

9.0 Chronic complications of diabetes

9.1 Recommendations

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9.2 Prevention and management of cardiovascular disease

Cardiovascular disease (CVD) is the major cause of mortality for individuals with diabetes. It is also a major contributor to morbidity, direct and indirect costs of diabetes. The main factors affecting increased mortality and morbidity are hypertension, dyslipidaemia, prothrombotic state, and smoking. Management of risk factors and screening for coronary artery disease involves blood pressure control, management of lipids, use of anti-platelet agents and actively supporting cessation of smoking.

9.2.1. Control of Blood Pressure:

9.1.1.1 Rationale

Hypertension is a common co-morbidity of diabetes, affecting 20-60% of people with diabetes. Hypertension is also a major risk factor for CVD and but also for microvascular complications such as retinopathy and nephropathy. In type 1 diabetes, hypertension is often the result of underlying nephropathy. In type 2 diabetes, hypertension is likely to be present as part of the metabolic syndrome (with abdominal obesity, hyperglycaemia, dyslipidaemia) that is accompanied by high rates of CVD, in particular stroke.

9.1.1.2 Recommendations

Screening and diagnosis:

- Blood pressure should be measured at every routine visit.
- Patients found to have a systolic blood pressure >130 mmHg or diastolic blood pressure \geq 80 mmHg should have blood pressure confirmed on a separate day.

Targets:

- Patients with diabetes should be treated to a blood pressure $\leq 130/80$ mmHg.

Treatment:

- Patients with blood pressure of $\geq 140/90$ mmHg should start drug therapy in addition to lifestyle and behavioural modification.
- Most patients would require two or more agents at proper doses to achieve blood pressure targets.
- Patients with a systolic blood pressure of 131 -139 mmHg or a diastolic blood pressure of 81-89 mmHg failing to achieve targets on lifestyle and behavioural modification alone within a maximum of 3 months should be started on pharmacological agents
- Initiate medication for lowering blood pressure in diabetes not complicated by raised albumin excretion rate, using any agent except for α -adrenergic blockers, and actively titrating dose according to response
- ACE-inhibitors and A2RBs may offer some advantages over other agents in some situations (prevention of microvascular disease)
- β start with β -adrenergic blockers in people with angina, β -adrenergic blockers or ACE-inhibitors in people with previous myocardial infarction, ACE inhibitors or diuretics in those with heart failure
- care should be taken with combined thiazide and β -adrenergic blockers because of risk of deterioration in metabolic control.
- Monitor renal function and serum potassium levels in patients treated with ACE inhibitors or ARBs.
- Add other anti-hypertensive medications as needed to achieve blood pressure control targets
- Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, labetalol, nifedipine LA, diltiazem, clonidine and prazosin. ACE-inhibitors and ARBS are contraindicated during pregnancy.
- In patients with wide fluctuation of blood pressure, 24-hour ambulatory monitoring should be considered.

9.2.1 Management of dyslipidaemia

9.2.1.1 Rationale

Diabetes is associated with a form of dyslipidaemia characterized by a modestly elevated total cholesterol, triglyceride and low HDL cholesterol. Lipid management aimed at lowering LDL cholesterol has been shown to reduce macrovascular disease and mortality in patients with type 2 diabetes, particularly those who have had prior cardiovascular events.

9.2.1.2 Recommendations

Assessment:

- Lipid assessments should be done annually or more often if not to target to monitor response to life style modification and therapy.

Treatment goals:

- Lifestyle modification focusing on the reduction of saturated fat, *trans* fatty acids, cholesterol intake and weight loss (if indicated), and increased physical activity have been shown to improve the lipid profile in patients with diabetes.
- The primary goal is:
 - LDL <100 mg/dl (≤ 70 mg/dl confers an added benefit).
 - HDL cholesterol to >40 mg/dl (>50 mg/dl may be considered in women).
 - Triglycerides level of <150 mg/dl.

Therapeutic options:

- For LDL-cholesterol of 100-130 mg/dl, life style modification should be advised; if targets are not achieved within 3 months a statin should be started
- For LDL-cholesterol >130 mg/dl a statin should be started along with life style modification
- High-risk patients such as those with cardiovascular disease should be started on a statin, irrespective of blood lipid level.
- Consider more aggressive therapy in high risk patients to achieve an LDL of <70 mg/dl
- If the HDL is <40 mg/dl and the LDL between 100 and 129 mg/dl, a fibric acid derivative, nicotinic acid derivatives, or concentrated fish oils might be used.
- If the triglycerides ≥ 400 mg/dl consider treatment after optimizing glycaemic control.

9.2.3 Anti-platelet agents

9.2.3.1 Recommendations

- Use aspirin (75–100 mg/day) in people with cardiovascular disease
- Consider aspirin (75–100 mg/day) as a primary prevention strategy in those with increased cardiovascular risk, including those who are >40 yr of age, or who have additional risk factors (family history of CVD, hypertension, smoking, dyslipidaemia, or albuminuria).

9.2.4. Smoking cessation

All people with diabetes should not smoke.

9.2.4.1 Recommendation

- Smoking cessation counselling and treatment should be offered to smokers.

