Evidence-based Approach to Diabetes Screening, Diagnosis and Treatment

David C. W. Lau, MD, PhD, FRCPC, Professor of Medicine, Biochemistry and Molecular Biology; Director, Julia McFarlane Diabetes Research Centre, University of Calgary, Calgary, AB.

As the population ages, the diagnosis of Type 2 diabetes is expected to skyrocket over the next two decades. Diabetes is diagnosed by a fasting venous plasma glucose level of equal to or greater than 7mmol/L or, in the presence of classic symptoms of hyperglycemia, a casual plasma glucose value greater than 11.1mmol/L. Early diagnosis, screening and prevention of diabetes in the elderly will greatly reduce the burden of this serious chronic disease that is associated with increased morbidity and mortality.

Key words: impaired glucose tolerance, diagnosis, screening, prevention, Type 2 diabetes

The Diabetes Epidemic

Diabetes is now reaching epidemic proportions in Canada and the U.S.[1,2] It has been estimated that one in five adults 65 years of age or older will develop Type 2 diabetes.[3] As the population ages, the diagnosis of Type 2 diabetes among elderly Canadians is expected to skyrocket over the next two decades. Since diabetes is a serious chronic disease associated with significantly increased morbidity and mortality, early screening and diagnosis, optimal management and, more importantly, its prevention in susceptible populations, are of paramount importance.

This article will review the screening and diagnosis of the elderly with diabetes and will focus on the current best evidence-based practice. The Canadian Diabetes Association clinical practice guidelines for the diagnosis and management of diabetes are currently being updated to reflect information accrued from recent clinical trials. Meanwhile, the reader is referred to the guidelines published in 1998.[4]

Diabetes in the Elderly

Epidemiologic data have provided compelling evidence to indicate that the absolute risk for diabetes in Canada increases progressively with age at a rate of 9% per year.[1] With over 50% of adult Canadians overweight or obese, we are witnessing the continuing dual epidemics of obesity and diabetes in the adult population in North America.[5,6] The increasing prevalence of being overweight or obese in our society will further augment the prevalence of diabetes in the elderly population.[5] An increase in insulin resistance and a slow but progressive failure of the pancreatic beta cells to respond to carbohydrate challenges are often cited as the age-related physiologic changes responsible for the increased risk of diabetes.[7]

Elderly people frequently do not experience the classic symptoms of hyperglycemia (fatigue, polyuria, polydipsia and unexplained weight loss) until blood glucose values are markedly elevated. This is largely attributable to the deterioration in renal function with age; the renal threshold for glucose doubles with a 50% reduction in glomerular filtration rate. Hence, the elderly person with diabetes may remain asymptomatic until the glucose exceeds the renal threshold, which could be much higher than the normal value of 10mmol/L. Health professionals could misinterpret this lack of symptoms as a "mild form" of diabetes when, in fact, it indicates more serious pathophysiology.

Diagnosis of Diabetes

The diagnostic criterion for diabetes is a fasting venous plasma glucose level of 7mmol/L or greater.[4] The test should be confirmed by repeat testing in the absence of unequivocal hyperglycemia. A casual plasma glucose value of 11.1mmol/L or greater, together with symptoms of diabetes, also fulfill the criterion. Diabetes also can be diagnosed by a plasma glucose value of 11.1mmol/L or greater at the two-hour sample after a 75g glucose load.

Impaired fasting glucose (IFG) is defined as a fasting plasma glucose value between 6.1 and 6.9mmol/L, whereas impaired glucose tolerance (IGT) refers to those individuals with two-hour plasma glucose values between 7.8 and 11mmol/L following a modified 75g glucose load.[4]

Screening for Diabetes in the Elderly

It has been estimated that there are as many unrecognized cases as there are diagnosed cases of diabetes.[3] Early screening can identify these people and may reduce the disease burden of diabetes and its complications. While mass screening is not recommended, annual evaluation for risk of diabetes in all elderly people on the basis of history and clinical information may be cost effective over the long term. Testing for diabetes using a fasting plasma glucose should be performed every three years in the elderly.[4] Annual or more frequent testing should be considered in those with additional risk factors (Table 1).

