The Use of Screening Tools for Cardiovascular Risk Assessment in Psoriasis – A Case- Control Study

Abstract

Background: Psoriasis is a common, T-cell-mediated disease, affecting 0.44-2.8% of the general population in India. It is associated with a higher risk of cardiovascular disease possibly due to chronic inflammation. Those patients with severe psoriasis are at a higher risk of death due to cardiovascular disease. The use of scoring tools may help the care providers to assess cardiovascular risks in these patients. Aims: The aim of this study was to assess the cardiovascular risks in patients with severe psoriasis using the commonly used risk-assessment tools (Framingham risk score [FRS] and Pooled cohort equations [PCE]) and to understand the utility of these tools in practice. Methods: It is a case-control study performed in the dermatology outpatient department of a tertiary care center during the study period from January to December 2020. Consenting adults with chronic plaque psoriasis and psoriasis area and severity index (PASI) more than 10 were included in the study. The FRS and PCE risk scores were calculated for the patients and age- and sex-matched healthy controls. Results: A total of 213 patients were assessed and 30 patients were excluded. Of the 183 patients, 152 patients were assessed using FRS and 135 patients using PCE. Equal number of age- and sex-matched healthy controls were also assessed. The mean age of the patients assessed using the FRS and PCE was 47 ± 10.9 and 52.84 ± 8.9 years, respectively. The mean age of the controls was 45.52 ± 8.7 and 51.76 ± 8.1 years in the FRS and PCE groups, respectively. The male to female ratio was 1.92:1 and 2:1 in the FRS and PCE risk-score groups, respectively. The mean PASI score was 16.45 ± 7.88 and 15.6 ± 7.6 in the two groups, respectively. The 10-year risk estimate using FRS in the patients ranged from 0 to 26.9%. The mean and median estimates were 4.95 ± 5.7 and 2.8%, respectively, while 2.65 ± 4.7 and 0.8% in the controls (P = 0.001). The 10-year risk estimate in the patients using the PCE risk score ranged from 0.3 to 39.6%. The mean and median estimate in the patients was 8.17 ± 9.9 and 5.2%, respectively while they were $5.68 \pm 7.5\%$ and 2.6% in the controls (P = 0.024). The agreement between the FRS and PCE was found to be poor (K, 0.049). There was no statistically significant correlation of PASI to either the PCE risk score (P = 0.498) or FRS (P = 0.630). Limitations: A small sample size, and study in a tertiary care center may have resulted in sampling bias. Conclusion: Psoriasis is associated with a higher risk of cardiovascular disease. These tools may help a dermatologist in the primary prevention of cardiovascular disease. It can also help in the awareness of the increased risk of cardiovascular disease in patients.

Keywords: Cardiovascular disease, coronary artery disease, Framingham risk score, pooled cohort equations, psoriasis

Introduction

Psoriasis is a common, chronic inflammatory disease affecting 0.44-2.8% of the general population.^[1,2] It is now considered а multisystem inflammatory disorder associated with comorbidities such as metabolic syndrome, coronary artery disease (CAD), obesity, diabetes mellitus, hypertension, non-alcoholic fatty liver disease (NAFLD), inflammatory bowel disease, and depression. The other comorbidities that are being explored are nephropathy,

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chronic obstructive pulmonary disease, obstructive sleep apnea, erectile dysfunction, and dementia.^[3] The "psoriatic march" is a relatively new concept suggesting that the chronic inflammation in psoriasis drives cardiovascular morbidity.^[4] However, the link between psoriasis and atherosclerosis is not a new hypothesis and it was observed and described as early as 1978 by McDonald and Calabresi.^[5] A population-based cohort study concluded that psoriasis is an independent risk factor for myocardial infarction even

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after controlling for the major risk factors of cardiovascular disease.^[6] Another case-control study found a higher prevalence and severity of coronary artery calcification in psoriasis patients after adjusting the cardiovascular risk factors.^[7] The exact mechanism for increased cardiovascular disease in psoriasis patients is not yet known. Chronic systemic inflammation induces insulin resistance that may result in endothelial dysfunction causing atherogenesis. There is an argument that suggests that the increased risk of CAD is likely due to a higher prevalence of traditional risk factors (obesity, hypertension, diabetes mellitus) in psoriasis patients than psoriasis *per se*. This association gets complicated by the increased prevalence of cardiovascular disease in patients suffering from NAFLD and depression, both of which are prevalent in psoriasis.^[8,9]

The dermatologists are the primary care providers for patients with psoriasis. This provides a unique opportunity to the dermatologists in primary prevention of CAD in this high-risk group. Various cardiovascular risk-assessment tools are available that incorporate traditional risk factors to estimate the risk of the development of cardiovascular disease. The most commonly used risk-assessment tools are the Framingham risk score (FRS) and pooled cohort equations (PCE) which can be utilized upfront by the dermatologists for patients of psoriasis.

