Clinical manifestations and risk factors of coronary artery disease in patients with diabetes mellitus in western Siberia

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ABSTRACT

Objective. To compare the prevalence of cardiovascular risk factors and clinical manifestations of coronary artery disease (CAD) between patients with type 2 diabetes mellitus (DM) and CAD who lived at northern latitudes vs. those who resided at southern latitudes in the Tyumen region, western Siberia.

Study design. This retrospective study involved 382 patients with type 2 DM selected from 8,573 patients with angiographic CAD (>50% stenosis). Out of the total, 243 patients were permanent residents at the high latitudes of the Tyumen region (“northern patients”), and 139 patients were permanent residents in areas south of the Tyumen region (“southern patients”).

Results. On average, northern patients were younger than southern patients (53 vs. 57 years, respectively). The odds ratio (OR) for living in the north was 2.1 (95% CI 0.99-4.53) for obesity (BMI≥30 kg/m²), 1.87 (95% CI 1.05-3.31) for smoking, 0.93 (95% CI 0.89-0.96) per 1 year increase in age, 0.84 (95% CI 0.76-0.94) per 1 mmol/L increase of fasting plasma glucose, and 1.15 (95% CI 1.04-1.28) per 1 mm increase of right ventricular end-diastolic diameter. The proportion of patients with 3 or more CAD risk factors was higher in the north. Most patients in both groups had a history of myocardial infarction, severe angina in class III/IV as defined by the Canadian Cardiovascular System (CCS), heart failure in class II/IV as defined by the New York Heart Association (NYHA) and hypertension.

Conclusions. A north–south gradient was observed in cardiovascular risk factors among patients with DM and CAD in the Tyumen region. The clinical manifestations of CAD in DM patients at high latitudes were comparable with those of patients who reside south of the Tyumen region of western Siberia, despite the younger age of northern patients.

Keywords: coronary artery disease, diabetes mellitus, cardiovascular risk factors, north–south gradient
INTRODUCTION

Previous investigations have demonstrated that high latitudes have a negative influence on the cardiovascular system. It has been shown that greater numbers of circumpolar residents in Russia have systemic hypertension than residents in other regions of the country (1–3). Diabetes mellitus increases the severity of symptoms caused by coronary artery disease (CAD) in patients with both diseases (4). The aim of the study was to compare the prevalence of cardiovascular risk factors and clinical manifestations of the disease between diabetic CAD patients living in northern and southern Siberia.

MATERIALS AND METHODS

Patients
Between January 1996 and February 2007, all 382 patients who had type 2 diabetes mellitus (DM) were selected from 8,573 patients with angiographic CAD (>50% stenosis) from admission records at the Tyumen Cardiology Center, Russia. Out of 382 patients, 243 were permanent residents in the north of the Tyumen region, (north of latitude 64°N), and 139 patients were permanent residents in the south of the Tyumen region (north of latitude 57°N). There is a significant difference in temperature between the north (where the mean temperature in winter is -29°C, and in summer is +8°C) and the south (-18° and +19°C, respectively) (5).

Coronary artery disease was defined using the criteria of the European Society of Cardiology and the American College of Cardiology (6). Type 2 DM was diagnosed using World Health Organization criteria (7). All patients had been clinically diagnosed with DM before they were recruited for the study. Cases of acute coronary syndrome were excluded. Sex, age, weight, height, body surface area and obesity (defined as a body mass index ≥ 30 kg/m²) were recorded during the initial examination. Blood pressure, concentrations of plasma, total cholesterol and plasma glucose were determined at baseline. Patients who were receiving antihypertensive treatment or whose blood pressure was above 140/90 mm Hg were classified as having hypertension. Patients who had smoked more than 100 cigarettes during their lifetimes and who either continued to smoke on a daily basis or occasionally were classified as smokers. Patients who consumed alcohol were classified as moderate drinkers if they consumed no more than 1 drink per day for women and no more than 2 drinks per day for men, and heavy drinkers if they consumed more than 2 drinks per day on average.

Echocardiography
The study was carried out using standard echocardiographic systems (Phillips Imagepoint HX, Agilent Technologies, US; Vivid 3, 4, 7 Systems, Vingmed-General Electric, Horten, Norway). Echocardiographic examinations were completed using standard apical, parasternal and subcostal views. Echocardiographic images were stored on videotapes and analyzed by 2 investigators; a third investigator blinded to the protocol was employed if there was a discrepancy in the diagnosis. Echocardiographic dimensions were measured according to the guidelines of the American Society of Echocardiography (8).
Coronary artery disease in diabetes patients

and recommendations for chamber quantification (9). Left ventricular (LV) ejection fractions were measured by the Simpson method. LV masses were calculated using the formula introduced by Devereux and co-workers (10). The extent of all LV wall motion abnormalities were identified using the method developed by Widimsky and co-workers (11).

Quantitative coronary angiography
All the patients in the study underwent elective coronary angiography using standard projections (12) by Diagnost ARC A, Poly Diagnost C, and Integris Allura (Phillips, Holland). The minimal luminal diameter, average proximal and distal reference diameters, percentage stenosis and lesion length were determined for each pair of orthogonal views and then averaged. Lesions were considered significant if stenosis severity was >50%.

