REVIEW

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Preventing and managing diabetic complications in elderly patients

ABSTRACT

Elderly patients with diabetes are prone to a number of complications, some of which take precedence over or hinder or preclude the intensive glucose control recommended for younger diabetic patients. This article reviews some of these complications, including coronary artery disease, retinopathy, neuropathy, nephropathy, and others.

KEY POINTS

Compared with strict glycemic control, treating cardiovascular risk factors offers more benefit in a shorter time and should be a higher priority.

Diabetic retinopathy is a leading cause of blindness. Yearly eye examinations are recommended.

Elderly patients with diabetes are prone to rapidly progressive nephropathy, especially after receiving iodinated contrast agents. Good glycemic control and control of blood pressure, especially with angiotensin-converting enzyme inhibitors, reduce the risk and the rate of progression.

Elderly patients with diabetes are at higher risk of cognitive decline, depression, and polypharmacy, all of which impede good diabetes management.

IN ELDERLY PATIENTS, as in all patients, diabetes is much more than the blood glucose level. However, in elderly patients the disease accelerates other common conditions of that population and markedly complicates their management.

Hypertension, coronary artery disease, and cerebrovascular attacks are more common in patients with diabetes.[1] Longitudinal studies of elderly and middle-aged people with diabetes show increased rates of cognitive decline and dementia.[2–4] Depression, urinary incontinence, and falls are also more common in elderly patients with diabetes. Physical disability is also increased: women with diabetes are half as likely to be able to manage ordinary physical tasks such as walking, climbing stairs, and doing housework as women without diabetes.[5]

In an earlier paper in this journal,[6] we reviewed the management of diabetes per se in elderly patients. In the pages that follow, we review the management of its associated conditions.

HEART RISK TRUMPS BLOOD SUGAR

Coronary artery disease is by far the leading cause of death in elderly people with diabetes: 40% to 50% of patients with type 2 diabetes die of cardiac disease.[7–9] The conventional risk factors—hypertension, hyperlipidemia, smoking, and diabetes—remain risk factors throughout old age. Risk reduction should focus on treating hypertension and dyslipidemia, smoking cessation, aspirin therapy, and exercise. While glycemic control reduces the risk of microvascular complications (eg, diabetic retinopathy and nephropathy) after about 8 years of treatment, benefits from con-

trol of elevated blood pressure and cholesterol occur after only 2 to 3 years.

Tight control of hypertension confers significant benefit

The United Kingdom Prospective Diabetes Study (UKPDS)[10] found that patients who had tight control of blood pressure (mean treated blood pressure 144/82 mm Hg) had 24% fewer diabetes-related end points, 32% fewer diabetes-related deaths, 44% fewer strokes, a 34% reduced risk of deterioration of retinopathy, and a 47% reduced risk of visual deterioration than patients who had usual control (mean treated blood pressure 157/87 mm Hg). The benefit of treating hypertension outweighed the benefits of tight glycemic control.

A strong focus on blood pressure control should be a major focus of any treatment program. The American Geriatrics Society goal for blood pressure is less than 140/80 mm Hg if tolerated. Others have proposed more stringent targets.

Lipid control

Coronary artery disease is by far the leading cause of death in elderly people with diabetes

Lipid control is integral to managing elderly patients with diabetes. In the Cholesterol and Recurrent Events trial[11] and the Heart Protection Study,[12] the cardiovascular benefits of reducing serum low-density lipoprotein cholesterol (LDL-C) levels were similar in elderly and younger patients with diabetes. In a meta-analysis of secondary prevention trials, absolute risk reduction was greatest in subjects older than 65 years with either diabetes or diastolic hypertension.

The American Diabetes Association,[13] the American Geriatrics Society,[14] and the Department of Veterans Affairs[15,16] have all set a goal for serum LDL-C of less than 100 mg/dL. In addition, the American Diabetes Association has set goal levels for triglycerides (< 150 mg/dL) and high-density lipoprotein cholesterol (> 40 mg/dL).

