CARDIOVASCULAR RISK IN PATIENTS WITH TYPE 2 DIABETES AND RETHINOPATHY

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Abstract

Aym: Type 2 diabetes is an independent risk factor for cardiovascular disease, and also generates multiple microvascular complications. We searched the association between diabetic retinopathy (as one of the most important long time microvascular complications in diabetes) and cardiovascular risk (calculated trought UKPDS risk engine) in subjects with T2DM without known cardiovascular diseases.

Material and methods: We examined 100 patients with type 2 diabetes, without clinical evidence of coronary, cerebrovascular or peripheral artery disease; 48 (48%) were women (mean age at examination 61.23±8.49) and 52 (52%) were men (mean age 60.75±8.43). Diabetic retinopathy was graded from retinal photograph according to Early Treatment for Diabetic Retinopathy Study severity scale. The cardiovascular risk was calculated for every patient using UKPDS Risk Engine. Statistically analysis was performed using Mann-Whitney U-test, Kruskal-Wallis and Oneway Anova tests.

Results: Diabetic retinopathy was found in 59.5% men and 40.5% women. Cardiovascular risk was significantly higher in patients with retinopathy compared with patients without retinopathy (28.05±14.33 vs. 16.42±12.72 for CHD; 20.06±12.46 vs. 10.34±9.63 for fatal CHD; 13.92±10.25 vs. 9.20±8.76 for stroke; 2.24±1.86 vs. 1.39±1.47 for fatal stroke) with p=0,000… in every cases.

Conclusions: We found a statistically significant correlation between retinopathy and cardiovascular risk, which sugested that in type 2 diabetes microvascular complications are likely developping in the same time with macrovascular complications and shares the sames pathogenic ways.

***Key words**: diabetic retinopathy, type 2 diabetes, cardiovascular risk.*

Introduction

It is known that diabetes currently affects 246 million people worldwide and the prevalence is estimated to increase around 380 million until 2025. In 2007 top 5 countries with the largest number of people suffering from diabetes were: India (40,9 million), China (39,8 million), USA (19,2 million), Russia (9,6 million), Germany (7,4 million). Every year, about 7 million people will develop diabetes. Besides, every year, 3,8 million deaths are also attributed to diabetes, but the number is even higher if we consider deaths due to cardio-vascular disease aggravated by the diabetes. Diabetes is therefore, the 4th cause of death worldwide. It is estimated that over 50% of people with

diabetes are not diagnosed, in some countries this percentage can reach up to 80% (1).

Macro-vascular complications make people suffering from diabetes to have a life expentancy of approximately 5-10 years smaller than those without diabetes.

Taking into account this data, results that prevention of specific complications of diabetes is the key issue because of the morbidity associated.

Type 2 diabetes is an independent risk factor for developing atherosclerosis. Accelerated atherosclerosis is responsable for most deaths of people with diabetes. In fact these are 4 times more prone to atherosclerosis comparing to those with normal blood glucose. Another well- known fact that raises problems is that the life expectancy of people suffering for diabetes is similar to a person without diabetes, but who had suffered a myocardial infarction. Diabetes is in fact equivalent for cardiovascular disease (2).

Earlier studies have shown that proliferative retinopathy predicts cardiovascular mortality and morbidity in both type 1 (3-6) and type 2 (7, 8) diabetic populations. Less well appreciated is the correlations between microvascular complications and cardiovascular risk, or, in other words, in what measure the presence and the severity of microvascular complications, such as diabetic retinopathy, can modify global cardiovascular risk. Recent data have also suggested that non-proliferative retinopathy predicts mortality from all causes and from cardiovascular disease (CVD) only in women with type 2 diabetes (9), thus suggesting a possible sex difference in the adverse impact of non-proliferative retinopathy on incident CVD events, although this hypothesis needs verification in larger studies. However, these observations suggest similar underlying, biological mechanisms in the pathophysiology of cardiovascular disease and retinopathy in diabetes.