Data analysis
The results were presented as means along with their standard deviations (SD) and, in cases of qualitative variables, as percentages of patients belonging to each category. The distributions were checked for normality with the Kolmogorov–Smirnov criterion. Comparisons between the 2 groups were carried out using Student’s t-test for normally distributed variables, and the Mann–Whitney U test for data with skewed distributions. A binary logistic regression analysis was carried out to test the independent association of each variable with northern residence. Only variables associated with a p-value of 0.05 or less were included in the final model.

RESULTS
The clinical characteristics of patients are summarized in Table I. Northern patients were significantly younger and had lower plasma glucose levels than southern patients. The prevalence of smoking and alcohol consumption was significantly higher in northern patients. Most patients in both groups were obese, but obesity was more prevalent in the northern group.

The proportion of patients with 3 or more CAD risk factors was significantly higher in the northern group than it was in the southern group (70.7 vs. 57.7%, respectively).

There were no significant differences in frequencies of hypertension, history of myocardial infarction (MI), painless myocardial ischemia, Canadian Cardiovascular System (CCS) angina classes, New York Heart Association (NYHA) classes and plasma total cholesterol levels between the groups. Most patients in both groups had a history of MI, hypertension, severe angina (CCS class III/IV), heart failure NYHA class II/IV and high plasma total cholesterol levels.

Echocardiographic examinations (Table II) showed that aortic root diameters, right ventricular (RV) end-diastolic dimensions and LV ejection fractions were all significantly higher in northern patients. The prevalence of aortic stenosis was significantly higher in southern patients. No differences were found in LV end-diastolic diameter, LV wall thickness and LV mass between the groups. Angiographic data demonstrated more frequent lesions of the left circumflex artery (60.9 vs. 45.3%, respectively), and a higher prevalence of coronary artery calcification (16.9 vs. 8.8%, respectively) in southern patients compared to northern patients.
## Table I. Demographic and clinical characteristics of the patients.

| Characteristic                              | Northern patients (n=243) | Southern patients (n=139) | p       |
|--------------------------------------------|---------------------------|---------------------------|---------|
| Age, years (mean, SD)                      | 53.4±6.7                  | 56.9±6.9                  | <0.001  |
| Male, %                                    | 81.1                      | 74.1                      | NS      |
| Obesity, %                                 | 83.8                      | 72.5                      | 0.008   |
| Smokers, %                                 | 58.8                      | 32.4                      | <0.001  |
| Alcohol consumption, %                     | 38.5                      | 20.9                      | 0.001   |
| Hypertensive, %                            | 89.7                      | 94.2                      | NS      |
| Prior myocardial infarction, %             | 60.9                      | 55.4                      | NS      |
| Duration of DM, years                      | 4.7±5.4                   | 6.1±6.8                   | NS      |
| Painless myocardial ischemia, %            | 1.6                       | 1.4                       | NS      |
| CCS angina class, %                        |                           |                           |         |
| I                                          | 9.2                       | 6.4                       | NS      |
| II                                         | 31.3                      | 23.6                      | NS      |
| III                                        | 54.8                      | 68.2                      | NS      |
| IV                                         | 4.6                       | 1.8                       | NS      |
| NYHA class, %                              |                           |                           |         |
| I                                          | 14.6                      | 12.4                      | NS      |
| II                                         | 60.1                      | 60.6                      | NS      |
| III                                        | 24.9                      | 26.3                      | NS      |
| IV                                         | 0.4                       | 0.7                       | NS      |
| Total cholesterol, mmol/L                  | 5.6±1.5                   | 5.8±1.5                   | NS      |
| Glucose, mmol/L                            | 7.8±2.8                   | 8.7±2.8                   | 0.001   |
| Treatment of DM, %                         |                           |                           |         |
| Diet                                       | 11.9                      | 13.3                      | NS      |
| Hypoglycemic medication:                   |                           |                           |         |
| Oral agents                                | 64.2                      | 66.3                      | NS      |
| Insulin                                    | 22.7                      | 19.3                      | NS      |
| Oral agents + insulin                      | 1.1                       | 1.2                       | NS      |

aData are means and SDs, or percentages  
\(^b\)NS – not significant  
\(^c\)DM – diabetes mellitus  
\(^d\)NYHA – New York Heart Association  
\(^e\)CCS – Canadian Cardiovascular System

