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Brief communication (Original)

Coronary artery events in Thai patients with psoriasis using Framingham and Ramathibodi–Electricity Generating Authority of Thailand risk scores

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Background: Psoriasis is an independent risk factor for cardiovascular disease. Several tools such as Framingham score (FRS) and Ramathibodi–Electricity Generating Authority of Thailand (RAMA-EGAT) score have been developed to predict the 10-year risk of coronary artery disease (CAD) and death. However, there are only few studies determine CAD risk using FRS and RAMA-EGAT score in Asian patients with psoriasis.

Objectives: To investigate the risk of CAD events using the FRS and RAMA-EGAT score in Thai patients with psoriasis.

Methods: Predictive factors that associated with intermediate and high risk (≥10%) of CAD events within 10-year were determined. Variables, including age, sex, blood pressure, cholesterol, high-density lipoprotein, diabetes mellitus, waist circumference, smoking, and alcohol intake were used to calculate scores.

Results: Of 145 patients with psoriasis and a mean age of 48.1 ± 14.1 years, 72 patients were men. Using FRS and RAMA-EGAT, 25% and 13% of the patients, respectively had a ≥10% risk of developing CAD events. A higher risk of CAD was predicted when severe psoriasis was considered. The duration of disease and treatment were associated with an increased risk of CAD using the FRS and RAMA-EGAT score by multivariate analysis.

Conclusions: A substantial portion of our patients had a CAD risk ≥10%, with significant relationship with duration of disease and treatment. Early screening of CAD and appropriate treatments of psoriasis may be helpful for preventing CAD in patients with psoriasis.

Keywords: Coronary artery diseases, Framingham score, psoriasis, RAMA-EGAT score, Thai

Coronary artery disease (CAD) has become an important cause of death and comorbid disease among the general population. Several assessment tools have been developed to predict the 10-year risk of developing CAD and coronary death. The Framingham Risk Score (FRS), which was developed in 1998, is probably the most well-known [1]. The FRS is validated in the U.S. population and performs well when applied to other populations with a similarly high background risk of CAD. However, application of the FRS overestimated the risk of CAD in cohorts in Europe, Asia, and even in newer cohorts in the US [2].

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The Ramathibodi–Electricity Generating Authority of Thailand (RAMA-EGAT) heart score was developed in 2005 to predict the risk of CAD in the Thai population. This equation was derived from a study that followed 3499 Thais who were employed by the Electricity Generating Authority of Thailand from 1985 to 1997 [3]. A subsequent study in 2007 showed that there was a good linear correlation between the RAMA-EGAT score and existence of plaques in coronary arteries [4]. Patients who had a RAMA-EGAT score ≥17, had a 45.7% chance of having significant coronary artery stenosis [4]. However, the major limitation of the RAMA-EGAT equation is that it is derived from the data of patients who had moderate-to-high risks for CAD events (middle-class income group). Therefore, the RAMA-EGAT equation may not be a good predictor when

applied to other Thais with different background risks for CAD.

Psoriasis is a chronic immune-mediated inflammatory disease that has been proposed as an independent risk factor for CAD. Chronic inflammation and inflammatory cytokines, such as tumor necrosis factor-alpha and interleukin-2 in psoriasis might play prominent roles in the pathogenesis of atherosclerosis [5]. This study aimed to assess the 10-year risk of CAD using FRS and RAMA-EGAT score in Thai patients with psoriasis. The predictive factors that associate with moderate-to-high risks of coronary artery events (≥10%) as predicted by FRS and RAMA-EGAT, were determined.

Methods

Ethics approval of this retrospective cohort study was obtained on 27th February 2014 from the Siriraj Institutional Review Board, Siriraj Hospital, Mahidol University (Si 118/2014). Psoriasis patients aged ≥18 years who attended the Dermatology Clinic, Siriraj Hospital, between 2013 and 2014, were included. Patients were excluded if they had a history of peripheral vascular diseases or past cardiovascular events, including myocardial infarction or stroke. Patients with secondary hyperlipidemia because of medical conditions, such as nephrotic syndrome, hypothyroidism, obstructive liver diseases, and connective tissue diseases, were also excluded.

