Assessment of P-wave indices as atrial fibrillation predictors in psoriasis patients

Nastaran Namazi, MD [1]
Maryam Helali, MD [1]
Mehdi Pishgahi, MD [2]
Yasaman Ketabi, MD [1]

1. Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Cardiology,Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author:
Yasaman Ketabi, MD
Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
PC: 1989934148
Fax: (98) 21-22744393
Tel: (98) 21-22741507
Email: yasamanketabi@gmail.com

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Background: Psoriasis is a prevalent chronic T cell mediated inflammatory skin disorder. Recent studies have reported an increase in the incidence of arrhythmia in psoriasis patients who run an excessive risk of metabolic syndrome and cardiovascular diseases. P-wave dispersion (PWD) and duration are important electrocardiographic (ECG) markers employed to anticipate the risk of atrial arrhythmias. The objective of this research was to investigate the risk of atrial arrhythmia by measuring PWD, and maximum and minimum p-wave duration in psoriasis patients without known cardio metabolic risk factors.

Materials and Methods: ECG was evaluated in Sixty-five adult patients with psoriasis and sixty-five age-, gender- and BMI-matched healthy individuals.

Results: Maximum P-wave duration (P max) and PWD were significantly higher in patients compare with the controls.

Conclusion: It seems that psoriasis patients run a higher risk of developing atrial arrhythmia even following the adjustment of cardio metabolic risk factors.

Keywords: psoriasis, P-wave dispersion, atrial fibrillation

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INTRODUCTION

Psoriasis, with 1 to 4% prevalence in population-based studies, is a common chronic inflammatory T cell mediated disorder affecting the skin, nails, and occasionally the joints [1-3]. Psoriasis has been associated with an increase in cardiovascular risk factors, such as metabolic syndrome, hypertension, diabetes mellitus, and mortality. Chronic inflammation and oxidative stress are thought to be responsible for the augmentation in the incidence of cardiometabolic events [4-6].

Atrial fibrillation (AF) is the most common sustained arrhythmia in the general population, which increases cardiovascular morbidity and mortality, while reducing the quality of life [6,7]. Certain studies have recently shown that AF and stroke are more widespread in psoriasis and such inflammatory diseases as rheumatoid arthritis [7-10]. The exact etiology is not fully recognized. Although a few studies were carried out on the prevalence of arrhythmia in psoriasis, there exist no data on the risk of arrhythmia after adjusting known cardiovascular disease risk factors.

ECG is considered as a noninvasive and inexpensive modality for evaluating cardiac disease. In comparison with other methods such as echocardiography, ECG is less expensive, more convenient and readily available. P-wave characteristics in electrocardiographs are commonly utilized to determine the risk of AF in myriad patient populations [11-15].

The difference between the maximum and minimum P-wave duration (P max, P min) in ECG is defined as PWD, which is regarded as an electrocardiographic marker of the prolongation of

intra- and inter-atrial conduction time in addition to the heterogeneous and discontinuous dissemination of sinus impulses in atrial areas [10,16,17]. Several studies have demonstrated the elongation of PWD to be a significant independent risk factor for the development of atrial arrhythmia and AF [18].

The aim of the present study was to assess P-wave characteristics as a major predictor for the development of AF.

MATERIALS AND METHODS

Included in the study were sixty-five patients with moderate to severe plaque type psoriasis (PASI>10) (referred to Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran) and sixty-five age, gender and body mass index (BMI) matched healthy controls. The diagnosis of psoriasis was confirmed by histopathology, and the severity of psoriasis was evaluated via PASI scoring system.

Exclusion criteria were hypertension, diabetes mellitus, personal or family history of cardiovascular disease/arrhythmia, abnormal echocardiogram, lung disease, pulmonary hypertension, liver/kidney disease, collagen vascular disease, cardiovascular drug use, abnormal thyroid function or serum electrolyte values, psoriatic arthritis, systemic psoriasis treatment within the past three months, alcohol consumption, obesity, and smoking (BMI $\geq$30 kg/m^2). All patients and controls had normal physical activity and were on regular diet. Participants, aged 18 years or older, provided a written informed consent.

