Cardiovascular Complications of Diabetes

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Objectives

- Review Diabetes Complications (and co-existing conditions)
- Discuss, understand, and implement screening for Diabetes Complications
- Learn guideline based treatment strategies for treatment and referral for Diabetes Complications

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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)

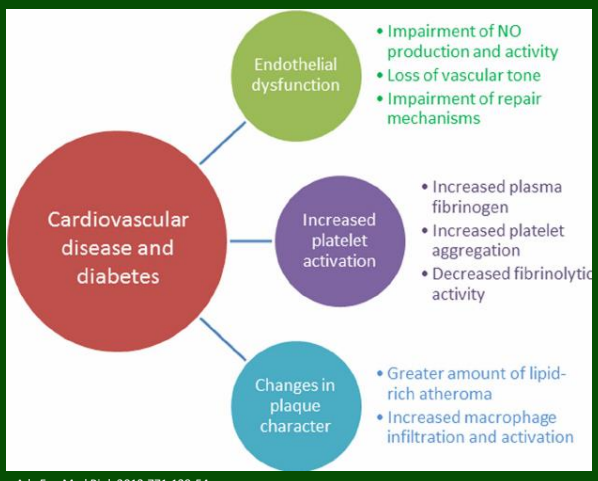
Diabetes Complications

Other complications

- Liver disease (NAFLD, NASH)
- All cause mortality risk

Pathophysiology of the connection between diabetes and cardiovascular disease

- Hyperglycemia
  - A1C? Variability, postprandial
- Chronic inflammation and thrombosis
- Dyslipidemia and atherogenesis
- Hypertension
- Inflammatory cytokines
- Endothelial dysfunction
- Oxidative stress



Adv Exp Med Biol. 2012;771:139-54
Current Cardiology Reports 17(3):566 · March 2015
Cardiovascular Endocrinology & Metabolism 7(1) 4-9: March 2018

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Risk Factors for Atherosclerotic Cardiovascular Disease (ASCVD)

- Diabetes/Insulin resistance
- Hypertension
- Hypercholesterolemia/dyslipidemia
- Cigarette smoking
- Family history
- Sedentary lifestyle/obesity
- Post-menopausal-women
- Over 45- men

Blood Pressure and Lipids

Cardiovascular Disease

Cardiovascular Disease

- Risk:
  - Stroke 2 to 4 times higher
  - Heart Disease 2 to 4 times higher
- ~75% of diabetes patients have high blood pressure (hypertension)
- ~75% of people with diabetes have a dyslipidemia (cholesterol disease)
- Diabetes confers risk about the same as pre-existing CVD in persons without diabetes

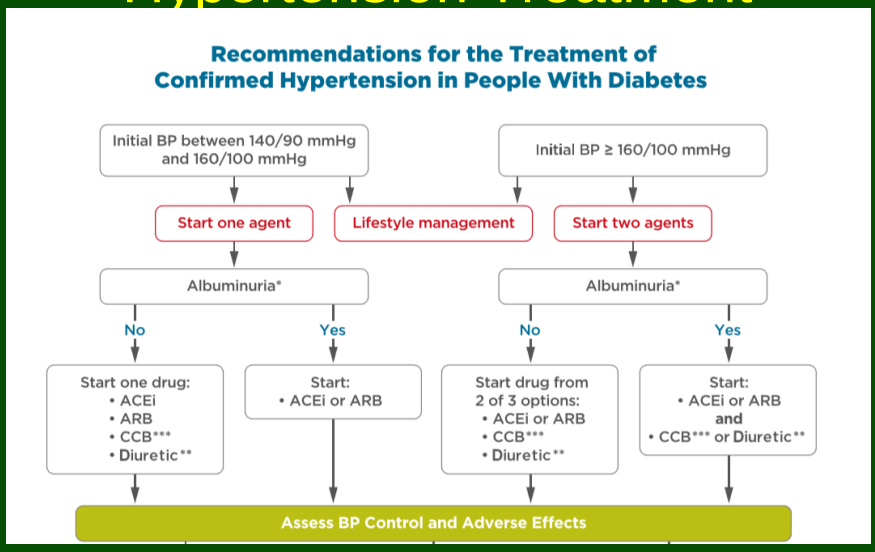
Cardiovascular Disease

- Heart disease and stroke ~65% of diabetes deaths
- **Routine screening of asymptomatic not recommended**
- Treat risk factors (lipids, BP, smoking, etc)

