Volume No. 7

Symposium On Diabetes

Cardiovascular Disease in Diabetes

Introduction

Symposium on diabetes is an effort towards disseminating information about various aspects of diabetes. In the year 2000, topics of clinical importance were discussed and we at Magnus Novo Nordisk are pleased to know about their overwhelming success.

We intend to continue our endeavor to provide information to empower you to achieve our common goal of improving the quality of life of our patients. The first publication of this year celebrated the insulin saga highlighting the ever changing role of insulin, from that of decreasing the mortality of patients with type 1 diabetes, to its increasing use in type 2 diabetes in preventing and delaying complications of diabetes.

Atherosclerosis accounts for some 80 percent of all diabetic mortality. About three-quarters of the cardiovascular deaths from diabetes result from coronary artery disease. The remaining quarter results from cerebral or peripheral vascular disease. Atherosclerotic disease causes some three-quarters of all hospitalizations for diabetic complications.

In the coming decades, the burden of diabetic cardiovascular disease will increase substantially. With an estimated annual cost of diabetes care at rupees 90,200 million in India, there is an urgent need to implement preventive measures.

Through this quarterly publication Magnus novo Nordisk promise to bring forth more information related to the practical aspects of diabetes. We are hopeful that you will find this series interesting and helpful in your day-to-day clinical practice.

Happy reading!

Cardiovascular Disease in Diabetes

Introduction

The American Heart Association in its recommendations for intervention to reduce the risk of cardiovascular complications in patients with diabetes mellitus, asserts that “From the point of cardiovascular medicine, it may be appropriate to say[1] diabetes is a cardiovascular disease.[2]”

The complications of diabetes are generally subdivided into the microvascular and the macrovascular variety. The microvascular complications are specific to diabetes with involvement of vascular cells of capillaries, arterioles and basement membrane of the retina, kidney and nerves. On the other hand, macrovascular complications resulting from atherosclerosis of the coronary, cerebral and lower extremity arteries and are not specific to diabetes. However, with contributing factors such as obesity, lipid abnormalities, hypertension and lifestyle changes they occur at an accelerated pace.

The risk of cardiovascular disease (CVD) is substantially increased in patients with both type 1 and type 2 diabetes. In type 1 diabetes, cardiovascular risk seems to be particularly high in those people who develop microalbuminuria and proteinuria, perhaps pointing to a common factor involving blood vessel integrity both in the kidney and elsewhere. In type 2 diabetes, cardiovascular risk also clusters with microalbuminuria in addition to a wide range of cardiovascular risk factors, which have been ascribed to insulin resistance[3].

Mortality from coronary arterial disease is two fold higher in men and fourfold higher in women with type 2 diabetes. Diabetes is the most common cause of disease in the young. At the time of diagnosis of type 2 diabetes, more than 50% patients are found to have preexisting coronary heart disease[4].

Atherogenic Mechanisms in Diabetes

Links between endothelial dysfunction, atherosclerosis and diabetes have been increasingly recognized. One of the earliest discernible atherogenic changes in diabetes is endothelial dysfunction, which is characterized by inhibited vasodilation, vascular smooth-muscle proliferation, increased thrombogenesis and proatherogenic cellular processes. Abnormal endothelium-dependent vasodilation also occurs in the microcirculation of patients with diabetes, where it may contribute to ischemia and its squeal.

Accelerated Atherosclerosis

Atherogenic factors

relating to artery wall
affecting thrombogensis
affecting lipoproteins
affecting vascular injury

Hyperglycemia

modification of lipoproteins
glycation of artery wall proteins
inducing advanced glycation end products
stimulating insulin secretion

Hyperglycemia and atherosclerosis in type 2 diabetes are related. Hyperglycemia causes glycosylation of virtually all proteins, inducing collagen cross-linking with other extracellular matrix proteins in the arterial wall. Long-term exposure to elevated glucose levels alone can cause the endothelial cell dysfunction observed in diabetes. Accelerated atherosclerosis, thrombosis, hypertension and hyperlipidemia all participate in the pathogenesis of vascular disease in patients of diabetes, and endothelial dysfunction is probably involved in each of these vascular abnormalities.

