Original Article

Assessing Framingham cardiovascular risk scores in subjects with diabetes and their correlation with diabetic retinopathy

Deepali R Damkondwar, Rajiv Raman, Suganeswari G, Vaitheeswaran Kulothungan[1], Tarun Sharma

Aim: To study the Framingham cardiovascular risk assessment scores in subjects with diabetes and their association with diabetic retinopathy in subjects with diabetes. **Materials and Methods:** In this population-based prospective study, subjects with diabetes were recruited (n=1248; age ≥40 years). The Framingham cardiovascular risk scores were calculated for 1248 subjects with type 2 diabetes. The scores were classified as high risk (>10%), and low risk (<10%). **Results:** Out of the 1248 subjects, 830 (66.5%) patients had a low risk of developing cardiovascular disease (CVD) in 10 years and 418 (33.5%) had a high risk of developing CVD in 10 years. The risk of developing CVD was more in males than females (56.8% vs. 7%) The prevalence of both diabetic retinopathy and sight-threatening retinopathy was more in the high-risk group (21% and 4.5%, respectively). The risk factors for developing diabetic retinopathy were similar in both the groups (low vs. high) – duration of diabetes (OR 1.14 vs. 1.08), higher HbA1c (OR 1.24 vs. 1.22), presence of macro- and microalbuminuria (OR 10.17 vs. 6.12 for macro-albuminuria) and use of insulin (OR 2.06 vs. 4.38). The additional risk factors in the high-risk group were presence of anemia (OR 2.65) and higher serum high density lipoprotein (HDL) cholesterol (OR 1.05). **Conclusion:** Framingham risk scoring, a global risk assessment tool to predict the 10-year risk of developing CVD, can also predict the occurrence and type of diabetic retinopathy. Those patients with high CVD scores should be followed up more frequently and treated adequately. This also warrants good interaction between the treating physician/cardiologist and the ophthalmologist.

Access this article online

Website: www.ijo.in

DOI: 10.4103/0301-4738.91344

Quick Response Code:

Key words: Cardiovascular disease, diabetes, diabetic retinopathy, framingham risk score

Cardiovascular disease (CVD) is the leading cause of death among individuals with type II diabetes mellitus.[1-4] Diabetics are twice more likely to die of CVD than non-diabetics.[5] There has been increasing evidence indicating an association between CVD and diabetic retinopathy (DR).[1-9] A recent evidence from the Atherosclerosis Risk In Communities (ARIC) study suggests that the risk of developing CVD increased twofold, with the presence of DR.[10] Thus, there seems to be an overlap of risk factors between CVD and DR.

The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and the Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) guidelines recommend using the Framingham risk scores to assess the absolute risk of type II diabetics developing CVD.[9] Framingham scoring is used for clinical management of asymptomatic patients for primary prevention.[9-11] However, whether the same scoring can predict the occurrence of DR or sight-threatening DR has not been explored.

Sankara Nethralaya Diabetic Retinopathy Epidemiology And Molecular Genetic Study (SN-DREAMS) was a population-based, cross-sectional study carried out to estimate the prevalence and risk factors of DR in urban India.[12]

Shri Bhagwan Mahavir Vitreoretinal Services Sankara Nethralaya, Chennai, [1]Elite School of Optometry, Department of Preventive Ophthalmology, Chennai, Tamil Nadu, India.

Correspondence to: Dr. Tarun Sharma, Shri Bhagwan Mahavir Vitreoretinal Services, Sankara Nethralaya, 18, College Road, Chennai – 600 006, Tamil Nadu, India. E-mail: drtaruns@gmail.com

Manuscript received: 11.12.10; Revision accepted: 05.06.11

The aim of the present study was to know the 10-year CVD risk among subjects with type II diabetes enrolled in SN-DREAMS, to elucidate the correlation between DR and Framingham risk scores, and to assess the risk factors for DR in subjects with low risk of developing CVD against those with high risk.