Blood Pressure

- Done at every visit (x2?)
- Target is <140/<90, <130/<80 if can be safely attained
- Consider weight loss if BP >120/>80

Hypertension Treatment



Be sure to check potassium levels, serum creatinine, and eGFR

Hypertension Treatment

- Lowering blood pressure reduces CVD and kidney disease
- Caveat: worsening renal function on ACEI or ARB warrants imaging of kidneys/renal arteries or nephrology referral
- If on more than one anti-hypertensive, consider giving one at bedtime

Lipids (Cholesterol)

- Increased cardiovascular risk (e.g., LDL cholesterol ≥100mg/dL [2.6 mmol/L], high blood pressure, smoking, albuminuria, and family history of premature ASCVD) and with ASCVD
- Obtain a lipid profile at initiation of statin therapy and periodically thereafter because doing so may help monitor the response to therapy and inform about adherence

American Diabetes Association
Standards of Care 2016

Lipids and Cardiovascular Complications:

"target normal"

– Total cholesterol <200

– Triglycerides <150

– HDL ("good") >40 men, >50 women

– LDL ("bad") <100, <70 high risk

These are no longer "targets", but abnormals represent "at risk"

CARDIOVASCULAR DISEASE AND RISK MANAGEMENT

Statin Treatment—Primary Prevention

10.19 For patients with diabetes aged 40–75 years without atherosclerotic cardiovascular disease, use moderate-intensity statin therapy in addition to lifestyle therapy. A

10.20 For patients with diabetes aged 20–39 years with additional atherosclerotic cardiovascular disease risk factors, it maybe reasonable to initiate statin therapy in addition to lifestyle therapy. C

10.21 In patients with diabetes at higher risk, especially those with multiple atherosclerotic cardiovascular disease risk factors or aged 50–70 years, it is reasonable to use high-intensity statin therapy. B

10.22 In adults with diabetes and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL cholesterol levels by 50% or more. C

CARDIOVASCULAR DISEASE AND RISK MANAGEMENT

Statin Treatment—Secondary Prevention

10.23 For patients of all ages with diabetes and ASCVD, high-intensity statin therapy should be added to lifestyle therapy. A

10.24 For patients with diabetes and ASCVD considered very high risk using specific criteria, if LDL cholesterol is ≥70 mg/dL on maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor). A Ezetimibe may be preferred due to lower cost.

10.25 For patients who do not tolerate the intended intensity, the maximally tolerated statin dose should be used. E

CARDIOVASCULAR DISEASE AND RISK MANAGEMENT

Statin Treatment—Secondary Prevention (continued)

10.26 In adults with diabetes aged >75 years already on statin therapy, it is reasonable to continue statin treatment. B

10.27 In adults with diabetes aged >75 years, it may be reasonable to initiate statin therapy after discussion of potential benefits and risks. C

10.28 Statin therapy is contraindicated in pregnancy. B

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Statin Intensity

High–intensity statin therapy	Moderate–intensity statin therapy
Lowers LDL by ≥ 50%: Atorvastatin 40–80 mg Rosuvastatin 20–40 mg	Lowers LDL by 30% to <50%: Atorvastatin 10–20 mg Rosuvastatin 5–10 mg Simvastatin 20–40 mg Pravastatin 40–80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Pitavastatin 2–4 mg

American Diabetes Association
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Commonly Used Anti-Lipid Medications

- Statins
  - Potent
  - Lower total cholesterol, LDL most effectively
  - Cut CVD risk by ~30%

Ezetimibe

PCSK-9 inhibitor

- Add to statin if high dose not tolerated, or if LDL is not <70 in those with CVD or high risk

Obtain a lipid profile at initiation of statins or other lipid-lowering therapy, 4–12 weeks after initiation or a change in dose, and annually thereafter as it may help to monitor the response to therapy and inform adherence.

What About Statin Intolerance?