The pathogenesis of atherosclerosis also involves oxidation of low-density lipoprotein (LDL) cholesterol. Exposure to glycosylation end products can prolong the half-life of LDL cholesterol, increasing the likelihood that it will be trapped in the vascular wall where it is more susceptible to oxidation.

Predisposing Risk Factors

Several predisposing factors simultaneously affect the development of CVD and diabetes mellitus. Among these concomitant factors are obesity, physical inactivity, heredity, sex and advancing age. The mechanisms whereby they predispose to chronic disease are complex and often overlapping to some extent, these predisposing factors exacerbate the major risk factors: dyslipidemia, hypertension, and glucose tolerance; and they may cause CVD and diabetes mellitus through other pathways as well. To a large extent, both CVD and diabetes must be prevented through control of the predisposing risk factors. Modification of life habits is at the heart of the public health strategy for prevention of CVD and diabetes mellitus. High priorities are the prevention (or treatment) of obesity and promotion of physical activity. Drug therapy nonetheless may be required to control the metabolic risk factors, particularly when they arise from genetic aberration and aging. Effective drugs are currently available for treatment of hypertension and dyslipidemia.

Insulin Resistance and the Metabolic Syndrome

Most patients with type 2 diabetes have insulin resistance. Indeed, insulin resistance seems to predispose to both CVD and diabetes. Research suggests that insulin resistance is a multisystem disorder that induces multiple metabolic alterations. Factors that contribute to insulin resistance are genetics, obesity, physical inactivity, and advancing age. Patients with insulin resistance often have abdominal obesity. Metabolic risk factors that occur commonly in-patient with insulin resistance are atherogenic dyslipidemia, hypertension, glucose intolerance, and a prothrombotic state. Each of these risk factors can be reviewed briefly.

Atherogenic Dyslipidemia

Atherogenic dyslipidemia is characterized by 3 lipoprotein abnormalities: elevated very-low-density lipoproteins (VLDL), small LDL particles, and low high-density-lipoprotein (HDL) cholesterol (the lipid triad). The lipid triad occurs frequently in patients with premature coronary heart disease (CHD) and appears to be an atherogenic lipoprotein phenotype independent of elevated LDL cholesterol. Most patients with atherogenic dyslipidemia are insulin resistant. Atherogenic dyslipidemia in diabetic patients often is called diabetic dyslipidemia. Many patients with atherogenic dyslipidemia also have an elevated serum total apolipoprotein B. Growing evidence suggests that all of the components of the lipid triad are independently atherogenic. Together they represent a set of lipoprotein abnormalities besides elevated LDL cholesterol that promote atherosclerosis.

Hypertension

Hypertension is a well-established major risk factor for CVD. It increases risk for both CHD and stroke and contributes to diabetic nephropathy. Several investigators report a positive association between insulin resistance and hypertension; this finding suggests that elevated blood pressure deserves to be listed among the components of the metabolic syndrome. Hypertension nonetheless is a multifactorial disorder, and the mechanistic connections between insulin resistance and hypertension are largely conjectural; even so, evidence for a causal link is growing. When hypertension coexists with overt diabetes, which it commonly does, the risk for CVD, including nephropathy, is doubly increased.

Elevated Plasma Glucose

For several years after onset of insulin resistance, fasting and postprandial glucose levels typically are normal. During this period, pancreatic ß-cells are able to increase insulin secretion in response resistance and thereby maintain normal plasma glucose levels. In some people, however, insulin secretion declines with aging, and elevated glucose concentrations appear. The first abnormality in

plasma glucose in patients with insulin resistance is IGT (or impaired glucose tolerance). The presence of IGT usually accompanies longstanding insulin resistance. Many prospective studies show that IGT (or impaired glucose tolerance) is a risk factor CVD; the degree of independence as a risk factor, however, is uncertain, because IGT commonly coexists with other components of the metabolic syndrome. A patient with IGT nonetheless must be considered at risk for both CVD and type 2 diabetes. As already indicated, once categorical hyperglycemia develops, it counts as an independent risk factor for CVD.

