

ORIGINAL ARTICLE

Characteristics of coronary artery disease in men with type 2 diabetes mellitus

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Abstract: **Background** – Ischemic heart disease is responsible for most serious morbidity and mortality in diabetic patients who have a 2 to 4 fold increase in the risk of coronary artery disease compared to non diabetic patients. **Objective** – To evaluate the particular features of ischemic heart disease in men with type 2 diabetes mellitus. **Materials and methods** – A retrospective, case-control study created by comparative analysis of anamnestic, paraclinical and coronarographycal data of 224 men angiographically investigated for ischemic heart disease that were divided according to the presence of diabetes into 2 groups with similar age distribution. **Results** – We objectified a high prevalence of ischemic heart disease in diabetic patients aged 60-69 (39.28%). The diabetic population more commonly presented obesity, hypertension, hypetriglyceridemia and low HDL cholesterol (43.75% versus 30.36%, 75% versus 66.06%, 62.50% versus 49.11% and 55.36% versus 50.89%, respectively). Diabetic men had more frequently three vessel disease (37.5% versus 34.82%), in-stent restenosis after angyoplasty and indication of coronary artery bypass grafting. **Conclusions** – In men with type 2 diabetes mellitus, the atherosclerosis risk factors (obesity, hypertension and atherogenic dyslipidemia) were better expressed and the coronary artery disease was more severe with complications after angyoplasty and required more often surgical myocardial revascularization.

Keywords: ischemic heart disease, diabetes mellitus, coronarography

Rezumat: **Introducere** – Boala cardiacă ischemică este responsabilă pentru o mare parte a morbidității grave și mortalității pacienților diabetici, care au risc de 2 - 4 ori mai mare pentru dezvoltarea unei boli coronariene comparativ cu pacienții fără diabet. **Obiectiv** – Evidențierea particularităților cardiopatiei ischemice la bărbații cu diabet zaharat tip 2. **Material și metodă** – Studiu retrospectiv, caz-martor, realizat prin analiza comparativă a datelor anamnestice, paraclinice și coronarografice a 224 bărbați investigați angiografic pentru cardiopatie ischemică divizați în funcție de prezența diabetului în 2 loturi cu distribuție similară pe grupe de vârstă. **Rezultate** – Am obiectivat o prevalență crescută a cardiopatiei ischemice la pacienții diabetici din grupa de vârstă 60-69 ani (39,28%). La populația diabetică au fost mai frecvent observate obezitatea, hipertensiunea arterială, hipetrigliceridemia și HDL colesterolul scăzut (43,75% versus 30,36%, 75% versus 66,06%, 62,50% versus 49,11% și respectiv 55,36% versus 50,89%). Pacienții cu diabet au prezentat mai frecvent afectare triconariană (37,5% versus 34,82%), restenoză intrastent postangioplastie și indicație de bypass aortocoronarian. **Concluzii** – La bărbații diabetici, anumiți factori de risc ai aterosclerozei - obezitatea, hipertensiunea arterială și dislipidemia aterogenă au fost mai bine exprimați iar afectarea coronariană a fost mai severă, cu complicații postangioplastie și indicație mai frecventă de revascularizare miocardică chirurgicală.

INTRODUCTION

Diabetes mellitus (DM) has become a major public health and economic problem. It is considered that the prevalence of diabetes worldwide, estimated at 2.8% (171 million) in 2000 will increase to 4.4% (366 milli-

on) in 2030¹. In this context, cardiovascular disease, the major cause of morbi / mortality among diabetic patients requires a comprehensive management with an aggressive strategy of risk factors control.

OBJECTIVE

To identify the characteristics of coronary heart disease in men with type 2 diabetes mellitus.

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MATERIALS AND METHODS

To achieve our goal we performed a retrospective, case - control study, analyzing clinical and laboratory data of patients with ischemic heart disease (IHD) with and without type 2 DM. The data were extracted from the observational sheets from the archives of the Institute of Cardiovascular Diseases „Prof. Dr. George IM Georgescu” (IBCV) Iasi.

The clinical spectrum of IHD included silent myocardial ischemia, various forms of angina pectoris (stable, unstable) and myocardial infarction. Glycemic status was evaluated according to American Diabetes Association criteria (ADA) 2003 as follows: normal glucose regulation was defined by the values of fasting plasma glucose (FPG) <5.6 mmol/L (100 mg/dl) and the diagnosis of diabetes was determined by two values of FPG ≥ 7.0 mmol/L (126 mg/dl) (venous plasma glucose).