The participants' weight (Kg), height (m), waist circumference (cm), BMI (kg/m2), systolic and diastolic blood pressure (after a 15-minute rest) were measured. Further determined were serum triglycerides, total cholesterol, HDL-C, LDL-C, and glucose levels in samples collected after a 12-hour fasting period.

Twelve-lead ECG of patients and controls was recorded in the supine position through the use of commercially available machinery (Marquette Case, Hellige Medical System, Cardiosmart Hellige Instrument Company, Freiburg, Germany). ECG recordings were obtained at 50 mm/s paper speed and 10 mm/mV amplitude. The beginning of P-wave was defined as the point where the first atrial deflection crossed the isoelectric line, and the end of P-wave was defined as the point where the atrial deflection returned to the isoelectric line.

All measurements, performed by an experienced cardiologist who was blinded to the study, were manually taken with the help of calipers and a magnifying glass to define the electrocardiographic deflection. The P-wave durations (P max, P min) were calculated in all 12 ECG leads; moreover, the difference between P max and P min was defined as PWD.

Continuous variables are presented as either mean ± SD or medians with total and interquartile ranges (25th-75th percentiles). Categorical data are reported as numbers (percentages). The normality of continuous variables was examined through the use of Shapiro-Wilk's W-test.

For data analysis, chi-square test and Fisher's exact test were performed wherever appropriate. The two groups were compared in terms of continuous variables using Mann-Whitney-U test, and the association between disease duration and other continuous variables was assessed via Spearman's correlation test.

All data analyses were conducted by the use of statistical software JMP, Version 7. SAS Institute Inc. Cary, NC, 1989-2007. P-values less than 0.05 were considered to be statistically significant, and all tests were two-sided.

Informed consent was obtained from all participants and the study protocol, performed according to the Declaration of Helsinki, and was approved by the institutional ethics committee.

RESULTS

Sixty-five patients with moderate to severe psoriasis (PASI>10) and sixty-five age-, gender- and BMI- matched healthy controls were included in the study. Table 1 shows the baseline demographics and laboratory findings of the participants. The two groups did not differ significantly in age, gender, BMI, systolic and diastolic blood pressure. Furthermore, no recognizable difference was observed concerning the median serum levels of total cholesterol, HDL-C, LDL-C, TG and serum glucose.

P-wave indices were not influenced by age and there was no significant difference between the genders of both groups (p=0.15).

The mean duration of disease was 10.5±3.7,

Table 1. Demographics and laboratory findings of patients with psoriasis and healthy controls

Characteristic	Patients with psoriasis (n=65)	Healthy controls (n=65)	*P*-value
Gender, no. (%)			1.00
Female	25 (38.5%)	24 (36.9%)	
Male	40 (61.5%)	41 (63.1%)	
Age, years	35 (18-85); (28.5-49.5)	35 (18-85); (28-51)	0.88
BMI	25.5 (19.3-29.8); (23.1-28)	25.8 (22-29.8); (24.2-27.2)	0.66
Waist circumference (cm)	95.4 ± 8.1	93.5 ± 7.5	0.9
Systolic BP, mmHg	110 (90-130); (105-120)	110 (100-135); (110-120)	0.76
Diastolic BP, mmHg	70 (60-90); (70-75)	70 (60-80); (60-70)	0.12
TG, mg/dL	126 (55-190); (95-154)	124 (73-188); (100.5-145.5)	0.89
Total cholesterol, mg/dL	167 (98-209); (127.5-192)	167 (100-204); (139-188)	1.00
LDL, mg/dL	99.42±25.04	99.95±20.70	0.89
HDL, mg/dL	38 (25-57); (32-42.5)	39 (23-54); (35-41)	0.40
Blood sugar, mg/dL	85.85±8.02	85.91±6.06	0.96
PASI	≥10		

Values are expressed as median (range); IQR or as mean±SD.
Abbreviations: BMI, Body Mass Index (calculated as weight in kilograms divided by height in meters squared); IQR, Interquartile range (25^{th} -75^{th} percentiles)

ranging from 2 to 24 years.

Patients with psoriasis had significantly longer P max duration than healthy controls (p<.0001, Table 2). P min durations, on the other hand, were similar in both groups (p=0.17, Table 2). Compared to the control group, patients had significantly higher PWD (p<.0001, Table 2). In patients with psoriasis, the duration of disease (2-32 years, mean 5.1 years) was not significantly associated with P-min (rs=0.24, p=0.06), P-max (rs=0.14, p=0.27) and PWD (rs=0.01, p=0.91). Neither was there a significant relationship between PASI and PWD or P-max and P-min.