We performed a case-control study to find the cardiovascular risk as assessed by these scoring tools in patients with severe psoriasis and to understand the utility of these tools in dermatology practice.

Methodology

The study was conducted in the dermatology outpatient department (OPD) of a tertiary care center in western Maharashtra during the study period from January to December 2020. The study was approved by the institutional ethics committee and written informed consent was taken from all the patients.

Patient selection

Consecutive patients with chronic plaque psoriasis with age more than 18 years and PASI more than 10 were included in the study. Patients with any of the following were excluded: (a) History of CAD, (b) History of cerebrovascular disease like stroke, (c) History suggestive of peripheral arterial disease, (d) Pregnant or lactating women, (e) Human immunodeficiency virus infection, (f) Unwilling to undergo investigations. Age- and sex-matched controls were selected from the relatives of the patients accompanying them to the dermatology OPD and patients reporting for unrelated illnesses like melasma or dermatophytosis.

Study protocol

All the patients were subjected to a thorough history taking including the history of diabetes, hypertension,

CAD, smoking, and duration of disease. The following investigations were undertaken: (a) Blood sugar fasting and post-prandial (b) Lipid profile including total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Age, gender, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded in pre-printed proforma. The disease severity was calculated using the PASI score. The CAD risk was assessed using the Framingham risk score version 2008 published by the National Institute of Health, USA, and PCE available as atherosclerotic cardiovascular disease (ASCVD) risk estimator version 2013 published by the American College of Cardiology.^[10,11] These risk-assessment tools are available on the web as well as on mobile applications for use by physicians. Both the risk-assessment tools were used for all patients as well as controls.

Framingham risk score

It is a risk-assessment tool for cardiovascular disease which estimates a 10-year risk of development of heart disease. It can be used in non-diabetic patients between the ages of 30 and 79 years with no prior history of CAD and peripheral claudication. The predictors used are age, gender, SBP, TC, HDL, treatment for hypertension, and smoking status. The risk is scored as low (<10%), intermediate (10–20%) and high (>20%).^[10]

Pooled cohort equations

It is a risk-assessment tool developed by the American College of Cardiology that estimates 10 years and lifetime risk of development of atherosclerotic CAD. It can be used in the assessment of risk in patients between the ages of 40 and 79 years. The predictors used are age, gender, ethnicity, SBP and DBP, TC, HDL, LDL, history of diabetes, smoking, hypertension treatment, and intake of statin and aspirin. The score is categorized as low risk (<5%), borderline risk (5–7.4%), intermediate risk (7.5–19.9%), and high risk (>20%).^[11]

Sample size calculation and statistical analysis

A convenience sampling method was used and all the patients who reported to the dermatology OPD and met the inclusion criteria were offered to be part of the study. Statistical analysis was performed using the statistical package for social sciences (SPSS version 20, Chicago). The categorical data are presented as numbers with percentages and continuous data as mean with standard deviation. The quantitative data were compared using the independent *t*-test and the categorical data using the Chi-square test. Bivariate analysis was done using Spearman correlation. The Kappa coefficient was calculated to find the agreement between the scores. All statistical tests were two-sided and were performed at a significance level of α : 0.05.