The inclusion criteria for the first group were: male gender, presence of diabetes mellitus, diagnosis of IHD, hospitalization and angiographic investigation in IBCV Iasi during the period of January 1 to December 31, 2008.

The inclusion criteria for the second group (control group) were: male gender, normal glucose control, diagnosis of IHD, angiographic investigation in IBCV Iasi in 2008, age distribution similar to the first group (we have chosen randomly from the non diabetic men, angiographically investigated for IHD in 2008 similar numbers of patients for each age group identified in the diabetic group).

For both groups, the presence of severe aortic stenosis represented exclusion criteria.

Statistical analysis with comparisons of the diabetic patients with matched controls was performed in Microsoft EXCEL program using *t* test (t-test assuming unequal variances for two samples) and coefficient of variation (CV). Statistic significance threshold was considered $p = 0.05$. According to the CV, a significance test that asses the representativeness of the mean, the mean was highly representative ($CV \leq 17\%$), moderate representative ($CV = 17-35\%$), weakly representative ($CV = 35-50\%$) or unrepresentative ($CV > 50\%$).

RESULTS

112 diabetic men without severe aortic stenosis were investigated for IHD in IBCV in the year 2008.

The mean age of the diabetic group was 61.32 years (CV 14.38%).

The age distribution of patients objectified a high prevalence of invasive coronary investigation in dia-

betic men from the age group of 60-69 years (39.28%) (Figure 1).

The majority of patients were from the urban area (84.82% in the first group and 72.32% in the second one).

There were no statistically significant differences in the duration of hospitalization in the 2 groups (the mean duration of hospitalization was 7 days).

The incidence of stroke was similar in the 2 groups (7.14% in the diabetic group versus 6.25% in the non diabetic group).

Cardiovascular heredity, smoking and chronic ethanol consumption were more frequent in the control group compared with the diabetic one (56.89% versus 55.17%, 66.07% versus 58.92% and 21.42% versus 7.14%, respectively).

All diabetic patients had type 2 DM. 18.75% of them had a positive family history of diabetes. There were 17 cases of newly diagnosed DM. The duration of diabetes varied largely (0-30 years) with a mean duration of 6.41 years. Insulin therapy was used in 20% of cases.

Glycated hemoglobin was measured in 66 patients and had a mean value of 8.31%. Diabetes mellitus was generally poorly controlled. 54.55% of the patients had a glycated hemoglobin $>8\%$, 30.3% presented a glycated hemoglobin of 6.5-8% and 15.15% a glycated hemoglobin $<6.5\%$. Only 6.25% had a fasting plasma glucose <108 mg/dl.

Patients were classified according to the body mass index (BMI) as follows: BMI = 18.5 to 24.99 kg/m^2 - normal weight, BMI = 25 to 29.99 kg/m^2 - overweight, BMI = 30 to 34.99 kg/m^2 - grade I obesity, BMI = 35 to 39.99 kg/m^2 - grade II obesity, BMI >40 kg/m^2 - grade III obesity.

We objectified statistically significant differences ($p = 0.00004$) in terms of weight status between the 2 groups. Normal weight status was 2 times more frequent in the control group compared with diabetic patients.

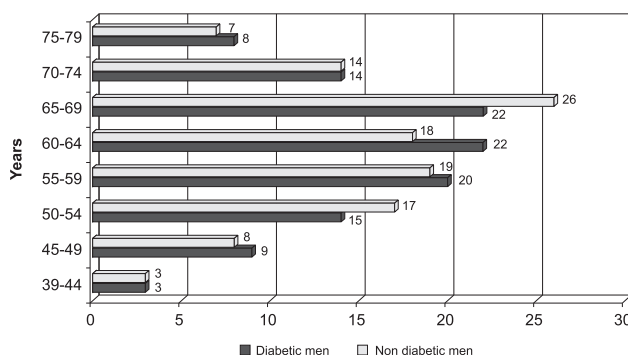


Figure 1. Distribution of the 2 groups according to age.

ts. The average body mass index was 29.46 kg/m² (CV 13.63%) in the diabetic group and 27.46 kg/m² (CV 12.52%) in matched controls. The diabetic men were superior in number in all 3 groups of obesity (**Figure 2**).

Depending upon the value of blood pressure, patients were divided in the following categories: normotensive - systolic blood pressure (SBP) <139 mmHg (men without DM) / <130 mmHg (diabetic men) and/or diastolic BP (DBP) <89 mmHg (men without diabetes) / 80 mmHg (diabetic men), grade 1 hypertension - SBP = 140-159 mmHg and/or DBP = 90-99 mmHg, grade 2 hypertension - SBP = 160-179 mmHg and/or DBP = 100-109 mmHg and grade 3 hypertension - SBP ≥180 mmHg and/or DBP ≥110 mmHg.

