The OD's Role in Diabetes

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Course Description

This course will provide the up-to-date information on diabetic retinopathy (DR). Emphasis will be on the OD's role in Diabetes by incorporating the latest in diagnostic modalities and therapeutic advances for vision-threatening diabetic retinopathy (VTDR), proliferative DR and diabetic macular edema (DME).

Goal

Provide attendees with recent developments in the early diagnostic strategies and therapeutic advances for diabetic retinopathy and discuss integration of these innovations into clinical practice.

Learning Objectives

At the conclusion of this course, attendees will be able to:

1) Describe the scope of diabetes in the US.
2) Appreciate the risks and goals in diabetes
3) Know the latest American Diabetes Association (ADA) recommendations.
4) Appreciate the latest technologies and methodologies to analyze DR/DME including fundus autofluorescence (FAF), wide-field imaging, multi-modal imaging with SD-OCT and OCT angiography (OCTA), and fluorescein angiography.
5) Recognize the importance of an interdisciplinary role in prevention of vision loss

Abstract

There is an alarming increase in diabetes among adults, with over 133 million Americans now living with diabetes or prediabetes- an increase of 11 million more Americans in the past two years. This course will provide the latest information on diabetic retinopathy (DR). Emphasis will be on the OD's role in diabetes by incorporating the latest in diagnostic modalities and therapeutic advances for vision-threatening diabetic retinopathy (VTDR), proliferative DR and diabetic macular edema (DME).

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COURSE OUTLINE

I. Latest on Diabetes and DR/DME *(National Diabetes Fact Sheet 2022)*

- Total: 37.3 million people have diabetes (11.3% of the US population)
- Diagnosed: 28.7 million people, including 28.5 million adults
- Undiagnosed: 8.5 million people (23.0% of adults are undiagnosed)
- Prediabetes: 96 million people aged 18 years or older have prediabetes (38.0% of the adult US population)

II. Diabetic Retinopathy (DR)-The leading cause of preventable blindness in working aged adults

- Currently~8 million Americans. Expected to increase to 11 million by 2030
- Initial sign of underlying disease (30% of type 2 DM) – case presentation
- Latest- 60% of diabetic patients do not receive regular follow-up eye examination
- American Diabetes Association (ADA) Position Statement:
    - Risk factors: Duration of diabetes, past glycemic control (HbA1c), medications, medical history (e.g., obesity, renal disease, systemic hypertension, serum lipid levels, pregnancy, neuropathy) and ocular history (e.g., trauma, other eye diseases, ocular injections, surgery, including retinal laser treatment and refractive surgery)
    - Prevent progression of DR/DME- good glycemic, blood pressure, cholesterol
- ***Time in Range (TIR***) - A new parameter to evaluate blood glucose control

III. DR Pathophysiology

- Hyperglycemia induce microvascular damage:
    - Alterations in biochemical pathways, such as increased flux of advanced glycation end products/receptors (AGE/RAGE), polyol pathway, protein kinase C (PKC) activation, and hexosamine pathway produce oxidative stress
    - Damages the pericytes and weakens capillary walls which causes retinal ischemia
    - Retinal ischemia
    - ↑ VEGF
    - ↑ vascular permeability
    - Fragile new vessels grow and rupture
    - Fibrovascular tissue causes retinal traction

IV. Innovation in Diagnosis- Case presentations

- Diabetic Retinopathy Severity Score (DRSS)

TABLE 1 DIABETIC RETINOPATHY DISEASE SEVERITY SCALE AND INTERNATIONAL CLINICAL DIABETIC RETINOPATHY DISEASE SEVERITY SCALE

Disease Severity Level	Findings Observable upon Dilated Ophthalmoscopy
No apparent retinopathy	No abnormalities
Mild NPDR (see Glossary)	Microaneurysms only
Moderate NPDR (see Glossary)	More than just microaneurysms but less than severe NPDR
Severe NPDR	
U.S. Definition	Any of the following (4-2-1 rule) and no signs of proliferative retinopathy: • Severe intraretinal hemorrhages and microaneurysms in each of **four** quadrants • Definite venous beading in **two** or more quadrants • Moderate IRMA in **one** or more quadrants
International Definition	Any of the following and no signs of proliferative retinopathy: • More than 20 intraretinal hemorrhages in each of **four** quadrants • Definite venous beading in **two** or more quadrants • Prominent IRMA in **one** or more quadrants
PDR	One or both of the following: • Neovascularization • Vitreous/preretinal hemorrhage

IRMA = intraretinal microvascular abnormalities; NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy

NOTE:
- Any patient with two or more of the characteristics of severe NPDR is considered to have very severe NPDR.
- PDR may be classified as high-risk and non-high-risk. See Table 6 for more information.