The fact that retinal changes may be a signal for cardio vascular events is not yet clearly demonstrated and is a theme which can offer us big surprises in the future. In this study we try to prove the link that seems to exist between diabetic retinopathy and cardiovascular risk in type 2 diabetes.

Material and methods

We studied 100 patients with type 2 diabetes recorded at Clinical Hospital C.F. Craiova. All patients were free of diagnosed CVD as ascertained by notes review, medical history and clinical examination, and electrocardiogram. In each patient we measured total cholesterol, HDL-C, triglicerides and calculated LDL-C using Fiedwald formula LDL-C=total cholesterol-(HDL-C+TG/5) mg/dl, when TG were under 400 mg/dl. We also questioned about diabetes duration, smoking and measured blood pressure, BMI and abdominal circumference. Blood pressure was recorded as the mean of three consecutive measurements in the sitting position taken 5 min apart. Hypertension was defined according to the current guidelines (10) as BP levels $\geq$ 140/90 mmHg or the use of anti-hypertensive drugs.

Cardiovascular risk was calculated for each patients using UKPDS Risk Engine (11). Diabetic retinopathy was graded from retinal photograph by a single ophthalmologist, according to Early Treatment for Diabetic Retinopathy Study severity scale (12). For this study, retinopathy was classified into three

categories as follows: no retinopathy, non-proliferative retinopathy (microaneurysms, intra-retinal haemorrhages and/or hard exudates) and proliferative/laser-treated retinopathy (new-vessel formation, fibrous proliferations, vitreous hemorrhages or previous laser coagulation therapy).

Statistical analysis

Statistical analysis was performed using programs available in the SPSS 17.0 statistical package. All variables were tested for normal distribution of the data. Data are presented as means ± standard deviation or percentages. Differences between the studied groups examined using t-test or the Mann-Whitney U-test for parametric and non-parametric data, respectively, while a chi-square test was used for categorical data. P-values < 0.05 were considered statistically significant.

Results

General characteristics:

Total number of subjects 100

Men 52 (52%) mean age at examination 60.75±8.43

Women 48 (48%) mean age at examination 61.23±8.49

Clasification of the groups – we found diabetic retinopathy in 42 (42%) subjects. Among these, 25 (59,5%) were men and 17 (40,5%) were women. The control group (patients without retinopathy) has 58 subjects, with 27 (46,6%) men and 31 (53,4%) women. Clinical and laboratory characteristics of the groups are shown in the table below (table 1).

Table 1. Baseline characteristics of diabetic patients grouped according to stages of diabetic retinopathy

Variable	Diabetic retinopathy		
	None	Nonproliferative	Proliferative
Sex m/f (n)	27 /31	19/16	6/1
Mean age (years)	60,69±8,79	61,71±7,95	59,71±8,60
Diabetes duration (years)	6,53±4,55	8,31±5,24	13,86±7,67
Total cholesterol(mg/dl)	199,84±45,73	221,89±42,39	228,86±45,26
TG (mg/dl)	172,53±104,53	178,03±114,33	188,14±111,66
HDL (mg/dl)	48,64±14,70	38,14±12,54	43,00±12,08
LDL (mg/dl)	117,33±45,35	153,44±41,64	146,71±49,40
HbA1c	6,52±0,70	7,64±1,35	6,60±1,04
Current smoker(%)	12 (20,7%)	16 (45,7%)	5 (71,4%)
Systolic blood pressure (mm Hg)	138,33±16,74	144,71±16,78	151,00±16,75
Diastolic blood pressure (mm Hg)	83,64±9,13	88,14±7,64	94,00±12,41
Hypertension (%)	40 (69,0%)	34 (97,1%)	7 (100%)
BMI (kg/m^2)	30,33±4,48	29,44±3,90	28,02±1,70
Abdominal circumference (cm)	100,17±10,79	98,03±13,61	99,00±7,05

As shown in table 1, patients with retinopathy were leaner, smoked more frequently, had higher frequency of hypertension, higher HbA1c and longer duration of diabetes than those without retinopathy.

