指导性意义[36]。Adhi等[46]分别对15例视网膜中央静脉阻塞和8例视网膜分支静脉阻塞进行了研究,RVO眼的平均FAZ面积均大于对侧眼和健康对照组。Ogasawara等[47]和Samara等[48]针对视网膜分支静脉阻塞的研究得出了相似的结论,视网膜分支静脉阻塞眼的FAZ扩大在深层更明显,且与患者的最矫正视力相关,FAZ更小的眼具有更好的视力。最佳矫正视力的提升可能与黄斑水肿消退有关,抗VEGF治疗能减轻黄斑水肿,维持RVO患者视网膜血流灌注和FAZ的稳定,从而改善视力预后[49]。Deng等[50]针对RVO患者FAZ的几何形态进行了研究,结果发现RVO组的AI显著高于健康对照组,且经过治疗后AI有减小的趋势,这可能与黄斑水肿导致的视网膜积液不均匀分布有关。FAZ大小及形态是否可以监测RVO的进展及治疗效果,还需要进一步的研究印证。

弱视是视觉发育期内由于视觉经验异常引起的单眼或双眼最佳矫正视力下降,形成机制包括单眼斜视、屈光参差、高度屈光不正和形觉剥夺[51]。Demirayak等[52]和Gao等[53]的研究发现,同一患者的弱视眼FAZ面积小于非弱视眼,但无统计学差异。而在Araki等[54]研究中,弱视眼与非弱视眼的浅层FAZ面积有统计学差异,但该研究样本量较小,临床意义仅供参考。

早产儿视网膜病变(retinopathy of prematurity, ROP)作为一种血管增殖型视网膜疾病,是导致儿童失明的主要原因。利用OCTA可以发现ROP患儿有明显的黄斑区视网膜微血管结构异常,FAZ的面积和体积较小[55]。Deng等[56]和Chen等[57]的研究均利用OCTA对ROP患者的FAZ进行了监测,对比了激光光凝和抗VEGF药物注射的

疗效和预后,并得出了相似的结论,经抗 VEGF 药物注射后的患儿 FAZ 扩大、血流密度减小,黄斑区血管结构发育更好。

FAZ 形态的改变也可见于 Coats 病[58]、黄斑毛细血管扩张症[59]、马凡综合征相关眼部并发症[60]等疾病当中,但目前相关研究并不全面,大多仅仅探索了 FAZ 面积的变化。针对 FAZ 尤其是其几何形态的研究在眼部疾病中的诊断及预测价值有待探索。

6 总结与展望

随着影像学技术的发展,OCTA 展现出的巨大价值使其成为眼科及各个领域重要的辅助检查工具。OCTA 不仅能够清晰显示视网膜各层血管的走形、结构和血流密度,还能将 FAZ 可视化和量化,并具有较高的重复性和可靠性。对于高度近视、DR、青光眼、RVO 等存在视网膜病变的疾病,有重要临床诊疗价值。然而利用 OCTA 进行眼底检查也存在一个公共问题,来自于不同生产公司的 OCTA 仪器对于视网膜解剖学层面分割标准不一致,这与软件设置的算法有关,希望在未来不同 OCTA 的视网膜分割能够做到精准且统一,这将有利于眼科疾病在不同研究之间的比较和探索。

临床医生可以通过监测 FAZ 的形态学参数,如面积、周长、CI、AI、轴比等,了解甚至预估疾病的进展,有助于识别疾病早期变化、精确分期、评估疾病的治疗效果和预后。在未来,通过 OCTA 对各类眼部疾病的 FAZ 进行大样本的纵向随访研究具有重要临床意义,进一步探索 FAZ 形态异常改变的机制,为疾病的诊断和治疗提供了新视角。

参考文献

[1] Mihailovic N, Eter N, Alnawaiseh M. Foveale avaskuläre zone und OCT - angiographie. eine übersicht aktueller erkenntnisse. Ophthalmologe, 2019,116(7):610-616.

[2] Kwon J,Choi J, Shin JW, et al. Glaucoma diagnostic capabilities of foveal avascular zone parameters using optical coherence tomography angiography according to visual field defect location. J Glaucoma, 2017, 26(12):1120-1129.

