ORIGINAL ARTICLE

Diabetic retinopathy: A predictor of coronary artery disease

Fawzia El Demerdash a, Wael Refaie a,*, Rashid Allakany b, Salah Tantawy c, Eid Dawood a

a Cardiology Department, Faculty of Medicine, Mansoura University, Egypt
b Ophthalmology Department, Faculty of Medicine, Mansoura University, Egypt
c Radiology Department, Faculty of Medicine, Mansoura University, Egypt

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KEYWORDS
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Abstract Background: Diabetes mellitus is a vascular disease with many microvascular manifestations as retinopathy and macrovascular complications as coronary artery disease. A large number of diabetics with retinopathy may have unidentified coronary artery disease.

Objective: Evaluate whether diabetic retinopathy is a valid predictor of coronary artery disease.

Study design: Cross section study.

Patients and methods: The study included 60 male patients chosen randomly from diabetic and ophtalmologic outpatient clinics. Twenty patients had type 2 diabetes mellitus with nonproliferative retinopathy, 20 patients with proliferative diabetic retinopathy and 20 patients with type 2 diabetes mellitus without retinopathy. All studied cases were not previously identified as coronary artery disease. Clinical examination stressed on conventional cardiovascular risk factors; duration, degree of control of hyperglycemia and erectile failure. Lipogram, urinary albumin excretion, resting, exercise ECG and echocardiography were carried out. All patients were subjected to fundus examination for evaluation of diabetic retinopathy and duplex ultrasound to assess carotid intimal medial thickness. Coronary angiography was undertaken for all cases.

Results: There was no significant difference regarding age, BMI and blood pressure between the groups. However, duration of diabetes, erectile dysfunction and neuropathy revealed significant difference between different groups particularly the proliferative in relation to the nonproliferative diabetic group. Hypertriglyceridemia, urinary albumin excretion and serum cholesterol differ.
1. Introduction

Chronic hyperglycemia results in microvascular and macrovascular complications. Diabetes is among the most important risk factors for coronary artery disease (CAD). The microvascular complications like diabetic retinopathy (DR) usually play a critical role in the life of diabetics. Fioretto et al. reported that for the prevention of progression of vasculopathy CVD (Gimeno-Orna et al.).

Weckbach et al. reported a high prevalence of occult atherosclerotic disease in DM and CAD may be silent in more than two thirds of long standing diabetics. Hernandez et al. concluded that true silent myocardial ischemia is a highly prevalent condition in type 2 diabetics especially in males and those with DR.

Some clinical findings may lead to suspecting CAD. Erectile dysfunction (ED) is frequently associated with multiple cardiovascular (CV) risk factors and complications like DR and CAD. The presence of xanthlasma that would suspect dyslipidemia was found to be significantly related to instent restenosis (Sukhija et al.). DR may be an independent risk marker for CVD (Gimeno-Orna et al.).

1.1. Study design

Cross section study.

1.2. Aim

To identify whether conventional atherosclerosis risk factors be a greater linking for CAD in long standing type 2 diabetic patients and to elucidate whether DR and/ or cIMT be valid predictors of CAD.

2. Subjects and methods

The study included 60 patients with long standing type 2 (> 10 years) Diabetes mellitus; 20 patients with proliferative diabetic retinopathy, 20 patients with nonproliferative diabetic retinopathy and 20 diabetic patients without retinopathy. They were randomly chosen from diabetic and ophthalmologic out-patient clinics. All were males with a mean age of 46.19 ± 0.9 years. Smokers were excluded. Diagnosis of DR was based on ophthalmoscopic examination and fundus photography. The examined groups were age and sex matched. Clinical examination stressed on conventional CV risk factors, duration of diabetes and degree of hyperglycemia, BMI and erectile dysfunction. Laboratory investigations were performed significantly between the studied groups. The ECG, echocardiography showed insignificant differences. Carotid intima media thickness showed an insignificant difference when comparing the three studied groups, however diabetic retinopathy group with coronary artery stenosis revealed a significant increase in carotid media thickness. Evidence of coronary artery stenosis was present in 80% of the proliferative diabetic retinopathy group and in 70% of the nonproliferative diabetic retinopathy group but was not present in nonretinopathic diabetic group. The stenotic lesions were involving one or two vessels. No one had left main disease.

Conclusion: Diabetic retinopathy is a good predictor of coronary artery disease that exceeds the conventional risk factors. Diabetics with retinopathy would benefit from early coronary angiography and diabetic retinocoronary clinics are warranted.

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diabetic retinopathy cases with stenotic lesion revealed significant increased cIMT.