9.3 Screening and treatment of diabetic kidney disease

9.3.1 Clinical classification:

- Incipient (sub-clinical) nephropathy (albumin excretion rate 30 -299 mg/24-h)
- Clinical (overt) nephropathy (albumin excretion rate ≥ 300 mg/24-h)
- Nephropathy with decrease in glomerular filtration rate
- End-stage renal disease, necessitating dialysis or renal transplantation.

9.3.2 Evidenced-based objective

- To reduce the risk and/or slow the progression of nephropathy, optimize glucose and blood pressure control.

9.3.3 Recommendations:

9.3.3.1 Screening

- Screen for microalbuminuria annually and pre- and during pregnancy.
- Assess microalbuminuria as albumin/creatinine ratio on a first pass urine sample.
- Diagnose microalbuminuria if A/C ratio is > 2.5 mg/mmol in women or > 3.5 mg/mmol in men in at least 2/3 samples.
- Measure serum creatinine annually and calculate eGFR.

9.3.3.2 Treatment:

- In the treatment of both micro- and macroalbuminuria, either ACE inhibitors or ARBs should be used except during pregnancy
- Reduction of protein intake may be advised in the later stages of CKD in conjunction with nephrologists
- In albuminuria or nephropathy, if patients are unable to tolerate ACE inhibitors and/or ARBs, use of non-DCCBs, β -blockers and diuretics for the management of blood pressure may be considered. Non-DCCBs may reduce albuminuria in people with diabetes including during pregnancy
- Consider referral to a physician experienced in the care of diabetic renal disease when the estimated GFR has fallen to < 45 ml/min/ 1.73 m².

9.4 Retinopathy screening and treatment

9.4.1 Screening

- People with diabetes should have a comprehensive eye examination annually by a retinal camera or an ophthalmologist or optometrist at diagnosis and annually.
- Examinations will be required more frequently if retinopathy is progressing

- Women who are planning pregnancy or become pregnant should have a comprehensive eye examination and should be counselled on the risk of development and/or progression of diabetic retinopathy. Eye examination should occur in the first trimester with close follow-up throughout pregnancy and for 1 year postpartum. This recommendation does not apply to women who develop GDM.

9.4.2 Treatment

- Optimize blood pressure and blood glucose control.
- Laser therapy should be available and should be done by well-trained ophthalmologists.

9.4.3 Referrals

Diabetes and eye clinics in each institution should agree and honour the criteria for emergency (same day, active vitreous haemorrhage), urgent (1 week; new vessels) and routine referrals (1 month).

In general, findings indicating the need for referral to an ophthalmologist within one month for further management are:

- Non-proliferative retinopathy with macular involvement, or without macular involvement but with large circinate hard exudates
- Hard exudates within one disc diameter of the macula
- Pre-proliferative retinopathy
- Unexplained decreased visual acuity.

9.5 Neuropathy

9.5.1 Clinical considerations

Manifestations may occur in both the peripheral and autonomic nervous systems.

Peripheral neuropathy includes:

- Polyneuropathies, including distal sensory-motor neuropathy and proximal motor neuropathy
- Focal neuropathies, including mono-neuropathies (including cranial) and entrapment neuropathies
- Multifocal neuropathies.

Autonomic neuropathy may involve the following systems:

- Cardiovascular: resting tachycardia, postural hypotension
- Gastrointestinal: gastroparesis, diarrhoea, constipation
- Genitourinary: atonic bladder, Erectile dysfunction

9.5.2 Recommendations

- Patients with diabetes should be screened annually for DPN using tests such as pinprick sensation and vibration perception (using a 128-Hz tuning fork), and 10-g monofilament pressure sensation at the distal plantar aspect of both great toes and ankle reflexes
- Simple inspection of insensate feet should be performed at 3- to 6-month intervals. An abnormality should trigger referral for podiatrist or special footwear, or podiatric care.
- Painful neuropathy requires symptomatic relief with tricyclic drugs, and if symptoms persist use gabapentin, pregabalin or duloxetine.
- Be alert to manifestations of autonomic neuropathy (resting tachycardia (>100 bpm), orthostatic hypotension (a fall in systolic blood pressure >20 mmHg upon standing), constipation, diarrhoea, faecal incontinence, gastroparesis, erectile dysfunction and hypoglycaemic unawareness.

9.6 Foot care

9.6.1 The high-risk foot

The risk of ulcers or amputations is increased with duration of diabetes and in males, smokers, people with poor glucose control, or with cardiovascular, retinal or renal complications.

The following are features of high risk foot:

- Peripheral neuropathy with loss of protective sensation
- Altered biomechanics (in the presence of neuropathy)
- Evidence of increased pressure (erythema, haemorrhage under a callus)
- Bony deformity
- Peripheral vascular disease (decreased or absent pedal pulses)
- A history of ulcers or amputation
- Severe nail pathology
- Poor hygiene

9.6.2 Recommendations:

- Educate all patients about the risk and prevention of foot problems and reinforce self-care behaviour
- Examine feet annually including the use of monofilament, tuning fork, palpation of peripheral pulses, and a visual examination
- Identify high risk feet (see above criteria) and provide:
 - referral to someone with professional skills in the management of at risk feet
 - reinforced diabetes foot education

- re-examination of feet at each clinical consultation
- In those with diminished peripheral pulses and symptoms of ischaemia consider Doppler examination and referral to vascular surgeons.