DISCUSSION

Cardiometabolic risk factors, such as hypertension, insulin resistance, dyslipidemia, obesity, alcohol consumption, and smoking are more common in psoriasis patients than the general population [19]. Certain studies have illustrated a clinically significant increased risk of accelerated atherosclerosis and cardiovascular disease and related mortality in psoriasis patients. They have further considered psoriasis as an independent risk factor for cardiovascular diseases. Instead of considering psoriasis as a clinically relevant risk factor for ischemic heart disease, some well-designed studies suggest that the high prevalence of comorbid conditions and certain other confounding factors like quality-of-life impairment, depression, altered life styles, use of systemic drugs and increased healthcare referral are in charge [20,21].

Rhythm disturbances, atrial fibrillation, atrioventricular block and sudden cardiac death are important manifestations of cardiac involvement in autoimmune diseases with increased inflammation including rheumatoid arthritis, ankylosing spondylitis and inflammatory bowel disease [8,22].

Arrhythmia and the concomitant effects like cerebrovascular disease, stroke, thrombophlebitis and pulmonary embolism have been reported as being more frequent in psoriasis patients. AF is responsible for up to 20% of all ischemic strokes,

Table 2. P-wave and heart rate in patients with psoriasis and healthy controls

Characteristic	Patients with psoriasis (n=65)	Healthy controls (n=65)	*P*-value
Pmax (msec)	100 (16-116); (88-112)	88 (68-112); (80-96)	<.0001
Pmin (msec)	48(30-76); (40-58)	48 (36-76); (44-56)	0.17
PWD (msec)	48 (24-82); (40-58)	36 (4-56); (28-46)	<.0001
Heart rate (bpm)	82 (72-94); (78.5-86)	84 (72-94); (80-88)	0.50

Values are expressed as median (range); IQR.
Abbreviations: PWD: P wave dispersion; IQR, Interquartile range (25^{th} -75^{th} percentiles)

augmenting the risk of ischemic stroke by 5-fold. Furthermore, AF-related strokes are more disabling, recurrent and fatal [17].

Markuszeski et al., reported that patients with psoriasis have more single supraventricular beats than controls [6]. Bacaksiz stated that psoriasis patients have impaired atrial conduction of sinus impulses and higher PWD indicating an augmented risk of AF [17]. A Danish nationwide study was the first cohort study to specify the prevalence of AF in psoriasis, where it was shown that psoriasis was related to an increased risk of AF, which is higher in severe and protracted diseases [7]. Armstrong appraised two cohorts and observed no association between moderate-to-severe or mild psoriasis and development of AF [12]. Another study reported that psoriasis was able to predict new-onset atrial fibrillation, yet included hypertensive patients with psoriasis and left ventricular hypertrophy [23].

Although the exact etiology of increased AF in psoriasis patients is yet to be fully understood, some mechanisms have been posited. Factors conducing to such increase might be atrial remodeling induced by chronic inflammation and oxidative stress, genetic predisposition, elevated levels of tumor necrosis factor-alpha, IL-2, IL-6 and IL-17, arterial wall inflammation and increased sympathetic activity [24-29]. A recent nationwide cohort study found that depression is associated with an increased risk of AF and stroke in patients with psoriasis [30]. The relationship between psoriasis, depression and inflammation is substantiated by the interesting observation that treatment with TNF-alpha inhibitors can reduce depressive symptoms in patients with psoriasis. In this regard, a recent study found that the use of antidepressants, such as serotonin reuptake inhibitors reduced the need for systemic psoriasis treatment [31-34]. Whether or not prescribing antidepressants can lower such risks is yet another issue that has to be further elucidated.

In this investigation, the P-wave variables were measured in patients and controls without traditional risk factors, where, consistent with certain studies, it was observed that PWD and P max values were significantly higher in the patients [17,25]. Unlike Bacaksiz et al., who showed that P min was shorter in patients [8], the present study showed that the P min values were not significantly different between psoriasis and normal individuals.