Prevention of Diabetes in the Elderly

Physical inactivity and weight gain are the major reasons for the increase in insulin resistance and pre-diabetic states. Two recent landmark clinical trials have provided compelling evidence that lifestyle modification can delay, if not prevent, diabetes in high-risk individuals.[8,9] Both the Finnish Diabetes Prevention Trial and the NIH-sponsored Diabetes

Prevention Program demonstrated remarkably similar results—a 5% body weight loss through lifestyle changes led to a 58% reduction in risk for the development of Type 2 diabetes.[8,9] Among those in the Diabetes Prevention Program who were between 60 and 85 years of age (20% of the study population), lifestyle modification appeared to have had an even greater effect, resulting in a 71% reduction in diabetes risk.[9]

Management of Diabetes in the Elderly

Over the years, the management of diabetes has evolved into a complex strategy with an interdisciplinary team approach recommended as the gold standard for best clinical practice. Much of the current best practice in diabetes management in general also applies to the elderly person with diabetes. Since few clinical trials have focused on diabetes in the elderly, referring to people over 70 years of age, the evidence for the various recommendations for the management of the elderly person with diabetes is less robust. Nonetheless, the elderly were included in randomized, double-blinded as well as cohort clinical trials on diabetes, and taken together, we can draw some meaningful conclusions.[10-14]

Since the elderly person differs from a middle-aged adult in ways ranging from differences in glucose homeostasis to drug metabolism, management of the elderly with diabetes should take these differences into consideration.[7] A variety of factors affecting the ability of the elderly to follow treatment plans also must be considered. A significant number of elderly people are in nursing homes or special institutions, presenting additional challenges for management.

Lifestyle Modification

Diabetic meal plans should be recommended to elderly people with diabetes. Nutrition education programs can improve metabolic control in ambulatory seniors with diabetes.[15] However, in those living in nursing homes, modified diets do not result in improved glycemic control and may compromise the nutritional status of these patients. All institutionalized patients should be managed with regular nursing home diets.[16] Elderly nursing home residents are more likely to have an appropriate meal plan if a registered dietician is associated with the facility.[17]

Although physical training programs can be implemented successfully in older patients with diabetes, comorbid conditions may prevent aerobic physical training in many patients and increased activity levels may be difficult to sustain. Resistance training appears to be a viable alternative and may even provide comparable improvement in insulin sensitivity. Furthermore, these programs may result in an improvement in lipid values and well being in older individuals.[18,19]

Glycemic Control

While there are no randomized controlled trials demonstrating improved health outcomes with improved glycemic control in the elderly with Type 2 diabetes, cohort studies consistently demonstrate that closer to normal blood glucose levels are associated with a lower risk of complications in elderly patients.[10-12] In the elderly with Type 2 diabetes, cognitive function improves when blood glucose values are brought down nearer to normal levels.[20] Hence, the same glucose targets apply to otherwise healthy elderly as to younger people with diabetes. Treatment efforts also should be directed at avoiding symptoms of hyperglycemia and preventing hypoglycemia. Whenever possible, elderly persons with diabetes should be referred to a diabetes health care team because interdisciplinary interventions have been shown to improve glycemic control.[21]

Pharmacological Therapy

Initial therapy in elderly people with diabetes depends on the underlying metabolic defects. Beta cell failure is more prevalent in lean older patients with Type 2 diabetes compared to obese elderly. This group of patients tends to benefit more from insulin secretagogues (sulfonylureas and meglitinides),[22,23] whereas the obese elderly should be treated with agents that improve insulin resistance, such as metformin and thiazolidinediones.[23-25]

Alpha-glucosidase inhibitors are modestly effective oral hypoglycemic agents in older patients with diabetes, but a substantial number of patients may not tolerate them because of gastrointestinal side effects.[26] The gastrointestinal side effects of alpha-glucosidase inhibitors can be minimized by starting with a low dose and increasing the dosage slowly.

Insulin therapy is indicated in elderly people with diabetes should they fail to achieve the established glycemic goals with an oral agent alone or in combination. In those people with metabolic decompensation, insulin therapy may be instituted as first-line therapy until the person is stabilized. In elderly people, the use of premixed insulins as an alternative to mixing insulins minimizes dosage errors.[27] Furthermore, glycemic control may be improved if elderly patients are treated with pre-filled insulin pens rather than conventional syringes.[28]

Table 1
Risk Factors for Diabetes

History of impaired fasting glucose or impaired glucose tolerance
Presence of complications of diabetes
Positive family history of diabetes in first-degree relative
Member of high-risk population (aboriginal peoples, Asian, Hispanic and African descent)
Presence of hypertension
Dyslipidemia characterized by elevated fasting plasma triglycerides or a low plasma high-density lipoprotein cholesterol level
Presence of coronary heart disease or stroke
Acanthosis nigricans
Polycystic ovary syndrome
Prior history of gestational diabetes

Combination therapy with several oral agents is increasingly common and often necessary to achieve glycemic targets. Equivalent glycemic control can be maintained in older people with either b.i.d. insulin injections or a combination of a single injection of insulin with an oral agent.[29]

Hypoglycemia and weight gain are frequent side effects that may compromise drug therapy and compliance. Insulin secretagogues and insulin injections both are associated with hypoglycemia and weight gain.[30] Among the sulfonylureas, hypoglycemia is two- to four-fold lower with gliclazide or glimepiride than with glyburide use.[30] Thiazolidinediones are insulin-sensitizing agents that can effectively lower blood glucose alone or in combination with other agents. These drugs are associated with greater incidence of fluid retention in older patients and should be used with caution in patients with cardiovascular disease.[31]

Cardiovascular Disease and Diabetes

Considering most elderly people with diabetes already have established macrovascular complications, the benefits of treating hypertension and dyslipidemia in the elderly are substantial and all elderly patients should be treated to decrease their cardiovascular disease (CVD) risk.

