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Management of Cardiovascular Risk Factors in Type 2 Diabetic Patients Undergoing Coronary Angiography

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Aim. To investigate risk factor management in diabetic patients undergoing coronary angiography.

Methods. Hemoglobin (Hgb) A_{1c}, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), blood pressure (BP), and body mass index (BMI) were cardiovascular risk factors analyzed in 284 consecutive type 2 diabetic patients who underwent coronary angiography.

Results. Coronary artery disease (CAD) was identified in 233 (82.0%) diabetic patients. The mean $HgbA_{1c}$ fraction for all patients at hospital admission was $9.7 \pm 1.4\%$. The mean concentration of LDL-C, HDL-C, and triglycerides was 2.82 ± 0.9, 0.92 ± 0.28, and 2.56 ± 0.81 mmol/L, respectively. One hundred and twenty-two (43.0%) patients had LDL-C < 2.6 mmol/L, 70 (24.7%) patients had a blood pressure of less than 130/85 mm Hg, and 158 (55.7%) had BMI < 30 kg/m^2. Only 26 (9.1%) patients had optimal control of the above cardiac risk factors. The average LDL-C, triglycerides, and blood pressure in patients with severe coronary artery disease were higher than those in patients with moderate to mild coronary artery disease ($p < 0.01$; unpaired t-test).

Conclusions. Cardiovascular risk factors were poorly controlled in type 2 diabetic patients. The average LDL-C, triglycerides, and blood pressure in patients with severe coronary artery disease were higher than those in patients with moderate to mild coronary artery disease.

Key words: *cholesterol; coronary angiography; diabetes mellitus; risk; risk management*

Cardiovascular morbidity and mortality are increased 4- to 6-fold in patients with type 2 diabetes (1-3). Diabetes seems to have greater impact on the risk of coronary death in women than in men (4). Diabetes is also associated with a worse short- and long-term outcome after percutaneous coronary angioplasty or coronary artery bypass grafting in patients with multivessel coronary disease (5-7). Furthermore, recent subgroup analyses of randomized clinical trials have suggested that diabetic patients, who comprise 15-25% of trial patients, have poorer long-term outcomes after percutaneous coronary intervention or conventional therapy, with a higher incidence of re-occlusion, re-infarction, and cardiac mortality than non-diabetics (8-11).

The mechanism of increased cardiovascular morbidity and mortality in diabetics is multifactorial and may be due to, at least in part, synergistic actions between coexistent cardiac risk factors such as hypertension, hyperlipidemia, hyperglycemia, smoking, and obesity. To prevent or reduce cardiac morbidity and mortality in type 2 diabetics, therapy should focus not only on insulin resistance and metabolic control, but also on cardiac risk factors, such as hypertension and hyperlipidemia (2). The purpose of the study was to investigate the level of management of multiple predetermined cardiovascular risk factors in a cohort of patients who underwent coronary angiogram for coronary artery disease.

Patients and Methods

Patients

Between 1998 and 2002, 1,480 consecutive patients were referred to Weifang Medical College Hospital for coronary angiography because of suspected anginal chest pain, unstable angina, or acute myocardial infarction before undergoing primary angioplasty or stenting. Only patients with type 2 diabetes mellitus were selected for the study. In the end, 284 patients with type 2 diabetes (219 men, 77.0%) were analyzed. The mean age ($\pm$ standard deviation) of patients was 61.0 ± 8.2 years. The duration of diabetes ranged from 0.5 to12 years (median, 6.3 years).

Thirty-two (38%) patients had previous myocardial infarction and seven (2.5%) had a history of coronary bypass surgery. Hypertension was found in 76 (26.8%) patients. A history of stroke and peripheral artery was found in six (2.1%) and nine (3.2%) patients, respectively.

Cardiovascular Risk Factors

The following parameters were used to define optimal treatment in these patients: hemoglobin (Hgb) A_{1c} fraction <7%, low-density lipoprotein cholesterol (LDL-C) <2.6 mmol/L, high-

density lipoprotein cholesterol (HDL-c) ≥1.2 mmol/L for men and ≥1.4 mmol/L for women, triglyceride (TG) level <2.3 mmol/L, blood pressure (BP) <130/85 mm Hg, and body mass index (BMI) <30 kg/m^2. In addition, the daily use of aspirin therapy and current smoking status were also evaluated.

