

V. TREATMENT OF COMORBID CONDITIONS

A. Hypertension

Screening and Diagnosis

- Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure above 130 mmHg or diastolic blood pressure above 80 mmHg should have blood pressure confirmed on a separate day.
- Orthostatic measurement of blood pressure should be performed to assess for the presence of autonomic neuropathy when clinically indicated.

Treatment

- Patients with diabetes should be treated to a systolic blood pressure <130 mmHg and a diastolic blood pressure <80 mmHg. However, many are now suggesting that lower blood pressure goals may be appropriate.
- Patients with a systolic blood pressure of 130-139 mmHg or a diastolic blood pressure of 80-89 mmHg should be given lifestyle/behavioral therapy alone for a maximum of 3 months. If targets are not achieved, pharmacological intervention should be initiated.
- Patients with systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg should receive drug therapy in addition to lifestyle/behavioral therapy.
- Some drug classes (ACE inhibitors, ARBs, β -blockers, calcium channel blockers and diuretics) have been repeatedly shown to be particularly beneficial in reducing CVD events during the treatment of uncomplicated hypertension and are therefore preferred agents for initial therapy. All patients should receive at least an ACE inhibitor or an ARB.
- If ACE inhibitors are not tolerated, ARBs may be used. Additional drugs may be chosen from these classes or another drug class to achieve blood pressure goals.
- If ACE inhibitors, ARBs, diuretics, or Tekturna (a direct renin inhibitor) are used, monitor renal function and serum potassium levels.
- Hypertensive patients with micro or macroalbuminuria:
 - In patients with type 1 diabetes, with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy.
 - In patients with type 2 diabetes, hypertension and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria.
 - In those with type 2 diabetes, hypertension and macroalbuminuria (>300 mg/day), nephropathy, or renal insufficiency, an ARB should be strongly considered and has been shown to delay the progression of nephropathy.
 - In patients with microalbuminuria or overt nephropathy, in whom ACE inhibitors or ARBs are not well tolerated, a non-dihydropyridine calcium channel blocker or β -blocker should be considered.
 - Whether or not Tekturna slows or prevents the progression of diabetic nephropathy is not yet known.
- In pregnant patients with diabetes and hypertension, blood pressure target goals of 110-129/65-79 mmHg are suggested in the interest of long-term maternal health and minimizing impaired fetal growth. ACE inhibitors and ARBs are contraindicated during pregnancy.
- In patients with a recent myocardial infarction, β -blockers should also be considered to reduce mortality.
- In elderly hypertensive patients, blood pressure should be lowered gradually to avoid complications.
- Patients not achieving target blood pressure on three drugs, including a diuretic, and patients with a significant renal disease should be referred to a nephrologist.
- See nutrition recommendations for medical nutrition therapy guidelines (pages 49-55).

B. Dyslipidemia

Screening

- Because of frequent changes in glycemic control in patients with diabetes and its effects on levels of lipoprotein, levels of LDL, HDL, total cholesterol, and triglyceride should be measured every year in adult patients.
- Patients with high risk levels who are under treatment for dyslipidemia, or who have high risk comorbid medical conditions, may require measurement of lipids more frequently.
- In children with diabetes, consideration should be given to measuring lipoproteins after age 2 years, as suggested by the National Cholesterol Education Program (NCEP) Report of the Expert Panel on Blood Cholesterol in Children and Adolescents. The recommended frequency for remeasuring lipoproteins in children with diabetes is unknown.

Treatment of Dyslipidemia

- Because all individuals who have diabetes should be considered a CVD risk equivalent:
 - The primary goal is an LDL <100 mg/dL (2.6 mmol/l).
 - Drug therapy is optional for an LDL of 101-129 mg/dL.
 - Drug therapy should be seriously considered for an LDL of >130 mg/dL.
 - A lower LDL cholesterol goal of <70 mg/dL (1.8 mmol/l), using a high dose of a statin, is an option for high risk patients.
- Aggressive therapy of dyslipidemia will reduce the risk of CAD in patients with diabetes.
- Primary therapy should be directed first at lowering LDL levels.
 - The initial therapy should be to use statins; however, if this fails to reach the goal, then the addition of a resin or ezetimibe should be considered.
 - HDL cholesterol goals should be >40 mg/dL (1.0 mmol/l) in men and >50 mg/dL in women.
 - If the HDL is below those levels, a fibric acid such as fenofibrate might be used in patients with LDL cholesterol between 100 and 129 mg/dL.
- The initial therapy for hypertriglyceridemia is improved glycemic control.
 - Triglycerides should be lowered to <150 mg/dL (1.7 mmol/l).
 - Behavioral modification with weight loss, increased physical activity, and moderation of alcohol consumption can be useful in treating hypertriglyceridemia. See nutrition recommendations for medical nutrition therapy guidelines on pages 49-55.
 - Additional triglyceride lowering can be achieved with very high dose statins (for subjects with both high LDL and triglyceride levels) or fibric acid derivatives (gemfibrozil or fenofibrate).
- In some cases when goals are not achieved, combination lipid therapy may be initiated. Several options are available, but these combinations have not been evaluated in outcome studies for either CVD event reduction or safety.
 - The combination of statins with nicotinic acid and especially with gemfibrozil or fenofibrate has been associated with increased risk of myositis, although the risk of clinical myositis (as opposed to elevated creatinine phosphokinase levels) appears to be low.
 - The combination of statins with nicotinic acid is effective in modifying diabetic dyslipidemia (with the largest increases in HDL cholesterol levels), but the combination may worsen hyperglycemia and thus frequent monitoring of glucose levels is recommended to observe for this.
 - Other available combinations include statin and a resin, ezetimibe or Omega-3 polyunsaturated fatty acids.

