

# A Comparative Study for the Assessment of Arterial Stiffness and Cardiovascular Risk Factors between Those Individuals With or Without Plaque Type Psoriasis

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**Background:** Psoriasis is a chronic inflammatory skin disease. Clinical manifestation with arterial stiffness (AS), atherosclerosis, metabolic syndrome, and cardiovascular diseases are common in psoriasis.

**Objective:** To compare AS evaluated by cardio-ankle vascular index (CAVI), clinical and laboratory cardiovascular parameters between psoriasis and non-psoriasis subjects.

**Materials and Methods:** A prospective, observational, analytic study enrolled 26 plaque psoriasis and 104 non-psoriasis participants as the controls, for a one-to-four ratio, at Mae Fah Luang Hospital, Bangkok, Thailand. AS measured by CAVI, clinical, and laboratory evaluation for cardiovascular risk factors were measured and determined between the two groups.

**Results:** The prevalent rate of arterial stiffness or CAVI greater than 8.0 in plaque psoriasis group was 73.1%, which is significantly higher than non-psoriasis subjects of 20.2% ( $p < 0.001$ ). Furthermore, those patients with psoriasis had a significantly higher percentage of those aged older than 40, fasting glucose greater than 100 mg/dL, triglyceride greater than 150 mg/dL, and LDL-cholesterol greater than 130 mg/dL than non-psoriasis group ( $p < 0.05$ ). Nevertheless, CAVI greater than 8.0 or AS was an only independent factor associated with plaque psoriasis after adjusting any other factors, with an adjusted odds ratio of 10.73 and a 95% confidence interval of 3.98 to 28.87 ( $p < 0.001$ ).

**Conclusion:** The patients with plaque psoriasis were 10.73 times significantly greater to predict CAVI greater than 8.0 or AS than non-psoriatic group. To prevent cardiovascular events and further long-term complications, early cardiovascular screening with CAVI in psoriasis patients is an optional evaluation tool.

**Keywords:** Psoriasis; Arterial stiffness; Cardiovascular risk; Cardio-ankle vascular index

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Psoriasis is a common skin inflammatory disorder that presents as chronic, well-demarcated erythematous papules and plaques with whitish scales. Psoriasis is caused by genetic and immune system malfunction with triggering factors such as emotional stress, infections, skin injuries, certain medications, cigarette smoking, and excessive alcoholic consumption. It characterizes with cellular

and humoral immune dysregulation that leads to skin inflammation, cellular proliferation, and hyperkeratinization<sup>(1)</sup>.

The World Health Organization (WHO) recognizes psoriasis as an important disease that significantly impacts patients' quality of life, physical and emotional disturbance, and social burdens. The majority of psoriatic patients were diagnosed before the age of 40<sup>(2)</sup>. Regarding disease severity, 75% of patients were classified as mild form while 25% with moderate to severe disease severity. The most common type is plaque type psoriasis<sup>(3)</sup>. Currently, psoriasis is still an incurable disease, and the treatments aim to control disease activities. The treatments of psoriasis include topical agents, systemic immunosuppressive or immune-modifying, and biologic agents, and phototherapy<sup>(4)</sup>.

The patients with psoriasis have a higher incidence of various comorbid conditions, including an immune-induced arthritis, diabetes mellitus,

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obesity, metabolic syndrome, and cardiovascular diseases<sup>(5)</sup>. Furthermore, vascular stiffness and atherosclerosis were commonly reported in psoriatic patients, caused by abnormal free fatty acid and lipoprotein accumulation. It leads to an oxidative stress reaction around the vascular walls. Since then, helper 1 T cells and regulatory T cells play a major role in inducing chronic inflammation and damaging the blood vessel wall, then turn to vascular stiffness and atherosclerosis later<sup>(6,7)</sup>. Studies have reported that psoriasis is an independent risk factor for cardiovascular events<sup>(8-10)</sup>. Because of higher risk of arterial stiffness, atherosclerosis, and metabolic syndrome, those patients with psoriasis develop major cardiovascular events, myocardial infarction (MI), and higher cardiovascular death in the long-term<sup>(9,10)</sup>. These findings raise concern about the need for early cardiovascular risk detection in psoriasis patients.

