Diabetes Microvascular Complications
Screening, Management, and Referral

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Diabetes Complications

Macrovascular Complications

• Cardiovascular disease
  – Coronary Heart disease (CHD)
  – Stroke
  – Peripheral arterial disease (PAD)/amputation
Diabetes Complications

**Microvascular Complications**

- Eye disease (retinopathy)
- Kidney disease (nephropathy)
- Nerve disease (neuropathy)
Type 1 Diabetes: DCCT

Microvascular Complications

Relative Risk vs. A1C (%)

- Retinopathy
- Nephropathy
- Neuropathy
- Microalbuminuria

Adapted with permission from Skyler J. Endocrinol Metab Clin North Am. 1996;25:243

DCCT/EDIC (type 1)

- Diabetic eye disease by 76 percent
- Advancement of eye disease by about half (54 percent), in people with some eye disease at the beginning of the study.
- Diabetic kidney disease by 50 percent.
- Diabetic nerve disease by 60 percent

NIDDK
Type 2 Diabetes: UKPDS

**UKPDS: 1% A1C Decrease and Reduced Risk of Complications**

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>43%</td>
<td>Lower-extremity amputation or fatal peripheral vascular disease†</td>
</tr>
<tr>
<td>37%</td>
<td>Microvascular disease†</td>
</tr>
<tr>
<td>19%</td>
<td>Cataract extraction†</td>
</tr>
<tr>
<td>16%</td>
<td>Heart failure*</td>
</tr>
<tr>
<td>14%</td>
<td>Myocardial infarction†</td>
</tr>
<tr>
<td>12%</td>
<td>Stroke*</td>
</tr>
</tbody>
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Cardiovascular complications

*†P < .05, ‡P < .001.
UKPDS = United Kingdom Prospective Diabetes Study.

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Goals of Glucose Management

Targets for glycemic control for many patients:

<table>
<thead>
<tr>
<th>A1c (%)</th>
<th>&lt;7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting (preprandial) plasma glucose</td>
<td>80-130 mg/dL</td>
</tr>
<tr>
<td>Postprandial (after meal) plasma glucose</td>
<td>&lt;180 mg/dL</td>
</tr>
</tbody>
</table>
Kidney Disease

Diabetic Kidney Disease

- Characterized by proteinuria and declining eGFR
- Occurs in 30% of type 1
- Occurs in 40% of type 2
- More common in African Americans, Asians, and Native Americans
- Associated with risk of CVD
- Diabetes is leading cause of ESRD

NKF
NIDDK
Am J Kid Dis June 2018
Chronic Kidney Disease—Screening New for 2020

• At least once a year, assess urinary albumin (e.g., spot urinary albumin-to-creatinine ratio) and estimated glomerular filtration rate (eGFR) in patients with type 1 diabetes with duration of ≥5 years and in all patients with type 2 diabetes regardless of treatment.

• Patients with urinary albumin >30 mg/g creatinine and/or an eGFR <60 mL/min/1.73m² should be monitored twice annually to guide therapy

• Start at 5 years in type 1, at or near diagnosis in type 2

Kidney Disease Management

• ACEI or ARB for albuminuria or proteinuria
• Serum creatinine and GFR monitoring
• Optimize blood pressure to target <140/<90 (<130/<80 without undue burden)
• Optimize blood glucose control (i.e., A1C <7) for appropriate patients
• Nephrology referral if eGFR<30, uncertain diagnosis, difficult to manage or rapid progression, albuminuria/proteinuria
• SGLT-2 for appropriate patients
Glucose-lowering Medication in Type 2 Diabetes: Overall Approach

Pharmacologic Approaches to Glycemic Management: Standards of Medical Care in Diabetes - 2020. Diabetes Care 2020;43(Suppl. 1):S98-S110
## Choosing Medications in DKD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Renal effect-progress of DKD</th>
<th>Renal effect-dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>neutral</td>
<td>Contraindicated GFR&lt;30</td>
</tr>
<tr>
<td>SGLT-2 inhibitors</td>
<td>benefit</td>
<td>Renal dosing, generally not used GFR&lt;45-60</td>
</tr>
<tr>
<td>GLP-1 RA</td>
<td>Beneft-liraglutide</td>
<td>Renal dosing for exenatide, lixisenatide</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Watch for dehydration, kidney injury</td>
</tr>
<tr>
<td>DPP-IV inhibitors</td>
<td>neutral</td>
<td>Renal dosing</td>
</tr>
<tr>
<td>TZD's</td>
<td>neutral</td>
<td>FDA Black box warning-HF, fluid retention</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>neutral</td>
<td>Glyburide-not recommended, watch for hypoglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(often not used)</td>
</tr>
<tr>
<td>insulin</td>
<td>neutral</td>
<td>Lower doses with lower GFR</td>
</tr>
</tbody>
</table>

Adapted from American Diabetes Association. Diabetes Care 2019 Jan; 42(Supplement 1): S90-S102

## Very Advanced Kidney Disease Diabetes Medications

- Insulin
- Maybe GLP-1
- Be sure to refer to nephrology
ACEI/ARB in Diabetes

• Not prescribed only for the diagnosis of diabetes
• Used for hypertension or albuminuria/proteinuria in the absence of hypertension

Retinopathy
Retinopathy Screening

• Type 1 annual starting after age 10 or after 5 years post diagnosis
• Type 2 annual starting shortly after diagnosis
• Consider less frequent if one or more normal exams (not usually done)

