

· 专家述评 ·

## 重视视网膜微血管改变在全身血管疾病诊疗中的作用

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**【摘要】** 作为全身微循环系统的组成部分,视网膜微血管和心脑血管微血管在病理状态下可能存在相似的改变。虽然目前尚无研究证实视网膜微血管改变与心脑血管疾病(CVD)之间存在明确的因果关系,但是认识到他们之间的相关性,对于临床医师综合评估全身微循环健康情况、预测 CVD 发生风险、早期进行有效的一级预防具有重要意义。此外,视网膜血管阻塞性疾病患者,尤其是那些尚未确诊为 CVD 等全身疾病的患者,往往因未进行全身疾病的检查而延误治疗,造成严重后果。因此,眼科医师须认识 CVD 与视网膜血管改变及疾病的关系,通过可视的视网膜微血管改变为全身血管性病变的一级预防、诊断和治疗提供有用的信息。

**【关键词】** 微循环; 微血管; 视网膜; 全身血管病变; 预防和治疗

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**【Abstract】** Being a part of the microcirculatory system, retinal microvasculature may have similar morphology change as cardio- and cerebro-microvasculature under the pathological conditions. Although no study has proved that there exists causal relationship between retinal microvasculature change and cardiovascular diseases (CVD), realizing their connection is extremely vital for ophthalmologists to evaluate the status of the systemic microcirculation, predict the occurrence of CVD, and proceed primary prevention by visible information of retinal microvascular alteration. In addition, for the patients suffering from retinal vascular occlusion, especially those with undiagnosed systemic diseases like CVD, ignoring systemic examinations may delay proper treatment and lead to the consequences of ill health. In conclusion, ophthalmologists should recognize the association of retinal microvasculature changes with systemic vascular diseases and provide useful information for primary prevention and early diagnosis and treatment of systemic vascular diseases.

**【Key words】** Microcirculatory system; Microvessel; Retina; Systemic vascular diseases; Prevention and treatment

微循环由直径在 150  $\mu\text{m}$  以下的血管组成,包括最小的阻力动脉、小动脉、毛细血管和小静脉,这些血管是循环系统的重要组成部分,在维持心血管健康方面起到重要的作用<sup>[1]</sup>。视网膜的微血管是观察全身微循环系统的窗口,且与心脏、肺和脑微血管同源,病理学研究显示视网膜血管病变的体征与其他器官的微血管病理性改变的程度密切相关<sup>[2]</sup>。因此视网膜微血管的病理改变有可能反映全身血管性疾病的病理生理

过程<sup>[3-4]</sup>。19 世纪晚期,研究者发现视网膜微血管改变与高血压、肾脏和心脑血管疾病有关,认为视网膜微血管异常可能提示存在心脑血管疾病(cardiovascular disease, CVD)和全身动脉粥样硬化<sup>[5-7]</sup>,视网膜微血管异常的严重程度可以预测高血压患者的死亡率<sup>[8]</sup>。然而近 10 年来,新型的、客观的视网膜微血管评估方法的出现使得视网膜微血管异常和 CVD 的相关性研究更加准确,关于视网膜血管改变的临床研究逐渐受到关注,随着近年来对眼底血管相关疾病发病机制研究的逐渐深入,研究者认为视网膜微血管研究在眼科血管性疾病的诊疗中发挥着越来越重要的作用,眼科医师须重新认识视网膜微血管的临床意义和作用。

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## 1 明确视网膜微血管异常的定义

视网膜微血管异常包括所有的视网膜微血管的病理改变。目前,各种研究对于视网膜微血管异常的命名有所不同,视网膜动脉改变包括弥漫性或局部动脉狭窄和动静脉压迹,动脉硬化指动脉壁的硬化和增厚,包括动脉粥样硬化和小动脉硬化,而视网膜血管病变是指所有的微血管病变,如视网膜出血、微血管瘤、棉絮斑、硬性渗出、黄斑水肿和视盘水肿。通常认为,视网膜血管病变的体征可能提示病变晚期微血管结构的改变,包括血-视网膜屏障的破坏<sup>[9-10]</sup>。有研究者将视网膜微血管改变分为 4 个阶段,血管收缩阶段表现为动脉变窄,硬化阶段表现为弥漫性的动脉变窄、动静脉压迹、动脉反射改变、动脉扭曲和动脉分支的角度变大,渗出阶段的特征性表现为视网膜出血和微血管瘤形成,并发症阶段即视网膜血管性疾病阶段,包括各种视网膜和玻璃体并发症,如动脉血栓、中央或分支视网膜动静脉阻塞、视网膜大动脉瘤、囊样黄斑水肿和增生性玻璃体视网膜病变<sup>[2,11]</sup>。