Decreased arterial compliance is one of the earliest detectable manifestations of adverse structural and functional changes within the vessel wall. This leads to the development of methods for detecting arterial stiffness, as it is a strong predictor of adverse cardiovascular outcomes. Previous studies confirmed pulse wave velocity (PWV), augmentation index, arterial distensibility, and cardio-ankle vascular index (CAVI) were used as clinical screening tools to detect arterial stiffness<sup>(11)</sup>. Although PWV measurement is widely accepted for assessing arterial stiffness, it is limited by its variability based on the changes in blood pressure. CAVI is a newer method theoretically independent of blood pressure. The CAVI device measurement is conducted through the aorta near the aortic valve, in comparison with the ankle artery<sup>(12)</sup>. Higher CAVI levels indicate elevated arterial stiffness, further the risks of cardiovascular events and can be clinically useful for assessing the risk of cardiovascular diseases<sup>(13)</sup>. A CAVI greater than 8.0 indicated an association with cardiovascular disorders<sup>(14)</sup>.

Although curative treatment for psoriasis is still undiscovered, improving the quality of life for these patients remains the main goal. Screening for cardiovascular risk in individuals with psoriasis should be a priority and easily accessible. The present research hypothesized that psoriasis patients would exhibit increased arterial stiffness, as evaluated by the CAVI technique, compared to the general population without psoriasis. Consequently, this could lead to the development of appropriate methods for screening cardiovascular risk in patients living with psoriasis.

The objectives of the present study were to compare arterial stiffness measured by CAVI and clinical and laboratory cardiovascular risk factors between plaque type psoriasis and non-psoriatic population.

## **MATERIALS AND METHODS**

The present study protocol was approved by the Ethics Committee on Human Research of Mae Fah Luang University (EC number 23119-20).

### **Study design and population.**

The present study was a prospective, analytic observational study. The sample size was calculated using an independent, two-group means comparison formula. A previous study reported the mean CAVI as  $6.79 \pm 1.08$  in patients with psoriasis, while the mean CAVI in those without psoriasis was  $6.52 \pm 0.54$ <sup>(15)</sup>. The predicted sample size for the psoriasis group was 26 subjects. Using a ratio of one-to-four, then the study enrolled 104 non-psoriasis subjects as the controls.

For psoriasis group, the study aimed to enroll 26 psoriasis patients, aged between 18 to 60 years, who visited the Mae Fah Luang University Hospital, Bangkok, Thailand, for regular annual check-up. Exclusion criteria included personal history of psoriatic arthritis, known case of malignancy, uncontrolled severe medical conditions such as end-stage renal or liver failure and cerebrovascular disease, chronic infection such as human immunodeficiency virus (HIV) and mycobacterium tuberculosis, and those subjects who are currently taking some medications that directly affect arterial measurement.

For the control group, the present study utilized secondary data from a study entitled 'Association of Age with Carotid Intima-Media Thickness, Arterial Stiffness, and Brachial Artery Systolic Time Intervals in Thai People Undergoing a Routine Annual Physical Exam' published by Jularattanaporn et al.<sup>(16)</sup> with formal permission. There were 104 healthy volunteers without a personal history of psoriasis, aged between 18 and 60 years, who were enrolled using simple random sampling technique as a control group. Exclusion criteria in control group were to known cases of malignancy, uncontrolled severe medical conditions such as end-stage renal or liver failure and cerebrovascular disease, chronic infection such as HIV and tuberculosis, and those subjects are currently taking medications that directly affect arterial measurement.

