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世界中医药学会联合会

World Federation of Chinese Medicine Societies

SCM \*\*-20\*\*

# 国际中医临床实践指南 糖尿病视网膜病变

International Clinical Practice Guideline of Chinese Medicine  
Diabetic Retinopathy

世界中联国际组织标准

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# 前 言

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## 引 言

本文件为进一步规范糖尿病视网膜病变的中医临床诊断与治疗，为国际中医师临床实践提供糖尿病视网膜病变的中医药治疗策略与方法而制定的临床实践指南。

本文件在以往的中医诊疗指南、专家共识基础上，结合中医学自身特点，应用循证医学方法和系统评价，经有关方面协商一致，在分析、比较、综合和验证的基础上，规范化编制的中医治疗糖尿病视网膜病变的纲领性文件，有助于循证医学原则在中医临床实践中得到更好的贯彻和实施，从而规范医生的医疗行为，提高中医防治疗效。

本文件是依据现有的研究证据、特定的方法制定出的声明性文件。在临床实践中，医师可参考本文件并结合患者具体情况进行个体化治疗。

本文件简明实用，可操作性强，可作为临床实践、诊疗规范和质量评价的重要参考依据。

WJECMS

# 国际中医临床实践指南 糖尿病视网膜病变

## 1 范围

本文件确定了糖尿病视网膜病变的中医诊断、辨证和治疗基本要求。

本文件适用于糖尿病视网膜病变的诊断和治疗；适用于各级医疗机构的中医和中西医结合眼科临床执业医师，作为对糖尿病视网膜病变的诊断和治疗依据。西医眼科医师和其他学科中医师也可参照本指南中的相关内容。

## 2 规范性引用文件

下列文件对于本文件的应用是必不可少的。凡是注日期的引用文件，仅注日期的版本适用于本文件。凡是不注日期的引用文件，其最新版本（包括所有的修改版）适用于本文件。

GB/T 16751.1 中医临床诊疗术语 疾病部分

GB/T 16751.2 中医临床诊疗术语 证候部分

GB/T 16751.3 中医临床诊疗术语 治法部分

2020 中国 2 型糖尿病防治指南（2020 年版）

2019 中国《中医临床诊疗指南-糖尿病视网膜病变》（2019 版）

2019 美国 AAO: Diabetic Retinopathy Preferred Practice Pattern（2019 年版）

SCM 2 中医基本名词术语中英对照国际标准

2009 WHO 西太平洋地区传统医学名词术语国际标准

## 3. 术语与定义

下列术语和定义适用于本文件。

### 3.1

#### 糖尿病视网膜病变

糖尿病导致的视网膜微血管损害所引起视网膜微血管瘤、出血、渗出、水肿、新生血管、玻璃体视网膜增殖性病变等特征性病变，是一种影响视力甚至致盲的慢性进行性疾病。

注：糖尿病视网膜病变属中医学“消渴内障”。

### 3.2

#### 消渴内障

为“消渴目病”之一，其部分临床表现属“视瞻昏渺”、“云雾移睛”、“暴盲”及“血灌瞳神”等内障眼病的范畴。

注：“消渴内障”相当于西医学糖尿病视网膜病变。

## 4. 诊断

### 4.1 临床表现

#### 4.1.1 症状

早期眼部多无自觉症状，病久可有不同程度视力减退，眼前黑影飞舞，或视物变形，甚至失明。

#### 4.1.2 体征

DR 的眼底表现包括微血管瘤、出血、硬性渗出、棉絮斑、静脉串珠状改变、视网膜内微血管异常、黄斑水肿、新生血管、视网膜前出血及玻璃体积血等。

### 4.2 眼科检查

a) 视力：裸眼视力（远近视力）和矫正视力，常有不同程度的视力下降，早期视力可无变化。

b) 眼压：眼压一般正常范围，晚期并发新生血管性青光眼可明显增高。

c) 裂隙灯显微镜检查：眼前段一般无变化，可能发现晶状体后囊浑浊，但无特异性。晚期并发新生血管性青光眼时可见睫状充血、角膜水肿、虹膜红变、瞳孔中等程度散大等。

d) 眼底检查：散瞳后进行眼底检查，可见微血管瘤、出血、渗出、新生血管、玻璃体积血等典型体征。

e) 彩色眼底照相

彩色眼底照相可见出血、硬性渗出、棉絮斑、静脉串珠状改变、视网膜内微血管异常、黄斑水肿、新生血管等体征。彩色眼底照相为无创检查，发现 DR 的重复性比其他检查要好，对于记录 DR 的明显进展和治疗的反应方面是有其价值的，常用于 DR 筛查和随访。

f) 荧光素眼底血管造影（fluorescein fundus angiography, FFA）

检眼镜下未见 DR 眼底表现的患者，FFA 检查可出现异常荧光，如微血管瘤样强荧光、毛细血管扩张或渗漏、视网膜血管无灌注区、新生血管及黄斑囊样水肿等。因此，FFA 可提高 DR 的诊断率，有助于评估疾病的严重程度，并指导治疗，评价临床疗效。