## 2 了解视网膜微血管异常与 CVD 的关系

作为全身微循环系统的组成部分,视网膜微血管和心脑血管在病理状态下可能存在相似的改变,如高血压患者心肌内小动脉的硬化改变与视网膜血管的改变非常相似<sup>[12]</sup>。虽然目前尚未有研究证实视网膜微血管改变与 CVD 之间存在明确的因果关系,但是认识他们之间的相关性对于综合评估全身微循环情况、预测 CVD 发生风险、早期进行有效的一级预防具有重要意义。

### 2.1 视网膜微血管异常与脑卒中

视网膜微血管的改变在一定程度上可以反映脑部小血管的健康状况,通过观察视网膜微血管的改变,临床医师可以对脑部微血管进行间接地、无创地评估<sup>[13-14]</sup>。既往研究显示,传统的视网膜微血管损害,如视网膜出血、微血管瘤和视网膜管径改变与临床诊断的脑卒中和亚临床的 MRI 诊断的脑梗死有关<sup>[15-17]</sup>,脑卒中患者中视网膜微血管改变的患病率较高<sup>[18]</sup>,视网膜微血管网血管稀疏并扭曲<sup>[13]</sup>。基于人群的队列研究显示,即使矫正了传统的危险因素,视网膜微血管异常者,即有视网膜血管病变体征和动静脉比值下降的个体,罹患脑卒中的可能性仍较大<sup>[19-20]</sup>。前瞻性研究也证实,视网膜微血管的改变在一定程度上可以预测脑卒中的发生<sup>[21-22]</sup>。将视网膜血管改变和脑部小血管疾病的其他指标相结合,可能更有助于评估脑部

小血管病变的严重程度<sup>[14]</sup>。

### 2.2 视网膜微血管异常与冠心病

越来越多的研究证实冠状微血管功能障碍在冠心病 (coronary heart disease, CHD) 的发生中起到重要作用,一些患者表现为心绞痛,但是冠状动脉导管和造影检查均未发现明显的冠状动脉异常,这种情况称为心脏病综合征,研究者认为此类患者存在冠状微血管功能障碍<sup>[23-24]</sup>。然而,由于缺乏冠状微循环的成像技术,微循环功能障碍很难诊断。视网膜血管的可见性为临床医师提供了直接观察微循环的途径,通过观察视网膜微血管的改变有可能发现与 CHD 相关的微血管病理性改变<sup>[25-26]</sup>,为该病的诊断、一级预防、病情评估、治疗和随访提供有用信息。此外,视网膜微血管直径的改变与 CHD 的危险因素有关,包括肥胖、代谢性疾病、高血压和全身的内皮功能障碍<sup>[27]</sup>。

在预测 CHD 发病风险方面,视网膜血管改变也存在一定价值。研究显示,女性患者中动脉越细,CHD 事件的 3 年发病率越高<sup>[28]</sup>,尽管将视网膜血管直径指标添加到传统的心血管事件风险评估模型 (如 Framingham 风险模型) 中后评估效率仅提高 1.7%,但是大规模的流行病学研究显示视网膜血管直径改变是 CHD 的独立危险因素<sup>[29]</sup>。

## 3 了解 CVD 与视网膜血管疾病的关系

视网膜血管疾病与患者的全身性血管疾病有关,常见的视网膜血管疾病包括高血压性视网膜病变、糖尿病视网膜病变 (diabetic retinopathy, DR)、视网膜血管阻塞性疾病。由于存在相关的全身病,高血压性视网膜病变和 DR 较易诊断并得到及时治疗,但视网膜血管阻塞性疾病患者,尤其是尚未诊断为 CVD 者往往因忽略全身疾病的检查而延误治疗。因此,眼科医师须认识 CVD 等全身疾病与视网膜血管疾病的关系,进行早期诊断及治疗。

视网膜中央动脉阻塞 (central retinal arterial occlusion, CRAO) 和视网膜静脉阻塞 (retinal vein occlusion, RVO) 可引起严重的视功能损害,患有 CVD 的患者罹患视网膜血管阻塞的风险增高,视网膜血管阻塞也是心血管病的危险因素<sup>[30-31]</sup>,此外动脉性高血压、冠心病、糖尿病等都是 CRAO 的潜在危险因素<sup>[32]</sup>。更重要的是,CRAO 及 RVO 患者发生脑卒中、急性冠状动脉综合征的风险明显高于正常对照组<sup>[33-35]</sup>,提示 CRAO 可能对 CVD 的发生有一定的预测作用,对于 CVD 的早期预防及诊治具有重要意义。

视网膜微血管的改变易于观察、评估及随访,通过

视网膜血管间接评估全身微循环健康情况对于其他重要器官如心脑血管微血管病理改变具有重要的临床意义,应引起临床医师的重视。

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