In our study, there was no association between PASI or duration of disease and PWD, P-max and P-min, which was probably due to the selection of patients with moderate to severe diseases (PASI>10). It can be further suggested that in moderate to severe psoriasis, there exists an increased risk of supraventricular arrhythmia from the onset of the diseases.

Among the limitations of the research, was the cross sectional design and the paucity of long-term clinical follow-up on the patients. Moreover, the inclusion of moderate to severe psoriasis patients in the study overestimates the risk. That said, large-scale long-term follow-up prospective studies are required to establish the predictive value of atrial conduction variables for the development of AF in patients with psoriasis.

CONCLUSION

Measuring PWD is a reliable, noninvasive and feasible approach to determining the risk of atrial fibrillation in patients with psoriasis. Needless to say, early detection and appropriate treatment are important if serious consequences are to be precluded.

Observing patients with increased PWD might result in earlier detection and intervention of arrhythmia, thereby reducing morbidity and the possibility of sudden death, stroke and pulmonary embolism. Cardiovascular risk factor modification has to be encouraged in all patients. Regarding the possible association of inflammation and cardiovascular events including arrhythmia, drugs with more favorable effect on inflammation can be selected, lowering cardiovascular events like methotrexate and TNF-alpha inhibitors in patients with elevated PWD.

Conflict of Interest: None declared.

REFERENCES

1. Christophers E. Psoriasis− epidemiology and clinical spectrum. Clin Exp Dermatol.2001;26(4):314-20.
2. Enamandram M, Kimball AB. Psoriasis epidemiology: the interplay of genes and the environment. J Invest Dermatol. 2013;133(2):287-9.
3. Zhang Z, Li G, Liu T. Psoriasis and risk of atrial fibrillation.

Int J Cardiol. 2015;185:301-3.