g) 光学相干断层扫描（optical coherence tomography, OCT）

糖尿病视网膜病变 OCT 检查的主要意义是监测黄斑水肿，另外 OCT 影像可以显示视网膜内出现的硬性渗出。

h) 光学相干断层扫描血管成像（optical coherence tomography angiography, OCTA）

光学相干断层扫描血管成像有助于发现 DR 临床症状出现前的微血管异常变化；可以量化黄斑无灌注区域，为黄斑缺血提供了更加定量的评估；可以早期发现视网膜新生血管。

i) 视觉电生理检查

糖尿病视网膜病变患者可出现暗适应功能异常，表现为杆阈、锥阈升高；多焦 ERG 检查表现为黄斑区反应密度降低；标准闪光 ERG 检查 a 波、b 波振幅降低；患病早期可见视网膜振荡电位（OPs）异常，表现为总波幅降低，潜伏期延长；病情加重时，各系波振幅明显下降。

j) 超声检查

当糖尿病患者因屈光间质浑浊（通常为白内障或玻璃体积血）而无法直接检查眼底情况时，B超检查可协助诊断玻璃体视网膜增生牵拉或视网膜脱离情况。

4.3 并发症

DR 的并发症有牵拉性视网膜脱离、虹膜新生血管及新生血管性青光眼等。

a) 牵拉性视网膜脱离

视网膜增殖膜及新生血管膜收缩，是引发牵拉性视网膜脱离的主要原因。

b) 虹膜新生血管及新生血管性青光眼

DR 广泛的视网膜缺血，诱生血管生长因子，刺激虹膜及房角产生新生血管。虹膜新生血管表现为虹膜表面出现的细小弯曲、不规则血管，多见于瞳孔缘，可向周边发展；房角新生血管阻塞或牵拉小梁网，或出血，影响房水引流，导致眼压升高，形成新生血管性青光眼。

4.4 DR 诊断、分期标准

4.4.1 DR 诊断、分期标准

参照 2014 年中华医学会眼科学会眼底病学组发布的我国《糖尿病视网膜病变临床诊疗指南》。

分期：糖尿病视网膜病变分期如下：

疾病严重水平		眼底所见	
I 期	NPDR	轻度非增生期 (Mild NPDR)	仅有视网膜微血管瘤
II 期		中度非增生期, (Moderate NPDR)	介于轻度到重度之间的视网膜病变, 可合并视网膜出血、硬性渗出和 (或) 棉絮斑
III 期		重度非增生期 (Severe NPDR)	有下列表现之一且无 PDR 表现: 每个象限视网膜内出血≥20 个出血点 累及至少 2 个象限的明确的静脉串珠样表现 累及至少 1 个象限的显著的 IRMA
IV 期	PDR	增生早期 (early PDR)	出现 NVE 或 NVD
		高危增生型 (high risk PDR)	当 NVD>1/4~1/3DA 或 NVE>1/2DA
V 期		纤维增生期 (fibrous proliferation)	出现纤维膜, 可伴视网膜前出血或玻璃体出血
VI 期		增生晚期 (advanced PDR)	牵拉性视网膜脱离, 合并纤维膜, 可合并或不合并玻璃体积血, 也包括虹膜和房角的新生血管

IRMA (intraretinal microvascular abnormalities) = 视网膜内微血管异常; NPDR

(non-proliferative diabetic retinopathy) = 非增殖性糖尿病视网膜病变; PDR

(proliferative diabetic retinopathy) =增殖性糖尿病视网膜病变；NVE (neovascular elsewhere) =视网膜新生血管；NVD (neovascular of the disc) =视乳头新生血管；DA (disc area) =视乳头直径。

#### 4.4.2 黄斑水肿定义及分型

参照国际糖尿病视网膜病变和黄斑水肿的国际临床分类法和我国关于《我国糖尿病视网膜病变临床诊疗指南(2014年)》。

糖尿病黄斑水肿的定义：黄斑区内毛细血管渗漏致黄斑中心 2 个视盘直径 (DA) 视网膜增厚，糖尿病黄斑水肿有局灶型和弥漫型，一般采用通用 DME (diabetic macular edema) 的国际临床分类：

糖尿病黄斑水肿 (DME) 国际临床分类：

DME 的严重程度	散瞳检眼镜可观察的病理改变
无明显的 DME	后极部无明显的视网膜增厚或硬性渗出
有明显的 DME	后极部有明显的视网膜增厚或硬性渗出
	轻度：有些视网膜增厚或硬性渗出，但远离黄斑中心
	中度：视网膜增厚或硬性渗出趋向，但没有累及中心
	重度：视网膜增厚或硬性渗出累及中心

#### 4.5 鉴别诊断

本病应与高血压性视网膜病变、视网膜静脉阻塞相鉴别。

##### 4.5.1 高血压性视网膜病变

有高血压病史，眼底可见视网膜动脉变细、反光增强，动、静脉交叉压迫现象明显，棉絮斑、硬性渗出、出血及广泛微血管改变。还可见视乳头水肿。

##### 4.5.2 视网膜静脉阻塞

有或无高血压病史，多为单眼发病，眼底出血为浅层、火焰状，沿视网膜静脉分布，后极部多，周边逐渐减少。静脉高度扩张迂曲，呈腊肠状。

#### 5. 辨证

##### 5.1 阴虚燥热证

视力正常或减退，病变为临床分期级 I~III 期；口渴多饮，口干咽燥，消谷善饥，大便干结，小便黄赤；舌质红，苔微黄，脉细数。

##### 5.2 气阴两虚证，

视物模糊，目睛干涩，或视物变形，或眼前黑花飘舞，视网膜病变多为 I~IV 期，神疲乏力，气短懒言，口干咽燥，自汗，便干或稀溏，舌胖嫩、紫暗或有瘀斑，脉沉细无力。

##### 5.3 肝肾亏虚证



视物模糊，目睛干涩，视网膜病变多为 I~III 期；头晕耳鸣，腰膝酸软，肢体麻木，大便干结，舌暗红少苔，脉细涩。

#### 5.4 脾虚湿滞证

视物模糊，或视物变形，或自觉眼前黑花漂移，视网膜病变多为 II~IV 期，以视网膜水肿、棉绒斑、出血为甚，并可出现黄斑水肿；面色萎黄或无华，神疲乏力、头晕耳鸣，小便量多清长；舌质淡，脉弱。