Glycemic control

The importance of tight glycemic control in preventing coronary heart disease in the elderly is somewhat controversial. Treatment guidelines for elderly patients with diabetes are mainly extrapolated from the UKPDS, in which patients were a mean of 54 years old at the start of the study. After 10 years, the mean hemoglobin A_{1c} levels were 7.9% in patients receiving conventional control and 7.0% in patients with intensive therapy. Every 1% reduction in hemoglobin A_{1c} was associated with a 37% decline in microvascular complications of diabetes, a 14% decline in myocardial infarctions, and a 21% decline in any diabetes-related outcome.[17]

In the original trial,[18] the rate of myocardial infarction was 17.4% in the conventional treatment group vs 14.7% in the intensive group ($P = .052$), and the risk of stroke did not differ. No thresholds for realizing benefits from reducing fasting glucose or hemoglobin A_{1c} levels were detected.

A recent cohort study involving about 10,000 participants aged 45 to 79 years found that the risk of cardiovascular disease and death from any cause increased continuously with increasing hemoglobin A_{1c} levels in people with or without diabetes.[19] However, the impact of treatment remains to be clarified. The Action to Control Cardiovascular Risk in Diabetes trial will address this question (and others), but results will not be available for several years.

RETINOPATHY IS A MAJOR CAUSE OF BLINDNESS

Diabetic retinopathy, a leading cause of blindness in the United States, is perhaps the most threatening of the chronic microvascular complications of diabetes for elderly patients. The strongest predictor of retinopathy is the duration of diabetes.[20–22] Retinopathy is classified as being nonproliferative, preproliferative, or proliferative.

Ischemia is believed to be the major cause of diabetic retinopathy, and glucose control has been shown to be of major benefit. A study of young adults with type 1 diabetes found that intensive therapy reduced the risk of developing retinopathy by 76% and slowed the progression of retinopathy by 54%. Comparable data for patients with type 2 diabetes are lacking.

Of some concern is a study in which retinopathy progressed more rapidly during the first year of aggressive insulin therapy in elderly patients with diabetes and baseline

retinopathy.[23] Further research is needed to identify which subgroups would benefit most from aggressive glycemic control.

In addition to specific ophthalmologic treatment, managing cardiovascular risk factors may reduce the progression of retinopathy: each cardiovascular risk factor has been found to also be a risk factor for retinopathy. Hypertension is an independent risk factor for any retinopathy, and its tight control reduces progression.[20,24] Aspirin therapy has not been found to confer either risk or benefit.[25,26]

Although guidelines typically call for yearly ophthalmic examinations to screen for retinopathy, whether this is cost-effective has been questioned.[27,28] But people older than 65 years with diabetes also have twice the risk of developing cataracts and three times the risk of developing glaucoma than those without diabetes. Considering the effects of visual loss on quality of life as well as the subsequent higher risk of accidents, eye examinations by an ophthalmologist at the time of diagnosis and annually thereafter are recommended. Tight glycemic and blood pressure control remains the cornerstone in the primary prevention of diabetic retinopathy. Panretinal and focal retinal laser photocoagulation reduces the risk of visual loss in patients with severe retinopathy and macular edema, respectively.[29]

NEUROPATHY PRESENTS IN MANY FORMS

Neuropathy is a particularly distressing complication and can lead to loss of sleep, limitation of activity, and depression.[26,30,31] Diabetic neuropathies include focal neuropathies (entrapment syndromes and mononeuropathies), polyneuropathy, and autonomic neuropathy.

Distal symmetric polyneuropathy ("glove and stocking" sensory symptoms) is the most common neuropathy of elderly people with diabetes. Pain, which can interrupt sleep and limit activity, can be treated with the anticonvulsants gabapentin (Gabarone, Neurontin), phenytoin (Dilantin, Phenytek) and carbamazepine (Carbatrol, Epitol, Equetro, Tegretol), and with tricyclic antidepressants. However, the anticholinergic effects of tricyclic antidepressants limit their use in older patients. Newer agents, such as duloxetine (Cymbalta) and pregabalin (Lyrica) show promise.[30,31] Dysesthesia of a burning quality is sometimes treated with topical capsaicin or with oral mexiletine (Mexitil), although their role in treating older patients is not well established.

