

THE ASSESSMENT OF THE GLUCOSE DIABETIC RETINOPATHY AND INTIMA-MEDIA THICKNESS IN TYPE 2 DIABETES

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Abstract

Background. Type 2 diabetes is an independent risk factor for cardiovascular disease, and also generates multiple microvascular complications. We searched the association between increased intima-media thickness, as an early sign of atherosclerosis, and diabetic retinopathy in a group of patients with type 2 diabetes.

Material and methods. We examined 100 patients with type 2 diabetes, registered in Clinical Hospital C.F. Craiova. Intima-media thickness was assessed in carotid artery by ultrasound and diabetic retinopathy was graded by retinal photography according to Early Treatment for Diabetic Retinopathy Study severity scale. Statistical analysis included Student's, Mann-Whitney, chi-square, Fisher tests and multiple regression.

Results. Diabetic retinopathy was found in 42% of patients. IMT correlates highly significant with the presence of retinopathy (mean value 0,83 mm in those without retinopathy vs. 0,90 mm in those with nonproliferative retinopathy, vs. 0,93 in those with proliferative retinopathy: $p = 0,000$). In multiple regression analysis, diabetic retinopathy was the most significant predictor of increased IMT, with a $p = 0,000$, along with smoking ($p = 0,031$).

Conclusions. Diabetic retinopathy was associated with an increased intima-media thickness in type 2 diabetes and, furthermore, could be an independent predictor for atherosclerosis.

Key words: diabetic retinopathy, intima-media thickness, atherosclerosis, type 2 diabetes.

Introduction

It is known that diabetes currently affects 246 million people worldwide and the prevalence is estimated to increase around 380 million until 2025 (1). 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 cardiovascular disease aggravated by the diabetes.

Diabetes is therefore, the 4th cause of death worldwide.

Type 2 diabetes is an independent risk factor for developing atherosclerosis and also generates multiple microvascular complications (2). Diabetic retinopathy it's the most important long time microvascular complication in diabetes and also a major cause of blindness among the people of working age worldwide. Micro and macroangiopathy frequently coexists and it

was shown that diabetic retinopathy increased the risk for cardiovascular events (3). The question is whether microangiopathy (for example diabetic retinopathy) can be an independent risk factor for the presence of atherosclerosis in type 2 diabetes mellitus. The number of relevant studies in this matter was limited and the results were unclear (4-7).

In this study we tried to find the association between diabetic retinopathy and intima media-thickness (as a sign of early stage of atherosclerosis) in a group of patients with type 2 diabetes without known cardiovascular disease.

Material and methods

We used the data of 100 patients with type 2 diabetes recorded at Clinical Hospital C.F. Craiova.

Exclusion criteria – clinical evidence of macrovascular complication (peripheral arterial disease, previous stroke or myocardial infarction, abnormal EKG), active liver disease.

Diabetic retinopathy was graded from retinal photograph according to Early Treatment for Diabetic Retinopathy Study severity scale (8).

Intima media thickness was measured ultrasonographically in the supine position on the right and left common carotid arteries 2 cm proximal to the carotid bulb and we used the mean value obtained in each patient.

In addition, we performed basic clinical laboratory analysis, such HbA1c and lipids. Total cholesterol, triglycerides and HDL-C were determined using enzymatic methods in C.F. Clinical hospital' laboratory. LDL-C was calculated using the Friedewald formula.

HbA1c was determined by chromatography method (Marius Nasta laboratory Bucharest). 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 (9) as BP levels $\geq 140/90$ mmHg or the use of anti-hypertensive drugs.

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 \pm 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

A multiple linear regression was utilized to define the independent predictors of IMT. The optimal regression models were built with stepwise method, and eliminates the independent values who did not reach statistical significance. *p* values $< 0,05$ were considered statistically significant.