#### 5.5 阴阳两虚证

视物模糊或视力严重障碍，目睛干涩，视网膜病变多为 IV~V 期，可出现黄斑水肿；神疲乏力，五心烦热，失眠健忘，腰酸肢冷，手足凉麻，阳痿早泄，下肢浮肿，大便溏结交替；舌淡胖少津或有瘀点，或唇舌紫暗，脉沉细无力。

### 6 治疗

#### 6.1 治疗原则

本病应在西医有效控制血糖、血压和血脂的基础上给予中医治疗。该病主要病机为气血阴阳失调，以气阴两虚、肝肾不足、阴阳两虚为本，脉络瘀阻、痰浊凝滞为标。以益气养阴，滋养肝肾，阴阳双补治其本；通络明目，活血化瘀，化痰散结治其标。临证要全身辨证与眼局部辨证相结合。首当辨全身虚实、寒热，根据眼底出血时间，酌加化瘀通络之品。早期出血以凉血化瘀为主，出血停止两周后以活血化瘀为主，后期加用化痰软坚散结之剂。微血管瘤、水肿、渗出等随证加减。

#### 6.2 辨证论治

##### 6.2.1 阴虚燥热证

治法：养阴生津，凉血润燥。

方药：玉泉丸（《中国中成药优选》）合知柏地黄丸（《医宗金鉴》）加减：葛根、天花粉、地黄、麦冬、五味子、知母、黄柏、山茱萸、山药、茯苓、泽泻、丹皮、糯米、甘草。若眼底以微血管瘤为主，可加丹参、郁金；出血明显者，可加生蒲黄、旱莲草、牛膝；有硬性渗出者，可加浙贝、海藻、昆布。（专家共识，弱推荐）

##### 6.2.2 气阴两虚证

治法：益气养阴，活血通络。

方药：生脉散（《内外伤辨惑论》）合杞菊地黄丸（《医级》）加减：人参、麦冬、五味子、枸杞、菊花、熟地黄、山茱萸、山药、茯苓、泽泻、丹皮、丹参、郁金。视网膜出血量多可酌加三七、旱莲草、蒲黄；伴有黄斑水肿者酌加白术、薏苡仁、车前子；自汗、盗汗可加白术、牡蛎、浮小麦。（证据级别 D，强推荐）

##### 6.2.3 肝肾亏虚证

治法：滋补肝肾，润燥通络。

方药：杞菊地黄丸（《医级》）加减：枸杞子、菊花、熟地黄、山茱萸、山药、茯苓、泽泻、丹皮。出血较多者可合用生蒲黄汤；出血静止期可合用桃红四物汤；出血久不吸收者，酌加浙贝、海藻、昆布（证据级别 D，强推荐）

#### 6.2.4 脾虚湿滞证

治法：健脾益气，利水消滞。

方药：补中益气汤（《脾胃论》）合五苓散（《伤寒论》）加减：人参、白术、炙甘草、黄芪、当归、陈皮、升麻、柴胡、猪苓、茯苓、泽泻、桂枝。可加巴戟天、郁金、车前子补肾活血利水；棉绒斑多者加法夏、浙贝、苍术；黄斑水肿者加薏苡仁、猪苓（专家共识，弱推荐）

#### 6.2.5 阴阳两虚证

治法：滋阴补阳，化痰祛瘀。

方药：偏阴虚者选左归丸（《景岳全书》），偏阳虚者选右归丸（《景岳全书》）加减：熟地黄、鹿角胶、龟板胶、山药、枸杞、山茱萸、川牛膝、菟丝子、附子、肉桂、杜仲、当归、淫羊藿。陈旧性瘀血、硬性渗出或玻璃体视网膜增生性纤维可酌加瓦楞子、浙贝、海藻、昆布软坚散结；有新生血管膜或出血较多时，加三七、生蒲黄、花蕊石化瘀止血；阳虚畏寒或视网膜水肿，可加菟丝子、淫羊藿补益肝肾助阳而明目。（专家共识，弱推荐）

### 6.3 中成药

芪明颗粒，用于肝肾亏虚，气阴两虚兼脉络瘀阻证。（证据级别 B，强推荐）

双丹明目胶囊，用于肝肾阴虚瘀血阻络证。（证据级别 B，强推荐）

明目地黄丸，用于肝肾阴虚，目涩畏光，视物模糊等。（证据级别 B，强推荐）

杞菊地黄丸，用于肝肾阴亏，瘀阻眼络，内障目暗，视物昏花等。（证据级别 D，强推荐）

复方血栓通胶囊，用于血瘀兼气阴两虚证，神疲乏力，咽干，口干，视物模糊。（证据级别 C，强推荐）

复方丹参滴丸，用于阴虚夹瘀兼气滞证。（证据级别 C，强推荐）

和血明目片，适用肝肾阴虚，兼血络瘀阻证。（证据级别 C，弱推荐）

### 6.4 针刺

对于 DR I～III期，出血较少者，可适度采用针刺疗法，取太阳、阳白、攒竹、足三里、三阴交、光明、肝俞、肾俞等穴，可分两组轮流取用，每次取眼区穴 1～2 个，四肢及背部 3～5 个，平补平泻。（专家共识，弱推荐）