Patients with distal sensory polyneuropathy are predisposed to develop Charcot joints, which may mimic gout or degenerative joint disease. Plain radiography of the foot can help differentiate these diseases. Distal sensory polyneuropathy also predisposes patients to neuropathic foot ulcer, the leading cause of foot amputation in the United States.[32]

Feet should be inspected at each office visit. Testing sensation with a monofilament detects sensory neuropathy. Patients should be encouraged to examine their feet daily. Therapeutic shoes, prescribed by a podiatrist and individually designed to prevent blisters, calluses, and ulcers, are covered by Medicare for peripheral neuropathy if any of the following are also present: callus formation, poor circulation, foot deformity, or a history of foot callus, ulcer, or amputation (partial or complete). Medicare will pay for one pair of shoes plus three pairs of inserts per year.

Proximal motor neuropathy (diabetic amyotrophy) primarily affects elderly patients. It begins with unilateral thigh pain, which becomes bilateral and progresses to proximal muscle weakness and wasting. Distal symmetric polyneuropathy may also be present. Treatment includes glycemic control (usually with insulin) and physical therapy. Some forms of amyotrophy respond to immunotherapy.

Autonomic neuropathy, although not painful, can be the most life-threatening form of diabetic neuropathy.[33] Tachycardia increases the risk of sudden death, while postural hypotension increases the risk of syncope, falling, and injury. Other forms of autonomic neuropathy include neurogenic bladder, sexual dysfunction, gastropathy (which is particularly sensitive to glycemic control), enteropathy, and gustatory sweating. Patients with autonomic neuropathy are more likely to have hypoglycemic unawareness.

Of concern: The risk of eye disease may increase in the first year of tight glucose control

NEPHROPATHY CAN PROGRESS RAPIDLY

Elderly patients with diabetes are especially at risk of developing nephropathy, which pro-

gresses from microalbuminuria to overt proteinuria to renal insufficiency and end-stage renal disease. Nephropathy may develop over a shorter time than the typical 10 to 20 years in younger patients. Independent risk factors for proteinuria and renal insufficiency include poor glycemic control over many years, hypertension, longer duration of diabetes, male sex, high serum total cholesterol levels, and smoking. Elderly patients are also at risk of renal insults such as receiving intravenous iodinated contrast agents in the course of radiologic procedures, nephrotoxic drugs, and comorbid illness such as congestive heart failure.

The diagnosis of diabetic nephropathy is usually made clinically and not by renal biopsy. Diabetic nephropathy can be diagnosed with almost 100% specificity in type 1 diabetes and more than 85% specificity in type 2 diabetes by a urinary albumin excretion of more than 300 mg per day and an appropriate time course in the absence of other obvious causes of renal disease. The urinary albumin-to-creatinine ratio can be used to screen for microalbuminuria (the precursor of frank proteinuria and renal insufficiency). A value of more than 30 mg of albumin per gram of creatinine suggests that albumin excretion exceeds 30 mg and that microalbuminuria is present.

End-stage renal disease may follow acute renal failure after a radiologic procedure with iodinated contrast

Prevention is a cornerstone of management. Good glycemic control reduces the risk of microalbuminuria, the progression of albuminuria, and the development of renal insufficiency. Lowering blood pressure reduces the decline in glomerular filtration rate and albuminuria. Angiotensin-converting enzyme (ACE) inhibitors reduce the rate of progression of proteinuria and reduce the rate of end-stage renal disease, although the data are stronger in patients with type 1 diabetes.[34] When side effects such as cough limit the use of ACE inhibitors, angiotensin receptor blockers can be used as an alternative. Blood pressure should be controlled to reduce stroke and cardiovascular complications, regardless of whether microalbuminuria is present.[35]

End-stage renal disease in elderly patients with diabetes is becoming increasingly frequent. Nephropathy in older patients is different from that in younger patients. In elderly patients, the pathologic findings may suggest ischemia and hypertension, and the classic Kimmelstiel-Wilson lesions may be absent. Patients may present with end-stage renal disease following an episode of acute renal failure that does not resolve, which may occur after a radiologic procedure involving an iodinated contrast agent.

NONKETOTIC HYPEROSMOLAR COMA

Nonketotic hyperosmolar coma occurs predominantly in elderly patients with type 2 diabetes. Predisposing factors include dementia, infection, stroke, and myocardial infarction. Coma results from osmotic diuresis due to hyperglycemia and consequent dehydration. A drop in the glomerular filtration rate promotes further hyperglycemia and dehydration in a vicious circle. Glucose levels commonly reach 600 mg/dL or more, and serum osmolality often exceeds 320 mOsm/L. A fluid deficit of 5 to 10 L is typical.