Treatment of isolated systolic hypertension or combined systolic and diastolic hypertension in elderly patients with diabetes confers greater benefits and significant reduction in CVD morbidity and mortality than in age-matched non-diabetic seniors.[32] Treatment of isolated systolic hypertension also may preserve renal function in elderly patients with diabetes.[33] Several different classes of antihypertensive agents have been shown to be effective, including thiazide diuretics, long-acting calcium channel blockers, beta blockers and angiotensin converting enzyme (ACE) inhibitors.[34-36] ACE inhibitors may be particularly valuable for people with diabetes because they improve endothelial dysfunction.[37]

For persons with diabetes and normal urinary albumin excretion (less than 30mg / day) and blood pressure greater than 130 / 80mmHg despite lifestyle interventions, an ACE inhibitor or an angiotensin II receptor blocker (ARB) is recommended by the 2001 Canadian Hypertension Recommendations Group.[36] If blood pressure targets cannot be reached despite an ACE inhibitor and / or ARB, then one or more of a long-acting calcium-channel blocker or low-dose thiazide diuretic should be added.[36] If treatment with an ACE inhibitor or ARB is contraindicated or cannot be tolerated, a cardioselective beta-adrenergic blocker, long-acting dihydropyridine calcium channel blocker or low-dose thiazide diuretic can be substituted.[36]

Treatment of hypercholesterolemia with statins for both primary and secondary prevention significantly reduces cardiovascular morbidity and mortality in older people without diabetes.[38] The diabetes sub-population in the Heart Protection Study also benefited from statin treatment to a similar if not greater extent.[39] When treating dyslipidemia in elderly patients with diabetes, it is reasonable to aim for the same target levels as in younger patients.

People with diabetes are considered at very high risk for cardiovascular disease, and treatment should aim to achieve the following target lipid values: LDL cholesterol level lowered to 2.5mmol / L or less; triglycerides less than 2mmol / L; and a total / HDL cholesterol ratio less than 4.4.[40] Aspirin is recommended to decrease the CVD risk in patients with diabetes and it appears reasonable that elderly patients also may benefit from such therapy.[4,41]

Summary

The elderly person with diabetes should be treated to achieve the same glucose and metabolic goal targets as their younger counterparts. A multidisciplinary team approach is ideal to provide education and counseling to make appropriate recommendations on lifestyle modification. Should medical therapy be considered to treat hyperglycemia, the choice of agents should take into consideration both pathophysiology and side effects—notably hypoglycemia—of the various agents. Combination therapy often is required to achieve target blood glucose, lipid and blood pressure values. ACE inhibitor and Aspirin therapy also are recommended to reduce CVD risk. ◆

References

1. Choi BC, Shi F. Risk factors for diabetes mellitus by age and sex: results of the National Population Health Survey. Diabetologia 2001;44:1221-31.
2. Mokdad AH, Ford ES, Bowman BA, et al. Diabetes trends in the U.S.: 1990-1998. Diabetes Care 2000;23:1278-83.
3. Harris MI. Diabetes in America: Epidemiology and scope of the problem. Diabetes Care 1988;21(suppl 3):C11-14.
4. Meltzer S, Leiter L, Daneman D, et al. 1998 clinical practice guidelines for the management of diabetes in Canada. Canadian Diabetes Association. CMAJ 1998;159 (Suppl 8):S1-29.
5. Mokdad AH, Bowman BA, Ford ES, et al. The continuing epidemics of obesity and diabetes in the United States. JAMA 2000;286:1195-200.
6. Katzmarzyk PT. The Canadian obesity epidemic: an historical perspective. Obesity Res 2002;10:666-74.
7. Meneilly GS, Elliott T. Metabolic alterations in middle-aged and elderly obese patients with type 2 diabetes. Diabetes Care 1999;22:112-8.
8. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.
9. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.
10. Kuusisto J, Mykkanen L, Pyörälä K, et al. Non-insulin-dependent diabetes and its metabolic control are important predictors of stroke in elderly subjects. Stroke 1994;25:1157-64.
11. Kuusisto J, Mykkanen L, Pyörälä K, et al. NIDDM and its metabolic control predict coronary heart disease in eldery subjects. Diabetes 1994;43:960-7.
12. Beks PJ, Mackay AJ, de Nelling JN, et al. Peripheral arterial disease in relatoin to glycaemic level in an elderly Caucasian population: the Hoorn study. Diabetologia 1995;38:86-96.