Materials and Methods

The study design and research methodology of SN-DREAMS 1 is described in detail elsewhere.[12] The study population was selected by multistage systematic random sampling, based on the socioeconomic status, which made the sample a true representation of Chennai, Tamil Nadu, India. Out of the 5999 individuals, aged ≥40 years, who were enumerated from the general population, 1816 subjects had diabetes (known 1349 and provisional 469); 1563 (86.1%) came for further evaluation at the base hospital out of whom only 1414 subjects were finally confirmed as diabetics (11 excluded due to non-gradable photographs); and 138 subjects with no diabetes were excluded.

The 10-year risk of developing CVD was evaluated for 1248 subjects (166 excluded due to previous history of CVD). Identified diabetics (based on the WHO criteria) underwent a detailed examination at the base hospital.[12] The fundi of all patients were photographed using the 45°, four-field stereoscopic digital photography. DR was diagnosed based on the modified Klein classification of the Early Treatment Diabetic Retinopathy Study scale.[12] Severe non-proliferative DR, proliferative DR and clinically significant macular edema were categorized as sight-threatening DR. This grading was done by two independent observers in a masked fashion; the grading agreement was high (k = 0.83).[12]

The study was approved by the organization's Institutional Review Board, and written consent was obtained from the subjects as per the Helsinki Declaration.[12]

Detailed history of the patients, including demographic data, socioeconomic status, physical activity, dietary habits, and anthropometric measurements, was collected. A detailed medical and ocular history and a comprehensive eye examination, including stereo fundus photographs, were taken at the base hospital. Biochemical investigations (blood sugar, total serum cholesterol, high-density lipoproteins, serum triglycerides, hemoglobin, glycosylated hemoglobin HbA1c) were conducted at the base hospital in fasting state.

The 10-year risk for developing CVD was estimated using the Framingham risk scores.[9-11] The different variables included in the scoring were age, serum total cholesterol, serum high density lipoprotein (HDL) cholesterol, systolic blood pressure, treatment for hypertension, and smoking status. Details about this tool are mentioned elsewhere.[9] The score was classified as high risk (>10%), and low risk (<10%).[9]

The proportion of a 10-year risk of developing CVD was calculated with the following formula:

Probability = $1 - S(t) \exp (\sum \beta x - \sum \beta \bar{x})$,

where S(t) = probability of survival at time "t", β = Cox parameter coefficient (total serum cholesterol, smoking status, HDL, systolic blood pressure), and exp = exponential.

Statistical analysis

SPSS (version 14.0) was used for statistical analysis. The prevalence was expressed as percentage with a 95% confidence interval (CI). The data were normally distributed. A test of significance such as chi-square test was performed for comparison of prevalence in of low and high risk for developing CVD. Univariate and stepwise multivariate logistic regression analyses were performed to elucidate the risk factors influencing the presence and severity of DR. The dependent variables were DR and no DR; duration of diabetes, HbA1c, presence of macro and microalbuminuria, use of insulin, etc. were the independent variables. Adjusted Odds ratios and their 95% CI values were estimated. A "*P*" value of less than 0.05 was considered statistically significant.

Results

Table 1 shows the prevalence of the 10-year risk of developing CVD among type II diabetes mellitus subjects to be 33.5% (95% CI 30.9–36.1). The risk of CVD was more in men than women (56.8% vs. 7%). The number of subjects with an increased risk of developing CVD increases up to 70 years (7.4% in 40–49 years to 38.8% in 60–69 years; $P < 0.0001$). The same trend was seen in both genders.

Fig. 1 shows the prevalence of DR and sight-threatening retinopathy among subjects with high and low risk of developing CVD. The prevalence of both DR and sight-threatening retinopathy was more in the high-risk group (21% and 4.5%, respectively) when compared to the low-risk group (16.6% and 2.4%, respectively; $P = 0.044$ and 0.041, respectively.