Regarding cardiovascular risk, we found a highly significant correlation between the presence and severity of diabetic retinopathy and the risk for cardiovascular disease, as shown in table 2 and fig. 1-4.

Table 2 Cardiovascular risk and diabetic retinopathy

Cardiovascular risk	Diabetic retinopathy	N.	Means	Standard deviation	Sig. (2-tailed)
Chd (%)	None	58	16,42	12,72	0,000
	Nonproliferative	35	27,54	14,02	
	Proliferative	7	30,64	16,75	
Fatal chd (%)	None	58	10,34	9,63	0,000
	Nonproliferative	35	19,71	12,05	
	Proliferative	7	21,80	15,28	
Stroke (%)	None	58	9,20	8,76	0,003
	Nonproliferative	35	13,08	9,75	
	Proliferative	7	18,13	12,43	
Fatal stroke (%)	None	58	1,39	1,48	0,001
	Nonproliferative	35	2,08	1,84	
	Proliferative	7	3,01	1,85	

As shown in fig. 1-4, the cardiovascular risk was remarkably higher in patients with proliferative/laser-treated retinopathy than in those with non-proliferative retinopathy and those without retinopathy, respectively.

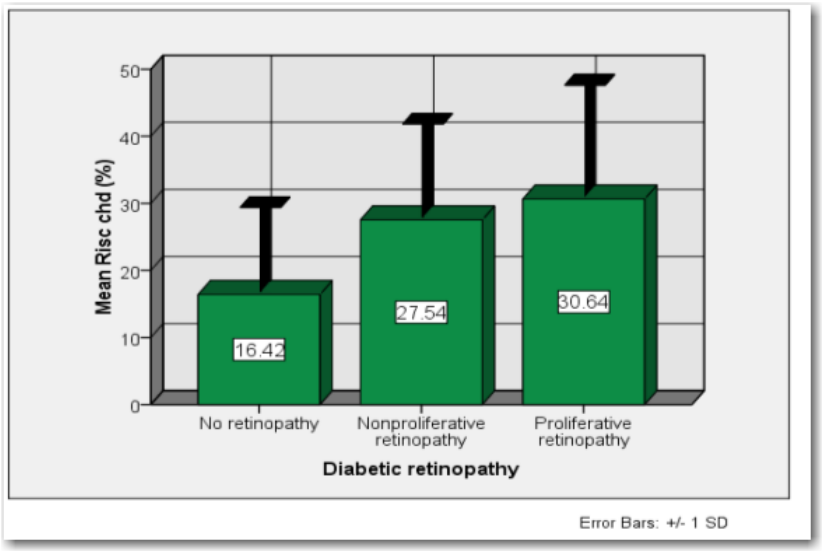

Fig. 1 Risk chd according to stage of diabetic retinopathy

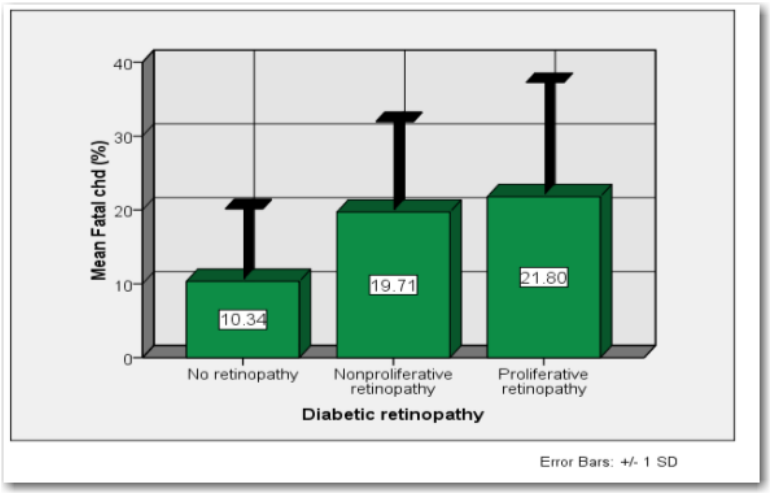

Fig. 2 Risk of fatal chd according to stage of diabetic retinopathy

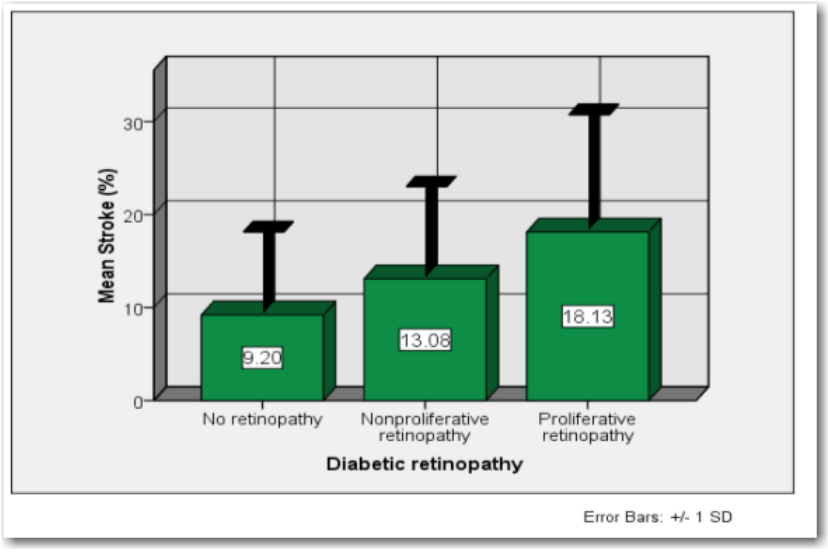