A history of psoriasis, smoking status, alcohol use, psoriasis treatment, and other medical conditions, such as diabetes mellitus (DM), dyslipidemia, and hypertension were recorded within 3-month follow-up visits using a questionnaire that was administered by a physician. Data regarding body mass index (BMI), waist circumference, blood pressure, severity of psoriasis, and blood chemistry were collected at the time point closest to or within a 6-month period before administration of the questionnaire. Waist circumference was measured at the midpoint between the lower costal margin and iliac crest. Obesity was defined as a BMI ≥25 kg/m^2 [6]. Severity of psoriasis was determined using the Psoriasis Area and Severity Index (PASI) score.

Two risk equations were used to predict the 10-year risk of CAD. The FRS was applied in patients aged 20–79 years. The FRS parameters include sex, age, total cholesterol, current smoking status, high density lipoprotein (HDL), and systolic blood pressure (including treated or untreated status). Those scoring less than 10% are at low risk, those scoring between 10% and 20% have a moderate risk, and those scoring 20% or more are at high risk [7, 8]. As the attributable risk of severe psoriasis (PASI ≥10) would increase yearly coronary artery events by an adjusted hazard ratio, an estimated value of 6.2% was added to the FRS in patients who had severe psoriasis, following recommendations by Mehta et al. [9].

The RAMA-EGAT score includes age, blood pressure, waist circumference, total cholesterol, HDL, DM, and current smoking, and alcohol consumption status. The RAMA-EGAT score stratifies patients into three risk categories: low (<10%), intermediate (10%–20%), and high (>20%). This cut-off was chosen based on the recommendations of the Adult Treatment Panel III (ATPIII) to determine goals for lipid-lowering therapy [3, 8].

The Statistical Package for the Social Sciences, version 18 (SPSS, Chicago, IL, USA) was used for analysis. Descriptive statistics, such as number, percentage, and mean ± standard deviation (SD), were used to describe demographic data and different risk categories according to different risk equations. A chi-square test, unpaired *t* test, and logistic regression were used to analyze the predictive factors that contributed to intermediate to high risk (≥10%) of CAD events. The variables that had $P < 0.20$ by univariate analysis or interested variables were selected to analyze for multivariate analysis. Statistical significance was set as a $P < 0.05$ for univariate and multivariate analysis.

Results

A total of 145 patients with psoriasis (72 men and 73 women; mean age, 48.1 ± 14.1 years) were included. Demographic data of the patients are shown in **Table 1**. At the time of the study, 64% of the patients commenced systemic treatment and 65% had mild disease (PASI <10). The most common underlying disease was obesity, followed by hypertension, dyslipidemia, and DM, respectively.

The FRS and RAMA-EGAT equation score were calculated for 145 patients. On the basis of FRS, 21% and 4% had an intermediate (10%–20%) and high risk (>20%) of developing CAD events within 10 years, compared with 12% and 1% of patients according to the RAMA-EGAT score, respectively. Using the FRS with and without an attributable risk of psoriasis, 7% and 4% of the patients, respectively, had a high risk of developing CAD events within 10 years (**Table 2**).

Table 1. Demographic data of Thai patients with psoriasis (n = 145)

Demographic data	Mean ± SD or n (%)
Age (years)	48.1 ± 14.1
Age of onset (years)	34.9 ± 14.0
Duration of psoriasis (years)	13.2 ± 9.2
Sex	
Male	72 (50)
Female	73 (50)
Type of psoriasis by age of onset	
Type I (≤40 years)	101 (70)
Type II (>40 years)	44 (30)
Clinical type of psoriasis	
Plaque-type psoriasis	133 (92)
Guttate psoriasis	5 (3)
Psoriasis erythroderma	4 (3)
Pustular psoriasis	3 (2)
Number of patients who had psoriatic arthritis	23 (16)
Disease severity (n = 142)	
PASI <10	92 (65)
PASI ≥10	50 (35)
Family history of psoriasis	26 (18)
Treatment of psoriasis	
Topical therapy alone	52 (36)
Systemic therapy	93 (64)
Underlying diseases	
Obesity(BMI ≥25 kg/m^2)	79 (59)
Hypertension	58 (40)
Dyslipidemia	27 (19)
Diabetes mellitus	23 (16)
Nonalcoholic fatty liver	7 (5)
HIV infection	4 (3)
BMI (kg/m^2)	26.6 ± 6.4
Waist circumference >90 cm	82 (43)
Fasting blood sugar level (mg/dL)	105.8 ± 23.8
Total cholesterol level (mg/dL)	198.3 ± 37.3
HDL cholesterol level (mg/dL)	51.5 ± 14.0
Current smoking	23 (16)