- Be sure that's what it is
- Consider pravastatin
- Ezetimibe

Anti-Lipid Medications

Caveats:

- Use with caution in known liver disease

(but may improve fatty liver-NAFLD)

- Use with caution in more advanced kidney disease (usually dose reduction)
- Increasing muscle aches- rare complication of rhabdomyolysis

Summary: Blood Pressure and Lipids Treatment

BP:

ACEI or ARB if albuminuria or proteinuria

Lipids:

- Statins first line +/- ezitimibe
- Fibrates, Fish Oil, Niacin, Colsevelam not a lot of data
- Icosapent ehthyl (Vascepa) some benefit with very high triglycerides (>500 md/dL)

Treating these appropriately aggressively reduces CVD and renal disease

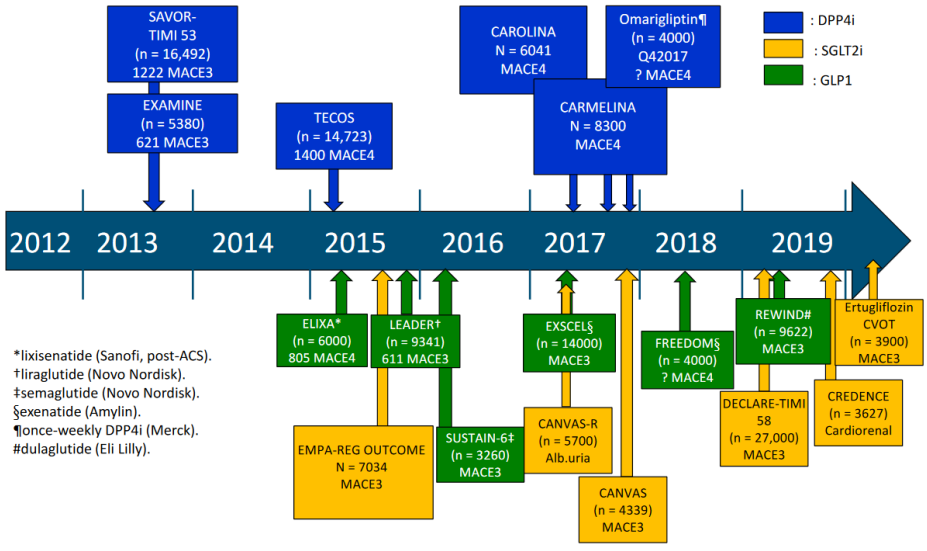
Anti-hyperglycemics and CVD

A1C and CVD Outcomes

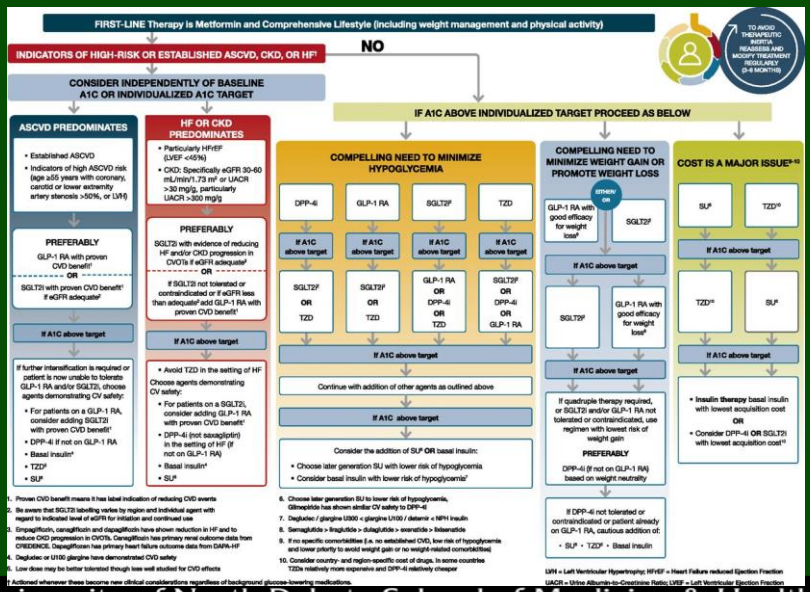
- DCCT: Trend toward lower risk of CVD events with intensive control (T1D)
- EDIC: 57% reduction in risk of nonfatal MI, stroke, or CVD death (T1D)
- UKPDS: nonsignificant reduction in CVD events (T2D).
- ACCORD, ADVANCE, VADT suggested no significant reduction in CVD outcomes with intensive glycemic control. (T2D)
- Post-prandial glucose and glucose variablility may be related to CVD

Diabetes Care 2017; 40 (Suppl. 1): S48-S56

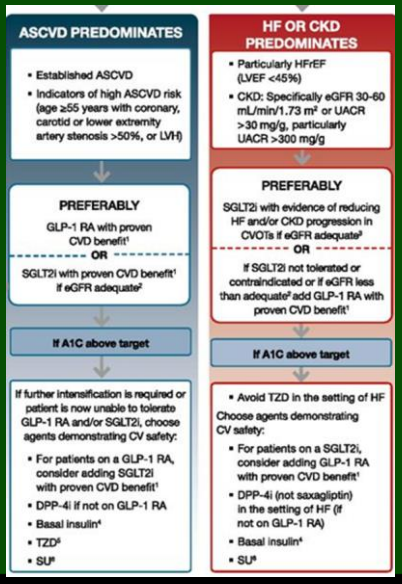
Major CV Outcome Trials in Type 2 Diabetes