Results

A total of 213 patients were assessed for inclusion during the study period. Thirty patients were excluded. Of the 183 patients, 152 patients were assessed using FRS as 31 (16.9%) patients had diabetes mellitus, and hence, FRS could not be used. A total of 135 patients were assessed using PCE and 134 patients could be assessed using both the scoring methods [Chart 1]. Equal number of age- and sex-matched controls (152-FRS, 135-PCE) were included in the study. The mean age of the patients and controls assessed using FRS was 47 ± 10.9 and 45.52 ± 8.7 years, respectively. The mean age of the patients and controls assessed using PCE was 52.84 ± 8.9 and 51.76 ± 8.1 years, respectively. The male to female ratio was 1.92:1 and 2:1 in FRS and PCE risk-score groups, respectively. In the FRS group, 24 (15.78%) patients were either current or past smokers and 15 (9.8%) were on treatment for hypertension. In the PCE group, 21 (15.5%) patients were smokers; 28 (20.7%) and 29 (21.7%) were on treatment for diabetes mellitus and hypertension, respectively. The mean PASI score was 16.45 ± 7.88 and 15.6 ± 7.6 in the two groups, respectively. The baseline characteristics of both the groups and comparison with controls have been discussed in Table 1.

The 10-year risk estimate for the cardiovascular event using FRS in the psoriasis patients ranged from 0 to 26.9%. The mean and median estimates in the patients were 4.95 ± 5.7 and 2.8%, respectively, while 2.65 ± 4.7 and 0.8% in the controls (P = 0.001). The 10-year risk estimate in the psoriasis patients using the PCE risk score ranged from 0.3 to 39.6%. The mean and median estimate in the patients were 8.17 \pm 9.9 and 5.2%, respectively, while 5.68 \pm 7.5 and 2.6% in the controls (P = 0.024) [Table 2].

The risk estimates can also be categorized as low (<10%), intermediate (10–20%), or high (>20%) in FRS and low (<5%), borderline (5–7.4%), intermediate (7.5–19.9%), and high (>20%) in the PCE risk score. Out of 152 patients and 152 controls assessed by FRS; low, intermediate, and high risks were seen in 120 (78.9%), 27 (17.7%), and 5 (3.2%) patients, respectively, and in 140 (92.1%), 9 (5.9%), and 3 (1.9%) controls, respectively. Out of the 135 patients and 135 controls assessed by PCE; 64 (47.4%), 31 (23%), 27 (20%), 13 (9.6%) patients had

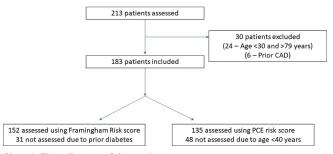


Chart 1: Flow-diagram of the study

low, borderline, intermediate, and high risk, respectively, and in 95 (70.4%), 14 (10.4%), 19 (14%), and 7 (5.2%) controls, respectively [Table 3]. The agreement between FRS and PCE was found to be poor (K, 0.049). There was no statistically significant correlation of PASI to either the PCE risk score (P = 0.498) or FRS (P = 0.630).

Discussion

Cardiovascular diseases are a common cause of morbidity and mortality across the globe. The underlying cause of cardiovascular diseases (CAD, cerebrovascular disease, and peripheral vascular disease) is atherosclerosis. The traditional risk factors for CAD are age, male gender, dyslipidemia, hypertension, diabetes mellitus, race, obesity, sedentary lifestyle, stress, and smoking.^[12] The prevalence of dyslipidemia, obesity, and hypertension is higher in the patients with psoriasis that may account for a higher prevalence of CAD in these patients.^[13] The study involving large databases have found that psoriasis per se contributes to an increased risk of CAD when adjusted for a higher prevalence of traditional risk factors. A population-based, prospective cohort study including 1,27,139 mild and 3837 severe psoriasis, conducted in the United Kingdom found a higher relative risk (RR) of myocardial infarction (MI) in patients with psoriasis. The RR was higher for severe psoriasis, but even mild psoriasis contributed to the risk of MI. The risk was higher in young patients with severe psoriasis.^[6] These findings were confirmed by the analysis of the healthcare database in the USA. The odds ratio for atherosclerosis, type 2 diabetes mellitus, and congestive cardiac failure was ≥ 1.20 .^[14] A cohort study found severe psoriasis to be a risk factor for major adverse cardiac events (hazard ratio 1.53, 95% confidence interval, 1.26-1.85). The authors concluded that after adjusting for age, gender, hypertension, dyslipidemia, and tobacco use; psoriasis confers an additional 6.2% absolute risk of major adverse cardiac events.^[15] A study using carotid intima-media thickness as a marker of subclinical atherosclerosis found an increased carotid intima-media thickness in patients with chronic psoriasis in the absence of traditional cardiovascular risk factors.^[16] Arterial stiffness is considered a measure of endothelial dysfunction. A cross-sectional study found carotid-femoral and carotid-radial pulse wave velocity, a marker for arterial stiffness, to be significantly higher in psoriasis patients.^[17,18]

The recent studies using novel tools have also substantiated these findings. Coronary artery calcification (CAC) is considered an indicator of cardiovascular disease. A case-control study found a higher prevalence (59.4% vs. 28.1%, P = 0.015) and severity (Agatston score 3.7 vs. 0, P = 0.019) of CAC in psoriasis patients as compared to controls.^[7] Vascular inflammation is considered a biomarker of cardiovascular risk. The aortic vascular inflammation can be detected using ¹⁸fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸ FDG PET/CT).

Table 1: Baseline characteristics of patients and controls						
	Framingham risk score (<i>n</i> =152)		Р	ASCVD (<i>n</i> =135)		Р
	Patient	Control		Patient	Control	
Age (years)	47±10.9	45.52±8.7	0.15	52.84±8.9	51.76±8.1	0.31
Sex (M: F)	100: 52	98: 54	0.8	90: 45	93: 42	0.69
PASI	16.45 ± 7.88			15.6±7.6		
Duration (years)	11.72±6.2			10.2 ± 6.8		
Smoking	24 (15.78%)	18 (11.84%)	0.31	21 (15.5%)	22 (16.2%)	0.86
History of DM	-	-		28 (20.7%)	13 (9.6%)	0.01
Hypertension treatment	15 (9.8%)	9 (5.9%)	0.2	29 (21.4%)	12 (8.8%)	0.003
SBP	128.41±16	$122.18{\pm}10.4$	0.001	132.3±15.9	125.3±12.7	0.001
DBP	83.49±10.6	79.6±6.26	0.001	85.19±10.8	80.9±7.4	0.001
TC	182.7±34.2	178.3±35.5	0.23	185.9±33.1	184±37.5	0.09
HDL	41.8±8.3	44.9±8.1	0.001	41.56±8.6	45.42±7.9	0.001
LDL	112.5±31.4	100.8±29	0.002	116.4±32.8	105.5 ± 29.1	0.017
BSF	97.5±23.9	86.2±11.9	0.001	106.19±34	91.6±22.2	0.001
BSPP	126.6±42.7	107.5±17.49	0.001	143.9±60.7	115.5±30.3	0.001

PASI – Psoriasis area and severity score; DM – diabetes mellitus; SBP – systolic blood pressure; DBP- diastolic blood pressure; TC – total cholesterol; HDL – High-density lipoprotein; LDL – Low-density lipoprotein; BSF – Blood sugar fasting; BSPP – Blood sugar post-prandial

Table 2: 10-year risk estimates of coronary artery disease in psoriasis patients							
	Patients	Controls	P				
Framingham risk score (<i>n</i> =152)	4.95±5.7	2.65±4.7	0.001				
PCE Risk score (<i>n</i> =135)	8.17±9.9	5.68 ± 7.5	0.024				

A prospective observational study found aortic vascular inflammation using ¹⁸ FDG PET/CT to correlate with the psoriasis severity.^[19] The exact cause of atherosclerosis in psoriasis is not known but it may be related to systemic inflammation and pro-inflammatory cytokine milieu like interleukin (IL) IL-1, IL-6, interferon γ , and tumor necrosis factor - alpha (TNF α).^[20] Systemic treatment of psoriasis may also adversely affect the cardiovascular risk factors; cyclosporine causes hypertension and dyslipidemia, retinoids decrease insulin sensitivity and methotrexate increases the homocysteine level which is atherogenic.^[21]

There are various risk-assessment scores available for the primary prevention of CAD. These tools estimate a 10-year risk of development of CAD and can be used for targeted therapies to lower the risk and follow-up. The commonest risk-score assessment tools used are FRS and PCE. The other risk scores being used are systemic coronary risk evaluation (SCORE) by the European Society of Cardiology, the World Health Organization/International Society of Hypertension (WHO/ISH) risk-assessment charts and the Joint British Societies (JBS) risk calculator.^[22] These are epidemiological tools that are to be used in specific settings. We used FRS and PCE in our study. FRS is validated in the USA, European Americans, and African Americans. For FRS, patients with type 2 DM were considered as coronary heart disease (CHD)-risk equivalent (same risk as patients with prior CHD), and hence, are excluded.^[10] PCE is used for 10 years and lifetime risk of CAD and