PASI = Psoriasis Area and Severity Index, BMI = Body Mass Index, HIV = human immunodeficiency virus, HDL = high density lipoprotein

Table 2. Ten-year risk for coronary events according to different risk equations

Equation scores	Mean ± SD	Number (%)		
		Low	Intermediate	High
FRS				
Without attributable risk of psoriasis	5.8 ± 6.9	109 (75)	30 (21)	6 (4)
With attributable risk of psoriasis	7.9 ± 7.3	97 (67)	38 (26)	10 (7)
RAMA-EGAT	5.5 ± 5.1	126 (87)	17 (12)	2 (1)

FRS = Framingham Risk Score (20–79 years; n = 145): low risk, <10%, intermediate risk, 10–20%; high risk, >20%

RAMA-EGAT = Ramathibodi–Electricity Generating Authority of Thailand (≥18 years; n = 145): low risk, <10%; intermediate risk, 10%–20%; high risk, >20%

In univariate analysis, duration of disease and type of treatment had significant association with intermediate-to-high CAD risk using FRS, whereas only duration of disease influenced CAD risk of ≥10% by RAMA-EGAT. However, the multivariate analysis for both scores showed that duration of disease and treatment were significantly associated with an increased risk of CAD (**Tables 3** and **4**).

Table 3. Logistic regression model to assess predictive factors that contribute to risk at ≥10% of coronary events as predicted by Framingham Risk Score

Variables	FRS		Univariate analysis		Multivariate analysis	
	<10% risk (n = 109)	≥10% risk (n = 36)	*P*	OR (95% CI)	*P*	OR (95% CI)
Duration of disease in years, mean ± SD	11.9 ± 8.3	17.1 ± 10.7	<0.001	1.14 (1.02, 1.11)	0.001	1.09 (1.04,1.14)
Severity[a], n (%)						
PASI <10	64 (59)	28 (78)	0.06	1		
PASI ≥10	42 (39)	8 (22)		0.44 (0.18, 1.05)		
Psoriatic arthritis, n (%)						
No	94 (86)	28 (78)	0.23	1		
Yes	15 (14)	8 (22)		1.79 (0.69, 4.66)		
Treatment, n (%)			0.005		0.002	
Topical	32 (29)	20 (56)		31.03 (1.39, 6.54)		4.63 (1.78, 12.05)
Systemic	77 (71)	16 (44)		1		
Obesity[b], n (%)						
No	55 (51)	24 (67)	0.07	1	0.04	
Yes	46 (42)	9 (25)		2.23 (0.94, 5.27)		2.88 (1.08, 7.68)
Diabetes mellitus, n (%)						
No	95 (87)	27 (75)	0.09	1	0.21	1.99 (0.68, 5.75)
Yes	14 (13)	9 (25)		2.26 (0.88, 5.79)		

[a,b]Only 142 and 134 patients were available for the data regarding severity and obesity, respectively, OR = odds ratio 95% CI = 95% confidence interval, SD = standard deviation, FRS = Framingham Risk Score, PASI = Psoriasis Area and Severity Index

Table 4. Logistic regression model to assess predictive factors that contribute to risk at ≥10% of coronary events as predicted by Ramathibodi–Electricity Generating Authority of Thailand (RAMA-EGAT) score

Variables	RAMA-EGAT score		Univariate analysis		Multivariate analysis	
	<10% risk (n = 126)	≥10% risk (n = 19)	*P*	OR (95% CI)	*P*	OR (95% CI)
Duration of disease in years, mean ± SD	12.5 ± 9.0	18.1 ± 9.7	0.02	1.06 (1.01,1.12)	0.02	1.08 (1.01, 1.14)
Severity[a], n (%)						
PASI <10	76 (62)	16 (84)	0.07	1	0.12	0.33 (0.08, 1.34)
PASI ≥ 10	47 (38)	3 (16)		0.30 (0.08,1.10)		
Psoriatic arthritis, n (%)						
No	108 (86)	14 (74)	0.19	1	0.48	1.64 (0.42, 6.39)
Yes	18 (14)	5 (26)		2.14 (0.69,6.68)		
Treatment, n (%)						
Topical	42 (33)	10 (53)	0.11	1	0.02	
Systemic	84 (67)	9 (47)		2.22 (0.84,5.88)		3.95 (1.23, 12.68)
Obesity[b], n (%)						
No	50 (43)	5 (28)	0.23	1	0.19	2.22 (0.67, 7.34)
Yes	66 (57)	13 (72)		1.97 (0.66,5.89)		