Prothrombotic State

A newly recognized component of the metabolic syndrome is a prothrombotic state. Patients with insulin resistance frequently manifest several alterations in coagulation mechanisms that predispose them to arterial thrombosis. These alterations include increased fibrinogen levels, increased plasminogen activator inhibitor-I, and various platelet abnormalities.

LDL Cholesterol and Atherogenesis in Diabetic patients

An elevated concentration of serum LDL cholesterol is a major risk factor for CHD. In fact, some elevation of LDL cholesterol appears to be necessary for the initiation and progression of atherosclerosis. In populations having very low LDL cholesterol levels, clinical CHD is relatively rare, even when other risk factors hypertension, cigarette smoking, and diabetes are common. In contrast, severe elevations in CHD in the complete absence of other risk factors.

The view has been expressed that most patients with diabetes do not have an elevated serum LDL cholesterol; if not, high LDL serum cholesterol would not be a common risk factor in patients with diabetes. It is true that most patients who have diabetes do not have marked elevations of LDL cholesterol, but these patients nonetheless carry high enough levels to support the development of atherosclerosis. A role for LDL in hyperglycemic patients became apparent in recent clinical trials wherein an aggressive LDL-lowering therapy reduced recurrent CHD events in patients with diabetes.

Cigarette Smoking

Cigarette smoking is a leading risk factor for CVD. Patients with diabetes who are smokers are doubly at risk. Unfortunately, many patients continue to smoke despite having diabetes; for these patients, the benefits that can be derived from modifying other risk factors are mitigated.

Diabetic Nephropathy

Microalbuminuria (urine albumin 30 to 300 mg/d or <300 mg/g creatinine) is the first clinical sign of diabetic damage to the kidney. Not only is microalbuminuria a harbinger of progressive kidney damage, but its presence also reflects a higher risk for CVD. Micro albuminuria (urine albumin >300 mg/d or >300 mg/g creatinine) usually denotes significant diabetic nephropathy and will be followed by a decline in glomerular filtration rate (GFR). The majority of patients with diabetes who have microalbuminuria also have hypertension; in these patients, control of hypertension slows the decline in GFR. Some patients with diabetes develop the nephrotic syndrome (urine protein >3 g/d); diabetic dyslipidemia in such patients often is compounded by nephrotic dyslipidemia, most notably by higher cholesterol levels. The nephritic syndrome usually heralds progressive renal insufficiency; thereafter, ESRD ensues an dialysis and/or transplantation become necessary to sustain life.

Management of CVD

Although evidence from randomized controlled studies is lacking, the American Diabetes Association Consensus Development Conference on the Diagnosis of Coronary Heart Disease in People With Diabetes has recommended that patients with an established coronary heart disease (CHD) history or who have had a prior cardiac event warrant cardiac testing for risk stratification. Further, in patients without a prior history of an event or symptoms strongly suggesting CHD, testing for CHD is warranted in patients with the following.

1. Typical or atypical cardiac symptoms;

2. Resting electrocardiogram suggestive of ischemia or infarction;

3. Peripheral or carotid occlusive arterial disease;

4. Sedentary lifestyle, age ^{3}35 years, and plans to begin a vigorous exercise program;

5. In addition to diabetes, two or more cardiac risk factors (total cholesterol ^{3}240 mg/dl, LDL cholesterol ^{3}160 mg/dl, or HDL cholesterol <35 mg/dl; blood pressure >140/90 mmHg; smoking; family history or premature CHD; positive micro-/microalbuminuria test).

   Cardiac testing might consist of exercise stress testing, stress perfusion imaging, stress echocardiography, or catheterization. The type of testing

and need for referral to a cardiologist depend on the severity of underlying or suspected coronary artery disease[5].

Risk Assessment and Clinical Evaluation

The first step in reducing the risk of cardiovascular disease in patients with diabetes is identification or risk factors such as cigarette smoking, hypertension, abnormal serum lipid levels, excess body weight and abdominal obesity, physical inactivity and a family history of cardiovascular disease (Table 1, 2 & 3).