附录 A  
(资料性)  
证据评价及推荐原则

A.1 证据评价和分级标准

参照 GRADE 分级方法，随机对照试验最初被定为高质量证据，其质量可因 5 个因素下降；观察性研究被定为低质量证据，其质量可因 3 个因素上升；最终证据质量被分为高、中、低、极低 4 级。

文献筛选和评价过程由两名评价员独立进行，如双方意见不一致，通过协商解决或由第三方裁决。具体内容见表 A.1:

表 A.1 证据评价和分级标准

研究设计	最初证据级别	降级/升级因素	证据级别	描述
随机对照试验	高	偏倚风险 -1 严重	高 (A)	非常确信真实值接近效应估计值
		-2 非常严重		
		不一致性 -1 严重	中 (B)	对效应估计值有中等程度信心：真实值可能接近估计疗效，但也可能有很大差别
		-2 非常严重		
		间接性 -1 严重		
不精确性 -1 严重	低 (C)	对效应估计值信心有限：真实值与估计值可能有很大差别		
-2 非常严重				
发表偏倚 -1 可能	-2 非常可能			
观察性研究	低	效应量大 +1 大	极低 (D)	对效应估计值几乎没有信心：真实值与估计值可能有很大差别
		+2 非常大		
		剂量-效应关系 +1 明显关联	+1 效应增加	
		混杂因素 +1 效应显著降低		

A.2 推荐原则

由于中医药治疗糖尿病视网膜病变的文献研究多数存在报告内容不全面、设计欠规范等问题，使研究结果可信性偏低，因此本文件的推荐原则为结合传统中医理论、文献研究和专家经验等综合因素考虑后制定，所有证据均需取得专家共识后方可列入推荐。

推荐强度确定原则：凡是对某项治疗措施强推荐人数超过总人数 75%，则强推荐使用该治疗措施；如果不推荐使用人数比例  $\geq 50\%$ ，则为不推荐；其他情况为弱推荐。

## 附录 B

(资料性)

### 利益冲突的宣言

《国际中医临床实践指南 糖尿病视网膜病变》指南制定小组所有成员均声明，完全独立进行本指南的编制工作，未与任何利益团体发生联系。

WFECMS

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## Foreword

Patent issues may have existed in this document, and WFCMS declared that they are not to blame.

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## Introduction

This Guideline aims to further standardize the TCM clinical diagnosis and treatment of diabetic retinopathy for all traditional Chinese medicine (TCM) practitioners worldwide. And it is a clinical directory for managing the disease with strategic tactics and methodology.

Based on the previous related TCM guidelines, expert's consensus, and characteristics of TCM, the Guideline also incorporates evidence-based medicine and systematic review. This standardized Guideline for managing DR in TCM has been accomplished with different aspects, such as analysis, comparison, integration, and authentication. It not only introduces evidence-based medicine principles into clinical TCM practice but also promotes the practitioner's standard and curative effect of DR prevention and treatment.

This document is a declarative document based on existing research evidence and specific methods. In clinical practice, physicians can refer to this document and make individualized treatments according to the specific conditions of patients.

It is a concise and practical guideline that can be served as an important reference in different aspects, such as clinical practice, specification of diagnosis and treatment, and quality evaluation.

# **International Clinical Practice Guideline of Traditional Chinese Medicine Diabetic Retinopathy**

## **1 Scope**

This Guideline defines the basic principles for the diagnosis, syndrome differentiation, and essential treatment of diabetic retinopathy in traditional Chinese medicine (TCM).

The Guideline applies to the diagnosis and treatment of diabetic retinopathy. It suits the needs of all ophthalmologists of TCM or integrated traditional Chinese and western medicine as the basis for diagnosing and treating diabetic retinopathy. In addition, ophthalmologists of western medicine and physicians of TCM in other disciplines may also refer to the relevant contents of this Guideline.

## **2 Normative references**

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

GB/T 16751.1 Clinic terminology of traditional Chinese medical diagnosis and treatment—Diseases

GB/T 16751.2 Clinic terminology of traditional Chinese medical diagnosis and treatment—Syndromes

GB/T 16751.3 Clinic terminology of traditional Chinese medical diagnosis and treatment—Therapeutic methods

《Guideline for the prevention and treatment of type 2 diabetes mellitus in China》 (2020)

《Clinical Practice Guideline of Traditional Chinese Medicine--Diabetic Retinopathy》 (2019)

《Diabetic Retinopathy Preferred Practice Pattern》 (2019)

International Standard Chinese-English Basic Nomenclature of Chinese Medicine (SCM 0002-2007)

《WHO International Standard Terminologies on Traditional Medicine in the Western Pacific Region》

### 3 Terms and definitions

The following terms and definitions are applicable in the Guideline.

3.1 Diabetic retinopathy (DR) is a chronic progressive disease affecting vision and leading to blindness. It presents a series of typical lesions caused by diabetic microvascular damage in the retina. Those lesions include microaneurysm, hemorrhage, exudate, edema, neovessel, and proliferative vitreoretinopathy.