Results

We studied 100 patients with type 2 diabetes. Among these, 52 (52%) were men (mean age at examination 60.75 ± 8.43) and 48 (48%) were women (mean age at examination 61.23 ± 8.49). We found diabetic retinopathy in 42 (42%) subjects (59,5% were men and

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 Clinic and laboratory characteristics of the groups

Variable	Without retinopathy	With retinopathy	p (2 tailed)
Male/female (%)	27 (46.6%)/31(53.4%)	25 (59.5%)/17(40.5%)	0,228
Mean age	60.69±8.79	61.38±7.99	0.690
Diabetes duration (years)	6.00 (3.00-9.00)	10.00 (4.00-12.25)	0.020
HbA1c (%)	6.52±0.70	7.46±1.35	0,000
Smoker (%)	12 (20.7%)	21 (50.0%)	0.003
Hypertension (%)	40 (69.0%)	41 (97.6%)	0.000
Total cholesterol (mg/dl)	199.84±45.73	223.05±42.39	0.011
Tryglicerides (mg/dl)	172.53±104,53	179.71±112,60	0.574
HDL-C (mg/dl)	48.64±14.70	38.95±12.46	0.001
LDL-C (mg/dl)	117.33±45.35	152.29±42.46	0.000
Systolic blood pressure (mm Hg)	138.33±16.74	145.76±16.74	0.031
Diastolic blood pressure (mm Hg)	83.64±9.13	89.12±8.70	0.003
Body mass index (kg/m ²)	30.33±4.48	29.20±3.65	0.183
Abdominal circumference (cm)	100.17±10.79	98.19±12.69	0.402

As shown in table 1, diabetes duration was significantly longer in patients with DR than in those without this complication (p=0,020). Diabetic retinopathy correlates highly significant with HbA1c (p=0,000), smoker status (p=0,003), hypertension (p=0,000), especially with diastolic value (p=0,003) and lipids value (p=0,001 for HDL-C and p=0,000 for LDL-C). We didn't find correlations between the presence of retinopathy and sex, although the percentage of nonproliferative

retinopathy had slightly increased in men versus women (36,54% vs 33,33%) and increased net in proliferative retinopathy (11,54% vs 2,08%), but without statistically significance.

In respect with mean value of IMT, patient with or without diabetic retinopathy different highly significant, as we shown in table 2. This significance is also maintained when we considered the stages of retinopathy (fig. 1).

Table 2 Intima media thickness (IMT) and diabetic retinopathy

Diabetic retinopathy	Number of patients	Mean value of IMT	Standard deviation	p (2-tailed)
Without retinopathy	58	0,827	0,080	0,000
Nonproliferative retinopathy	35	0,901	0,076	
Proliferative retinopathy	7	0,931	0,040	

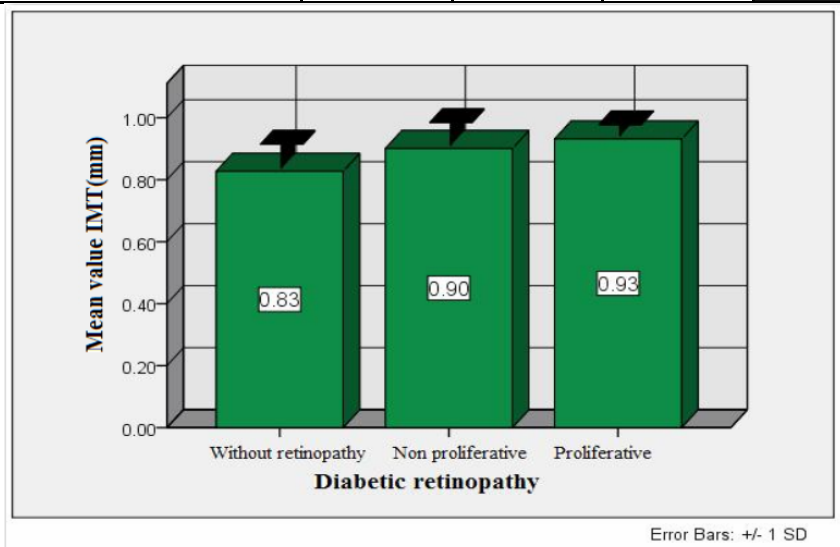


Fig 1 Relation between mean value of IMT and retinopathy

A multiple linear regression was utilized to test whether diabetic retinopathy was an independent predictor of mean IMT. Additionally, we tested other variables who presented statistical significance for the value of IMT, such as HbA1c, diabetes duration, smoking status, total cholesterol, HDL-C, hypertension. In each models, diabetic retinopathy was an independent risk factor for increased IMT, with a $p=0,000$. Other significant predictor was smoking status ($p=0,031$); diabetes duration was slightly over statistical significance ($p=0,51$).