Early detection of cardiovascular disease may reduce morbidity and mortality in patients with diabetes. Detection of subclinical disease require a careful assessment for evidence of claudication, angina, dyspnea or exertion of cerebrovascular disease. Carotid and femoral arteries should be assessed for bruits and peripheral pulses should be evaluated. The ratio of ankle-to-brachial artery systolic blood pressure may serve as a marker for peripheral vascular disease. The urine should be checked for microalbuminuria. Electrocardiographic evidence of left ventricular hypertrophy is a strong predictor of morbidity and mortality from coronary heart disease.

Special consideration for exercise stress testing include the blunted blood pressure and heart rate responses that are often present in patients with diabetes. In addition, painless ST-segment depression is common in these patients, and the diagnostic specificity of ST-segment depression is often reduced in patients with diabetes because of a previous silent myocardial infarction, conduction abnormalities and increased left ventricular mass. An alternative to exercise testing is perfusion scintigraphy. Although not recommended routinely, ambulatory electrocardiographic monitoring may be useful for detecting silent ischemia.

Autonomic dysfunction is associated with a 50 percent mortality rate at five years. Periodic evaluation should include an assessment for evidence of autonomic dysfunction. Autonomic dysfunction increases the risk of general anesthesia and complications following elective surgery. Autonomic dysfunction may be present if two or more of the following abnormalities are found on examination: a resting heart rate (supine) of 100 beats per minute, and excessive diastolic blood pressure response to hand-grip exercise, an abnormal expiratory/inspiratory RR-interval ration and postural hypotension.

Table 1. Evaluation of Major Risk Factors in Diabetic Patients

Cigarette Smoking

History : Record current and part smoking habits; list smoking duration (years of use) and intensity (number of cigarettes smoked per day); determine passive smoke exposure (at work and at home)

Blood Pressure

History: Record history of blood pressure (BP) and measures of treatment, including current and past antihypertensive agents. Also determine acquired factors affecting BP: body weight, physical activity level, sodium intake, and alcohol consumption.

Physical examination: Define current BP from multiple measurements; measure BP supine, sitting, and standing in elderly patients; consider 24-hour automated, ambulatory BP monitoring in older patients (detects absence of nocturnal fall in Bp [autonomic dysfunction], episodic hypertension, resistant hypertension).

Serum lipids and lipoproteins

History: Assess dietary habits and alcohol intake, exercise habits, efforts to modify lifestyle habits, use of medication that influence lipoprotein levels, family history of premature vascular disease and dyslipidemia, history of thyroid disorders or pancreatitis

Physical examination: Check for eruptive xanthomas and lipemia retinalis (signs of severe hypertriglyceridemia), tuberoeruptive xanthomas (sign of dysbetalipoproteinemia), xanthelasma (suggestive of hyperlipidemia), and signs of hypothyroidism.

Albuminuria

Measure serum creatinine

Test urine with a dipstick for protein: If dipstick is negative, measure urine albumin-to-creatinine ratio in the first morning urine specimen

Glycemic status

History: Age of onset of hyperglycemia; course of diabetes management; family history of diabetes, history of diabetic complications.

Physical examination: Cardiovascular status, retinopathy and other diabetic complications.

Laboratory : Fasting plasma glucose (FPG); hemoglobin A1c (periodically); diabetes=FPG>126 mg/dL (x2) impaired fasting glucose=110 to 126 mg/dL (x2).

2. Evaluation of Predisposing Risk Factors in Diabetic Patients

Body weight and fat distribution

History: Assess history of body weight, age at onset of overweight, history of weight loss and weight gain; assess eating and exercise habits, social and occupational factors affecting body weight, family support, history of body weights in family members in childhood and adulthood, attitude and motivation for weight control.