Fluid replacement is the mainstay of treatment. Because free water is typically lost in an osmotic diuresis, 0.9% (normal) saline is usually given if hemodynamic instability is present or 0.45% (half-normal) saline otherwise. Insulin is also required, as is specific treatment of the precipitating cause, eg, infection. Ketoacidosis may also occur in the elderly.

Recovery from coma or improvement in mental status may lag behind correction of the serum osmolality and may take several days. Mortality rates can be high: severe hyperosmolarity, advanced age, and nursing home residence are the major risk factors for death.

INFECTIONS: SEVERE AND UNUSUAL

Elderly patients with diabetes are at increased risk of developing severe and unusual infections, particularly malignant external otitis. Necrotizing *Pseudomonas aeruginosa* infection initially involves the external ear canal and progresses to the mastoid air cells, the skull base, or temporal bone. The clinical presentation consists of fever, otalgia, otorrhea, and less commonly, cranial nerve palsy. Treatment involves surgical debridement and antibiotics.

Other infections associated with diabetes include rhinocerebral mucormycosis, necrotizing fasciitis, emphysematous cholecystitis, and

emphysematous pyelonephritis. An elderly patient with diabetes is also at increased risk of renal papillary necrosis, which presents as insidious renal failure.

COGNITIVE IMPAIRMENT

Elderly people with diabetes are at increased risk of cognitive impairment, which poses a barrier to taking medications appropriately and performing other tasks of self-management.

Because dementia may go undetected, particularly in the early stages, cognitive function should be assessed in elderly patients when they fail to take therapy correctly or have frequent episodes of hypoglycemia, or if glycemic control deteriorates without an obvious explanation. Caregivers play a critical role in detecting and reporting early cognitive impairment.

DEPRESSION IS OFTEN UNDETECTED

Elderly patients with diabetes have a higher rate of depression than do age-matched controls, but it is commonly underdetected and undertreated.[5,36] Depression has been associated with poor glycemic control, and treatment of depression is associated with improved control. Routine screening for depression should be performed; a variety of diagnostic instruments are available. Particular attention should be given to medications that are associated with depression.

POLYPHARMACY

Many elderly patients take multiple medications. Polypharmacy increases the risk of drug side effects, interactions, and nonadherence to taking medications.[37–39] This problem is increased in diabetes, in which several medications are necessary to manage hyperglycemia, hyperlipidemia, hypertension, and other associated conditions.

Patients should keep accurate medication lists, including over-the-counter medications, herbs, and nutritional supplements. Physicians should carefully review each medication to check if it is appropriate and used correctly.

FALLS

Elderly patients with diabetes mellitus are at increased risk of injurious falls, which are associated with high rates of complications, death, and functional decline.[40,41] Risk factors include frailty and functional disability, visual impairment, peripheral or autonomic neuropathy, hypoglycemia, and polypharmacy.

Elderly patients should be screened for their risk of falls, and appropriate measures should be instituted. The American Geriatrics Society has guidelines for preventing falls in the elderly.[41]

URINARY INCONTINENCE

Elderly women with diabetes are at increased risk of developing urinary incontinence. Risk factors include autonomic neuropathy (causing either neurogenic bladder or fecal impaction), polyuria due to hyperglycemia, and urinary tract and vaginal infections. Although evidence is lacking that urinary incontinence affects glycemic control, assessing and treating the condition improves quality of life.

SUMMARY

Diabetes is a common problem in the elderly, accounting for considerable morbidity and mortality. In a large longitudinal analysis (> 50,000 patients), elderly persons newly diagnosed as having diabetes experienced high rates of complications during 10-year follow-up, far in excess of elderly persons without diabetes.[42] Diabetes is underdiagnosed in the elderly and is frequently undertreated. Management of the elderly with diabetes presents unique challenges because of associated comorbidities, but with attention to detail and individualized approaches, quality and duration of life can be optimized. The greatest attention should be given to reduction of overall cardiovascular risk. Glycemic goals and the treatment regimens to achieve those goals should be individualized and chosen to control hyperglycemic symptoms and achieve the maximal glycemic control possible while minimizing the risk of hypoglycemia. Diabetes will continue to be a challenge to the patient, the physician, the care team, and the health care system. ■

Review the patient's meds, including herbs, supplements, and over-the-counter drugs

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