[a,b]Only 142 and 134 patients were available for the data regarding severity and obesity, respectively, OR = odds ratio, 95% CI = 95% confidence interval, SD = standard deviation

Discussion

CAD is worldwide health problem, including in developing countries. Major cardiovascular risk factors include obesity, hypertension, hyperlipidemia, and DM. A national health survey in 21,960 Thais in 2009 (aged ≥15 years) showed that 30% of men and 40% of women were obese (BMI ≥25 kg/m^2). The mean BMI values of 23.1 kg/m^2 in men and 24.4 kg/m^2 in women in the 2009 survey are comparable to those in a previous survey in 2000 (5305 adults, aged ≥35 years, mean BMI of 23 kg/m^2 in men and 24.8 kg/m^2 in women) [10, 11]. A recent study suggested that psoriasis increases the risk of obesity and cardiovascular events [5]. Our study showed that there was a higher percentage of obesity in patients with psoriasis (59%) than in average Thais, and that the mean BMI value of these patients was 26.4 kg/m^2. The common comorbid diseases in our patients were obesity, hypertension, dyslipidemia, and DM. These may emphasize the greater risk of Thai patients with psoriasis developing CAD events compared with the general population.

The application of FRS and RAMA-EGAT score to other populations with different background risk of CAD remains questionable. Both scores have been validated in 785 HIV-infected Thai patients [12]. The study showed that the prevalence of 10-year risk of CAD ≥10% in HIV-infected Thai patients was 9.9% and 2.1% by FRS and RAMA-EGAT score respectively. However, it seemed that FRS probably overestimated risk of CAD in HIV-infected Thai patients because RAMA-EGAT score demonstrated better agreement with the D:A:D risk equation (Data Collection on Adverse Effects of Anti-HIV Drugs) than FRS and D:A:D risk equations. The D:A:D risk equation was developed from a data set of 22,625 HIV-infected individuals in 20 countries across Europe and Australia [13]. Similarly, the FRS equation predicted a higher risk of CAD than the RAMA-EGAT equation especially when the risk of severe psoriasis was taken into account in our study. Observed events from long-term follow-up data are required to determine whether the FRS overestimated or the RAMA-EGAT score underestimated the 10-year risk of CAD in Thai patients with psoriasis. It should be noted that the prevalence of 10-year risk of CAD ≥10% of Thai patients with psoriasis in our study was higher than that of HIV-infected Thai patients by FRS and RAMA-EGAT score [12]. There are a limited number of studies regarding FRS in Asian patients with psoriasis. A previous study on the FRS in 159 Koreans with psoriasis showed that most of them were at low-to-intermediate risk of developing CAD, similar to the FRS of Thai patients in our study [14]. Previous studies using the FRS in patients with psoriasis from Brazil, Spain, Portugal, and the USA showed that 7%–18.6% of the patients were at high risk (>20%), while 4% of our patients, and 5.1% of Korean patients were at high risk (>20%) [15-19]. These studies suggest that Asian patients with psoriasis have a lower 10-year risk of CAD than white patients of European ancestry with psoriasis. Asian lifestyle, dietary habits, and genetic susceptibility may be other reasons for these different outcomes.

Previous studies from Spain (395 patients), Brazil (98 patients), and the USA (1591 patients) showed that the severity, duration, and treatment of psoriasis did not affect high cardiovascular risk scores using the FRS equation [15-17]. By contrast, our study showed that duration of disease and treatment had significant association with an increased CAD risk using multivariate analysis for both scores. The wide range of inflammatory cytokines in the long disease duration of psoriasis, such as tumor necrosis factor, interleukin-1 and interleukin-2 are probably risk factors for CAD in psoriasis patients [5]. Our study only included a relatively small number of patients compared with other studies, and estimation of CAD risk was investigated on the basis of risk equations instead of observed risk. More studies with a large number of psoriasis patients are warranted to determine predictive factors that contribute to high CAD risk in Asian populations.

In conclusion, Thai patients with psoriasis had several comorbid diseases that contributed to CAD events. A substantial portion of patients had intermediate-to-high risk of developing CAD events within 10-years using the FRS and RAMA-EGAT score. Early screening for CAD and appropriate treatments for psoriasis may be helpful to prevent CAD in psoriasis patients.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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