

OCT 血管成像在眼科的应用

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收稿日期:2017-05-24 修回日期:2017-09-19

Application of OCT angiography in ophthalmology

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Received:2017-05-24 Accepted:2017-09-19

Abstract

• Optical coherence tomography angiography (OCTA) is a new technology of angiography in recent years. In addition to the advantages of traditional OCT, it can observe blood flow in different retinal and choroidal segmentation slab. By using the pseudo-color, abnormal vascular structure can be distinguished from normal vascular structure of the retina. Dye injection is not needed with OCTA, which is different from fundus fluorescein angiography (FFA) and indocyanine green angiography (ICGA). OCTA provides more and more accurate blood flow information. However, like other biometric technology, OCTA has its limitations and shortcomings. This review will analyze and summarize the operating principle of OCTA, its application in ophthalmology, as well as its advantages and limitations.

• **KEYWORDS:** optical coherence tomography; fluorescein fundus angiography; indocyanine green angiography; retinal blood vessels; choroidal neovascularization; optic nerve; glaucoma

Citation: Yang AP, Wang H. Application of OCT angiography in ophthalmology. *Guoji Yanke Zazhi (Int Eye Sci)* 2017; 17(11): 2073-2076

摘要

光学相干断层扫描血管成像(OCTA)是近年来新兴的血管成像技术,除具备传统OCT的优点外,还能够分层观察视网膜脉络膜血管形态及血流改变情况,使用伪彩可区分

正常与异常的血管结构,并且能够对血流信号进行探测和量化分析。此外,与传统的荧光素眼底血管造影(FFA)和吲哚菁绿造影(ICGA)技术不同,OCTA无需静脉注射造影剂就能提供比传统眼底血管造影技术更多、更准确的血流信息。但是,任何技术的临床应用都有其局限性。本文将对OCTA的基本原理及其在眼科的应用、局限性进行综述。

关键词: 光学相干断层扫描; 荧光素眼底血管造影; 吲哚菁绿血管造影; 视网膜血管; 脉络膜新生血管; 视神经; 青光眼

DOI:10.3980/j.issn.1672-5123.2017.11.19

引用: 杨爱萍,汪浩. OCT血管成像在眼科的应用. 国际眼科杂志 2017;17(11):2073-2076

0 引言

光学相干断层扫描血管成像(optical coherence tomography angiography, OCTA)是一种无创、方便和快捷的新型血管影像学工具,除具备传统OCT的优点,可获得血管的结构信息外;此项新技术能够分层观察视网膜脉络膜血管形态及血流改变情况,使用伪彩可区分正常与异常的血管结构,并且能够对血流信号进行探测和量化分析。此外,与传统的荧光素眼底血管造影(FFA)和吲哚菁绿造影(ICGA)技术不同,OCTA无需静脉注射造影剂,通过更密集的扫描模式对同一位置进行多次快速扫描,提取变化的OCT信号,通过不同的算法去除伪迹并转化成血流,快速得到视网膜脉络膜微血管的三维成像^[1]。OCTA可以说是视网膜影像检查技术发展的里程碑,有助于我们更好地认识视网膜脉络膜疾病、青光眼和神经眼科疾病的血管改变,进一步加深对这些疾病发病机制的理解,从而对相关眼病进行有效地监测及随访^[2-4]。但是,OCTA检查仍存在检测范围有限、对患者的固视及屈光间质的清晰度要求高等限制^[5]。本文将对OCTA的工作原理及其在眼科的应用、局限性进行综述。

1 OCTA的基本原理及其与传统血管造影检查的对比

近年来,OCT技术在眼科领域发展迅速,成为21世纪最重要的眼科影像学发明与进展,从早期的时域OCT(time domain OCT)到扫描速度更快、分辨率更高的频域OCT(spectral domain OCT),再到深度分辨率更好的扫描光源OCT(swept-source OCT),使得我们能够从临床上观察到与组织切片相当的纵向视网膜、视神经,甚至脉络膜等的细微结构。最近开发应用的OCTA利用频谱振幅去相干血管成像(split-spectrum amplitude-decorrelation angiography, SSADA)算法,将原始全频谱图像分裂为数个不同频谱图像并减少其噪声,提高信噪比,然后再将其合并,从而达到视网膜、脉络膜各层血管形态在横断面的清晰成像^[6-8]。与FFA和ICGA等传统的血管造影检查相

比,OCTA是无创的,不需要注射任何染料,避免了造影剂可能引起的各种不良反应,诸如恶心、呕吐、皮肤瘙痒、呼吸困难、过敏性休克,严重者可以导致死亡^[9]。传统的眼底血管造影检查需要观察造影剂注射后眼底血管荧光的动态变化,此过程需要10~30min,而OCTA对眼底各层血管的成像仅需要5~6s。此外,FFA和ICGA显示的是造影剂在视网膜脉络膜全层的渗漏、着染等情况,而OCTA能够分层清晰地显示视网膜脉络膜的血流形态和分布情况,并且可以对视网膜的血流灌注进行定性及定量分析^[10-11]。然而,目前临床上应用的OCTA最大扫描范围为8mm×8mm,比传统血管造影的观察范围小,无法显示周边部的血流改变情况,这也是目前OCTA的主要不足。