Retinopathy Screening
New for 2020

Screening for diabetic retinopathy recommendations were revised to include consideration of retinal photograph with remote reading or use of a validated assessment tool as a way to improve screening access
Retinopathy Management

• A1C < 7 for appropriate patients
• Laser photocoagulation by ophthalmologist or retinologist

Diabetic Neuropathy
Diabetic Distal Symmetric Polyneuropathy

- DSPN
  - At least 20% of type 1 diabetes after 20 years
  - 10-15% of new type 2 diabetes
  - 50% after 10 years of type 2 diabetes

- Feet typical initial presentation, burning, tingling, numbness
- Neuropathy contributes to amputations
- Up to 50% of DSPN may be asymptomatic

Neuropathy Position Statement
Diabetes Care 2017;40:136-154

Neuropathy Screening

- Screen at diagnosis for type 2, 5 years after diagnosis for type 1, and annual thereafter
- Foot inspection every visit plus annual/prn:
  - 10g monofilament testing
  - Vibratory testing (128 HZ)
  - Temperature and pinprick
  - Reflexes
- Assess for autonomic neuropathy in those with DSPN
Neuropathy: Treatment

- Optimize blood glucose control (i.e., A1C <7) for appropriate individuals for reducing incidence of DPN and CV autonomic neuropathy in those with type 1 diabetes (better evidence in type 1 diabetes)

- Optimize blood glucose control to prevent progression of DSPN in persons with type 2 diabetes

- Pregabalin or duloxetine recommended first line

- Gabapentin may also be considered first line

- Opioids not recommended

- Tricyclic antidepressants use with caution

Other neuropathies

- Autonomic
  - Cardiovascular
  - Gastrointestinal
  - Urogenital
  - Sudomotor

- Mononeuropathy
  - Cranial or peripheral nerve

- Radiculopathy

- Pressure palsies

- B12 deficiency from long term metformin use

- Related hypothyroidism
Case 1: MT

- MT is a 58-year-old Hispanic female
- T2DM x 11 years with dyslipidemia, HTN, albuminuria, non-painful peripheral neuropathy, obesity, non-alcoholic fatty liver disease (NAFLD), history of myocardial infarction (MI) 3 years ago
- Current medications:
  - Metformin 1000 mg orally twice a day
  - Glipizide 10 mg orally once daily
  - Pioglitazone 30 mg orally once daily
  - Lisinopril 20 mg orally once daily
  - Metoprolol XL 25 mg orally once daily
  - Atorvastatin 80 mg orally once daily
  - Aspirin 81 mg orally once daily

Case 1: MT

- Physical exam
  - Nonproliferative retinopathy, normal heart and lung sounds, obese, decreased vibratory and filament sensation in otherwise healthy appearing feet
- Concerns
  - Many blood sugars in 200-300s mg/dL, but occasionally less than 70 mg/dL
  - Fatigue
  - Difficulty losing weight
  - Urinary frequency
- Labs
  - A1C 10.2%
  - Lipids in target range (on high intensity statin), serum creatinine 0.9 mg/dL, GFR 54 mL/minute/1.73 m², hepatic function revealing minor transaminase elevation, urine albumin 110 mg/24 hr (normal <30 mg/24 hr)

What next?
Case 1: MT

• This patient has **macrovascular** disease  
  – ASCVD

• This patient has **microvascular** disease  
  – Early CKD, neuropathy, early retinopathy

Case 1: MT

• Recall current standards of care recommend an **SGLT-2 inhibitor** or a **GLP-1 agonist** in the patient with established cardiovascular disease

• Recall current standards of care recommend an **SGLT-2 inhibitor** in the patient with chronic kidney disease with appropriate GFR

• One of patient’s main complaints is difficulty losing weight, both of these drug classes are weight-neutral or may promote weight loss

• Basal insulin could also be considered here- A1C greater than 10% with symptoms
Case 1: MT

• Could do any of the following in the patient with established CVD
  – Add drug class: GLP-1 agonist
  – Add drug class: SGLT-2 inhibitor
  – Using both GLP-1 agonist or SGLT-2 inhibitor for maximal weight loss

• Could do any of the following in the patient with established CKD
  – Preferentially add drug class SGLT-2 inhibitor if eGFR is satisfactory

• Would definitely
  – Continue metformin (renal function is OK for this)
  – Refer to diabetes educator and dietician for interprofessional team care
  – Assess well-being/lifestyle factors

• Would consider
  – Stop glipizide
  – Stop pioglitazone
  – As we have onboarded more appropriate medications for this patient's individual needs

Case 1: MT Summary

• What if A1C was not at target in 3 months?
  – if not on insulin yet, would definitely consider

• Advance therapy, avoid clinical inertia

• Remember appropriate interprofessional team-based diabetes self-management education and support
Case 2: CG

• 60 year old Hispanic male
• Metformin, DPP-IV inhibitor
• Started on ACEI for HTN
• Serum creatinine at start 1.1
• 4 weeks later 2.9
• Now what?

Case 2: CG

• Renal ultrasound shows bilateral renal artery stenosis
Standards of Care Resources

- Full version available
- Abridged version for PCPs
- Free app, with interactive tools
- Pocket cards with key figures
- Free webcast for continuing education credit

Professional.Diabetes.org/SOC

Summary

- Diabetes complications can be avoided or minimized with good glucose control
- Appropriate, guideline based screening is important for early detection
- Know when to make appropriate referrals