Note: diabetes retinopathy belongs to the traditional Chinese medicine "Internal visual obstruction by dispersion-thirst" .

3.2 "Internal visual obstruction by dispersion-thirst" is one of the "ocular diseases by dispersion-thirst" (diabetes mellitus corresponds to "dispersion-thirst"), whereas DR corresponds to "internal visual obstruction by dispersion-thirst". Moreover, the disease belongs to the category "internal visual obstruction eye diseases" and is commonly classified under the diseases such as "blurring vision", "vitreous opacity", "pupillary hemorrhage", or "sudden blindness".

Note: "Internal visual obstruction by dispersion-thirst" is equivalent to diabetic retinopathy in western medicine.

### 4 Diagnosis

#### 4.1 Clinical Features

##### 4.1.1 Symptoms

There is no conscious ocular symptom in the early stage of DR. However, varying degrees of vision loss may occur in a prolonged illness. The symptoms are blur vision, black shadow fluttering, metamorphopsia, or blindness.

##### 4.1.2 Signs

The fundus manifestations of DR include aneurysms, hemorrhage, hard exudate, cotton-wool spots, venous bead, intraretinal microvascular abnormality (IRMA), macular edema, neovascularization, pre-retinal hemorrhage, vitreous hemorrhage.

#### 4.2 Ophthalmic examination and ancillary testing

(1) Visual acuity: unaided and best-corrected visual acuity at distance and near, often varying degrees of vision loss, early vision may not change.

(2) Intraocular pressure is generally normal, Late-stage complicated by neovascular glaucoma can be markedly increased.

(3) Biomicroscopy: slit-lamp microscopic examination: The anterior segment of the eye is usually unchanged, and clouding of the posterior lens capsule may be found, but it is nonspecific. ciliary congestion, corneal edema, iris redness, and moderate pupil dilatation are seen in late complications of neovascular glaucoma.

(4) Ophthalmoscopy: Fundus examination was performed after mydriasis, and typical signs such as microhemangioma, hemorrhage, exudation, neovascularization, and vitreous hemorrhage were seen

(5) Color fundus photography

Color fundus photography shows hemorrhage, hard exudation, cotton wool spots, beading of veins, abnormal microvessels in the retina, macular edema, neovascularization, and other symptoms. Color fundus photography is a non-invasive examination, and the repeatability of finding DR is better than other examinations. It is valuable for recording the obvious progress of DR and the response to treatment and is often used for DR screening and follow-up.

(6) Fluorescein fundus angiography (FFA)

FFA can detect abnormal fluorescence in patients with insignificant fundus manifestations by ophthalmoscopy. Those abnormalities include microaneurysm strong fluorescence, telangiectasia or vascular leakage, retinal vascular non-perfusion area, neovascularization, cystoid macular edema, and so forth. Therefore, FFA can improve the rate of DR diagnosis. Moreover, it helps to guide the treatment and evaluate the disease's severity and treatment efficacy.

(7) Optical Coherence Tomography (OCT)

The main significance of OCT examination for diabetic retinopathy is to monitor macular edema, and the images can show the presence of hard exudation in the retina.

(8) Optical Coherence Tomography Angiography, (OCTA)

OCTA is helpful to detect abnormal microvascular changes before the onset of clinical symptoms, providing a more quantitative evaluation of macular ischemia; quantifying macular nonperfusion areas, and detecting retinal neovessel at an early stage.

(9) Visual electrophysiology examination

Diabetic retinopathy patients may have abnormal dark adaptation function, which is manifested as elevated rod threshold and cone threshold. Multifocal ERG examination showed that the reaction density in the macular region decreased. Standard flash ERG to check a wave, b wave amplitude reduction; At the early stage of the disease, abnormal retinal oscillating potential (OPs) can be seen, which is characterized by decreased total amplitude and prolonged latency. The amplitude of each wave decreased significantly when the disease worsened.

(10) Ultrasonography

B-ultrasound can assist in the diagnosis of vitreoretinal hyperplasia or retinal detachment in diabetic patients who cannot directly examine the fundus due to refractive interstitial opacity (usually cataract or vitreous hemophilia)

### 4.3 Complications

Complications of DR include tractional retina detachment, rubeosis iridis, and neovascular glaucoma.

#### (1) Tractional retinal detachment

Retinal proliferative membrane and neovascularization membrane contraction are the main causes of tractional retinal detachment.

#### (2) Rubeosis iridis and neovascular glaucoma

Extensive retinal ischemia of DR induces angiogenin that stimulates the iris and anterior chamber angle to develop neovessels. The characteristics of rubeosis iridis are small curved and irregular abnormal vessels on the iris surface, primarily found in the pupil margin, which can proliferate to the periphery. Also, the neovascularization in the anterior chamber angle obstructs or drags trabecular meshwork or bleeds, which affects the drainage of aqueous humor, resulting in increased intraocular pressure, thus neovascular glaucoma.

### 4.4 Standard for diagnosis and staging of DR

#### 4.4.1 Standard for diagnosis and staging of DR

Refer to the “Guidelines for the Clinical Diagnosis and Treatment of Diabetic Retinopathy” issued by the Ophthalmology Group of the Chinese Medical Association in 2014.