C. Cardiac Disease

Screening

Screening protocols for hypertension and dyslipidemia are often indicators of coronary risk (see Hypertension and Dyslipidemia Sections). According to a Consensus Panel of the American Diabetes Association (ADA) and American College of Cardiology (ACC), stress testing should be performed for patients with diabetes who have any of the following:

1. Typical or atypical cardiac symptoms
2. Resting ECG suggestive of ischemia or infarction
3. Peripheral or carotid occlusive arterial disease
4. Sedentary lifestyle, age 35 or older, and plans to begin a vigorous exercise program

Positive screening is an indication for stress echocardiogram or nuclear stress test and/or cardiac catheterization. Referral to a cardiologist should be initiated.

There are no evidenced-based guidelines for screening the asymptomatic patient with diabetes for CAD.

Treatment

1. Aspirin at 81 mg/day or higher
2. Treat hypertension and dyslipidemia (see Hypertension and Dyslipidemia sections)
3. Aggressive treatment of diabetes
4. An ACE inhibitor should be considered in patients >55 years of age, with or without hypertension, who have another CVD risk factor (history of CVD, dyslipidemia, microalbuminuria or tobacco use)
5. Beta-blockers should be considered to reduce mortality in patients undergoing major surgery or with a prior myocardial infarction
6. Metformin use is contraindicated in patients with treated CHF
7. TZDs are associated with fluid retention and their use can be complicated by the development of CHF; caution in their use is advised

D. Peripheral Vascular Disease

Screening

Annually perform a comprehensive foot examination and provide self-care education for patients with diabetes to identify risk factors predictive of ulcers and amputations.

Routine foot examination is the most important means for assessing vascular insufficiency in the lower extremities of patients with diabetes. This should include the use of a monofilament, tuning fork, palpation, and a visual examination including the assessment of:

- Pallor or dependent rubor
- Loss of hair
- Atrophy of skin
- Cornification of the nails
- Fissures or ulcerations
- Temperature demarcation
- Venous-filling time
- Pulse

People with neuropathy should have a visual inspection of their feet at every visit with a health care professional.

Patients at risk should understand the implications of the loss of protective sensation; the importance of foot monitoring on a daily basis; the proper care of the foot, including nail and skin care; and the selection of appropriate foot wear.

Treatment

- Refer patients who smoke or who have prior lower extremity complications to foot care specialists for on-going preventive care and lifelong surveillance.
- Initial screening for peripheral arterial disease should include a history for claudication and an assessment of the pedal pulses. Consider obtaining an ankle-brachial index (ABI), as many patients with peripheral arterial disease (PAD) are asymptomatic.
- The following foot related risk conditions are associated with an increased risk of amputation:
 - Peripheral neuropathy with loss of protective sensation
 - Altered biomechanics in the presence of neuropathy
 - Evidence of increased pressure, such as erythema or hemorrhage under a callous
 - Bony deformity
 - Peripheral vascular disease with decreased or absent pedal pulses
 - A history of ulcers or amputation
 - Severe nail pathology
- Refer patients with significant claudication or a positive ABI to a vascular surgeon for further assessment and consider exercise, medications, and surgical options.
- People with neuropathy or evidence of increased plantar pressure may need to be managed with well-fitted walking shoes or athletic shoes.
- Hypertension, diabetes, and dyslipidemia must be treated vigorously.

Noninvasive vascular testing may include:

- Doppler systolic pressure measurements
- Ankle/brachial index
- Doppler waveform analysis
- Transcutaneous oxygen pressure
- Duplex color flow scanning
- Magnetic resonance angiography (MRA)

Any question of ischemia should necessitate a vascular consultation for the possible need for revascularization.

REFERENCE SECTION V

Aliskiren (Tekturna) for Hypertension. *The Medical Letter on Drugs and Therapeutics*. Issue 1258. 49:29-31. April 2007

American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus. The AACE System of Intensive Diabetes Self-Management, 2002 Update. *Endocrine Practice*. 8:Supplement 1. January/February 2002

American College of Physicians PIER (Physicians Information and Education Resource). <http://pier.acponlin.org>

American Diabetes Association. Clinical Practice Recommendations. *Diabetes Care*. 30(Suppl. 1):S15-S16, S16-S17, S18-19, S22-S24. 2007

Aspirin for Primary Prevention of Cardiovascular Disease (Revisited). *The Medical Letter on Drugs and Therapeutics*. Issue 1258. 48:53. July 2006

Detection, Evaluation and Treatment of High Blood Cholesterol. Adult Treatment Panel III. National Cholesterol Education Program. National Heart, Lung and Blood Institute. National Institutes of Health. NIH Publication No. 01-2670. May 2001

Johnstone M, Veves A. *Diabetes and Cardiovascular Disease*. Totowa, NJ. Humana Press. 2nd Edition. 2005

Leahy J, Clark N, Cefalu W. *Medical Management of Diabetes Mellitus*. New York, NY. Marcel Dekker, Inc. 2000