Fig. 3 Risk of stroke according to stage of diabetic retinopathy

Discussion

The association of diabetic retinopathy and an increased cardiovascular risk has been described before (13), but the information on the impact of diabetic retinopathy on the incidence of CVD in large type 2 diabetic populations is limited and conflicting

Diabetic retinopathy and microalbuminuria are expressions of microvascular damage. They often appear together and point toward possible future macrovascular events (14).

In this article we found a statistically significant correlation between retinopathy and cardiovascular risk, which sugested that in type 2 diabetes microvascular complications are likely developping in the same time with macrovascular complications and shares the sames pathogenic ways.

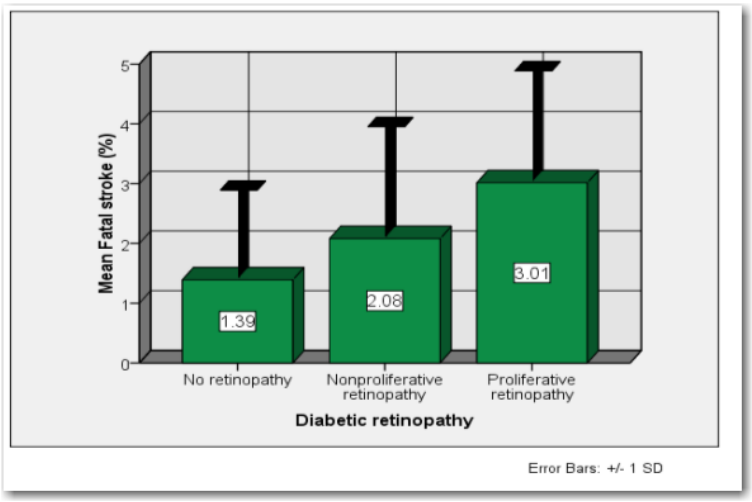

Fig. 4 Risk of fatal stroke according to stage of diabetic retinopathy

Multifactorial intervention can lessen the consequences of these pathological conditions. Interdisciplinary collaboration between diabetologists, nephrologists, cardiologists and ophthalmologists, as well as general practitioners and internists seems to be necessary for these diseases.

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