We noted statistically significant differences in the tensional status between the 2 groups ($p = 0.013$) (**Figure 3**).

Normal blood pressure was more common in men without diabetes (33.94% versus 25%). The majority of diabetic men had high grade hypertension (54.46% versus 41.96%).

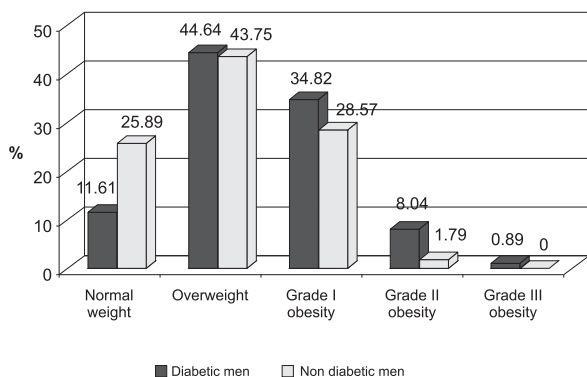


Figure 2. Distribution of the 2 groups according to weight status.

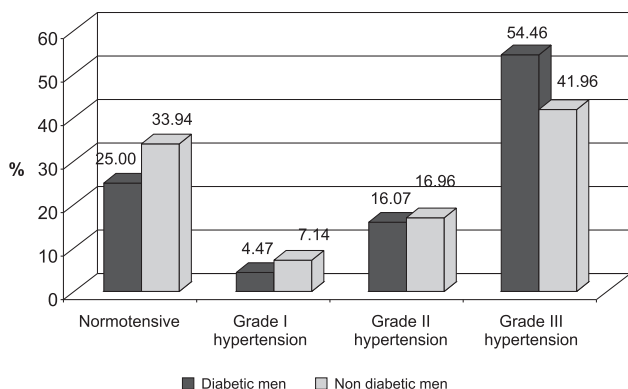


Figure 3. Distribution of the 2 groups according to blood pressure.

Orthostatic hypotension was 3 times more common in the diabetic group (8.92% versus 2.67% in matched controls).

We objectified statistically significant differences ($p = 0.028$) in the values of resting heart rate between the 2 groups. 10.71% of diabetic men compared with 5.35% of matched controls had a resting heart rate >90 beats/minute while a resting heart rate <70 beats/minute was encountered in 42.85% of diabetics compared with 60.71% of non diabetic patients.

The lipid status was evaluated by the values of triglycerides (TG), total cholesterol (Col T), LDL cholesterol (LDL c) and HDL cholesterol (HDL c). The lipid profile of diabetic patients was characterized by elevated TG (62.50% versus 49.11%) ($p = 0.034$) (**Figure 4**). The mean value of TG was 178 mg% in the diabetic group compared with 160 mg% in the control group.

Diabetic men more frequently presented low HDL cholesterol (55.36% versus 50.89%) but without reaching statistical significance threshold ($p = 0.29$). No statistically significant differences were registered between total cholesterol ($p = 0.24$) and LDL cholesterol ($p = 0.08$). The mean value of total cholesterol was 174 mg% (CV 27.07%) in the diabetic group and 178 mg% (CV 21.67%) in the control group, and the LDL cholesterol had a mean value of 98.5 mg % in the first group (CV 39.34%) and 105.21 mg% in the second one (CV 29.98%).

There were statistically significant differences ($p = 0.039$) in the values of serum creatinine between the 2 groups. The mean value of creatinine was 1.18 mg% in diabetic patients and 1.09 mg% in matched controls. 12.5% of diabetic patients compared with 7.14% of matched controls presented a serum creatinine >1.5

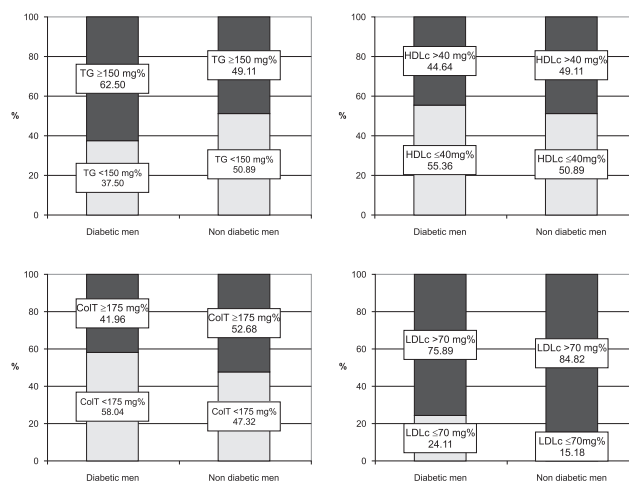


Figure 4. Distribution of the 2 groups according to lipid pattern.

mg /dl. 19.67% of diabetic patients presented proteinuria and 38,8% glycosuria.