Tables 2 and 3 represent the results of stepwise forward and backward logistic regression analyses in two groups: subjects who had low risk of developing CVD and those who had a high risk of developing CVD, respectively. In the low-risk group, the risk factors independently associated with any DR, in order of importance, included increasing duration of diabetes (Odds

Table 1: Age and gender prevalence of subjects with low and increased 10-year risk of developing cardiovascular diseases

Age group	10-year low risk of CVD (n = 830) Framingham Risk Score < 10%		10-year increased risk of CVD (n = 418) Framingham Risk Score > 10%		
	n (%)	(95% CI)	n (%)	*P*	(95% CI)
Over all					
40–49	342 (41.2)		31 (7.4)	<0.0001	
50–59	321 (38.7)		119 (28.4)	<0.0001	
60–69	143 (17.2)		162 (38.8)	<0.0001	
>69	24 (2.9)		106 (25.4)	<0.0001	
Subtotal (n = 1248)	830 (66.5)	(63.9–69.1)	418 (33.5)		(30.9–36.1)
Men					
40–49	173 (60.3)		31 (8.2)	<0.0001	
50–59	104 (36.2)		119 (31.6)	<0.0001	
60–69	10 (3.5)		146 (38.7)	0.207	
>69	0 (0.0)		81 (21.5)	<0.0001	
Subtotal (n= 664)	287 (43.2)	(39.4–46.9)	377 (56.8)		(53.0–60.5)
Women					
40–49	169 (31.1)		0 (0.0)	<0.0001	
50–59	217 (40.0)		0 (0.0)	<0.0001	
60–69	133 (24.5)		16 (39.0)	0.379	
>69	24 (4.4)		25 (61.0)	<0.0001	
Subtotal (n= 584)	543 (93.0)	(90.9–95.0)	41 (7.0)		(4.9–9.1)

CVD: Cardiovascular diseases, *P*<0.005 statistically significant

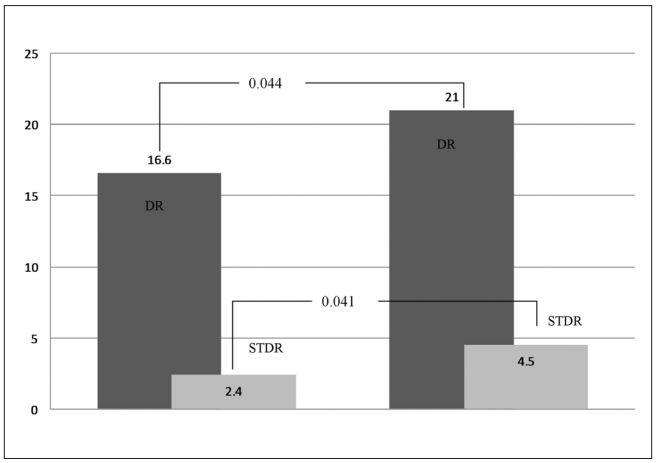

Figure 1: Prevalence of diabetic retinopathy and sight-threatening diabetic retinopathy in subgroups (DR: Diabetic retinopathy, STDR: Sight threatening diabetic retinopathy, CVD: Cardiovascular diseases)

Table 2: Stepwise multiple regression model for risk factors for the presence of any diabetic retinopathy in the group with 10-year low risk of cardiovascular diseases

Risk factors	Step in selection	No DR vs. DR OR (95% CI)	*P*
Duration of DM (years)	1	1.14 (1.09–1.18)	<0.0001
HbA1c (%)	2	1.24 (1.13–1.35)	<0.0001
Presence of macroalbuminuria	3	10.17 (3.04–33.94)	<0.0001
BMI	4	0.93 (0.88–0.98)	0.010
Presence of microalbuminuria	5	1.87 (1.11–3.15)	0.019
Use of insulin	6	2.06 (1.02–4.17)	0.044

DR: Diabetic retinopathy, OR: Odds ratio, HbA1c: glycosylated hemoglobin, BMI: body mass index, *P*<0.005 statistically significant

Table 3: Stepwise multiple logistic regression analysis for risk factors for presence of any diabetic retinopathy in the group with 10-year increased risk of cardiovascular diseases

