Prevention of MACROvascular Complications of Diabetes

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Conflicts of Interest

None
Objectives

1. To recognize macrovascular complications as the leading cause of death in people with diabetes
2. To be familiar with risk factors for macrovascular complications of diabetes
3. To understand the impact of multifactorial risk reduction on outcomes in patients with diabetes
Microvascular = small vessel disease

Macrovascular = large vessel disease
Overview of Diabetic Complications

**Macrovascular**
- Stroke
- Heart disease and hypertension

**Microvascular**
- Diabetic eye disease (retinopathy and cataracts)
- Renal disease
- Neuropathy

*Foot problems

Leading cause of death in people with diabetes
AMERICAN DIABETES ASSOCIATION

STANDARDS OF MEDICAL CARE IN DIABETES—2018

Diabetes Care 2018;41(S1).
Screening for Coronary Artery Disease (CAD)

Screening

- In asymptomatic patients, routine screening for coronary artery disease is not recommended as it does not improve outcomes as long as atherosclerotic cardiovascular disease risk factors are treated. A

Diabetes Care 2018;41(S1).
No ADA guidelines for screening for cerebrovascular disease in asymptomatic patients
Peripheral Arterial Disease (PAD)

Cholesterol (plaque) embolization

Severe ischemia in setting of infection
Screening for Peripheral Arterial Disease (PAD)

**PAD**
- Routine foot examination (including pulses)
- Ankle brachial index (ABI)
  - Symptomatic patients (claudication)
  - Asymptomatic
    - Not specifically addressed in 2018 ADA guidelines
Why isn’t there greater emphasis on screening for these macrovascular complications?
A1c target: < 7-8%

Blood pressure target: < 140/90

Cholesterol treatment: Statins
Therapies added to metformin should be based on presence or absence of CVD.
See Table 8.1 for a helpful comparison of CV/renal effects of available hyperglycemic agents.

<table>
<thead>
<tr>
<th>Efficacy*</th>
<th>Hypoglycemia</th>
<th>Weight Change</th>
<th>CV Effects</th>
<th>Cost</th>
<th>Oral/SQ</th>
<th>Renal Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ASCVD</td>
<td></td>
<td></td>
<td>Progression of DKD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CHF</td>
<td></td>
<td></td>
<td>Dosing/Use considerations</td>
</tr>
</tbody>
</table>

*Efficacy* refers to the effectiveness of the treatment in managing diabetes.

*Diabetes Care 2018;41(S1).*
Which of the following antihyperglycemic therapies has NOT been linked to a reduction in cardiovascular events or mortality?

A. Liraglutide  
B. Pioglitazone  
C. Empagliflozin  
D. Sitagliptin
A1c target: < 7-8%

Blood pressure target: < 140/90

2018 ADA Guidelines:
Management of hypertension in the patient with diabetes

Matt Bouchonville, MD
Endo ECHO
March 27, 2018

Cholesterol treatment: Statins

(Happy to share these slides with you!)

Diabetes Care 2018;41(S1).
A1c target: < 7-8%

Blood pressure target: < 140/90

Cholesterol treatment: Statins
Revised statin guidelines for 2018

- Consolidated middle and older ages
- Less aggressive recommendations for younger patients
- Increased emphasis on LDL targets

Table 9.2—Recommendations for statin and combination treatment in adults with diabetes

<table>
<thead>
<tr>
<th>Age</th>
<th>ASCVD</th>
<th>Recommended statin intensity and combination treatment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>No</td>
<td>None†</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>High, if LDL cholesterol ≥ 70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#</td>
</tr>
<tr>
<td>≥40 years</td>
<td>No</td>
<td>Moderate‡</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>High, if LDL cholesterol ≥ 70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)</td>
</tr>
</tbody>
</table>

*In addition to lifestyle therapy. †For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used. ‡Moderate-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. ASCVD risk factors include LDL cholesterol ≥ 100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD. ‡High-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. #Adults aged <40 years with prevalent ASCVD were not well represented in clinical trials of non-statin–based LDL reduction. Before initiating combination lipid-lowering therapy, consider the potential for further ASCVD risk reduction, drug-specific adverse effects, and patient preferences.