[3] Piao HL, Guo Y, Zhang HW, et al. Acircularity and circularity indexes of the foveal avascular zone in high myopia. Sci Rep, 2021,11(1):16808.

[4] Krawitz BD, Mo S, Geyman LS, et al. Acircularity index and axis ratio of the foveal avascular zone in diabetic eyes and healthy controls measured by optical coherence tomography angiography. Vision Res, 2017,139:177-186.

[5] Choi J, Kwon J, Shin JW, et al. Quantitative optical coherence tomography angiography of macular vascular structure and foveal avascular zone in glaucoma. PLoS One, 2017,12(9):e0184948.

[6] Alnawaiseh M, Brand C, Bormann E, et al. Quantitative analysis of retinal perfusion in mice using optical coherence tomography angiography. Exp Eye Res, 2017,164:151-156.

[7] Alnawaiseh M, Schubert F, Heiduschka P, et al. Optical coherence tomography angiography in patients with retinitis pigmentosa. Retina, 2019,39(1):210-217.

[8] Krajewski P, Turczyńska M, Gołębiewska J, et al. Optical coherence tomography angiography findings in patients with chronic thromboembolic pulmonary hypertension. Retina, 2022, 42(12): 2354-2360.

[9] Shin YU, Kim S, Lee BR, et al. Novel noninvasive detection of the fovea avascular zone using confocal red - free imaging in diabetic retinopathy and retinal vein occlusion. Invest Ophthalmol Vis Sci, 2012, 53(1):309-315.

[10] Mendis KR, Balaratnasingam C, Yu P, et al. Correlation of histologic and clinical images to determine the diagnostic value of fluorescein angiography for studying retinal capillary detail. Invest Ophthalmol Vis Sci, 2010,51(11):5864-5869.

[11] Jia YL, Bailey ST, Hwang TS, et al. Quantitative optical coherence tomography angiography of vascular abnormalities in the living human eye. Proc Natl Acad Sci USA, 2015,112(18):E2395-E2402.

[12] Sampson DM, Gong PJ, An D, et al. Axial length variation impacts on superficial retinal vessel density and foveal avascular zone area measurements using optical coherence tomography angiography. Invest Ophthalmol Vis Sci, 2017,58(7):3065-3072.

[13] Kwon J, Choi J, Shin JW, et al. Alterations of the foveal avascular zone measured by optical coherence tomography angiography in glaucoma patients with central visual field defects. Invest Ophthalmol Vis Sci, 2017,58(3):1637.

[14] Al-Sheikh M,Tepelus TC, Nazikyan T, et al. Repeatability of automated vessel density measurements using optical coherence tomography angiography. Br J Ophthalmol, 2017,101(4):449-452.

[15] Mastropasqua R, Toto L, Mattei PA, et al. Reproducibility and repeatability of foveal avascular zone area measurements using swept-source optical coherence tomography angiography in healthy subjects. Eur J Ophthalmol, 2017,27(3):336-341.

[16] Freiberg FJ,Pfau M, Wons J, et al. Optical coherence tomography angiography of the foveal avascular zone in diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol, 2016,254(6):1051-1058.

[17] Linderman R, Salmon AE, Strampe M, et al. Assessing the accuracy of foveal avascular zone measurements using optical coherence tomography angiography: segmentation and scaling. Transl Vis Sci Technol, 2017,6(3):16.

[18] 鲁鑫, 赵星星, 伊恩晖, 等. OCTA 定量分析糖尿病视网膜病变患者黄斑区微循环变化. 国际眼科杂志, 2023,23(6):1033-1039.

[19] Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology, 2016,123(5):1036-1042.

[20] Wolf S, Balciuniene VJ, Laganovska G, et al. RADIANCE: a randomized controlled study of ranibizumab in patients with choroidal neovascularization secondary to pathologic myopia. Ophthalmology, 2014,121(3):682-692.e2.

[21] Ruiz-Medrano J, Montero JA, Flores-Moreno I, et al. Myopic maculopathy: current status and proposal for a new classification and grading system (ATN). Prog Retin Eye Res, 2019,69:80-115.

[22] Cheng D, Chen Q, Wu YF, et al. Deepperifoveal vessel density as an indicator of capillary loss in high myopia. Eye, 2019, 33(12): 1961-1968.