4. Rosa D, Machado R, Matias F, et al. Influence of severity of the cutaneous manifestations and age on the prevalence of several cardiovascular risk factors in patients with psoriasis. J Eur Acad Dermatol Venereol. 2012;26(3):348-53.
5. Markuszeski L BA, Janusz I, Narbutt J, et al. Heart rate and arrhythmia in patients with psoriasis vulgaris. Arch Med Res. 2007;38:64-9.
6. Chiu H-Y, Chang WL, Huang WF, et al. Increased risk of arrhythmia in patients with psoriatic disease: a nationwide population-based matched cohort study. J Am Acad Dermatol. 2015;73(3):429-38.
7. Ahlehoff O, Gislason GH, Jørgensen CH,et al. Psoriasis and risk of atrial fibrillation and ischaemic stroke: a Danish nationwide cohort study. Eur Heart J. 2012;33:2054-64.
8. Lindhardsen J, Ahlehoff O, Gislason GH, et al. Risk of atrial fibrillation and stroke in rheumatoid arthritis: Danish nationwide cohort study.Br J Dermatol. 2012;344:e1257.
9. Lazzerini PE, Capecchi PL, Acampa M, et al. Arrhythmic risk in rheumatoid arthritis: the driving role of systemic inflammation. Autoimmun Rev. 2014;13(9):936-44.
10. Simsek H, Sahin M, Akyol A, et al. Increased risk of atrial and ventricular arrhythmia in long-lasting psoriasis patients.Sci World J. 2013;2013.
11. Yavuzkir M, Ozturk A, Dagli N, et al. Effect of ongoing inflammation in rheumatoid arthritis on P-wave dispersion. J Int Med Res. 2007;35(6):796-802.
12. Turgut O, Tandogan I, Yilmaz MB, et al. Association of P wave duration and dispersion with the risk for atrial fibrillation: Practical considerations in the setting of coronary artery disease. Int J Cardiol. 2010;144(2):322-4.
13. Dilaveris PE, Stefanadis CI. P wave dispersion. A valuable non-invasive marker of vulnerability to atrial arrhythmias. Hosp Chron. 2006;1(3):130-7.
14. Centurión OA. Clinical implications of the P wave duration and dispersion: relationship between atrial conduction defects and abnormally prolonged and fractionated atrial endocardial electrograms. Int J Cardiol. 2009;134(1):6-8.
15. Michelucci A, Bagliani G, Colella A, et al. P wave assessment: state of the art update. Card Electrophysiol Rev. 2002;6(3):215-20.
16. Centurion OA. Clinical implications of the P wave duration and dispersion: relationship between atrial conduction defects and abnormally prolonged and fractionated atrial endocardial electrograms. Int J Cardiol. 2009;134:6-8.
17. Bacaksiz A, Erdogan E, Tasal A, et al. Electrocardiographic P-wave characteristics in patients with psoriasis vulgaris. Ups J Med Sci. 2013;118(1):35-41.
18. Gonna H, Gallagher MM, Guo XH, et al. P wave abnormality predicts recurrence of atrial fibrillation after electrical cardioversion: a prospective study. Ann Noninvasive Electrocardiol. 2014;19(1):57-62.
19. Neimann AL, Shin DB, Wang X, et al. Prevalence of cardiovascular risk factors in patients with psoriasis. J Am Acad Dermatol. 2006;55(5):829-35.
20. Parisi R, Rutter M, Lunt M, et al. Identification and Management of Psoriasis Associated ComorbidiTy (IMPACT) project team. Psoriasis and the risk of major cardiovascular events: cohort study using the clinical practice research datalink. J Invest Dermatol. 2015;135(9):2189-97.
21. Wakkee M, Herings RM, Nijsten T. Psoriasis may not be an independent risk factor for acute ischemic heart disease hospitalizations: results of a large population-based Dutch cohort. J Invest Dermatol. 2010;130(4):962-7.
22. Thomsen N, Hørslev-Petersen K, Beyer J. Ambulatory 24-hour continuous electrocardiographic monitoring in 54 patients with ankylosing spondylitis. Eur Heart J. 1986;7(3):240-6.
23. Bang CN, Okin PM, Køber L, et al. Psoriasis is associated with subsequent atrial fibrillation in hypertensive patients with left ventricular hypertrophy: the losartan intervention for endpoint study. J Hypertens.2014;32(3):667-72.
24. Fu G, Cao Y, Lu J, et al. Programmed cell death-1 deficiency results in atrial remodeling in C57BL/6 mice. Int J Mol Med. 2013;31(2):423-9.
25. Korantzopoulos P, Kolettis TM, Galaris D, et al. The role of oxidative stress in the pathogenesis and perpetuation of atrial fibrillation. Int J Cardiol. 2007;115(2):135-43.
26. Liu T, Li G, Li L, et al. Association between C-reactive protein and recurrence of atrial fibrillation after successful electrical cardioversion: a meta-analysis. J Am Coll Cardiol. 2007;49(15):1642-8.
27. Saba S, Janczewski AM, Baker LC, et al. Atrial contractile dysfunction, fibrosis, and arrhythmias in a mouse model of cardiomyopathy secondary to cardiac-specific overexpression of tumor necrosis factor-α. Am G Physiol Heart Circ Physiol. 2005;289(4):H1456-H67.
28. Sawaya SE, Rajawat YS, Rami TG, et al. Downregulation of connexin40 and increased prevalence of atrial arrhythmias in transgenic mice with cardiac-restricted overexpression of tumor necrosis factor. Am G Physiol Heart Circ Physiol. 2007;292(3):H1561-H7.
29. Dave J, Ahlman MA, Lockshin BN, et al. Vascular inflammation in psoriasis localizes to the arterial wall using a novel imaging technique. J Am Acad Dermatol. 2014;70(6):1137-8.
30. Egeberg A, Khalid U, Gislason G, et al. Association between depression and risk of atrial fibrillation and stroke in patients with psoriasis: a Danish nationwide cohort study. Br J Dermatol. 2015;173(2):471-9.
31. Leonard BE. The immune system, depression and the action of antidepressants. Prog Neuropsychopharmacol Biol Psychiatry. 2001;25(4):767-80.
32. Menter A, Augustin M, Signorovitch J, et al. The effect of adalimumab on reducing depression symptoms in patients with moderate to severe psoriasis: a randomized clinical trial. J Am Acad Dermatol. 2010;62(5):812-8.
33. Thorslund K, Svensson T, Nordlind K, et al. Use of serotonin reuptake inhibitors in patients with psoriasis is associated with a decreased need for systemic psoriasis treatment: a population based cohort study. J Intern Med. 2013;274(3):281-7.
34. Miller AH, Maletic V, Raison CL. Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. Biol Psychiatry. 2009;65(9):732-41.