Physical examination: Measure body weight (kg) and height (m); calculate body mass index (BMI) (kg/m^2); categorize body weight (BMI 25 to 29.9=overweight; >30=obesity); measure waist circumference (abdominal obesity=>40 in [102cm] in men >36 in [88cm] in women; borderline abdominal obesity in men, 88 to 102 cm)

Physical activity

History: Assess housework, childcare; determine opportunities and available facilities for regular exercise

Physical examination: Assess level of cardiovascular fitness in cardiac rehabilitation facilities.

Family history

History: Access family history for CVD or sudden death. (Family history is positive if CVD or sudden death occurred in first-degree male relatives before age 55 years of first-degree female relatives before age 65 years). Determine presence or absence of other risk factors high cholesterol levels, cigarette smoking, hypertension, diabetes in first-degree relatives (biological parents, siblings, offspring). If possible, expand family tree to second-degree relatives (grandparents, uncles, aunts). Create a simple family tree.

Laboratory: Measure glucose and past and current levels of physical activity; ascertain activity on the job, participation in sports, regular walking, jogging, or swimming. In women, ask about activity in lipids (cholesterol, triglycerides, and HDL cholesterol) in first-degree relatives.

Table 3. Detection of Clinical and Subclinical Cardiovascular Disease in the Diabetic Patient

Stress testing for coronary heart disease
Consult AHA guideline for exercise treadmill testing
Special considerations for exercise testing in diabetic patients
Blood pressure and heart rate responses often blunted (due to elevated resting heart rate)
Painless ST-segment depression in common in diabetic patients
Diagnosis specificity of ST-segment depression often reduced (due to previous silent myocardial infarction, conduction abnormalities, and increases in LV mass)
Exercise or pharmacological stress 201TI (or 99Tc) perfusion scintigarphy favorable alternative for exercise testing in diabetic patients
Ambulatory ECG monitoring for silent ischemia: may be helpful in some diabetic patients, but not recommended routinely
Echocardiography (with Doppler) and radionuclide ventriculography
Special considerations for diabetic patients
Diastolic dysfunction common in asymptomatic diabetic patients
Diastolic dysfunction often precedes systolic dysfunction
LV wall motion abnormalities: suggests diabetic cardiomyopathy
Evaluation of autonomic dysfunction
Beside evaluation of autonomic dysfunction
Two or more of the following tests are abnormal
Resting heart rate (supine) 100 bpm
Excess diastolic blood pressure response to hand-grip exercise
Abnormal expiratory/ inspiratory RR-interval ratio
Postural hypotension
Significance of autonomic dysfunction in diabetic patients
Carries poor prognosis (50% mortality in 5 years)
Sudden death common; consider electrophysiological study for syncope workup
Enhanced complications after elective surgical procedures
Increased danger with general anesthesia
Detection of subclinical cardiovascular disease

History: Access carefully for claudication, angina, dyspnea on exertion, cerebrovascular disease

Physical exam: Routine cardiovascular examination; assess for carotid and femoral artery bruits; evaluate peripheral artery pulses; ratio of ankle-to-brachial artery systolic blood pressure (marker of subclinical peripheral vascular disease)

Laboratory: Check for microalbuminuria

ECG: LV hypertrophy strong predictor of CHD morbidity and mortality.

Electron beam CT: Coronary calcium score highly correlated with total coronary atherosclerosis burden (role in risk assessment currently under investigation)

Carotid ultrasound: Detects subclinical carotid atherosclerosis (role in risk assessment currently under investigation)

Primary Prevention

Type 2 diabetes can be viewed as the end product of years of metabolic stress accompanying insulin resistance. As the report states, “the clock starts ticking for acceleration of atherogenesis long before onset of hyperglycemia.” Early detection of risk factors associated with the metabolic syndrome is needed to institute primary prevention measures in patients in risk of diabetes. Evidence of insulin resistance includes the presence of abdominal obesity or borderline abdominal obesity, high-normal blood pressure or mild hypertension, high-normal triglycerides (150 to 250 mg per dL [1.70 to 2.82 mmol per L]), reduced HDL cholesterol (less than 40mg per dL [1.05 mmol per L] in men and less than 50 mg per dL [1.30 mmol per L] in women) and borderline high-risk LDL cholesterol (130 to 159 mg per dL [3.35 to 4.10 mmol per L]). In some patients, impaired fasting glucose (110 to 126 mg per dL [6.10 to 7.00 mmol per L]) may be present. Impaired fasting glucose usually signifies longstanding insulin resistance and is a strong risk factor for type 2 diabetes. Early implementation of primary measures for prevention of cardiovascular disease will probably delay the onset of type 2 diabetes as well as reduce the risk of cardiovascular disease (Table 4).