Echocardiographic evidences of diastolic dysfunction were present in 6, 5, 4 cases of the studied PDR, nonPDR and the nonretinopathic diabetic groups respectively. Coronary angiography performed on all the studied diabetic groups revealed CA stenosis in 80% of the PDR, 70% of the nonPDR and was absent in the nonretinopathic group. The differences were statistically significant.

Comparing all the stenotic cases (30 cases) to the nonstenotic cases (30 cases) illustrated that the risk factors of atherosclerosis were significantly more evident in the stenotic CAD in comparison to the nonstenotic CAD. Stenotic CAD was more evident in PDR (80%) than the nonPDR (70%) and was not present in the NRD group. cIMT showed insignificant differences when comparing the three studied groups but calculating the difference between stenotic lesions the nonstenotic groups demonstrated a significant increase in cIMT than in the stenotic CAD group.

4. Discussion

The studied cases were recruited from diabetic and ophthalmologic clinics for the study assessment. They were known to be long standing diabetics. Patients with other traditional risk factors for atherosclerosis were not included. Smokers, known hypertensive and those under hypotensives or antidyslipidemics were excluded. Clinical examination revealed significant differences between the retinopathic and the nonretinopathic groups in the presence of the history of erectile dysfunction and peripheral neuropathy.

History of ED was present in 50%, 40% and 10% of the PDR, nonPDR and NRD groups respectively. This is lower than that reported by Hermans et al. who found the frequency of ED in the retinopathic groups to be 84.3%. This could be attributed to the difference in the way of detecting ED. Males with ED in our region may mask their ED considering that ED is against manhood. Hermans et al. reported that ED is now considered a surrogate marker of endothelial dysfunction as well as a sentinel predictor of new onset macroangiopathic events.

HBA1-c which is an index of the degree of control of the hyperglycemic state was found to be elevated in the three studied groups. Higher HBA1-c was found to be one of the important factors related to the development of PDR.

Serum TG was significantly elevated in the studied diabetic groups especially in PDR. The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study support the use of fenofibrate for CVD and DR prevention.

The present finding of a significant elevation of UAE in diabetics with retinopathy confirms the findings of Parving et al. and Savage et al. who found that UAE is more than an indicator of renal disease in NIDDM patients and in fact may reflect a state of generalized vascular damage that occurs throughout the body. Tong et al. concluded that in patients with type 2 DM, retinopathy interacts with microalbuminuria to increase the risk of CV events. Donnelly et al. proved that UAE rate is associated with 2-4 fold increases in CV and all cause mortality.

Resting ECG showed insignificant changes in relation to the different DR groups while exercise stress ECG revealed that 15%, 10% and 5% have ischemic changes in PDR, non-PDR and NDR groups respectively. This is coinciding with Bailey and Sparrow who found that only 15% of diabetics with CAD could have ECG changes. Positive exercise ECG testing in patients with DR was reported many decades ago. The lower frequency of silent ischemia in the present study is not in accordance with Nakagawa et al. who found silent ischemia in 69% but are in agreement with Hernandez et al. who detected silent ischemia in 21.9%.

Echocardiography evidences LV diastolic dysfunction in PDR together with significant prolonged relaxation and delayed abnormal valve opening. The peak rates of cavity dimension increase and posterior wall thinning were reduced.

| Table 1 | Demographic and clinical characteristics of the examined cases. |
|---------|-----------------|-----------------|-----------------|-----------------|
| DPR(1) 20 cases | DNPR (2) 20 cases | NRD (3) 20 cases | P1–3 | P2–3 |
| Age (years) | 47.1 ± 1.9 | 46.19 ± 1.9 | 46.21 ± 0.9 | 0.066 | 0.96 |
| Duration of DM (years) | 11.1 ± 1.1 | 10.1 ± 1.2 | 8.9 ± 1.3 | <0.001 | 0.004 |
| BMI | 33.1 ± 1.1 | 32.5 ± 1.1 | 32.2 ± 2.9 | 0.201 | 0.667 |
| BP (mmHg) | | | | |
| SBP | 143.1 ± 4.6 | 142.2 ± 4.5 | 141.1 ± 1.9 | 0.079 | 0.319 |
| DBP | 90.87 ± 1.1 | 91.69 ± 2.9 | 91.1 ± 1.1 | 0.531 | 0.399 |
| PN | 28.22 ± 2.5 | 26.11 ± 1.7 | 20.12 ± 1.7 | <0.001 | <0.001 |
| Chest pain no. (%) | 3/20 (15%) | 2/20 (10%) | 1/20 (5%) | 0.291 | 0.553 |
| Erectile dysfunction no. (%) | 10/20 (50%) | 8/20 (40%) | 2/20 (10%) | 0.006 | 0.030 |