Study procedure

All eligible participants were informed about the research process and enrolled in all subjects who voluntarily signed in informed consent form in psoriasis group. The participants' baseline information included age, sex, body weight, body mass index (BMI), systolic and diastolic blood pressure, waist circumference and waist-hip ratio, personal history for underlying diseases, cigarette smoking status, alcohol consumption, current medications, and family history in cardiovascular diseases were interviewed and recorded. The psoriasis participants were asked to fast any kind of food and drink at least 8 hours during an overnight period. A blood drawn of 12 mL was collected and tested for fasting blood glucose, total cholesterol, triglyceride (TG), high density lipoprotein-cholesterol (HDL-Chol), low density lipoprotein-cholesterol (LDL-Chol) and serum creatinine for kidney function.

CAVI measurement

Psoriasis participants were measured for CAVI, assessed by VaSera VS-1500 device (Fukuda Denshi, Tokyo, Japan). The participants were instructed to lie in supine position on the examination bed, placing blood pressure cuffs on all extremities and electrocardiogram monitoring pads and heart sound devices on the chest wall. PWV and CAVI was measured and recorded<sup>(17,18)</sup>.

Statistical analysis

The means and standard deviation were reported for continuous data, while frequency and percentage for categorical data were used. The independent t-test was tested for the two independent groups mean comparison. The chi-square or Fisher's exact test was used to compare categorical data.

Univariate and multivariate data analysis using binary logistic regression model was performed to compare associated cardiovascular risks, laboratory findings and arterial stiffness measured by CAVI, for CAVI greater than 8.0, between plaque psoriasis and non-psoriasis groups. Any variables with a p-value of less than 0.10 in univariate analysis were selected in multiple binary logistic regression models. Crude and adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were reported. A p-value of less than 0.05 was considered statistically significant. IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA) was used as statistical software.

Table 1. Baseline characteristics

| Variables                       | Psoriatic subjects (n=26)<br>Mean (SD) | Non-psoriatic subjects (n=104)<br>Mean (SD) | p-value* |
|---------------------------------|--|---|----------|
| Age (years)                     | 45.5 (9.3)                             | 40.0 (11.3)                                 | 0.0239   |
| CAVI                            | 8.4 (0.7)                              | 6.9 (1.2)                                   | <0.001   |
| Systolic blood pressure (mmHg)  | 131.9 (13.2)                           | 133.9 (16.3)                                | 0.5672   |
| Diastolic blood pressure (mmHg) | 82.3 (10.9)                            | 83.9 (11.0)                                 | 0.4971   |
| Body weight (kg)                | 71.7 (10.2)                            | 65.8 (13.4)                                 | 0.0400   |
| BMI (kg/m <sup>2</sup> )        | 25.8 (3.1)                             | 24.7 (4.2)                                  | 0.2051   |
| Waist circumference (cm)        | 87.6 (11.2)                            | 86.6 (10.9)                                 | 0.8438   |
| Waist-hip ratio                 | 0.91 (0.07)                            | 0.87 (0.07)                                 | 0.0113   |
| FBS (mg/dL)                     | 112.5 (37.2)                           | 98.6 (31.2)                                 | 0.0520   |
| Total Chol (mg/dL)              | 226.8 (40.7)                           | 207.8 (42.7)                                | 0.0422   |
| Triglyceride (mg/dL)            | 205.8 (63.6)                           | 126.3 (84.5)                                | <0.001   |
| HDL-Chol (mg/dL)                | 48.5 (4.1)                             | 57.2 (13.2)                                 | 0.0015   |
| LDL-Chol (mg/dL)                | 163.5 (35.5)                           | 119.7 (35.2)                                | <0.001   |
| Creatinine (mg/dL)              | 1.02 (0.12)                            | 0.97 (0.21)                                 | 0.3015   |

CAVI=cardio-ankle vascular index; SD=standard deviation; BMI=body mass index; FBS=fasting blood sugar; Total Chol=total cholesterol; HDL-Chol=high density lipoprotein-cholesterol; LDL-Chol=low density lipoprotein-cholesterol

\* Independent student t-test was applied to compare clinical and laboratory outcomes between psoriatic subjects versus non-psoriatic subjects.