Table 4. Guide to Primary Prevention of Cardiovascular Diseases in Patients With Diabetes

<table>
<tr><th>Risk Intervention</th><th colspan="4">Recommendations</th></tr>
<tr><td>Smoking

Goal: complete cessation</td><td colspan="4">Ask about smoking status as part of routine evaluation. Reinforce nonsmoking status.

Strongly encourage patients and family to stop smoking

Provide counseling, nicotine replacement, and formal cessation program as appropriate</td></tr>
<tr><td>Blood pressure control

Goal:
<130/85 mm HG</td><td colspan="4">Measure blood pressure at each visit. Consider home blood pressure monitoring.

Promote lifestyle modification: weight control, physical activity, and moderation in alcohol, moderate sodium restriction.

Consider blood pressure medication: If blood press [3]140/90 mm Hg after 3 months of life habit modification or if initial blood pressure >160/100 mm Hg: individualize thereby to patient's other requirements and characteristics.</td></tr>
<tr><td rowspan="5">Cholesterol management

Primary goal:
LDL<130mg/dL

Some authorities recommend LDL
~ 100 mg/dL for diabetic patients with multiple risk factors)

Rule out secondary causes of high LDL (liver function tests, thyroid function tests, urinalysis)

Secondary goals: HDL>35 mg/dL; TG<200 mg/dL</td><td colspan="4">Ask about dietary habits as part of routine evaluation

Measure total and HDL cholesterol and TG; estimate LDL</td></tr>
<tr><td colspan="3">Start AHA Step II Diet (~ 130% fat, <7% saturated fat, <200 mg/dL cholesterol) and weight control

Consider adding drug therapy to diet therapy for LDL levels >130 mg/dL</td><td rowspan="3">Risk factors to consider for more aggressive LDL-lowering therapy, i.e. LDL goal ~100 mg/dL; age (men [3]45 y, women [3]55 y or postmenopausal), hypertension, diabetes, smoking. HDL <35 mg/dL, family history of CHD in first-degree relatives (in male relatives<55y, female relatives <65 y)</td></tr>
<tr><td colspan="3">Suggested drug therapy for LDL levels >130 mg/dL (drug selection priority modified according to TG level)</td></tr>
<tr><td>TG<200 mg/dL</td><td>TG 200-400 mg/dL</td><td>TG>400 mg/dL</td></tr>
<tr><td>Statin Resin</td><td>Statin Fibrate</td><td>Consider Combined drug therapy (statin+fibrate)</td><td>HDL <35 mg/dL

Emphasize weight management and physical activity, avoidance of cigarette smoking</td></tr>
<tr><td colspan="4">If HDL, goal not achieved, consider combination drug therapy</td></tr>
</table>

Glucose control Near normal fasting glucose HbA1c ~ 1% above normal	First-step therapy: weight reduction and exercise Second-step therapy oral hypoglycemic agents (sulfonylureas and/or metformin; ancillary: acarbose, glitazone) Third-step therapy: Insulin therapy
Antiplatelet agents	Some authorities recommend aspirin 80 to 325 mg/d if not contraindicated for primary prevention in high-risk diabetic patients.
Physical activity Goal : Increase amount; exercise regularly 3-4 times per week for 30 minutes	Ask about physical activity status and exercise habits as part of routine evaluation. Encourage 30 minutes of moderate-intensity exercise 3 to 4 times per week as well as increased physical activity in daily life habits for persons who are inactive. Encourage regular exercise to improve conditioning and optimize fitness level. Advise medically supervised programs for those with low functional capacity and/or co morbidities. Promote environmental factors conducive to health (i.e. golf courses that permit walking)
Weight management Goal : Achieve and maintain desirable BMI and waist circumstances	Measure patient's weight and height, BMI, and waist circumference at each visit as part of routine evaluation Desirable BMI range: 21 to 25 kg/m^2. Desirable waist circumference for men <102 cm and women <88 cm Start weight management and physical activity as appropriate.
Estrogens	Consider estrogen replacement therapy in postmenopausal women, especially those with multiple CHD risk factors, such as elevated LDL; efficacy for CVD risk reduction in diabetic women not proved. Individualized estrogen replacement therapy recommendation consistent with other health risks.