[23] He JN, Chen QY, Yin Y, et al. Association between retinal microvasculature and optic disc alterations in high myopia. Eye, 2019,33(9):1494-1503.

[24] Sung MS, Lee TH, Heo H, et al. Association between optic nerve head deformation and retinal microvasculature in high myopia. Am J Ophthalmol, 2018,188:81-90.

[25] Min CH, Al-Qattan HM, Lee JY, et al. Macular microvasculature in high myopia without pathologic changes: an optical coherence tomography angiography study. Korean J Ophthalmol, 2020, 34(2): 106-112.

[26] Lee KM,Choung HK, Kim M, et al. Positional change of optic nerve head vasculature during axial elongation as evidence of Lamina cribrosa shifting: boramae myopia cohort study report 2. Ophthalmology, 2018,125(8):1224-1233.

[27] Kur J, Newman EA, Chan-Ling T. Cellular and physiological mechanisms underlying blood flow regulation in the retina and choroid in health and disease. Prog Retin Eye Res, 2012,31(5):377-406.
[28] Yau JWY, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care, 2012,35(3):556-564.
[29] Samara WA,Shahlaee A, Adam MK, et al. Quantification of diabetic macular ischemia using optical coherence tomography angiography and its relationship with visual acuity. Ophthalmology, 2017, 124(2):235-244.
[30] Conrath J, Giorgi R, Raccah D, et al. Foveal avascular zone in diabetic retinopathy: quantitative vs qualitative assessment. Eye, 2005, 19(3):322-326.
[31] Alipour SHM, Rabbani H, Akhlaghi M, et al. Analysis of foveal avascular zone for grading of diabetic retinopathy severity based on curvelet transform. Graefes Arch Clin Exp Ophthalmol, 2012,250(11):1607-1614.
[32] Balaratnasingam C, Inoue M, Ahn S, et al. Visual acuity is correlated with the area of the foveal avascular zone in diabetic retinopathy and retinal vein occlusion. Ophthalmology, 2016,123(11):2352-2367.
[33] Takase N, Nozaki M, Kato A, et al. Enlargement of foveal avascular zone in diabetic eyes evaluated by en face optical coherence tomography angiography. Retina, 2015,35(11):2377-2383.
[34] 纪风涛, 王慧, 魏科, 等. SS-OCTA 评估增殖性糖尿病视网膜病变玻璃体切除术后黄斑微血管的变化. 国际眼科杂志, 2023,23(5):747-753.
[35] Li ZJ,Alzogool M, Xiao JH, et al. Optical coherence tomography angiography findings of neurovascular changes in type 2 diabetes mellitus patients without clinical diabetic retinopathy. Acta Diabetol, 2018,55(10):1075-1082.
[36] Miwa Y, Murakami T,Suzuma K, et al. Relationship between functional and structural changes in diabetic vessels in optical coherence tomography angiography. Sci Rep, 2016,6:29064.
[37] Tang FY, Ng DS, LamA, et al. Determinants of quantitative optical coherence tomography angiography metrics in patients with diabetes. Sci Rep, 2017,7(1):2575.
[38] Kim K, Kim ES, Yu SY. Optical coherence tomography angiography analysis of foveal microvascular changes and inner retinal layer thinning in patients with diabetes. Br J Ophthalmol, 2018,102(9):1226-1231.
[39] Bates NM,Tian J, Smiddy WE, et al. Relationship between the morphology of the foveal avascular zone, retinal structure, and macular circulation in patients with diabetes mellitus. Sci Rep, 2018,8(1):5355.
[40] 曾运考, 杨大卫, 曹丹, 等. 早期不同分期糖尿病视网膜病变黄斑区血流密度及血管结构改变. 中华实验眼科杂志, 2020,38(9):783-787.
[41] Özdemir HB, Ali Şekeroğlu M. The effect of topical tropicamide and phenylephrine on macular and peripapillary microvasculature: an optical coherence tomography angiography study. Int Ophthalmol, 2020, 40(8):1969-1976.
[42] Liu KC,Xu HZ, Jiang HB, et al. Macular vessel density and foveal avascular zone parameters in patients after acute primary angle closure determined by OCT angiography. Sci Rep, 2020,10(1):18717.
[43] Zivkovic M, Dayanir V, Kocaturk T, et al. Foveal avascular zone in normal tension glaucoma measured by optical coherence tomography angiography. Biomed Res Int, 2017,2017:3079141.