Adapted with permission from Wilkinson CP, Ferris FL III, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003;110:1679.

- OCTA clinical findings-
    - Subclinical DR- Microaneurysms (MAs), vascular anomalies (loops and dilations)
    - Diabetic macular ischemia (DMI)
        - Capillary non-perfusion
        - Disruption and enlargement of the foveal avascular zone (FAZ)
            - FAZ was 0.348mm^2 in diabetic eyes and 0.288mm^2 in normal eyes.
        - Neovascularization
- Centered involved (CI-DME) vs non-centered DME
- Ultra-wide field imaging of DR
    - Updates EDTRS
    - Early detection of peripheral DR lesions
        - Eyes with predominantly peripheral lesions (PPL) (defined as outside of ETDRS 7 standard field) had a 4.7- fold increased risk of progression to proliferative diabetic retinopathy (PDR)
- Fundus autofluorescence (FAF)
    - Lipofuscin accumulation in DR
    - HyperFAF in DME

V. Standard of Care

- PDR: PRP versus Anti-VEGF (Protocol S)
- Anti-VEGF for CI-DME
    - RIDE/RISE, RESTORE, and VISTA/VIVID
- FDA Approved therapy for DME:
    - Ranibizumab (Lucentis 0.3 mg) – RIDE/RISE ($1150)
    - Aflibercept (Eylea) – VIVID/VISTA ($2000)
    - Dexamethasone implant (Ozurdex) – MEAD ($1400)
    - Fluocinolone implant (Iluvien) –FAME ($9300)
    - Off label therapy
        - Bevacizumab (Avastin) – DRCR.net ($70)
        - Intravitreal Triamcinolone (Triessence) - $150
    - FDA approves Lucentis 0.3mg approval for the monthly treatment of

all different forms of diabetic retinopathy

- Latest on Protocol V
  - Anti-VEGF for CI-DME in patients with good vision (20/25 vision or better)
  - DME can be clinically sub-divided into three relevant categories
    - CI-DME with VA impairment
    - CI-DME with good VA
    - Non-CI-DME.
- PANORAMA study
  - The trial confirmed that moderately severe and severe non-proliferative diabetic retinopathy is not a benign condition, with patients at high risk of rapidly progressing to vision-threatening events.
  - In untreated patients with severe NPDR, 53% developed complications, the EYLEA treatment prevented approximately 74% of complications at one year.
- Protocol W
  - Protocol W is a prospective multicenter study by the DRCR Retina Network that included eyes with moderate-to-severe NPDR and without baseline CI-DME (Figure).
  - The study was designed as a long-term evaluation of intravitreal aflibercept's ability to prevent PDR and CI-DME in eyes with advanced DR.
  - Preventive treatment with aflibercept resulted in a threefold reduction in the development of CI-DME with vision loss (14.8% in the sham group vs 4.1% in the aflibercept group).
  - Treatment was also associated with a nearly twofold reduction in the development of new-onset PDR (33.2% in the sham group vs 13.5% in the aflibercept group
- New Bispecific treatment (Faricimab)
  - Anti–Ang-2 Fab- Enhanced activity through Ang-2 inhibition
  - Anti-VEGF

V. American Diabetes Association (ADA Position Statement on Diabetic Retinopathy)

- First such update by the ADA since 2002
- Emphasize the importance of good diabetes control (blood glucose, blood pressure and lipids)
- Eye examination frequency recommendations for people with diabetes
- Recognition of anti-VEGF agents as the 'gold standard' for diabetic macular edema (DME)
- Retinal photography may serve as a screening tool for retinopathy.
- Diabetic teleretinal screening

VI. Conclusion

- Diabetes and the risk of vision-threatening retinopathy is on the rise.
- Early diagnosis and treatment have significantly improved the patient visual

prognosis and outcome.

- Multidisciplinary diabetes care team.
- OD's play a vital role by incorporating the latest in diagnostic modalities and therapeutic advances for vision-threatening diabetic retinopathy (VTDR), proliferative DR and diabetic macular edema (DME).

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