| Table 2 | The studied CV risk factors. |
|---------|-----------------|-----------------|-----------------|-----------------|
| DPR(1) 20 cases | DNPR (2) 20 cases | NRD (3) 20 cases | P1–3 | P2–3 |
| HBA1-c | 9.01 ± 0.9 | 8.09 ± 1.1 | 7.99 ± 1.2 | 0.004 | 0.016 |
| Cholesterol (mg/dl) | 233.9 ± 12.9 | 200.5 ± 15.7 | 190.90 ± 17.9 | <0.001 | 0.091 |
| Triglyceride (mg/dl) | 201.8 ± 11.1 | 170.1 ± 22.1 | 160.8 ± 11.9 | <0.001 | 0.105 |
| LDL-cl (mg/dl) | 140.29 ± 10.9 | 137.26 ± 12.5 | 134.24 ± 0.5 | 0.017 | 0.286 |
| HDL-cl (mg/dl) | 38.25 ± 7.9 | 36.40 ± 6.8 | 35.49 ± 7.2 | 0.255 | 0.683 |
| UAE mg/24 h | 360.35 ± 22.9 | 280.90 ± 21.2 | 260.29 ± 24.1 | <0.001 | 0.006 |
from normal and patients with severe retinopathy (PDR). Seg-mental hypokinesia were not reported in any of the studied groups.

Measuring cIMT revealed insignificant differences when comparing the three studied groups but the DR group with stenotic CAD lesion showed a significant increase in cIMT. The insignificant differences in the cIMT between the three studied groups although are different from most studies yet they are in accordance with Adams et al.\textsuperscript{22} who found that the relationship between the cIMT and the severity of CAD is weak.

The present finding of a significant increase in cIMT in the stenotic CAD group is confirmatory to many studies.\textsuperscript{23–25} The present findings are in accordance with those of Koch et al.\textsuperscript{26} who found that the clinical symptoms as well as conventional CV risk profile are not valid predictors of CAD and that coronary angiography should be performed in all diabetic patients prior to renal transplantation. Williams et al.\textsuperscript{27} found combined microvascular and macrovascular sequelae in 24\% of diabetics.

Coronary angiography is the surest method and the cornerstone for diagnosing CAD,\textsuperscript{27} although not always feasible in many cardiovascular units in developing countries.

Reaching no definitive diagnosis of CAD, coronary angiography was accepted and performed for the studied cases. 80\% of patients with PDR and 70\% of patients with nonPDR had significant stenotic CAD lesion. This is coinciding with many recent studies.\textsuperscript{28,7,29,30} In the present study; old age, longer duration of DM and uncontrolled hyperglycemic state were
significantly evident in the stenotic lesion when compared to the nonstenotic group. Ohno et al.29 reported that patients with DR having a significant stenotic CAD and needing early CABG might well go unrecognized to face serious cardiac events; cardiac death, MI and repeat revascularization.31 B mode carotid US as a useful measure of CAD23,24 was previously confirmed by the autopathy studies which showed that the extent of carotid and CAD are coinciding.32 In the present study cIMT revealed insignificant differences on comparing the three studied groups although it was significantly thicker in the stenotic CAD group.

Diagnosis of DR is an easy outpatient clinical maneuver. Its presence is a call for a complete evaluation for CVD risk factors together with stress ECG, echocardiography and coronary angiography and measuring cIMT. The present findings are confirmatory to Targher et al.33 and Cheung et al.34 who concluded that DR especially in its more advanced stages is confirmatory to Targher et al.33 and Cheung et al.34 who associated with an increased CVD and CHD risk independent of other known CV risk factors. The present results are also coinciding with Gimeno-Orna et al.7 who found that DR is an independent risk marker for CAD and also confirmatory to Baiely and Sparrow,20 who found that 24% of diabetics with retinopathy have angina and myocardial infarction. The availability of PCI and CABG intervention nowadays mandates coronary angiography for type 2 diabetic patients especially in the presence of increased cIMT and DR with or without conventional CV risk factors.35

5. Conclusion

Long standing diabetics should undergo repeated fundus examination at least yearly not only for preserving their vision but also for early suspicion of CAD events. Detection of DR and/or increased cIMT should be a trigger to investigate CAD and coronary angiography has to be performed once retinopathy is diagnosed and special diabetic retinocoronary clinics are warranted.

References