Coronary Angiography

Coronary angiography was performed with the standard Judkins technique. Coronary artery disease was defined as at least one stenosis of a coronary artery of ≥50%. The following criteria were used to define the characteristics of severe coronary artery disease: 1) multivessel disease – a stenosis in more than three of the following arteries: left main, left anterior descending, left circumflex, and right coronary artery; 2) multi-lesion disease – more than three significant (>50%) segmental stenosis in the same coronary artery; 3) extensive lesion – a stenoses of more than 10 mm in length.

Coronary artery disease was defined as severe if one or more of the three types of coronary lesions mentioned above were found by coronary angiography.

Statistical Analysis

Data were expressed as means ± SD. Differences in cardiac risk factors between those with severe and mild to moderate forms of coronary artery disease were analyzed by an unpaired t-test, whereas the comparison of categorical data such as smokers, aspirin users between patients with severe and mild to moderate coronary artery disease was performed by a chi-square test. The SPSS statistical package, Release 10.0.0. (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Significance level was set at $p<0.05$.

Results

General Therapeutic Measures

Among the diabetic patients, 162 (57.0%) were smoking more than 20 cigarettes a day at hospital admission. Seventy-two (25.4%) were taking oral aspirin at a dose ranging between 75 and 300 mg/day for the prevention of coronary artery disease.

Of the 284 diabetic patients, 88 (31.0%) were using diet control of hyperglycemia without any specific medication at hospital admission. Ninety-five (33.5%) were taking one of the following oral hypoglycemic drugs: metformin, glipizide, or tolbutamide. Fifty-four (19.0%) were on insulin, whereas the remaining 47 (16.6%) patients had no specific therapy for diabetes.

Management of Cardiac Risk Factors

Less than half of our diabetic patients had showed optimal management of $HgbA_{1c}$, LDL-C, HDL-C, and blood pressure at admission (Table 1). Thirty-four men and 10 women had HDL-C of more than 1.2 and 1.4 mmol/L, respectively. Less than 11% of patients had normal $HgbA_{1c}$. Overall, only 26 (9.2%) patients had normal values of all parameters (Table 1).

Table 1. Characteristics of 233 diabetic patients at admission to hospital

Parameter*	Value (mean ± SD; range)	No. (%) of patients with values within normal range
$HgbA_{1c}$ (%)	9.7 ± 1.4 (5.2-14.6)	25 (8.9)
LDL-C (mmol/L)	2.84 ± 0.91 (2.30-4.81)	122 (43.0)
HDL-C (mmol/L)	0.92 ± 0.28 (0.59-1.64)	33 (11.5)
TG (mmol/L)	2.56 ± 0.81 (1.75-5.37)	165 (58.0)
BP (mm Hg)	146 ± 34 (108-178)	70 (24.7)
BMI (kg/m^2)	24.3 ± 6.7 (18-28)	158 (55.7)

*Abbreviations: $HgbA_{1c}$ – hemoglobin A_{1c}; LDL-c – low-density lipoprotein cholesterol; HDL-c – high-density lipoprotein cholesterol; TG – triglyceride; BP – blood pressure; BMI – body mass index.

Relationship between cardiac risk factors and the severity of coronary artery disease was identified in 233 (82.0%) patients following coronary angiography. One hundred and thirty-five patients (58.0%) were found to have severe coronary artery disease. Patients with severe coronary artery disease had increased values of $HgbA_{1c}$, LDL-C, triglycerides, and blood pressure ($p<0.01$; Table 2). They also had a lower HDL-C and a higher BMI, but these differences did not reach statistical significance. There were more heavy smokers in the severe coronary artery disease group than in the mild-to-moderate coronary artery disease group ($p<0.05$).

Table 2. Relationship between cardiovascular risk factor control and severity of coronary artery disease (CAD) in 233 diabetic patients

Parameter*	Severe CAD (n = 135)	Mild-moderate CAD (n = 98)	p†
Age	54 ± 13	57 ± 16	>0.05
No. of men (%)	98 (72.6)	72 (73.5)	>0.05
Duration of DM (years)	6 ± 3	5 ± 3	>0.05
$HgbA_{1c}$ (%)	10.9 ± 1.9	7.9 ± 1.1	<0.01
LDL-C (mmol/L)	3.44 ± 0.51	2.77 ± 0.31	<0.01
HDL-C (mmol/L)	0.82 ± 0.26	0.97 ± 0.33	0.10
TG (mmol/L)	2.90 ± 1.15	2.37 ± 0.83	<0.01
BP (mm Hg)	156 ± 24	132 ± 29	<0.01
BMI (kg/m^2)	25.3 ± 6.9	23.6 ± 5.6	0.07
Smokers (No., %)	101 (74.8)	41 (41.8)	<0.05
Aspirin users (No.,%)	25 (18.5)	18 (18.6)	>0.05

*Abbreviations: DM – diabetes mellitus; $HgbA_{1c}$ – hemoglobin A_{1c}; LDL-c – low-density lipoprotein cholesterol; HDL-c – high-density lipoprotein cholesterol; TG – triglyceride; BP – blood pressure; BMI – body mass index. Data expressed as mean ± standard deviation for continous variables.
†Unpaired t-test for continous variables and chi-square for fractions.