Risk factors	Step in selection	No DR vs. DR OR (95% CI)	*P*
Duration of DM (years)	1	1.08 (1.04–1.12)	<0.0001
HbA1c	2	1.22 (1.08–1.38)	0.001
Presence of anemia	3	2.65 (1.39–5.03)	0.003
Use of insulin	4	4.38 (1.28–15.00)	0.019
Serum HDL cholesterol, mg/dl	5	1.05 (1.02–1.08)	0.003
Presence of macroalbuminuria	6	6.12 (1.64–22.82)	0.007
Presence of microalbuminuria	7	2.28 (1.23–4.22)	0.009

DM: Diabetes mellitus, DR: Diabetic retinopathy, HDL: High density lipoprotein, *P*<0.005 statistically significant

for per year increase 1.14), glycosylated hemoglobin (Odds for per unit increase 1.24), presence of macroalbuminuria (Odds 10.17), body mass index (BMI; Odds for per unit increase 0.93), presence of microalbuminuria (Odds 1.87) and use of insulin (Odds 2.06).

In the high-risk group, the risk factors independently associated with any DR, in order of importance, included increasing duration of diabetes (Odds for per year increase 1.08), glycosylated hemoglobin (Odds for per unit increase 1.22), presence of anemia (Odds 2.65), use of insulin (Odds 4.38), serum HDL cholesterol (Odds for per unit increase 1.05), presence of macroalbuminuria (Odds 6.12) and presence of microalbuminuria (Odds 2.28).

Discussion

We reported the 10-year risk of developing CVD among type II diabetic subjects in a population-based study. On the basis of the Framingham risk scores, nearly one-third of the subjects recruited for the study will have CVD at the end of 10 years. For over a decade, the Framingham risk score has been used to predict the 10-year risk of developing CVD in people with no history of CVD.[13-15]

We found that the risk of developing CVD was more in males than in females. In general, males have a higher risk of CVD than females, but the gender difference was smaller in subjects with type II diabetes.[13-18]

The United kingdom Prospective Diabetes Study (UKPDS) used the Framingham scores and found that among subjects with type II diabetes, the 10-year risk of developing CVD was 28%; however, on longitudinal follow-up, there was an underestimation of the risk by 32%.[16-20] Similarly, another study in Spain found that the scores overestimated the risk in both genders.[19] There is no longitudinal study from India which can suggest whether the scores underestimate or overestimate the CVD risk among subjects with type II diabetes.

We found that the severity of DR and sight-threatening DR was more in subjects in the high-risk group than in the low-risk group. Similar to our study, the ARIC study also found that the chances of developing CVD, over 7.8 years of follow-up, increased twofold with the presence of DR.[10,20] Gimeno-Orna *et al*. also found that the presence of baseline retinopathy was associated with CVD irrespective of other cardiovascular risk factors.[21]

We also described the risk factors for DR in the low-risk and high-risk groups. The unique factors in the high-risk group included presence of anemia and higher serum HDL cholesterol. Other factors were common in both the groups. Anemia and serum HDL cholesterol were associated with both CVD and DR.

The strengths of this study are its standardized photographic documentation and its population-based sample. The findings of the study can be extrapolated to the urban Indian population. The inherent cross-sectional design and the lack of follow-up are the limitations of this study.

In conclusion, the Framingham risk score, a global risk assessment tool for predicting the 10-year risk of developing CVD, can also predict the occurrence of DR. Understanding the risk factors in subjects with a high risk of developing CVD can help implement preventive strategies like frequent follow-up

and early and adequate laser treatment to reduce the burden of blindness due to DR.

Further follow-up studies are warranted to know the incidence of CVD and DR in population-based samples.