[44] Wang YM, Hui VWK, Shi J, et al. Characterization of macular choroid in normal-tension glaucoma: a swept-source optical coherence tomography study. Acta Ophthalmol, 2021,99(8):e1421-e1429.
[45] Scott IU,VanVeldhuisen PC, Oden NL, et al. Baseline predictors of visual acuity and retinal thickness outcomes in patients with retinal vein occlusion: standard Care Versus COrticosteroid for REtinal Vein Occlusion Study report 10. Ophthalmology, 2011,118(2):345-352.
[46] Adhi M, Filho MA, Louzada RN, et al. Retinal capillary network and foveal avascular zone in eyes with vein occlusion and fellow eyes analyzed with optical coherence tomography angiography. Invest Ophthalmol Vis Sci, 2016,57(9):OCT486-OCT494.
[47] Ogasawara Y, Iwase T, Yamamoto K, et al. Relationship between abnormalities of photoreceptor microstructures and microvascular structures determined by optical coherence tomography angiography in eyes with branch retinal vein occlusion. Retina, 2020,40(2):350-358.
[48] Samara WA,Shahlaee A, Sridhar J, et al. Quantitative optical coherence tomography angiography features and visual function in eyes with branch retinal vein occlusion. Am J Ophthalmol, 2016,166:76-83.
[49] Winegarner A, Wakabayashi T, Fukushima Y, et al. Changes in retinal microvasculature and visual acuity after antivascular endothelial growth factor therapy in retinal vein occlusion. Invest Ophthalmol Vis Sci, 2018,59(7):2708-2716.
[50] Deng Y,Zhong QW, Zhang AQ, et al. Microvascular changes after conbercept therapy in central retinal vein occlusion analyzed by optical coherence tomography angiography. Int J Ophthalmol, 2019,12(5):802-808.
[51] Murray J, Gupta P,Dulaney C, et al. Effect of viewing conditions on fixation eye movements and eye alignment in amblyopia. Invest Ophthalmol Vis Sci, 2022,63(2):33.
[52] Demirayak B, Vural A, Sonbahar O, et al. Analysis of macular vessel density and foveal avascular zone in adults with amblyopia. Curr Eye Res, 2019,44(12):1381-1385.
[53] Gao L, Gao Y, Hong FR, et al. Assessment of foveal avascular zone and macular vascular plexus density in children with unilateral amblyopia: a systemic review and meta-analysis. Front Pediatr, 2021, 9:620565.
[54] Araki S, Miki A,Goto K, et al. Foveal avascular zone and macular vessel density after correction for magnification error in unilateral amblyopia using optical coherence tomography angiography. BMC Ophthalmol, 2019,19(1):171.
[55] Chen YC, Chen YT, Chen SN. Foveal microvascular anomalies on optical coherence tomography angiography and the correlation with foveal thickness and visual acuity in retinopathy of prematurity. Graefes Arch Clin Exp Ophthalmol, 2019,257(1):23-30.
[56] Deng X, Cheng Y, Zhu XM, et al. Foveal structure changes in infants treated with anti-VEGF therapy or laser therapy guided by optical coherence tomography angiography for retinopathy of prematurity. Int J Ophthalmol, 2022,15(1):106-112.
[57] Chen YC, Chen SN. Foveal microvasculature, refractive errors, optical biometry and their correlations in school-aged children with retinopathy of prematurity after intravitreal antivascular endothelial growth factors or laser photocoagulation. Br J Ophthalmol, 2020,104(5):691-696.
[58] Schwartz R,Sivaprasad S, MacPhee R, et al. Subclinical macular changes and disease laterality in pediatric Coats disease determined by quantitative optical coherence tomography angiography. Retina, 2019,39(12):2392-2398.
[59] Venkatesh R, Reddy NG, Mishra P, et al. Structural-vascular-functional correlation in type 2 non-proliferative macular telangiectasia. Int J Retina Vitreous, 2022,8(1):59.
[60] Chen H, Ng KY, Li SS, et al. Characteristics of the foveal microvasculature in children withMarfan syndrome: an optical coherence tomography angiography study. Retina, 2022,42(1):138-151.