## Table II. Comparison of echocardiography results from the northern and southern patients.

| Characteristic                              | Northern patients (n=243) | Southern patients (n=139) | p       |
|--------------------------------------------|---------------------------|---------------------------|---------|
| IVS, mm                                    | 13.3±2.3                  | 13.4±2.1                  | NS      |
| LVPW, mm                                   | 11.4±1.5                  | 11.4±1.5                  | NS      |
| LV end-diastolic diameter, mm              | 52.0±4.7                  | 51.1±5.0                  | NS      |
| LV mass (grams)                            | 316.3±72.9                | 318.2±73.9                | NS      |
| LV ejection fraction, %                    | 55.5±8.0                  | 52.8±9.0                  | 0.003   |
| Extent of LV wall-motion abnormalities, %  | 11.8±14.8                 | 13.4±15.7                 | NS      |
| LV aneurysm, %                             | 10.0                      | 11.1                      | NS      |
| RV end-diastolic diameter, mm              | 26.2±3.5                  | 25.3±2.7                  | 0.012   |
| Left atrial dimension, mm                  | 43.3±4.5                  | 44.2±5.7                  | NS      |
| Aortic root diameter, mm                   | 35.3±3.5                  | 34.6±2.5                  | 0.018   |
| Signs of aortic atherosclerosis, %         | 85.1                      | 84.4                      | NS      |
| Aortic stenosis, %                         |                           |                           |         |
| Mild                                       | 4.6                       | 10.4                      | NS      |
| Moderate                                   | 0.8                       | 0.7                       | 0.009   |
| Severe                                     | -                         | 1.5                       |         |

aData are means and SDs, or percentages  
\(^b\)NS – not significant  
\(^c\)IVS – interventricular septum  
\(^d\)LV – left ventricular  
\(^e\)LVPW – left ventricular posterior wall  
\(^f\)RV – right ventricular
The multivariable analysis in Table III shows that compared to the south, northern residence was associated with a 2.1-fold increase in odds for being obese, with an 87% increased likelihood of being a smoker and a 15% increase for having a RV end-diastolic diameter 1 mm thicker than normal. Living in the north was also associated with younger age (a 7% decrease in odds per 1 year change in age) and lower blood glucose (a 16% decrease in 1 mmol/L change). Alcohol consumption, LV ejection fraction, aortic stenosis, lesions of the left circumflex artery and coronary artery calcification were initially entered into the model, but failed to meet the inclusion criteria and were excluded.

Table III. Odds ratios (OR) derived from logistic regression of northern residence on age, obesity, smoking, blood glucose and right ventricular (RV) end-diastolic diameter.

| Explanatory variables                        | OR   | 95% confidence interval |
|----------------------------------------------|------|-------------------------|
| Age (yr)                                     | 0.93 | 0.89–0.98*              |
| Obesity (body mass index ≥30 kg/m²)          | 2.12 | 0.99–4.53**             |
| Smoking                                      | 1.87 | 1.05–3.31***            |
| Glucose (mmol/L)                             | 0.84 | 0.76–0.94****           |
| RV end-diastolic diameter (mm)               | 1.15 | 1.04–1.28******         |

**DISCUSSION**

The relationship between mortality and environment temperature can be expressed as “cold weather being more deadly than hot weather” (13). The greater significance of cold was also confirmed in the Eurowinter study (14). This study did not assess CAD mortality in relation to temperature in the north and south of the Tyumen region; rather, we suggested that CAD clinical manifestations could be more severe in the north. Geographic variations in CAD have long been observed in different countries, with more severe clinical manifestations of CAD being seen in the north than those seen in the south (15–18). The frequency of cardiovascular risk factors followed the same north–south gradient as the one known for cardiovascular mortality (19,20). We hypothesized that the clinical manifestations of CAD in patients with DM could be more severe in the north of the Tyumen region compared to the south.

More frequent smoking, alcohol consumption, obesity and the prevalence of 3 or more CAD risk factors in the northern group confirmed that the prevalence of CAD risk factors among patients with DM in the Tyumen region followed the trend expected from previous studies (15–20).

We showed the independent association of CAD risk factors with northern residence. The results are similar to previous data that reported a high prevalence of smoking and obesity in circumpolar populations (21–23). There were no significant north–south differences in most of the clinical, echocardiographic and angiographic parameters, indicating that the CAD clinical manifestations
Coronary artery disease in diabetes patients

in DM patients were comparable in severity throughout the Tyumen region, despite the younger age of northern patients. We attribute the absence of such differences, at least partly, to the unwillingness of sick individuals to live and work in cold environments, which has increased the north–south difference.

The more frequent aortic stenoses in the southern group can be explained by the older age of these patients. The age difference could also explain the higher prevalence of impaired LV ejection fraction, coronary artery calcifications and circumflex artery lesions in southern patients. The severity of CAD clinical manifestations are affected not only by age and climate but also by social conditions (15,24,25), which are poorer in the north.

Limitations
The primary limitation of this study was its retrospective character. This may have caused information bias during data collection. Another limitation was associated with the long period of data collection. From 1996 to 2007, new generations of monitoring equipment were used in our clinic. These devices provided better (but different) image quality by the end of the investigation compared with the images that were taken at the start of it.

Conclusions
The north–south difference of cardiovascular risk factors was observed among patients with DM and CAD in the Tyumen region. The clinical manifestations of CAD in DM patients were comparable at high latitudes and in the south of the Tyumen region of western Siberia, despite the younger age of northern patients, which perhaps can be attributed to the selection of healthier individuals in the north. In addition, a combination of CAD and DM is unfavourable regardless of where patients reside in the Tyumen region.

Ethics
This investigation has been approved by the Ethics Committee of the Tyumen Cardiology Center.

Conflict of interest statement
The authors declare no conflict of interest.

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