References

1. Valmadrid CT, Klein R, Moss SE, Klein BE. The risk of cardiovascular disease mortality associated with microalbuminuria and gross proteinuria in persons with older-onset diabetes mellitus. Arch Intern Med 2000;160:1093-100.
2. Srinath Reddy K, Shah B, Varghese C, Ramadoss A. Responding to the threat of chronic diseases in India. Lancet 2005;366:1744-9.
3. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part I: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001;104:2746-53.
4. Grundy SM. Diabetes and cardiovascular disease: A statement for healthcare professionals from the American Heart Association. Circulation 1999;100:1134-46.
5. Selvin E. Meta-Analysis: Glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med 2004;141:421-31.
6. Goyal A, Yusuf S. The burden of cardiovascular disease in the Indian subcontinent. Indian J Med Res 2006;124:235-44.
7. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part II: Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. Circulation 2001;104:2855-64.
8. Collins P. Management of cardiovascular risk in the peri-menopausal woman: A consensus statement of European cardiologists and gynaecologists. Eur Heart J 2007;28:2028-40.
9. Kanjilal S, Rao VS, Mukherjee M, Natesha BK, Renuka KS, Sibi K, *et al*. Application of cardiovascular disease risk prediction models and the relevance of novel biomarkers to risk stratification in Asian Indians. Vasc Health Risk Manag 2008;4:199-211.
10. Myerson M, Coady S, Taylor H, Rosamond WD, Goff DC Jr; ARIC Investigators. Declining severity of myocardial infarction from 1987 to 2002: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation 2009;119:503-14.
11. Chamnan P, Simmons RK, Sharp SJ, Griffin SJ, Wareham NJ. Cardiovascular risk assessment score for people with diabetes: A systemic review. Diabetologia 2009;52:2001-14.
12. Agarwal S. Sankara Nethralaya-Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN DREAMS I): Study design and research methodology. Ophthalmic Epidemiol 2005;12:143-53.
13. McGuire DK, Granger CB. Diabetes and ischemic heart disease. Am Heart J 1999;138:S366-75.
14. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation 1998; 97:1837-47.
15. Eichler K, Puhan MA, Steurer J, Bachmann LM. Prediction of first coronary events with the Framingham score: A systematic review. Am Heart J 2007;153:722-31.
16. Coleman RL, Stevens RJ, Retnakaran R, Holman RR. Framingham, SCORE, and DECODE risk equations do not provide reliable cardiovascular risk estimates in type 2 diabetes. Diabetes Care 2007;30:1292-3.
17. Guzder RN, Gatling W, Mullee MA, Mehta RL, Byrne CD. Prognostic value of the Framingham cardiovascular risk equation and the UKPDS risk engine for coronary heart disease in newly diagnosed type 2 diabetes: Results from a United Kingdom study. Diabet Med 2005;22:554-62.
18. McEwan P, Williams JE, Griffiths JD, Bagust A, Peters JR, Hopkinson P, *et al*. Evaluating the performance of the Framingham risk equations in a population with diabetes. Diabet Med 2004;21:318-23.
19. Jimeno Mollet J, Molist Brunet N, Franch Nadal J, Serrano Borraz V, Serrano Barragán L, Gracia Giménez R. Variability in the calculation of coronary risk in type-2 diabetes mellitus. Aten Primaria 2005;35:30-6.
20. Cheung N, Wang JJ, Klein R, Couper DJ, Sharrett AR, Wong TY. Diabetic retinopathy and the risk of coronary heart disease: The Atherosclerosis Risk in Communities Study. Diabetes Care 2007;30:1742-6.
21. Gimeno-Orna JA, Faure-Nogueras E, Castro-Alonso FJ, Boned-Juliani B. Ability of retinopathy to predict cardiovascular disease in patients with type 2 diabetes mellitus. Am J Cardiol 2009;103:1364-7.

Cite this article as: Damkondwar DR, Raman R, Suganeswari G, Kulothungan V, Sharma T. Assessing Framingham cardiovascular risk scores in subjects with diabetes and their correlation with diabetic retinopathy. Indian J Ophthalmol 2012;60:45-8.

Source of Support: Nil. **Conflict of Interest:** None declared.