**The stages of diabetic retinopathy are as follows:**

Disease Severity Level			Findings upon Dilated Ophthalmoscopy
I	NPDR	Mild NPDR	Microaneurysm only
II		Moderate NPDR	Retinopathy between mild and severe, with retinal hemorrhage, hard exudate, and/or cotton wool spots
III		Severe NPDR	Any of the following and no signs of PDR: Extensive (>20) intraretinal hemorrhages in each of 4 quadrants Definite venous beading in 2 or more quadrants Prominent IRMA in 1 or more quadrants
IV	PDR	Early PDR	NVE or NVD appears
		High-risk PDR	When NVD > 1/4 ~ 1/3 DA or NVE > 1/2 DA
V		Fibrous proliferation	Fibrous membranes may appear with pre-retinal or vitreous hemorrhage
VI		Advanced PDR	Tractional retinal detachment accompanied with fibrous membranes, with or without vitreous hemorrhage, neovascularization of the iris, and anterior chamber angle

IRMA=Intraretinal microvascular abnormalities; NPDR=Non-Proliferative Diabetic Retinopathy; PDR=Proliferative Diabetic Retinopathy; NVE=Retinal Neovascularization Elsewhere; NVD= Neovascularization of the Optic Disc; DA=Disc area.

#### 4.4.2 Definition and classification of macular edema

Regards the international clinical classification of diabetic retinopathy and macular edema and China’s “Clinical Guidelines for the Diagnosis and Treatment of Diabetic Retinopathy in China (2014)”.

Definition of diabetic macular edema (DME): The leakage of capillaries in the macular area causes thickening within 2 optic disc diameters at the macular center. DME classifies into 2 types, the focal and diffuse types. Generally, the international clinical classification of DME is employed.

International Clinical Classification of Diabetic Macular Edema (DME):

Severity of DME	Findings upon Dilated Ophthalmoscopy
Without obvious DME	No noticeable retinal thickening or hard exudate in the posterior pole.
With obvious DME	Apparent retinal thickening or hard exudate in the posterior pole. Mild: Some retinal thickening or hard exudate, but away from the macular center. Moderate: Retinal thickening or hard exudative predispositions, but not involving the macular center. Severe: Retinal thickening or hard exudation involving the macular center.

#### 4.5 Differential diagnosis

This disease should be distinguished from hypertensive retinopathy and retinal vein occlusion.

##### 4.5.1 Hypertensive retinopathy

With a history of hypertension, retinal arteries become thinner with more prominent light reflections. Moreover, arteriovenous crossing compression is noticeable. Cotton wool spots, hard exudate, bleeding, and extensive microvascular changes are observable. Also, optic disc edema may present.

##### 4.5.2 Retinal vein occlusion

With or without a history of hypertension, most cases are unilateral. Superficial and flame-shaped retinal hemorrhages are present along the retinal veins. They are more prominent in the posterior pole and gradually lessened towards the periphery. The veins are highly distended, tortuous, and sausage-shaped.

## **5 Syndrome differentiation**

### **5.1 Yin Deficiency And Dryness Heat syndrome**

Features: normal or reduced vision and pathological change from grade 1 to grade 3. Other features include dry mouth and throat, polydipsia, swift digestion with rapid hungering, dry and hard stool, dark urine, red tongue with slightly yellow fur, and thready and rapid pulse.

### **5.2 Qi and Yin Deficiency syndrome**

Features: blurred vision, dry eyes, distorted images, or black flowers fluttering floaters seen, pathological change from grade 1 to grade 4, mental fatigue, lack of strength, shortness of breath, lazy for speech, dry mouth and dry throat, spontaneous sweating, dry or loose stools, enlarged and tender tongue, purple tongue with or without ecchymosis, weak pulse.

### **5.3 Liver-kidney depletion syndrome**

Features: blurred vision, dry eyes, retinopathy from grade 1 to 3, dizziness, tinnitus, soreness and weakness of waist and knees, limb numbness, dry and hard stool, dark red tongue with little fur, unsmooth and thready pulse.

### **5.4 Spleen deficiency and dampness stagnation syndrome**

Features: blurred vision, distorted images, or black flowers fluttering floaters seen, retinopathy from grade 2 to 4 with apparent retinal edema, cotton wool spots, significant hemorrhage, and macular edema may also occur, shallow yellow or dull complexion, mental fatigue, lack of strength, dizziness, tinnitus, a large volume of urine; pale tongue, weak pulse.

### **5.5 Deficiency of both Yin and Yang syndrome**

Features: blurred vision or a severe visual impairment, retinopathy from grade 4 to 5, and macular edema may occur; mental fatigue, dry eyes, lack of strength, vexing heat in chest and palms and soles, insomnia and amnesia, backache and cold limbs, cold hands and feet, impotence and premature ejaculation, lower limbs edema, hard and loose stools alternately, pale and enlarged tongue with little saliva or petechiae, dark purple lips, and tongue, deep thready weak pulse.

## **6 Treatment**

### **6.1 Treatment Principles**

The disease should be treated by traditional Chinese medicine based on well-controlled blood glucose, blood pressure, and blood lipids with western medicine. The disease is mainly due to the disharmony of Qi and blood, as well as Yin and Yang. The root causes mostly are deficiency of both Qi and Yin, liver-kidney deficiency, or deficiency of both Yin and Yang while accompanied by



static blood obstructing collateral and phlegm stagnation. Thus it should be treated by replenishing Qi and nourishing Yin, nourishing the liver and kidney, and supplementing Yin and Yang to cure the root cause. Moreover, dredging collaterals, brightening the eyes, activating blood and resolving stasis, resolving phlegm, and dissipating mass are the ways to treat the presenting symptoms.