RESULTS

One hundred thirty participants were enrolled, dividing to 26 psoriatic subjects and 104 non-psoriatic healthy subjects.

Baseline characteristics

Those subjects with the psoriasis group had significantly higher mean age, body weight, and waist-hip ratio than those without psoriasis group (p<0.05). Moreover, psoriatic group had significantly higher CAVI or risk of arterial stiffness than non-psoriasis group. In terms of laboratory findings, those patients with psoriasis had significantly higher serum total cholesterol, TG, and LDL-Chol level while lower HDL-Chol level than those without psoriasis (p<0.05) (Table 1).

Comparison of clinical and laboratory factors between psoriatic and non-psoriatic subjects, categorized with the standard cut-off point.

The data shown in Table 2 used standardized cut-off points to categorize participants in both groups. The prevalent rate of arterials stiffness or CAVI greater than 8.0 in plaque psoriasis group was 73.1%, which is significantly higher than in non-psoriasis subjects at 20.2% (p<0.001). Furthermore, the psoriasis group had higher percentages of those subjects with age over 40 years than those without psoriasis. For laboratory findings, the psoriatic group

**Table 2.** Comparing clinical and laboratory factors between psoriatic and non-psoriatic subjects, categorized with the standard cut-off point

| Variables  | Psoriatic subjects; n (%) | Non-psoriatic subjects; n (%) | p-value* |
|--|---------------------------|-------------------------------|----------|
| Sex  |                           |                               |          |
| Female   | 15 (57.7)                 | 51 (49.0)                     | 0.430    |
| Male   | 11 (42.3)                 | 53 (51.0)                     |          |
| CAVI >8.0  | 19 (73.1)                 | 21 (20.2)                     | <0.001   |
| Age >40 years                                    | 18 (69.2)                 | 43 (41.3)                     | 0.011    |
| Cigarette smoking                                | 2 (7.7)                   | 9 (8.6)                       | 0.875    |
| Known case of hypertension                       | 7 (26.9)                  | 41 (39.4)                     | 0.237    |
| Known case of diabetes                           | 2 (7.7)                   | 10 (9.6)                      | 0.762    |
| BMI >25 kg/m <sup>2</sup>                        | 16 (61.5)                 | 43 (41.3)                     | 0.064    |
| Excess WC: >90 cm (male) or >85 cm (female)      | 14 (53.8)                 | 46 (44.2)                     | 0.379    |
| Waist-hip ratio: >0.90 (male) or >0.85 (female)  | 14 (53.8)                 | 44 (42.3)                     | 0.296    |
| SBP >130 mmHg                                    | 14 (53.8)                 | 57 (54.8)                     | 0.930    |
| DBP >85 mmHg                                     | 11 (42.3)                 | 51 (49.0)                     | 0.539    |
| FBS >100 mg/dL                                   | 10 (38.5)                 | 13 (12.5)                     | 0.002    |
| Total Chol >200 mg/dL                            | 19 (73.1)                 | 56 (53.8)                     | 0.076    |
| TG >150 mg/dL                                    | 18 (69.2)                 | 30 (28.9)                     | <0.001   |
| HDL-Chol: <40 mg/dL (male) or <50 mg/dL (female) | 6 (23.1)                  | 20 (24.7)                     | 0.867    |
| LDL-Chol >130 mg/dL                              | 23 (88.5)                 | 30 (37.0)                     | <0.001   |
| Metabolic syndrome#                              | 12 (46.2)                 | 21 (20.2)                     | 0.007    |

CAVI=cardio-ankle vascular index; BMI=body mass index; WC=waist circumference; SBP=systolic blood pressure; DBP=diastolic blood pressure; FBS=fasting blood sugar; Total Chol=total cholesterol; TG=triglyceride; HDL-Chol=high density lipoprotein-cholesterol; LDL-Chol=low density lipoprotein-cholesterol

# Metabolic syndrome: Central obesity with WC >90 cm (men) or 80 cm (women) with two or more of the following five criteria are met: blood pressure >130/85 mmHg, TG level >150 mg/dL, HDL cholesterol level <40 mg/dL (men) or 50 mg/dL (women) and FBS >100 mg/dL

\* Chi-square and Fisher's exact test were applied to compare between psoriatic subjects versus non-psoriatic subjects.