13. Morisaski N, Watanabe S, Kobyashi J, et al. Diabetic control and progression of retinopathy in elderly patients: five-year follow-up study. J Am Geriatr Soc 1994;42:142-5.
14. Stolk RP, Vingerling JR, de Jong PT, et al. Retinopathy, glucose and insulin in an elderly population. The Rotterdam Study. Diabetes 1995;44:11-5.
15. Miller CK, Edwards L, Kissling G, et al. Nutrition education improves metabolic outcomes among older adults with diabetes mellitus: results from a randomized controlled trial. Prev Med 2002;34: 252-9.
16. Coulston AM, Mandelbaum D, Reaven GM. Dietary management of nursing home residents with non-insulin-dependent diabetes mellitus. Am J Clin Nutr 1990; 51:67-71.
17. Funnell MM, Herman WH. Diabetes care policies and practices in Michigan nursing homes, 1991. Diabetes Care 1995;18:862-6.
18. Skarfors ET, Wegener TA, Lithell H, et al. Physical training as treatment for type 2 (non-insulin-dependent) diabetes in elderly men: a feasibility study over 2 years. Diabetologia 1987;30:930-3.
19. Ligtenberg PC, Hoekstra JB, Bol E, et al. Effects of physical training on metabolic control in elderly type 2 diabetes mellitus patients. Clin Sci (Lond) 1997;93:127-35.
20. Sinclair AJ, Allard I, Bayer A. Observations of diabetes care in long-term institutional settings with measures of cognitive function and dependency. Diabetes Care 1997;20:778-84.
21. Kronsbein P, Jorgens V, Muhlhauser I, et al. Evaluation of a structured treatment and teaching programme on non-insulin-dependent diabetes. Lancet 1988;2:1407-11.
22. Groop L. Sulfonylureas in NIDDM. Diabetes Care 1992;15:737-54.
23. Turner RC, Cull CA, Frighi V, et al. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). JAMA 1999;281:2005-12.
24. Group UPDSU. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998;352: 854-65.
25. Inzucchi SE, Maggs DG, Spollett GR, et al. Efficacy and metabolic effects of metformin and troglitazone in type II diabetes mellitus. New Engl J Med 1998;338:867-72.
26. Meneilly GS, Ryan EA, Radziuk J, et al. Effect of acarbose on insulin sensitivity in elderly patients with diabetes. Diabetes Care 2000;23:1162-7.
27. Coscelli C, Calabrese G, Fedele D, et al. Use of premixed insulin among the elderly: reduction of errors in patient preparation of mixtures. Diabetes Care 1992;15:1628-30.
28. Coscelli C, Lostia S, Lunetta M, et al. Safety, efficacy acceptability of a pre-filled insulin pen in diabetic patients over 60 years old. Diabetes Res Clin Pract 1995;28:173-7.
29. Wolffenbuttel BH, Sels JP, Rondas-Colbers GJ, et al. Comparison of different insulin regimens in elderly patients with NIDDM. Diabetes Care 1996;19:1326-32.
30. Shorr RI, Ray WA, Daugherty JR, et al. Individual sulfonylureas and serious hypoglycemia in older people. J Am Geriatr Soc 1996;44:751-5.
31. Nathan DM. Initial management of glycemia in type 2 diabetes mellitus. New Engl J Med 2002;347:1342-9.
32. Curb JD, Pressel SC, Cutler JA, et al. Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. JAMA 1996;276:1886-92.
33. Voyak SM, Straessen JA, Thijs L, et al. Follow-up of renal function in treated and untreated older patients with isolated systolic hypertension. J Hypertens 2001;19:511-9.
34. Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated hypertension. Lancet 1997;350:757-64.
35. UK Prospective Diabetes Study (UKPDS) Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. Br Med J 1998;317:703-13.
36. McAlister FA, Zarnke KB, Campbell NR, et al. The 2001 Canadian recommendations for the management of hypertension: Part two- Therapy. Can J Cardiol 2002;18:625-41.
37. Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Lancet 2000;355:253-9.
38. LaRosa JC, He J, Vupputuri S. Effect of statins on risk coronary disease: a meta-analysis of randomized controlled trials. JAMA 1999;282:2340-6.
39. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7-22.
40. Fodor JG, Frohlich JJ, Genest JGJ, et al. Dyslipidemias ftWGoHaO. Recommendations for the management and treatment of dyslipidemia. Report of the Working Group on Hypercholesterolemia and Other Dyslipidemias. CMAJ 2000;162:1441-7.
41. ETDRS Investigators. Aspirin effects on mortality and morbidity in patients with diabetes mellitus. Early Treatment Diabetic Retinopathy Study Report 14. JAMA 1992;268:1292-1300.