Clinically, the whole process should be undertaken by integrating systemic and local ocular syndrome differentiation. First, the practitioner should differentiate the whole body status in deficiency or excess, cold or heat, and so forth. Then, according to the bleeding time, add the medicines for dredging meridians and collaterals appropriately.

In the early stage of hemorrhage, the principal treatment direction is cooling blood, stopping bleeding, and resolving stasis. After bleeding stops for two weeks, the direction should switch to primarily promote activating blood and resolving stasis. In the late stage of hemorrhage, add the agents to resolve and soften hardness and dissipate mass appropriately.

Furthermore, modify the prescription formula corresponding to the syndrome with other signs such as microaneurysm, edema, exudate, and so forth.

## **6.2 Syndrome differentiation and treatment**

### **6.2.1 Yin Deficiency And Dryness Heat syndrome**

Treatment: nourishing Yin and engendering fluid, cooling blood, and moistening dryness.

Formula and herbs: Yuquan Wan (“Optimization of Chinese Patent Medicine”) combined with Zhibai Dihuangwan (“Yi Zong Jin Jian”). Commonly used drugs: Radix Puerariae, Radix Trichosanthis, Radix Rehmanniae Recent, Radix Ophiopogonis, Fructus Schisandrae Chinensis, Rhizoma Anemarrhenae, Cortex Phellodendri, Fructus Corni, Rhizoma Dioscoreae, Poria, Rhizoma Alismatis, Cortex Moutan Radicis, glutinous rice, and Radix Glycyrrhizae. If the fundus is dominated by microhemangioma, Radix Salviae Miltiorrhizae and radix curcumae can be added; If the bleeding is obvious, you can add raw Typha pollen, eclipta, Radix Achyranthis Bidentatae; If there is hard exudation, Bulbus Fritillariae Thunbergii, Sargassum, and Thallus Eckloniae can be added

(expert consensus, weak recommendation)

### **6.2.2 Deficiency of both Qi and Yin, syndrome**

Treatment: replenishing Qi and nourishing Yin, activating blood, and dredging collaterals.

Formula and herbs: Shengmai San (“Internal and External Injury Differentiation”) combined with Qi Ju Di Huang Wan (“Medical

Grade”). Commonly used drugs: Radix Ginseng, Radix Ophiopogonis, Fructus Schisandrae Chinensis, Fructus Lycii, Flos Chrysanthemi, Radix Rehmanniae Praeparata, Fructus Corni, Rhizoma Dioscoreae, Poria, Rhizoma Alismatis, Cortex Moutan Racidis, Radix Salviae Miltiorrhizae, and Radix Curcumae. For high retinal hemorrhage, add Radix Notoginseng, eclipta, and raw typha pollen; for macular edema, add atractylodes, Semen Coicis, and Plantago; for spontaneous sweating, and night sweating, add atractylodes, Concha Ostreae and Fructus Tritici Levis. (quality of evidence: D, strong recommendation)

### **6.2.3 Liver-kidney depletion, syndrome**

Treatment: nourishing and tonifying both liver and kidney, moistening dryness, and dredging collaterals.

Formula and herbs: Qi Ju Di Huang Wan (“Medical Grade”) with modification according to the disorder. Commonly used drugs: Fructus Lycii, Flos Chrysanthemi, Radix Rehmanniae Praeparata, Fructus Corni, Rhizoma Dioscoreae, Poria, Rhizoma Alismatis, and Cortex Moutan Racidis. Those with excessive bleeding can be combined with Pollen decoction; During the stationary phase of bleeding, Taohongsiwu decoction can be combined; If the bleeding is not absorbed for a long time, add Bulbus Fritillariae Thunbergii, Sargassum, and Thallus Eckloniae. (quality of evidence: D, strong recommendation)

### **6.2.4 Spleen deficiency and dampness stagnation syndrome**

Treatment: invigorate the spleen and Qi, excrete water and disperse stagnation.

Formula and herbs: Buzhong Yiqi Decoction (“Spleen and Stomach Theory”) combined with Wuling Powder (“Treatise on Febrile Diseases”). Modify the content according to the disorder. Commonly used drugs: Radix Ginseng, Rhizoma Atractylodis Macrocephalae, Radix Glycyrrhizae cum Melle, Radix Astragali seu Hedysari, Radix Angelicae Sinensis, Pericarpium Citri Reticulatae, Rhizoma Cimicifugae, Radix Bupleuri, Polyporus, Poria, Rhizoma Alismatis, and Ramulus Cinnamomi. Add Radix Morindae Officinaliscu,rcuma, Plantago to tonify the kidney, promote blood circulation, and inducing diuresis; for excessive cotton-wool spots add Rhizoma Pinelliae Preparatum, Bulbus Fritillariae Thunbergii, atractylodes; for macular edema add Semen Coicis, Polyporus. (expert consensus, weak recommendation)

### **6.2.5 Deficiency of both Yin and Yang, blood stasis, and phlegm coagulation syndrome**

Treatment: nourishing Yin and tonifying Yang, resolving phlegm, and

dispelling blood stasis.

