

Research Article

Early detection of coronary artery disease in asymptomatic type 2 diabetes mellitus patients

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ABSTRACT

Background: Type II Diabetes Mellitus (DM) is a major risk factor for Coronary Artery Disease (CAD). Patients remain mostly asymptomatic and thus diagnosed at an advance stage of the disease. Our aim of study was to detect the CAD at an early stage in asymptomatic diabetic patients.

Methods: 136 asymptomatic type II diabetes mellitus patients were enrolled prospectively for treadmill test (TMT) and subsequent coronary angiography (CAG) was performed on 96 (70.87%) TMT positive patients. Diabetic status, clinical parameters including risk factors, TMT and angiographic findings were analyzed.

Results: The patients were divided into two groups, high risk group A (risk factor ≥ 2) and low risk group B (risk factor ≥ 1). 34 patients of group A (36.95%) were CAD positive out of 92 patients of high risk group and 4 patients group B (9.09%) out of 44 patients of low risk group. Duration of diabetes mellitus and multiple risk factors were correlated with coronary artery disease (CAD) as well as multiple coronary artery involvement.

Conclusions: A routine TMT of all long standing asymptomatic type 2 diabetic patients (≥ 10 years) with family history of CAD and subsequent CAG should be done on all TMT positive patients for early detection of CAD to take early appropriate revascularization measure.

Keywords: Type 2 diabetes mellitus, Risk factor, TMT, CAG, Early detection of CAD, Revascularization

INTRODUCTION

Type 2 diabetes mellitus is an important risk factor for Coronary Artery Disease (CAD). The Framingham Heart study revealed increase incidence from one to five fold of CAD, MI, CHF, PAD and sudden death in type 2 diabetes mellitus patients.¹ CAD accounts for 70-80% of mortalities in DM.⁵ The absence of chest pain is common (silent ischemia) in type 2 DM patients. It is difficult to diagnose CAD at proper time because of asymptomatic nature of the disease progression.^{2,7} The prognosis of individual with type 2 diabetes who have coronary artery

involvement worse than non-diabetic due to involvement of multiple vessels.^{1,5,6}

American Diabetes Association (ADA) recommends that treadmill exercise test (TMT) and/or coronary angiography should be done in diabetic patients having additional cardiovascular risk factors.² More sensitive diagnostic methods such as Single Photon Emission Computerized Tomography (SPECT) and multi-detector coronary MDCT may be done. But those diagnostic approaches cannot be done for asymptomatic patients on an out patients basis.⁷ No unanimous accepted test suggested for early diagnosis of asymptomatic CAD.

However severe CAD may be diagnosed noninvasively by TMT with fewer cardiac risk factors on out patients basis.⁷ In the present study TMT was performed in asymptomatic type 2 DM patients irrespective of cardiac risk factors and CAG in positive TMT cases for early detection of Coronary Artery Disease (CAD).

METHODS

This study was performed from January 2012 to July 2014 at Shri Aurobindo medical college and PG Institute in the department of cardiology amongst the type 2 DM patients who came for routine cardiology checkup in the OPD. Exclusion criteria 1) Typical history of angina 2) Know non coronary heart disease such as congenital or acquired valvular heart disease, heart failure (CCF) or arrhythmia 3) Abnormal ECG finding 4) Diagnosed CAD by invasive and non-invasive procedure.

Clinical feature, blood biochemistry and 5 cardiac risk factors, such as hypertension, dyslipidemia, family history of CAD, smoking habit and macro-micro albuminuria were noted. Patients were placed in 2 groups group A with risk factor ≥ 2 and group B with risk factor ≥ 1 .

Type 2 DM were defined as 1) Random blood sugar level ≥ 200 mg/dl and diabetic symptoms based on ADA diagnostic criteria 2) Fasting blood sugar level ≥ 126 mg/dl. 3) Diagnosed and receiving treatment for DM. Duration of type 2 DM is taken a time period between diagnosis of DM to CAD evaluation in years. Diabetic retinopathy, neuropathy and nephropathy were evaluated

with appropriate clinical and laboratory testing. Lipid profile was done in every patients.

TMT was performed in all patients irrespective of number of cardiac risk factors. Coronary angiography (CAG) was performed in positive, inconclusive and equivocal TMT result. This study was approved by hospital ethical committee and informal consent was taken from all TMT positive patients.

