Examining the Diabetic Patient: What Matters Most

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Objectives

- Simplify strategy for evaluating the eyes of diabetics
- Identify the threats to vision and treatments
- Develop patient education that helps diabetics understand the importance of controlling their disease

Preretinal Neovascularization = Proliferative Disease

Proliferative Diabetic Retinopathy (PDR)
Proliferative Diabetic Retinopathy (PDR)

NVD = on or within 1DD of ONH

Proliferative Disease:
Preretinal hemorrhage

Proliferative Disease:
Vitreous Hemorrhage

Proliferative Disease:
Tractional Retinal Detachment
Proliferative Disease: Tractional Retinal Detachment

Clinically Significant Macular Edema

- Retinal thickening within 500 microns of fovea
- Exudate within 500 microns of fovea with adjacent thickening
- Retinal thickening of at least one disc area any part within one disc diameter of center of fovea

ETDRS. Ophthalmology. 1985; 103:1796-1806
ETDRS. Ophthalmology. 1987; 94:761-774

What are the chances?

<table>
<thead>
<tr>
<th>No Tx</th>
<th>Tx</th>
<th>RBR</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>90%</td>
<td>45%</td>
<td>50%</td>
<td>45%</td>
<td>2</td>
</tr>
<tr>
<td>25%</td>
<td>12.5%</td>
<td>50%</td>
<td>12.5%</td>
<td>8</td>
</tr>
<tr>
<td>10%</td>
<td>5%</td>
<td>50%</td>
<td>5%</td>
<td>20</td>
</tr>
<tr>
<td>2/million</td>
<td>1/million</td>
<td>50%</td>
<td>0.0001%</td>
<td>1,000,000</td>
</tr>
</tbody>
</table>

ETDRS: Focal laser for CSME
DRS: PRP for High Risk PDR

Treatments DME

- Laser
- Steroids
- Anti-VEGF

RESTORE
DA VINCI
VIVID/VISTA
Early Treatment Diabetic Retinopathy Study (ETDRS)

- Moderate vision loss (15 letters on ETDRS) at 3 years:
  - 24% untreated
  - 12% treated

- ARR 12%
- NNT 8

- Few (<3%) had improvement of 15 letters or more

Diabetic Retinopathy Clinical Research Network (DRCR.net)

- DME
  - 20/40 – 20/320
  - N = 840

- 1mg triamcinolone
  - N = 256

- 4mg triamcinolone
  - N = 254

- Macular laser
  - N = 330

DRCR.net

- 4 mg > 1 mg/laser
  - 4 months

- 4 mg = 1 mg/laser
  - 1 year

- Laser > 4 mg/laser
  - 2 years

DRCR.net

- Complications (%)
  - Laser
  - 1 mg
  - 4 mg

- IOP ≥ 10mmHg
  - 16

- Cataract Surgery
  - 33

- 20/40 BCVA or better in patients with mild visual loss

- Ranibizumab + sham laser:
  - 20% à 53%

- Ranibizumab + active laser:
  - 16% à 45%

- Active laser + sham injections:
  - 15% à 24%

RESTORE

- Average change in visual acuity from baseline to month 12
  - Ranibizumab + sham laser: +6.1 ± 6.4 letters (p<.0001)
  - Ranibizumab + active laser: +5.9 ± 7.6 letters (p<.0001)
  - Active laser + sham injections: +0.8 ± 6.4 letters

- 20/40 BCVA or better in patients with mild visual loss
  - Ranibizumab + sham laser:
    - 20%
    - 12%

  - Ranibizumab + active laser:
    - 15%
    - 15%

  - Active laser + sham injections:
    - 10%
    - 24%

- ARR 33%, NNT 3
- ARR 29%, NNT 3
- ARR 9%, NNT 11
RISE and RIDE

RISE
- 0.3mg ranibizumab: N = 127
- 0.5mg ranibizumab: N = 127
- Sham: N = 127

RIDE
- 0.3mg ranibizumab: N = 125
- 0.5mg ranibizumab: N = 125
- Sham: N = 130

RISE and RIDE. Ophthalmology 2012: 119: 789-801

≥ 15 letters ETDRS chart

24 months

RISE
- 44% 0.3mg ARR 26% NNT 4
- 39% 0.5mg ARR 21% NNT 5
- 18% sham

RIDE
- 34% 0.3mg ARR 22% NNT 5
- 46% 0.5mg ARR 34% NNT 3
- 12% sham

RISE and RIDE. Ophthalmology 2012: 119: 789-801

Progression to PDR and needing PRP
< 1%

ranibizumab
11% sham

% with BCVA ≥ 20/40

60% ranibizumab 36% sham ARR 24% NNT 4

Mean change from baseline BCVA
+8.5-9.9 letters more in ranibizumab vs. sham

ARR 27% NNT 3

Eyes gained ≥ 3 lines BCVA

Trap-Eye: 36% Laser: 11%

AR 22% NNT 3
Trap-Eye (aflibercept) was FDA approved for treatment of DME in 2014

Summary DME Treatment

DME Tx
- Laser maintains vision rather than improving it
- Steroids work as well as laser but the side effects are worse
- Anti-VEGF has shown to improve vision although requires a lengthy course of treatment of monthly injections

Threats to vision
- Diabetic Retinopathy
- NPDR
- Macular Disease
- Ischemia
- Edema
- PDR
- Macular Disease
- Ischemia
- Edema