Discussion

We investigated in this study if diabetic retinopathy is correlated with the early stage of atherosclerosis in type 2 diabetes. We found

that retinopathy is an independent predictor of intima media thickness, even after taking into account, in the multiple regression analysis conventional atherosclerosis risk factors, such as diabetes duration and control, lipid abnormalities, smoking status or arterial hypertension.

There are a few studies regarding this problem and the results are contradictory. For example, CURES-2 study (10) demonstrates an association between diabetic retinopathy and increased IMT in type 2 diabetes. Also, a most recent study, published in 2008, demonstrates the links between retinopathy, IMT and endothelial dysfunction (11). Other studies sustained that patients with type 2 diabetes and retinopathy have an increased risk for cardiovascular events (12). On the other hand, the large, prospective,

observational Valpolicella Heart Diabetes Study in T2DM did not confirm this association after adjusting for classical cardiovascular risk factors, including hypertension (13). Anyway, these contradictory data shows that the obvious link that exists between macro and microvascular complication in type 2 diabetes goes beyond

our current knowledge and requires much more informations.

In conclusion we demonstrates in our study that in type 2 diabetes intima media thickness, as a sign of early atherosclerosis, is strongly correlated with both presence and gravity of retinopathy and, therefore, patients who presented this complication need particulary intensive cardiovascular screening.

REFERENCES

1. Diabetes Atlas, third edition, International Diabetes Federation, 2007.
2. **Gerstein HC, Capes SE.** Dysglycemia: a key cardiovascular risk factor. *Semin Vasc Med.* 2002; 2:165–174
3. **Hiller R, Sperduto RD, Podgor MJ, Ferris FL 3rd, Wilson PW.** Diabetic retinopathy and cardiovascular disease in type II diabetics. The Framingham Heart Study and the Framingham Eye Study *Am J Epidemiol* 1988;28:402–9.
4. **Targher G, Bertolini L, Tessari R, Zenari L, Arcaro G.** Retinopathy predicts future cardiovascular events among type 2 diabetic patients: the Valpolicella Heart Diabetes Study. *Diabetes Care* 2006;29:1178.
5. **van Hecke MV, Dekker JM, Nijpels G, Stolk RP, Henry RM, Heine RJ et al.** Are retinal microvascular abnormalities associated with large artery endothelial dysfunction and intima-media thickness? The Hoorn Study. *Clin Sci (Lond)* 2006;110:597–604.
6. **Juutilainen A, Lehto S, Rönnemaa T, Pyörälä K, Laakso M.** Retinopathy predicts cardiovascular mortality in type 2 diabetic men and women. *Diabetes Care* 2007;30:292–9.
7. **Targher G, Bertolini L, Zenari L, Lippi G, Pichiri I, Zoppini G et al.** Diabetic retinopathy is associated with an increased incidence of cardiovascular events in Type 2 diabetic patients. *Diabet Med* 2008;25:45–50.
8. Early treatment for Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs-An extension of the modified Airle House Classification. ETDRS report n° 10. *Ophthalmol* 1991; 98: 786-806.
9. **Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jr, et al.** Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee: Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension.* 2003;42:1206–1252. doi: 10.1161/01.HYP.0000107251.49515.c2.
10. **Rema M, Mohan V, Deepa R, Ravikumar R;** Chennai Urban Rural Epidemiology Study-2. Association of carotid intima-media thickness and arterial stiffness with diabetic retinopathy: the Chennai Urban Rural Epidemiology Study (CURES-2). *Diabetes Care* 2004;27:1962–7
11. **M. T. Malecki, G. Osmenda, M. Walus-Miarka, J. Skupien, K. Cyganek, B. Mirkiewicz-Sieradzka, T. A. damek-Guzik, T. J. Guzik and J. Sieradzki** Retinopathy in type 2 diabetes mellitus is associated with increased intima-media thickness and endothelial dysfunction *Eur J Clin Invest* 2008; 38 (12): 925–930
12. **van Hecke MV, Dekker JM, Stehouwer CD, Polak BC, Fuller JH, Sjolie AK, et al.** Diabetic retinopathy is associated with mortality and

cardiovascular disease incidence: the EURODIAB prospective complications study. *Diabetes Care* 2005;28:1383–1389.

cardiovascular events among type 2 diabetic patients: the Valpolicella Heart Diabetes Study. *Diabetes Care* 2006;29:1178.

13. Targher G, Bertolini L, Tessari R, Zenari L, Arcaro G. Retinopathy predicts future