TG indicates triglycerides; BMI body mass index

Interventions for Risk Reduction in Cardiovascular Disease

Comprehensive medical intervention in patients with diabetes and atherosclerotic cardiovascular disease can have a considerable impact. It can extend the overall rate of survival, improve quality of life, decrease the need for intervention procedures such as angioplasty and coronary artery bypass surgery, and reduce the incidence of subsequent myocardial infarction (Table 5).

Conclusion

Cardiovascular complications have emerged over the last decade as the key target to reduce morbidity and mortality in diabetics. The focus in treatment of diabetes is shifting from blood sugar to the blood vessel. As health care providers, caring for persons with diabetes, it is needless to say that only a concerted effort on our behalf to provide comprehensive risk reduction, primary and secondary prevention of cardiovascular disease will enable our patients to live longer and healthier.

Table 5. Guide to Comprehensive Risk Reduction for Patients with Coronary and other Vascular Disease who have Diabetes

<table>
<tr><th>Risk Intervention</th><th colspan="5">Recommendations</th></tr>
<tr><td>Smoking

Goal: Complete Cessation</td><td colspan="5">Strongly encourage patient and family to stop smoking

Provide counseling, nicotine replacement, and formal cessation program as appropriate.</td></tr>
<tr><td>Blood pressure control

Goal: ~ 135/85 mm Hg</td><td colspan="5">Initiate lifestyle modification - weight control, physical activity, alcohol moderation, and moderate sodium restriction – in all patients with blood pressure >135 mm Hg systolic or 85 mm Hg diastolic.

Add blood pressure medication, individualized to other patient requirements and characteristics (i.e. age, race, need for drugs with specific benefits) if blood pressure is not <140 mm Hg systolic or <90 mm Hg diastolic in 3 months or if initial blood pressure is >160 mm Hg diastolic.</td></tr>
<tr><td rowspan="4">Lipid management

Primary goal:
LDL ~ 100 mg/dL

Secondary goals:
HDL>35 mg/dL;
TG<200 mg/dL</td><td colspan="5">Start AHA Step II Diet in all patients: 30% fat, <7% saturated fat, <200 mg/d cholesterol

Access fasting lipid profile. Immediately start cholesterol lowering drugs when baseline LDL>130 mg/dL.</td></tr>
<tr><td>LDL <100 mg/dL No drug therapy</td><td colspan="3">LDL 100 to 129 mg/dL Consider adding drug therapy to diet, as follows

LDL 130 mg/dL Add drug therapy to diet, as follows</td><td>HDL <35 mg/dL Emphasize weight management and physical activity

Advise smoking cessation</td></tr>
<tr><td rowspan="2"></td><td colspan="3">Suggested drug therapy</td><td rowspan="2"></td></tr>
<tr><td>TG<200 mg/dL</td><td>TG 200 to 400 mg/dL</td><td>TG>400 mg/dL</td></tr>
</table>