Kinetic disorders were recorded in similar percentages in both groups (52.52% in the diabetic group and 52.23% in the non diabetic group). We objectified statistically significant differences between the thickness of interventricular septum (IVS) ($p = 0.03$) and left ventricular posterior wall (LVPW) ($p = 0.0012$). Average thickness of the IVS was 13.08 mm (CV 15.19%) in the diabetic group compared with 12.35 mm (CV 15.55%) in the control group and the LVPW was 12.42 mm (CV 13.61%) in the first group compared with 11.69 mm (CV 14.6%) in the second one.

Men without diabetes that were angiographically investigated for IHD more frequently presented the diagnosis of myocardial infarction (MI) - acute (AMI - 11.61% versus 9.82%) or in their medical history (56.25% versus 45.54%) (**Figure 5**).

Among patients with myocardial infarction thrombolysis was performed in 6 diabetic patients and 18 patients without diabetes.

The analysis of angiographic data showed that diabetic men had more frequent multivessel disease compared with non diabetics (three vessel disease 37.50% versus 34.82%) (**Figure 6**). The incidence of IHD without coronary lesions was very low in both groups.

The left main coronary artery was more commonly affected in people without diabetes (8.92% versus 5.35% in diabetic patients).

The majority of patients with one vessel disease presented left descending artery lesions (51.43% in the diabetic group and 47.37% in the control group), followed by stenosis of right coronary artery (25.71% and 39.47%, respectively) and left circumflex artery (22.86% and 13.16%, respectively).

For the two vessel disease, the most common association was in both groups the lesions on left descending and right coronary artery (54.84% in diabetic patients and 46.67% in matched controls).

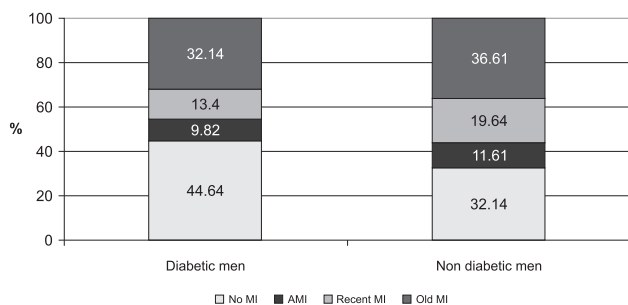


Figure 5. Distribution of the 2 groups according to the presence of myocardial infarction.

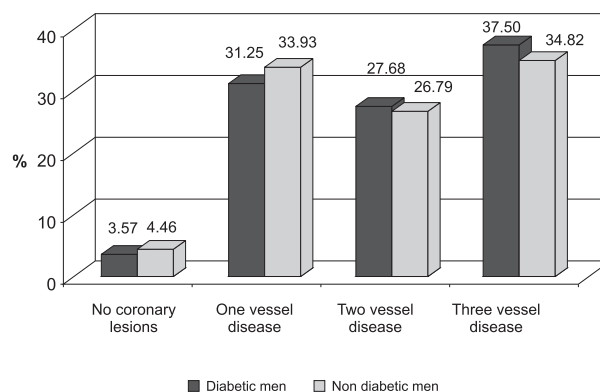


Figure 6. Distribution of the 2 groups according to the coronary lesions.

Percutaneous coronary angioplasty with stenting was performed in equal percentages in the 2 groups (60.71%) but the use of pharmacologically active stents was predominant in the diabetic group (22.05% versus 10.29%).

Acute stent thrombosis was diagnosed in 2 diabetics and caused the death of the patients.

12.5% of diabetic patients compared with 4.46% of patients without diabetes required intervention for in-stent restenosis.

More diabetic men presented surgical myocardial revascularization indication (27.67% versus 25% of patients without diabetes).

DISCUSSIONS

Diabetic patients accumulate more atherogenic risk factors than patients without diabetes, including hypertension, obesity and lipid abnormalities and the coronary risk increases proportionally with the intensity of these factors².