Treadmill exercise test (TMT) was performed according to Bruce protocol. TMT was defined as +ve if there was ≥ 1 mm horizontal/down sloping ST-segment for 0.08 sec. after the J point. Coronary angiography was performed in all TMT +ve, inconclusive and equivocal cases. Coronary artery disease was considered if there was more than 60% stenosis. In case of $>80\%$ stenosis then appropriate Percutaneous Coronary Intervention (PCI) and CABG were done.

Statistical analysis

The data obtained were input into the SPSS statistical software, version 20.0. A descriptive statistical analysis was performed. P value was set significant at <0.05 .

RESULTS

There were 136 asymptomatic type 2 diabetic patients male (n-65), female (n-20). The clinical characteristics are shown in Table 1. The Mean BMI was 24.8 of which more than 50% of the patients were overweight. Mean duration of DM was 10.1 years. Most of the patients were dyslipidemic. The average CAD risk factors were two.

Table 1: CVD risk factors, clinical characteristics & diabetic complications evaluation of the studied patients.

	Total No. of patients			P value
	(N-136)	Yes (N-38)	No (N-98)	
Age (years)	56.2 \pm 6.4	58 \pm 6	54.6 \pm 6.5	0.004
Male/female	116/20	34/4	82/16	0.5899
DM duration years	10.44 \pm 6.4	12.8 \pm 6	8.4 \pm 6.4	0.0002
F/H/O DM	52 (38.2%)	22 (57.8%)	30 (30.6%)	0.0055
Retinopathy	22 (16.1%)	10 (26.3%)	12 (12.2%)	0.0818
Neuropathy	30 (22.0%)	10 (26.3%)	20 (20.4%)	0.0672
Hypertension	60 (44.11%)	28 (73.6%)	32 (32.6%)	0.0001
F/H/o CAD	20 (14.7%)	16 (42.1%)	4 (4.8%)	0.00001
Smoking	80 (58.8%)	30 (78.9%)	50 (51.0%)	0.0034
No. risk factor	2.0 \pm 1	3 \pm 1	2 \pm 1	0.0001
HBA _{1c} %	8 \pm 2	8 \pm 1	9 \pm 1	<0.0001
Creatinine (mg/dl)	1.1 \pm 0.8	1.3 \pm 0.6	1 \pm 0.4	<0.0009
Total cholesterol (mg/dl)	196 \pm 40.2	210 \pm 38	196 \pm 41	0.0706
HDL (mg/dl)	40 \pm 10	42 \pm 6	44 \pm 9	0.2085
LDL (mg/dl)	126 \pm 32	122 \pm 36	114 \pm 38	0.2657
Triglyceride (mg/dl)	206 \pm 132	202 \pm 119	226 \pm 120	0.2961

We compared CVD risk factors between patients with CAD & patients without CAD (Table 1). Those with CAD were older, smoker, hypertensive, positive family history of CAD, long duration of diabetes, high HBA_{1C}, high serum creatinine level & more number of CVD risk factors. No significant differences were found in gender, diabetic complications, total cholesterol, HDL/LDL cholesterol & triglyceride level.

Analysis of risk factors

The total enrolled 136 patients were divided into two groups (Table 2). High risk group Gr-A (risk factors ≥ 2) and low risk group (Group B) (risk factors ≥ 1). 92 patients (76.64%) had ≥ 2 risk factors (Group A) and 44 patients (32.36%) had ≥ 1 risk factor (Group B). No significant difference in age, gender, BMI, family history of DM, duration of DM, HBA_{1C} level & complications of diabetes were found between group A & group B (Table 2). The prevalence of CAD in group A and group B was 36.95% and 9.09% respectively. These data correlates the risk factors with CAD incidence. The more the risk factors, the more chance of CAD incidence. The multi vessel involvement in group A was 66% & group B 62% and didn't differ much between the two groups. Thus we can conclude that even asymptomatic diabetic patients with fewer risk factors may have multi vessel involvement.

Table 2: comparison of risk factor and CAD findings.