has been validated in the US population. The guidelines suggest that it may underestimate the risk in the South Asians (Indians, Pakistanis) while overestimating the risk in the East Asians (Chinese and Japanese).[11] However, the American College of Cardiology (ACC) clinical practice guidelines advise the use of PCE as a starting point in these populations also. These risk-assessment tools may also underestimate the risk in patients with chronic inflammation like psoriasis, rheumatoid arthritis, and human immunodeficiency virus infection.^[23] Though the data are scarce on the comparative performance of these scores, a study comparing the accuracy of the different risk scores (FRS, WHO/ISH, JBS, PCE) in the Indians found that JBS identified the largest proportion of patients as high-risk followed by PCE and FRS. The risk estimate provided by the WHO/ISH was the lowest.^[24] In our study, we found that risk was assessed to be higher with PCE as compared to FRS (8.17 ± 9.9 vs. $4.95 \pm 5.7\%$). A total of 32 (21%) patients versus 12 (7.8%) controls had a higher risk of heart disease as per FRS while 71 (52.6%) patients versus 40 (29.6%) controls had a higher risk as calculated by the PCE risk score. We also found a poor agreement between FRS and PCE in our study (K, 0.049). The dose-response relationship between psoriasis severity and cardiovascular mortality and morbidity has been noted in many studies. In a historical cohort study, increased cardiovascular mortality was noted in psoriasis inpatients but not outpatients. Severe psoriasis measured as repeated admission and younger age at first admission was associated with higher cardiovascular mortality.^[25] The study involving the research practice database also found a higher risk of cardiovascular mortality in severe psoriasis which was defined as the administration of systemic therapy.^[26] In our study, we could not find any correlation between PASI and PCE (P = value, 0.630) or FRS (P = value, 0.498). This might be explained as we defined severity based on

Table 3: Comparison of risk estimates using FRS and PCE in psoriasis patients									
FRS (<i>n</i> =152)			PCE (<i>n</i> =135)						
Risk	Patients	Controls	Risk	Patients	Controls				
Low (<10%)	120 (78.9%)	140 (92.1%)	Low (<5%)	64 (47.4%)	95 (70.4%)				
Intermediate (10-20%)	27 (17.7%)	9 (5.9%)	Borderline (5-7.4%)	31 (23%)	14 (10.4%)				
High (> 20%)	5 (3.2%)	3 (1.9%)	Intermediate (7.5-19.9%)	27 (20%)	19 (14%)				
			High (>20%)	13 (9.6%)	7 (5.2%)				

PASI, which may vary during the disease. The patient at first presentation may have a higher PASI when compared to those with a longer duration of the disease, especially on systemic therapy.

The cardiovascular risk scores are used in risk assessment for primary prevention of cardiovascular disease. The treatment can be initiated based on the risk factors and reduction in the risk assessed temporally. A systematic review and meta-analysis of 10 years of risk assessment using FRS and PCE suggested that these scoring systems overestimate the risk, especially in high-risk individuals.^[27] Another overview of the systematic review comparing the total risk assessment to the standard care concluded that there is no effect on fatal or non-fatal cardiovascular events compared to conventional care. The use of risk-assessment tools lead to a slight reduction in blood pressure, TC, and smoking level and it does not harm the patients.^[28] The psoriasis patients are high-risk patients and, in our study, we found that they had a higher 10-year cardiovascular risk. The use of the scoring systems may help in an increased awareness of the dermatologist to the cardiovascular risk factors in the patients with psoriasis that may prove helpful in the primary prevention of CAD when remedial measures are taken upfront. A healthy lifestyle including a healthy diet, exercise, moderation in alcohol intake, and smoking cessation should be advised to all patients of psoriasis. The pharmacological intervention for hypertension, diabetes mellitus, and dyslipidemia should be started when deemed necessary.[23]

The study has several limitations. A small sample size, convenience sampling method, and study in a tertiary care center may have resulted in a bias in sampling. Most patients had a long duration of the disease and many were on systemic treatment that may have modified these risk factors.

Conclusion

Severe psoriasis is associated with a higher risk of CAD. Dermatologists are primary care physicians for patients with psoriasis. Screening psoriasis patients for cardiovascular risk factors and the use of scoring systems may help in the primary prevention of CAD and holistic management of these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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