Formula and herbs: Those with partial Yin deficiency choose the Zuogui pill (“Jingyue Quanshu”), and those with partial Yang deficiency choose the Yougui pill (“Jingyue Quanshu”). Modify the content according to the disorder. Commonly used drugs: Radix Rehmanniae Praeparata, Colla Cornus Cervi, Colla Carapax et Plastrum Testudinis, Rhizoma Dioscoreae, Fructus Lycii, Fructus Corni, Radix Cyathulae, Semen Cuscutae, Radix Aconiti Lateralis Praeparata, Cortex Cinnamomi, Cortex Eucommiae, Radix Angelicae Sinensis, and Herba Epimedii. For stale blood stasis, hard exudate, or vitreoretinal hyperplastic fibers, add Concha Arcae, Bulbus Fritillariae Thunbergii, Sargassum, Thallus Eckloniae to softening hardness to dissipate stagnation; for neovascular membranes or excessive bleeding, add Radix Notoginseng, raw typha pollen and Ophicalciturum to petrify blood stasis and stop bleeding; for intolerance of cold with yang deficiency or retinal edema, add dodder and Herba Epimedii to improve acuity of vision by tonifying the liver, kidney, and Yang.

(expert consensus, weak recommendation)

### **6.3 Chinese patent medicine**

Qiming Granule is used for liver-kidney depletion, Qi and Yin deficiency, and collateral blood stasis syndrome. (quality of evidence: B, strong recommendation)

Shuangdan mingmu capsule is used for liver-kidney depletion and blood stasis obstructing the collaterals syndrome. (quality of evidence: B, strong recommendation)

Mingmu Dihuang Wan is used for liver-kidney Yin deficiency, dry eye and photophobia, blurred vision, and so forth. (quality of evidence: B, strong recommendation)

Qi Ju Di Huang Wan is used for liver-kidney Yin deficiency, ocular collateral blood stasis, internal visual obstruction and dim vision, blurred vision, and so forth. (quality of evidence: D, strong recommendation)

Compound Xueshuantong Capsule is used for blood stasis with Qi and Yin deficiency, mental fatigue, lack of strength, dry throat, dry mouth, and blurred vision. (quality of evidence: C, strong recommendation)

Compound Danshen dropping pills are used for Yin deficiency and blood stasis with Qi stagnation. (quality of evidence: C, strong recommendation)

He Xue Ming Mu Pian is used for liver-kidney Yin deficiency with obstruction of collateral blood. (quality of evidence: C, weak recommendation)

### **6.4 Acupuncture and moxibustion**

Acupuncture therapy can be utilized for patients with DR grades from 1 to 3

with mild bleeding. Suggested acupoints are Taiyang (EX-HN 5), Yangbai (GB 14), Cuanzhu (BL 2), Zusanli (ST 36), Sanyinjiao (SP 6), Guangming (GB 37), Gansu (BL 18), Shenshu (BL 23) and others appropriate in the prescription. Allocates those acupoints into two groups and applies in turn. In each treatment session, apply 1 or 2 acupoints in the eye area and 3 to 5 points in the limbs and the back, manipulating in neutral reinforcement and reduction. (expert consensus, weak recommendation)

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## ANNEX A (Informative Appendix)

### Evidence Evaluation and Recommendation Principle

#### A.1 Evaluation and Grade

The evidence classification principle of this document is based on the GRADE, randomized controlled trials were initially designated as high-quality evidence, the quality of which could be reduced by five factors, while observational studies were rated as low-quality evidence, but their quality could be increased by three factors. Finally, the quality of evidence is sorted into high, moderate, low, and very low.

The process of screening and evaluation of the literatures are carried out independently by two evaluators. If the views of the two parties are inconsistent, they would resolve through negotiation or adjudication by a third one. See table A1 below for details:

**Table A1: Evaluation and Grade**

Initial quality of a			Lower/Higher	Quality level	Definition
Study design	body of evidence				
Randomized controlled trials	High	Risk of Bias	-1 Serious	High(A)	We are very confident that the true effect lies close to that of the estimate of the effect trials
			-2 Very serious		
		Inconsistency	-1 Serious	Moderate(B)	
			-2 Very serious		
		Indirectness	-1 Serious	Low(C)	
			-2 Very serious		
Imprecision	-1 Serious	Very low(D)			
	-2 Very serious				
Publication bias	-1 Likely	Very low(D)			
	-2 Very likely				
Observational studies	Low	Large effect	+1 Large	Very low(D)	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
			+2 Very large		
		Dose response	+1 Evidence of a gradient		
		All plausible residual confounding	+1 Would reduce a demonstrate effect		
			+1 Would suggest a spurious effect if no effect was observed		

#### A.2 Recommended principle

The fact that most studies on the treatment of diabetic retinopathy in TCM are not comprehensive, the design of studies is often less standardized, the selection of formula is diverse, and the efficacy standard is not uniform, which

attribute to the outcome bias. Therefore, the evidence is required to obtain expert consensus before being included in the recommendation.

The general principle of the expert consensus is that if the total number of experts who strongly recommend one treatment exceeds 75%, then it is a strong recommendation. If the number of experts who recommend it is below or equal to 50%, then it is not recommended; other situations are sorted into weak recommendations.

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**ANNEX B**  
**(Informative Appendix)**

**Announcement of Interest Conflicts and Fund Sources**

All members of the guideline development group of the international clinical practice guideline of traditional Chinese medicine diabetes retinopathy declared that they were completely independent in the preparation of this guideline and had no contact with any interest groups.

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