Refresh: ADA Type 2 Medication Algorithm 2020



Choosing an anti-hyperglycemic agent



SGLT-2 with CVD Benefit:
Canagliflozin
Dapagliflozin
Empaglifolozin

GLP-1 with CVD Benefit:
Liraglutide
Semaglutide
Dulaglutide

Aspirin

- If no contraindications
- Men >50 years of age
- Women >50 years of age
- Younger if higher risk

American Diabetes Association. *Diabetes Care.* 2013;37(suppl 1)

Smoking

- Refer to appropriate resources
- Consider FDA approved medications
- E-cigs are NOT recommended at this time

American Diabetes Assocation
Standards of Care 2016

Heart Disease and Stroke Symptoms

- Educate patients about heart disease and stroke symptoms
- I have seen patients with fairly advanced disease without a lot of symptomotology
- Large knowledge gaps exist with patients

Pregnancy

- Statins, ACE, ARB contraindicated
- BP usually methyldopa
- Be sure to talk about this preconception

Cases

Case #1

- 32 year old with type 1 diabetes
- BP 144/86, 148/90 2 separate occasions
- No albuminuria/proteinuria
- “I’ve never had high blood pressure before”
- What next?

Case #1

- Hard for persons with type 1 to "get their heads around" having high blood pressure

Clear indication for HTN treatment

Case #2

- 56 year old female 10 years duration type 2 diabetes
- HTN on ARB
- 20 pack year history smoking, quit 3 years ago
- Chol 202 TG 260 HDL 34 LDL 104
- Now what?

Case #2

- Should be on aspirin 81 mg daily
- High risk (2 additional CVD risk factors)
- Would be tempting to use low dose statin to start
- 40-75, risk factors, high dose statin
  - Atorvastatin 40–80 mg
  - Rosuvastatin 20–40 mg

  Take time to explain why

Case 3

- TG, a 58-year-old African American, has had T2D for 8 years
- Currently being treated for hypertension (12 years) and dyslipidemia (10 years)
- History of acute coronary syndrome
- Concerned about uncontrolled blood glucose level, a recent increase in weight (5 lbs)
- Non-smoker and only occasionally consumes alcohol
- Walks 15-20 minutes, three times a week
- Diet has improved over last 5 years after consult with RD, but she admits to having a “sweet tooth”

(Continued…)

Case 3

- Physical exam:
  - General examination normal, No pallor, cyanosis, clubbing or lymphadenopathy
  - Height, 5'2" (157 cm); weight, 152 lbs (69 kg)
  - BMI, 27.8 kg/m²
  - BP, 132/86 mmHg
  - Pulse 80/min, regular, peripheral pulses well felt
  - Systemic examination- normal
  - Foot examination is normal
  - Fundus examination :Grade I non proliferative diabetic retinopathy

(Continued…)

Case 3

- Medications
  - Glimepiride 2 mg daily BID
  - Metformin sustained release preparation 1000 mg daily
  - Telmisartan 40 mg daily
  - Atorvastatin 80 mg at night
  - Aspirin 81 mg at night

(Continued…)

Case 3

- Labs:
  - A1C 8.3 %
  - Lipids TC 160, TG's 210, HDL 35, LDL 68
  - Fasting, preprandial blood glucose values 150's-160's
  - Post-prandial blood glucose values 190's-220's
  - GFR 55, serum creatinine 1.2, hepatic chemistries normal
  - Urine normal (no albuminuria)

Case 3

From the lab results, which plasma glucose patterns of hyperglycemia are present?

A. Fasting
B. Preprandial
C. Postprandial
D. Nocturnal

Case 3

A drug from which of the following drug classes could you suggest to intensify Mrs. G's treatment to manage her hyperglycemia?

A. GLP-1 receptor agonist
B. DPP-4 inhibitor
C. SGLT2 inhibitor
D. Basal insulin

Summary

- Diabetes complications can be avoided or minimized with good glucose control
- Appropriate, guideline based screening is important for early detection
- Cardiovascular is disease is extremely common in diabetes, treat risk factors appropriately
- Know when to make appropriate referrals