		Statin Resin	Statin Fibrate	Consider Combined drug therapy (statin+fibrate)	
Glucose control Goal: near normal fasting glucose Goal: HbA1c ~1% above normal	First-step therapy: weight reduction and exercise Second-step therapy: oral hypoglycemic agents (sulfonylureas and/or metformin; ancillary: acarbose, glitazone) Third-step therapy: Insulin therapy				
Physical activity: Goal: minimum goal 30 minutes 3 to 4 times per week	Assess risk, preferably with exercise test, to guide prescription Encourage minimum of 30 to 60 minutes of moderate – intensity activity 3 or 4 times weekly (walking, jogging, cycling, or other aerobic activity) supplemented by an increase in daily lifestyle activities (e.g. walking breaks at work, using stairs, gardening, household work) Maximum benefit 5 to 6 hours a week Advise medically supervised programs for moderate – to high-risk patients.				
Weight management	Start intensive dietary therapy and appropriate physical activity as outlined above, in patients whose BMI is $^{3}25kg/m^{2}$. Particularly emphasize need for weight loss in patients with hypertension, elevated triglycerides, or elevated glucose levels.				
Antiplatelet agents / anticoagulants	Start aspirin 80 to 325 mg/d if not contraindicated Manage warfarin to international normalized ration 2 to 3.5 for post-MI patients not able to take aspirin.				
ACE inhibitors in post-MI patients	Start early post-MI in stable high-risk patients (anterior MI, previous MI, Killip Class II (S_3 gallop, rates, radiographic congestive heart failure) Continue indefinitely for all with LV dysfunction (ejection fraction ~ 40%) or symptoms of failure. Use as needed to manage blood pressure or symptoms in all other patients.				
ß-Blockers	Start in high-risk post-MI patients (arrhythmia, LV dysfunction, inducible ischemia) at 5 to 28 days. Continue 6 months minimum. Observe usual contraindications. Appropriate use of ß-blockers not contraindicated in patients with diabetes. Use as needed to manage angina, rhythm, or blood pressure in all other patients.				
Estrogen	Observational studies (but not clinical trials) suggest benefit. Limited data in diabetic women individualize recommendation consistent with other health risks.				

TG indicates triglycerides; MI myocardial infarction; and LV left ventricular

References

1. Burden of diabetes and its complications in India. A Ramachandran, NNDU 2000 p 51-7

2. Diabetes and Cardiovascular Disease - A Statement for Healthcare professionals from the American Heart Association. DM Grundy, IJ Benamin, GL Burke et. Al, Circulation. 1999; 1000; p 1134-1146.

3. The Aetiology of Vascular Disease in Diabetes. JS Yudkin, NNDU 2000 p 43-7.

4. Hyperglycemia and Hyperinsulinemia – Role and Relevance in Diabetic Macrovascular Disease, SP Pendsey, NNDU 99 p 45-51.

5. Standards of medical Care of patients with Diabetes Mellitus. Position Statement. American Diabetes Association: Clinical Practice Recommendations Diabetes Care, Jan 2001; Vol. 24 Suppl. 1.

Experts Opinion

P. J. Geeverghese
Risk factors of CVD are mainly diabetes itself. Endothelial dysfunction is the root cause of the macro-angiopathy. During MI, diabetics control of diabetics with IV insulin and thrombolytic therapy is useful.

Kochi

Manoj Chadha
IHD is in 2-5 times commoner in a diabetic as compare to a non-diabetic. In addition to increase in frequency, CAD is more severe in the form of multivessel and multi segmental involvement. Therapeutic invention to decrease CAD should begin at the stage of impaired glucose as by the time the patients becomes diabetic atherosclerotic, changes are well established.

Mumbai

Sunil Gupta
70% of diabetics suffer with coronary artery disease. A diabetic without MI has the same risk of a MI as that of a non-diabetic with MI, for the second MI. hyperglycaemic and atherosclerosis in type 2 diabetes are related. So a good control of glycaemic level is desirable along with a low dose aspirin for primary prevention of all diabetes.

Nagpur

Madan C. Phadnis
Microvascular complication like diabetes retinopathy, diabetes nephropathy are seen only in diabetics. Meticulous control of hyperglycemia is the most effective measure in preventing and delaying these complications. Macro vascular complications like CAD, cerebrovascular accidents & peripheral vascular disease are seen in non-diabetics also. But their incidence in diabetes multiplies. Along with control of diabetics one has to take care of many other aspects like control of BP, hyperlipidemia obesity, cessation of smoking, regular exercise program and management of stress. Life style modification becomes the mainstay of comprehensive management of Diabetes.

Pune