2 OCTA与眼科疾病

2.1 脉络膜新生血管性疾病的血流成像

2.1.1 脉络膜新生血管 脉络膜新生血管(choroidal neovascularization,CNV)是新生血管性老年性黄斑变性、病理性近视继发脉络膜新生血管、特发性脉络膜新生血管、眼组织胞浆菌病综合征等多种眼内疾病的主要病理改变。由于CNV血管壁发育不完整,血管脆性大,极易引起出血和炎性细胞以及富含脂质液体外渗,继而结缔组织增生形成瘢痕,最终导致不可逆性盲的发生^[12-14]。视网膜外层或脉络膜层均质背景中出现异常的血管信号是CNV的表现,也是OCTA检查中CNV的诊断标准^[15-16]。Bonini等研究发现OCTA检查对CNV诊断的敏感度为50%~100%,特异度可以达到92%~100%^[17-18]。FFA、ICGA检查是诊断CNV的金标准^[19],但是FFA、ICGA只能提供二维的血管图像,对病灶的准确定位较困难,并且其有创性也限制了应用范围及使用频率^[20]。而OCTA检查能够提供视网膜和脉络膜微血管的三维图像,同时可以对视网膜脉络膜血管的形态进行分层观察^[21]。此外,OCTA与传统的FFA和ICGA相比能够更准确地鉴定1型CNV,其在OCTA检查中可呈扇形、不规则形以及海蛇头^[22]。也有研究表明,OCTA检查可能是临床常规诊断2型CNV的新型影像学方法,其在OCTA检查中经常呈现为肾小球型或者水母样,然而其特异性仍需要进一步观察^[23]。Nora等在一项研究中应用OCTA来观察抗VEGF治疗初次未治疗CNV患者6例6眼的病变CNV面积、RPE层隆起高度等指标来量化OCTA检查对于仅经历抗VEGF治疗的初次CNV患者的疗效,这使得OCTA亦成为评价抗VEGF药物疗效的一个有价值的指标^[24]。值得注意的是,有研究显示,OCTA检查能快捷而且无创地诊断中心性浆液性脉络膜视网膜病变(CSC)合并CNV的患者,其作用优于FFA^[25]。由此可见,OCTA不仅可以显示CNV类型及获得高分辨率的CNV图像,而且还可以对CNV的血流和面积进行定量分析,从而为CNV的检测及治疗效果的评估提供了更加精确的证据^[26-27]。

2.1.2 息肉样脉络膜血管病变 息肉样脉络膜血管病变(polypoidal choroidal vasculopathy,PCV)的主要表现为脉络膜异常分支血管网(branch vascular network,BVN)和血管网末端的息肉样病变(polyps)。目前ICGA是PCV的主要检查手段,其检查中发现BVN及polyps是息肉状脉络膜血管病变诊断的“金标准”^[28]。然而对比ICGA的有创性、耗时性及重复应用次数少等限制,OCTA能较好地显示BVN的血管形态,并且能更清晰地显示BVN的血流

信号位于RPE与Bruch膜之间^[29-30]。但是OCTA检查对polyps的成像检出率却低于ICGA检查,仅为50%^[31],其可能的原因与OCTA对polyps信号的捕获方式有关,某些慢流速、小体积的息肉样病变检测难度较大。随着OCTA的临床应用增多,通过手工调节分层,对polyps的检出率增加为75%~85%^[30,32]。此外,在已检出polyps的病例中,OCTA检查显示其血流信号位于陡峭的色素上皮脱离的顶端,这是在ICGA检查中无法显示的^[33]。因此OCTA检查为PCV患眼BVN及polyps的观察提供了新的可能,对PCV的诊断及其随访发挥了重要的作用。