Discussion

The main finding of the study was that less than 50% of the diabetic patients had optimal management of blood glucose, lipids, and blood pressure. In addition, less than 10% of the patients had normal values of $HgbA_{1c}$, LDL-C, HDL-C, and blood pressure at the time of coronary angiography.

Type 2 diabetes has become a world pandemic. By 2025, the number of adults with diabetes will rise to 300 million worldwide, compared with 135 million six years ago (12). Patients with coronary heart disease have a higher prevalence of diabetes than the general population (13). The prevalence of type 2 diabetes has traditionally been low in China, but in the last two decades, the prevalence of the disorder has rapidly increased (12).

Type 2 diabetes is characterized by insulin resistance, hyperinsulinemia, and altered carbohydrate and lipid metabolism. Diabetes-associated hyperglycemia, increased LDL-C and decreased HDL-C blood concentrations may lead to vasculopathy through lipid deposition into vessel walls accompanied by monocyte infiltration, vascular smooth muscle cell proliferation, arterial mural fibrosis, and thrombosis (2). Angiographic measures of coronary artery disease are closely associated with risk factors for atherosclerosis, such as levels of LDL-C, hypertension, and smoking in non-diabetic patients (14,15). Semiquantitative assessments of coronary artery disease in our di-

abetic patients showed that patients with severe coronary artery disease had a higher level of LDL-c and triglycerides than those with mild to moderate coronary artery disease. These findings were consistent with the results of prospective studies showing that levels of these lipoproteins are associated with incidence of clinical cardiovascular events among type 2 diabetic patients (16,17).

An intreresting finding was that, although all patients underwent coronary angiography because of the symptoms of coronary artery disease, in 12% of them no significant coronary artery disease was detected by angiography. Review of these patients' medical records showed that the pain was not associated with typical ST-T changes in body surface electrocardiography, although most of them had chest discomfort or pain suggestive of angina before angiography.

Adequate management of cardiovascular risk factors offers significant benefits in slowing the progression of atherosclerosis and prevention of cardiac events in diabetics. Improved treatment of hyperglycemia in patients with type 2 diabetes mellitus delays the onset and progression of microvascular complications (19-21). Large clinical trials have shown that lowering LDL-C with statins in diabetics with preexisting coronary artery disease significantly reduces subsequent cardiac events (22,23). A recent mega-trial in patients with coronary artery disease, other occlusive vascular disease, or diabetes showed that simvastatin at a daily dose of 40 mg reduced the rates of myocardial infarction, stroke, and revascularization by about one-quarter, irrespective of patients' initial cholesterol concentrations (24). Furthermore, optimal control of risk factors in diabetics, including blood pressure with ramipril, reduces cardiovascular death by 37% and total mortality by 24% (25).

It is important to note that, despite large evidence of the benefits of cardiac risk factor control in type 2 diabetes and the recommendation from the US National Cholesterol Education Program (26), most of our patients did not achieve optimal management of the cardiac risk factors known to have adverse impact on short- and long-term prognosis. More than half of the patients were still smoking, and nearly 90% were exposed to long-term hyperglycemia as reflected by an increased blood $HgbA_{1c}$. Overall, only 9.1% of the patients had reached our predetermined management targets at hospital admission.

Inadequate control of cardiovascular risk factors in patients with cardiovascular disease also exists in other regions. In Europe, there is still a high prevalence of smoking, obesity, hyperlipidemia, and uncontrolled hypertension (27). In the United States, only one-third of patients with hyperlipidemia manage to maintain LDL-C concentration as defined in the National Cholesterol Education Program guidelines (28). These data, together with the results from our study, should incite both cardiologists and primary care physicians to improve the standards of care of diabetic patients and thus reduce cardiac risk factors to a minimum.

In conclusion, the present study has demonstrated that the management of cardiovascular risk factors is unsatisfactory in the majority of type 2 diabetic patients in our population. To reduce the severity of coronary artery disease and improve the overall prognosis of these patients, specialist as well as primary care physicians should make greater efforts to improve their cardiovascular risk factor management.

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