**Table 3.** Univariate and multivariate data analysis

| Variables                 | Univariate analysis |               |          | Multivariate analysis |               |          |
|---------------------------|---------------------|---------------|----------|-----------------------|---------------|----------|
|                           | Crude OR            | 95% CI        | p-value* | Adjusted OR           | 95% CI        | p-value* |
| CAVI >8.0                 | 10.73               | 3.98 to 28.87 | <0.001   | 10.73                 | 3.98 to 28.87 | <0.001   |
| Age >40 years             | 3.19                | 1.27 to 8.00  | 0.013    |                       |               |          |
| BMI >25 kg/m <sup>2</sup> | 2.27                | 0.94 to 5.47  | 0.068    |                       |               |          |
| Metabolic syndrome#       | 3.39                | 1.37 to 8.40  | 0.008    |                       |               |          |

CAVI=cardio-ankle vascular index; BMI=body mass index; OR=odds ratio; CI=confidence interval

# Metabolic syndrome: Central obesity with waist circumference >90 cm (men) or 80 cm (women) with two or more of the following five criteria are met: blood pressure >130/85 mmHg, TG level >150 mg/dL, HDL cholesterol level <40 mg/dL (men) or 50 mg/dL (women) and FBS >100 mg/dL

\* Simple and multiple binary logistic regression models were tested.

also significantly greater proportion of those subject with fasting blood sugar (FBS) greater than 100 mg/dL, TG greater than 150 mg/dL, and LDL-Chol greater than 130 mg/dL than in non-psoriatic group. In the present study, 46.2% of psoriatic participants were diagnosed with metabolic syndrome, which is significantly higher than in non-psoriatic participants at 20.2% (Table 2).

### Univariate and multivariate data analysis

The variables with a p-value less than 0.10 in univariate analysis, including CAVI greater than 8.0,

age older than 40 years, BMI greater than 25 kg/m<sup>2</sup>, and metabolic syndrome were selected in multivariate data analysis. Independent variables such as FBS greater than 100 mg/dL, total cholesterol greater than 200 mg/dL, TG greater than 150 mg/dL, and LDL-Chol greater than 130 mg/dL were excluded from the model because of the correlation with metabolic syndrome. In the final analysis, those subjects with psoriasis were 10.73 times significantly greater to predict CAVI greater than 8.0 or arterial stiffness than non-psoriatic group (AOR 10.73, 95% CI 3.98 to 28.87, p<0.001) (Table 3).

## DISCUSSION

The present study confirmed that the patients diagnosed with plaque psoriasis strongly associated with arterial stiffness using CAVI technique. Arterial stiffness is defined as CAVI greater than 9.0 in most studies, however, the population with borderline elevated CAVI greater than 8.0 is associated with increased prevalence of obstructive coronary heart disease<sup>(14)</sup>. Three quarters of patients with plaque psoriasis (73.1%) are related to arterial stiffness or CAVI greater than 8.0. In addition, the authors reported that psoriasis had 10.73 times greater risk of CAVI greater than 8.0 than non-psoriatic group. This evidence supported previous studies that confirmed the association between psoriasis with atherosclerosis and cardiac events<sup>(9,10)</sup>. Previous studies also linked between higher CAVI, or arterial stiffness associated with cardiovascular events and increased cardiovascular-related mortality<sup>(19)</sup>.