4-2-1 Rule: Raising the (Risk) Bar

1. IRMA in 1 quadrant
2. Venous beading in 2 quadrants
4. Severe retinal hemorrhages in 4 quadrants

NPDR → PDR in 1 year

Mild
- 3% risk of progression to PDR

Moderate
- 15% risk of progression to PDR

Severe
- 62% risk of progression to PDR
- Meets DME criteria of 4-2-1 Rule

Very Severe
- 75% risk of progression to PDR
- Meets TWO criteria of 4-2-1 rule

Follow-up intervals in months

<table>
<thead>
<tr>
<th>Severity of NPDR</th>
<th>American Academy of Ophthalmology</th>
<th>American Optometric Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Mild</td>
<td>6-12</td>
<td>12</td>
</tr>
<tr>
<td>Moderate</td>
<td>6-12</td>
<td>12</td>
</tr>
<tr>
<td>Severe</td>
<td>2-4</td>
<td>3-4</td>
</tr>
<tr>
<td>Very Severe</td>
<td>2-4</td>
<td>2-3</td>
</tr>
</tbody>
</table>
8-year Incidence of CHD and Stroke as a Hazard Ratio (HR) in Japanese Type 2 Diabetics (N=2033)

<table>
<thead>
<tr>
<th>Retinal Finding</th>
<th>Coronary Heart Disease</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild-Moderate NPDR</td>
<td>1.69 (95% CI 1.17-2.97)</td>
<td>2.69 (95% CI 1.03-4.86)</td>
</tr>
<tr>
<td>Retinal hemes/MA</td>
<td>1.63 (95% CI 1.04-2.56)</td>
<td>Not associated (P=0.06)</td>
</tr>
<tr>
<td>CWS</td>
<td>Not associated (P=0.66)</td>
<td>2.39 (95% CI 1.35-4.24)</td>
</tr>
</tbody>
</table>

Communicate Diabetic Eye Exam Results to PCP!

High Risk Characteristics

- HRC: NVD ≥ ¼ disc area
- Any NVD or NVE with pre-retinal or vitreous hemorrhage

Diabetic Retinopathy Study (DRS)

- Severe vision loss (20/800) in eyes that met HRC of 2 years
  - 26% untreated
  - 11% treated
  - ARR 15%
  - NNT 8

- Severe vision loss (20/800) in eyes with PDR < HRC of 2 years
  - 7% untreated
  - 3% treated
  - ARR 4%
  - NNT 25

"My vision was fine until you sent me to that retinal specialist for laser"

PRP for PDR

- 5-9 letters loss from baseline
  - 1 sitting (N=84) • 4 sittings (N=71)

- % decrease over time:
  - 3 day
  - 4 weeks
  - 17 weeks
  - 34 weeks
PRP for PDR

<table>
<thead>
<tr>
<th>≥ 10 letters loss from baseline</th>
<th>1 sitting (N=84)</th>
<th>4 sittings (N=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25%</td>
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<tr>
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<tr>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>34 weeks</td>
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Anti-VEGF for PDR

BCVA ≥ 20/320
No Previous PRP
N = 394 eyes

Lucents® 0.5mg q1 month
N = 160 eyes

PRP over 1-3 visits
N = 168 eyes

Anti-VEGF for PDR: 2 Year Results

- Mean change in visual acuity:
  - Lucentis: +2.8 letters
  - PRP: +0.2 letters
- Change in visual field total point score:
  - Lucentis: -23 dB
  - PRP: -422 dB
- DME development:
  - Lucentis: 9%
  - PRP: 28%
- Eyes without PDR on fundus photos:
  - Lucentis: 35%
  - PRP: 30%

“Every time a doctor sees a patient, the patient should feel better as a result”
Anonymous MD

After 20 years of known diabetes the prevalence of DME was approximately 28% in both type 1 and type 2 diabetes

Recorded at TEDMED
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www.TEDMED.com
The most widely accepted methods to reduce vision loss from DME and reduce progression of DR are:

1. Intensive glycemic control
2. Blood pressure control
3. Lipid management

The frequency of remission of type 2 diabetes achievable with lifestyle intervention is 8.6% (95% CI, 5.3%-7.4%) at year 1 and 8.1% (95% CI, 5.6%-7.3%) at year 4, compared with 2.3% (95% CI, 1.9%-2.7%) for the DSE group at both time points (95% CIs, 1.4%-2.6% at year 1 and 1.5%-2.7% at year 4). The absolute reduction in HbA1c from year 1 to year 4 for the ILI group is 15.4% (95% CI, 13.7%-17.0%) and at year 4 (6.4%; 95% CI, 4.7%-8.1%).

**Table 1: Duration of Any Remission (Partial or Complete) by Intervention Group and Duration of Sustained Remission**

- **Intensive lifestyle intervention**
- Diabetes support and education

**Figure 3: Prevalence Any Remission (Partial or Complete) by Intervention Condition and Year**

- Intensive lifestyle intervention
- Diabetes support and education

**Figure 4: Duration of Any Remission (Partial or Complete) by Intervention**

- Intensive lifestyle intervention
- Diabetes support and education

**Figure 5: Success of any Remission (Partial or Complete) by Intervention**

- Intensive lifestyle intervention
- Diabetes support and education
Highest probabilities of 1-year remission

<table>
<thead>
<tr>
<th>Condition</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 2-year history of diabetes</td>
<td>21.2%</td>
</tr>
<tr>
<td>More than 6.5% weight loss</td>
<td>16.4%</td>
</tr>
<tr>
<td>Fitness improvements</td>
<td>15.6%</td>
</tr>
<tr>
<td>Low initial HbA1c</td>
<td>17.1%</td>
</tr>
<tr>
<td>Not taking antihypertensive medications</td>
<td>15.2%</td>
</tr>
</tbody>
</table>

Avoid words that maim
Encourage with words that heal

Teach well

Summary

- Inquire about blood sugar, HbA1c, year of diagnosis, blood pressure, cholesterol, PCP visits (send a report to them), diet/exercise
- Look carefully for the threats to vision
- Engage in conversation with empathy, compassion and educate well

Contact Information
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