Hypertension is present at diagnosis in many patients with type 2 diabetes³. Most convincing evidence for the importance of hypertension in diabetes comes from the United Kingdom Prospective Diabetes Study in which at nine years follow-up each 10 mmHg reduction in mean systolic blood pressure was associated with a 12% decrease in the risk of developing a cardiovascular complication, the lowest risk occurring at a systolic blood pressure below 120 mmHg⁴. Our study confirms the high prevalence of hypertension in diabetic patients. Only one quarter of diabetic patients were normotensive in our study while the majority had high grade hypertension.

Obesity is also an independent risk factor for cardiovascular disease⁵. Eighty percent of patients with type 2 DM are either obese or overweight and obesity independently predicts cardiovascular disease and coro-

nary atherosclerosis⁶. Our study objectified statistically significant differences between weight status in the 2 groups with a marked prevalence of obesity in diabetic patients.

- There are some differences in the lipid profile in diabetic patients compared with those without diabetes that may explain the accelerated development of atherosclerosis. Lipid abnormalities characteristic of type 2 diabetes include elevated triglycerides, low levels of HDL cholesterol and elevated concentrations of small and dense LDL cholesterol particles⁷. In addition, for any concentration of plasma lipoproteins, patients with diabetes have more severe coronary artery disease compared with patients without diabetes. This increased risk may be due in part to qualitative differences of lipoprotein fractions (small and dense LDL cholesterol) that are more susceptible to oxidation and penetrate more easily the intima of the vessel⁸. In our study we objectified statistically significant differences in the levels of triglycerides between the 2 groups. The mean values of total cholesterol and LDL cholesterol were higher in men without diabetes but without statistical significance ($p = 0.24$ respectively 0.078). For technical reasons we could not qualitatively evaluate the LDL particles and similar total LDL cholesterol concentrations cannot exclude the presence of high concentrations of small dense particles. Unlike data on lipid profile in diabetic women that we obtained in a previous study⁹, there were no statistically significant differences in the level of HDL cholesterol that had a mean value of 42 mg/dl in both groups. We noted a modest percentage of achievement of lipid therapeutic target values¹⁰ in the diabetic population 58.04% for total cholesterol, 24.11% for LDL cholesterol, 44.64% for HDL cholesterol and 37.5% for triglycerides.

A particularity of our study is that more non diabetic patients angiographically investigated for IHD in 2008 in our center had a history of myocardial infarction compared with diabetic patients. A possible explanation is the higher addressability of diabetic patients who are referred for exploration due to the frequent presence of multiple risk factors, the better medical education that allows presentation for investigation before the instauration of a clinical major cardiovascular event but also the fact that patients with type 2 diabetes have a high rate of asymptomatic coronary disease¹¹. However, even though 55.36% of diabetic patients compared with

67.86% of matched controls had a major cardiovascular event, angiographic data revealed no statistically significant differences between the number of coronary lesions in the 2 groups ($p = 0.28$), an argument that diabetes mellitus is a coronary heart disease equivalent¹². Moreover, we noted a tendency of diabetic patients to have three vessel disease. Our data are consistent with the literature on the susceptibility of diabetic patients to develop multivessel disease^{13,14}.

Although procedural success rates are similar in patients with and without diabetes receiving elective percutaneous coronary intervention with stent^{15,16}, diabetic patients have higher rates of short and long term complications. Diabetic patients have higher rates of restenosis and coronary artery disease progression compared with patients without diabetes¹⁷⁻¹⁹ requiring repeat revascularization even though restenosis was reduced by the use of drug eluting stents instead of bare metal stents in diabetic patients with stable or unstable coronary disease with similar risk of death or MI²⁰. The use of drug eluting stents compared with bare metal stents has drastically reduced the rate of restenosis in diabetic patients. Furthermore, DM is an independent predictor of acute stent thrombosis²¹. In our study acute stent thrombosis was present only in the diabetic group with a fatal outcome and the rate of repeat revascularization for in stent restenosis was greater in diabetics compared to matched controls. In addition, due to the characteristics of the coronary lesions, more diabetic patients compared to controls were referred for surgical myocardial revascularization.

CONCLUSIONS

There are statistically significant differences between certain risk factors for coronary heart disease in men with type 2 diabetes mellitus compared with non diabetic patients. Men with diabetes are more frequently hypertensive, obese, have higher triglycerides levels and left ventricular hypertrophy.

Diabetic men present more frequently coronary multivessel disease that require surgical myocardial revascularization techniques and develop more commonly complications when percutaneous angioplasty with stenting is performed.

The diabetic patients with coronary heart disease require a cardio diabetological approach with a better control of diabetes and aggressive strategy against all cardiovascular risk factors.

Conflict of interests: none declared.

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