2.2 视网膜血管性疾病的血流成像

2.2.1 糖尿病视网膜病变 糖尿病视网膜病变(diabetic retinopathy,DR)是糖尿病的并发症之一,与长期高血糖、代谢异常、组织缺氧、氧化损伤、血流动力学改变和免疫损伤等因素有关,若未给予及时有效地治疗将会进展为增生性DR(proliferative diabetic retinopathy,PDR),严重影响视力甚至致盲^[34-35]。目前FFA仍然是临床诊断糖尿病视网膜病变的金标准,通过动态观察造影剂的循环和渗漏,可以清楚地显示视网膜无灌注(NP)、血管渗漏和新生血管(NV)及微血管瘤等DR的主要病理生理学改变^[36]。然而,由于OCTA没有荧光素渗漏的干扰,可以更好地显示视网膜中央无血管区(foveal avascular zone,FAZ)的扩大、周围血管的重塑以及小无灌注区^[37]。但是OCTA对微血管瘤的显示数量比FFA检查显示的数量少,这可能是由于太小的微血管瘤拥有较低的血流速度,OCTA难以捕获此种血流信号^[38]。Hwang等^[39]研究报道,OCTA检查可以量化DR患者黄斑旁中心凹以及中心凹周围的血管密度、无血管区的总面积和中心凹无血管区,并且发现DR患者组的黄斑旁中心凹和中心凹周围的血管密度对比健康个体组依次减少12.6%和10.4%,DR患者组的无血管区总面积和中心凹无血管区对比健康个体组分别扩大0.82mm²和0.16mm²。他们认为,将来OCTA检查可能会成为糖尿病患者在系统诊断前迅速无创筛查糖尿病视网膜病变的有效手段。此外,Samara等^[40]应用OCTA对比观察DR患者55例84眼和年龄相仿健康人群27例34眼,根据临床阶段对糖尿病眼进行分组,分别获得各组的浅层视网膜毛细血管、深层毛细血管各自对应的中心凹无血管区面积(FAZ)、平均血管密度(VAD)、血管长度密度(VLD),通过定量测量FAZ、VAD、VLD分析其与视力的相关性发现:FAZ在DR人群几乎所有分组的浅层和深层毛细血管都较正常对照组受检眼扩大;两组VAD和VLD比较,DR组几乎所有分组的深浅毛细血管层都低于健康对照组;并且观察发现深浅毛细血管层的FAZ值均与其相对应的视力呈正相关。还有研究报道,OCTA在诊断糖尿病性黄斑缺血时,甚至可能替代FFA^[41]。综上所述,OCTA检查为DR疾病的早期筛查及疾病进展提供了一个客观的检测方法,同时为今后进一步研究DR病因学提供了新的途径^[42-43]。

2.2.2 视网膜静脉阻塞 视网膜静脉阻塞(retinal vein occlusion,RVO)是一类视网膜静脉解剖和(或)功能发生异常的眼底血管性疾病,其发生率仅次于糖尿病性视网膜病变,而且其发生率随年龄增长而增加^[44]。继发性黄斑水肿是导致RVO患者视力减退的常见原因。目前,荧光素眼底血管造影检查依然是诊断和治疗视网膜静脉阻塞的主要依据^[45]。OCTA检查可以很好地显示RVO患者视

网膜后极部血管弓内深层和浅层毛细血管的改变;血管扩张、迂曲、重塑以及异常吻合;同时可以清晰地显示毛细血管无灌注、微血管瘤以及视盘水肿等改变^[46]。而 FFA 检查只能观察到黄斑区视网膜小血管,且容易受出血遮蔽或水肿渗漏的影响。当 RVO 患者继发黄斑水肿时,OCTA 可以检测到黄斑无血管区的扩大以及黄斑区血管密度的降低,对 RVO 患者视力预后的判断及研究发病机制和病理过程具有重要的价值^[46]。但是由于受到扫描范围的限制,OCTA 无法动态检测周边有无灌注区,所以临床上 FFA 检查仍具有指导意义。

2.3 OCTA 在其他眼科疾病的应用 青光眼和神经眼科疾病可以导致视网膜神经节细胞和神经纤维的损害,OCTA 检查为进一步研究两者的丢失与血流的变化之间的相关性提供了重要的参考手段。Jia 等^[47]研究提出,视盘血流指数的降低与其自身的严重程度相关。Jia 等^[3]在另一项研究中发现,视盘血流灌注的减少发生在视野损害发生前,通过视盘血流灌注的定量检查对早期青光眼的诊断与评估预后具有重要的价值。胡立影等^[48]使用 OCTA 检查观察前部缺血性视神经病变(AION)患者视盘血流灌注的情况,发现 OCTA 可以更加直观准确地显示视盘供血状态,从而判断疾病的严重程度。由此可见,OCTA 并不能作为确诊青光眼和神经眼科疾病的主要影像学检查方法,但可以让从血流变化的角度深入了解并认识青光眼和神经眼科的发病机制。

3 OCTA 检查的局限性

OCTA 检查虽然具有很多优势,但是作为一种新兴技术,其本身也存在一定的局限性:(1)OCTA 的扫描范围较局限,不能对视网膜进行大面积的扫描,主要的扫描区域为黄斑及视盘。(2)OCTA 无法显示眼底血流的动态变化,不能像 FFA 一样可以通过造影剂的渗漏和着染情况,来判断病变血管的活跃度。(3)患者固视能力差、眼球震颤等原因,容易产生伪影,影响 OCTA 对异常血管的识别,为疾病的诊断增加困难^[49]。(4)OCTA 检查的自动化分割算法识别特定视网膜血管层的可靠性较低,当视网膜发生病变时自动分割误差明显化,此时需要手动调节分层,而此过程耗时较长^[50]。

综上所述,作为一种无创、方便、快捷、可重复的新型血管成像技术,OCTA 检查可以对眼科多种疾病进行观察,提供直观的诊断依据,从而更好地理解眼底疾病的病理生理机制以辅助治疗。但是 OCTA 检查也存在一定的局限性,相信随着技术的不断改进与完善,OCTA 检查在眼科临床将拥有广阔的发展前景。

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