Overweight, obesity, and metabolic syndrome were not associated with psoriasis in the present study. This differs from previous meta-analysis study by Mirghani et al. which confirms that psoriasis is slightly associated with obesity<sup>(20)</sup>. Previous study by Choi et al. reported a significant association between arterial stiffness and psoriasis but was not related to high BMI<sup>(15)</sup>. The reason the researchers could not find the association is because it was uncommon to develop morbid obesity in Asian population.

The present study reported dyslipidemia. The psoriatic group had a greater proportion of those subjects with TG greater than 150 mg/dL, at 69.2%, and LDL-Chol greater than 130 mg/dL, at 88.5%, than non-psoriatic groups. The present study found 46.2% of psoriatic participants diagnosed with metabolic syndrome, which is significantly higher than in the non-psoriatic participants at 20.2%. Studies reported on the relationship between psoriasis and dyslipidemia. A study by Salihbegovic et al, reported 62.8% psoriatic patients linked with dyslipidemia<sup>(21)</sup>. A study by Nakhwa et al. also documented a strong association between dyslipidemia and psoriasis when comparing with the control group<sup>(22)</sup>. It hypothesized that lipid accumulation in the psoriatic scales directly correlated with an increased blood level of cholesterol<sup>(23)</sup>. Furthermore, dyslipidemia might associate with disease severity. With the increase in Psoriasis Area Severity Index (PASI), the hyperlipidemia becomes more present<sup>(21)</sup>.

The present study reported that 38.5% of psoriasis had impaired FBS or FBS greater than 100 mg/dL in significantly greater proportion than in non-

psoriatic groups, which was at 12.5%. Those patients with psoriasis were more likely to have insulin resistance than healthy subjects<sup>(24)</sup>. Several studies raised the concerns and made the hypothesis between psoriasis and insulin resistance, but it remained inconclusive<sup>(25)</sup>. Moreover, a meta-analysis study by Armstrong et al. supported the evidence that psoriasis had slightly greater risk of diabetes mellitus<sup>(26)</sup>.

In addition to increased cardiovascular disease risk contributed by arterial stiffness, decline in arterial distensibility is also an indicator of endothelial dysfunction and associates with atherosclerosis, deterioration of glomerular filtration rate, and microvascular damages<sup>(27)</sup>. Lifestyle factors are known as the modifiers of arterial distensibility, which also change the natural history of psoriasis<sup>(28)</sup>. According to these reasons, arterial stiffness measurement in psoriatic patients may serve as an indicator of increased cardiovascular disease risk and a target of lifestyle intervention for disease management.

## LIMITATION AND FUTURE RESEARCH

The present study conducted a single snapshot data collection that limited temporal-causal relationships between the factors and disease occurrence. Long-term, follow-up study should be done. Factors such as small sample size, selection bias in control group, disease severity (PASI), the duration of psoriasis, systemic therapy, daily alcoholic or tobacco consumption, and lifestyle that might influence study outcomes were not mentioned in the study.

## WHAT IS ALREADY KNOWN ABOUT THIS TOPIC?

The patients with plaque psoriasis were 10.73 times significantly greater to predict CAVI greater than 8.0 or arterial stiffness than non-psoriatic group. To prevent long term cardiovascular events and further complications, early cardiovascular screening with CAVI in psoriasis patients is an optional evaluation tool.

## WHAT DOES THIS STUDY ADD?

- Arterial stiffness or CAVI greater than 8.0 are common in plaque psoriasis.
- Arterial stiffness is linked to long-term cardiovascular complications and increased mortality from cardiac events.
- Early cardiovascular screening with CAVI measurement in psoriasis patients is important and recommended for early detection and prevention.



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## AUTHORS' CONTRIBUTIONS

TO, VJ, and TC contributed to the concept of study and study design. TO and TC collected and analyzed the data. TO and TC wrote the original draft. VJ and TC contributed critically to its revision for important intellectual content. All the authors approved the final version submitted for publication and took responsibility for the statements made in the published article.

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## CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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