	Group A (risk factors ≥ 2) N-92	Group B (risk factors ≥ 1) N-44	P value
Age (years)	56.4 \pm 8.6	55.4 \pm 8.1	0.519
Male/female	80/12	38/6	0.924
BMI (kg/m ²)	26 \pm 2.6	25.8 \pm 4.8	0.753
F/H type 2 DM	30 (32%)	14 (31%)	0.926
Duration of type 2 DM	10.4 \pm 6.5	8.9 \pm 6.8	0.217
Retinopathy	25 (27%)	8 (18%)	0.3521
Neuropathy	20 (21%)	10 (22%)	0.066
HBA _{1C} %	8.2 \pm 2.2	7.6 \pm 2.0	0.1281
Incidence of CAD	34 (36.95%)	4 (9.09%)	0.0015
Multivessel disease	20 (66%)	5 (62%)	0.2207

DISCUSSION

Diabetes is a major risk factor of Ischemic heart disease as revealed by Framingham study. There is marked increase in PAD, CHF, CAD and SCD (risk increased from one to five fold).¹ AHA has designated DM as a "CAD risk equivalent" type 2 DM patients without prior MI have a similar risk for CAD related events as non-diabetic individuals who had a prior MI. Prognosis of individuals with diabetes who have CAD or MI is worse than for non-diabetic.² CAD is more likely involve

multiple vessels in individuals with DM due to silent nature of CAD in type 2 DM. Mostly the patients are diagnosed at the advance stage of disease with multiple organ failure and leads to high mortality rate.⁸⁻¹¹

The mortality and morbidity of type 2 DM are mostly due to cardiovascular disease. The common pathophysiology of CAD in DM is due to endothelial dysfunction. The vascular tone, leukocyte attraction, vascular smooth muscle growth, nutrient delivery and end product nutrient removal, inflammation, coagulation, thrombosis and fibrinolysis are regulated by vascular endothelium. The alteration of vasoconstriction, inflammation thrombosis and fibrinolysis collectively causes endothelial dysfunction and along with vascular smooth muscle and platelets dysfunction cause the micro and macro vascular complication of type 2 DM. Type 2 DM leads to dyslipidemia in the form of hypertriglyceridemia, reduced HDL and increase LDL level which is more atherogenic and more easily glycosylated and susceptible to oxidation. This dyslipidemia with hyperinsulinemia enhance initiation and growth of atherosclerotic coronary plaques formation. Diabetic patients commonly show higher incidence of cardiac ischemia than non-diabetic patients. Silent Ischemia may delay or mask the diagnosis of CAD. When CAD is diagnosed it is most advanced and multivessel diseases. Autonomic neuropathy which damage the afferent sympathetic fibers may be the causative pathophysiology along with dysfunction of opioid receptors damage to the nerve ending may be the cause silent ischemia in type 2 DM.¹⁷⁻¹⁹

ADA recommended specific guideline for search of risk factors in asymptomatic diabetic patients.² The approach is based on CVD risk factor such as smoking, dyslipidemia, hypertension, family story of CAD and micro-macro albuminuria. Those risk factors are well known CVD risk factors.^{12,16} Our study corroborates with those risk factors for CAD. Our patients were truly asymptomatic and enrolled from the out patients department. ADA did not include duration of DM among CAD risk factors. Several studies concluded a positive relation of duration of DM with CAD.^{12,14,15} Our study also revealed positive correlation of duration of DM with CAD incidence.

Diagnostic approach of CAD may fail if consideration strict to number of risk factors only. Our study revealed and suggests an active CAD evaluation in relatively older patients with duration of type 2 DM $> \pm 10$ years and positive family history of CAD. It is advisable to consider the duration of DM as a primary risk factor regardless of symptoms. To overcome the delay of diagnosis of CAD more sensitive diagnostic techniques are evolved such MDCT and SPECT.^{3,7} These modern tools are more promising with higher accuracy but they are costly and can only be done at referral hospital. TMT is less costly and can be done for screening CAD in asymptomatic type 2 DM patients in on outpatient basis.

CONCLUSIONS

TMT & subsequent CAG in TMT positive patient is the right approach considering the cost benefit ratio of all asymptomatic relatively older diabetic patients with ≥ 10 years of duration and positive family history of CAD with even fewer CVD risk factors for early detection of CAD & necessary revascularization before multivessel involvement and multiple organ failure.

Our study results are limited as the sample size is small. Larger sample size & using more modern diagnostic techniques may corroborate our findings.

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Ethical approval: The study was approved by the hospital ethics committee

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