Diabetes Care 2018;41(S1).
How about other interventions besides blood glucose, blood pressure, and cholesterol lowering?
Which of the following interventions has the greatest impact on survival in patients with diabetes?

A. Blood pressure control
B. Lipid lowering
C. Aspirin
D. Smoking cessation
Smoking cessation

Meta-analysis: Smoking cessation has greater impact on survival than several other interventions
Aspirin

Secondary prevention

- Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of atherosclerotic cardiovascular disease. 

Primary prevention

- Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy in those with type 1 or type 2 diabetes who are at increased cardiovascular risk. This includes most men and women with diabetes aged ≥50 years who have at least one additional major risk factor (family history of premature atherosclerotic cardiovascular disease, hypertension, dyslipidemia, smoking, or albuminuria) and are not at increased risk of bleeding.

*Diabetes Care* 2018;41(S1).
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D., Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D., Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutierrez, Ph.D., Miguel Fiol, M.D., Ph.D., José Lapetra, M.D., Ph.D., Rosa María Lamuela-Raventos, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D., Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D., José Alfredo Martínez, D.Pharm, M.D., Ph.D, and Miguel Angel Martinez-González, M.D., Ph.D., for the PREDIMED Study Investigators

- ~7500 participants with high CV risk but NO known CVD (~50% with diabetes)
- Mediterranean diet vs low fat diet; no caloric restriction

<table>
<thead>
<tr>
<th>Mediterranean diet</th>
<th>Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olive oil*</td>
<td>≥4 tbsp/day</td>
</tr>
<tr>
<td>Tree nuts and peanuts†</td>
<td>≥3 servings/wk</td>
</tr>
<tr>
<td>Fresh fruits</td>
<td>≥3 servings/day</td>
</tr>
<tr>
<td>Vegetables</td>
<td>≥2 servings/day</td>
</tr>
<tr>
<td>Fish (especially fatty fish), seafood</td>
<td>≥3 servings/wk</td>
</tr>
<tr>
<td>Legumes</td>
<td>≥3 servings/wk</td>
</tr>
<tr>
<td>Sofrito‡</td>
<td>≥2 servings/wk</td>
</tr>
<tr>
<td>White meat</td>
<td>Instead of red meat</td>
</tr>
<tr>
<td>Wine with meals (optionally, only for habitual drinkers)</td>
<td>≥7 glasses/wk</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Discouraged</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Soda drinks</td>
<td>&lt;1 drink/day</td>
</tr>
<tr>
<td>Commercial bakery goods, sweets, and pastries‡</td>
<td>&lt;3 servings/wk</td>
</tr>
<tr>
<td>Spread fats</td>
<td>&lt;1 serving/day</td>
</tr>
<tr>
<td>Red and processed meats</td>
<td>&lt;1 serving/day</td>
</tr>
</tbody>
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José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D.,
for the PREIDMED Study Investigators*

• Cardiovascular events cut by 30%
• NNT: 61 patients
• No adverse effects

Trial stopped early at median of 4.8 yrs based on interim analysis
What happens when we combine all of these interventions?
Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Multifactorial Intervention

• Subjects
  – T2D (n=160)
  – Microalbuminuria
  – Mean age 55 yrs
  – Randomized to conventional vs intensive therapy

• Goals of intervention
  – A1c < 6.5%
  – Chol < 175 mg/dL
  – Trig < 150 mg/dL
  – SBP < 130 mmHg
  – DBP < 80 mmHg
  – ACE/ARB
  – ASA 81 mg/day
Cardiovascular death reduced by 57%
Real world experience:

How is greater recognition of the impact of multifactorial intervention affecting cardiovascular outcomes in patients with diabetes?
Fewer patients with type 2 diabetes dying of CVD.
Fewer patients with type 1 diabetes dying of CVD.
Questions?