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# Angiotensin-converting enzyme I/D polymorphism and susceptibility of psoriasis.

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## Abstract

**The role of angiotensin-converting enzyme (ACE) I/D polymorphism in psoriasis have not been determined. Thus, in this study, we aimed to analyse ACE I/D polymorphism for the association with the risk of psoriasis in a Chinese Han population. A total of 161 cases (72 men and 89 women; mean age, 43.8 ± 5.5 years) and 256 controls (119 men and 137 women; mean age, 42.1 ± 6.9 years) were included in the study. The observed frequencies of all tested genotypes in controls did not deviate from Hardy-Weinberg equilibrium (HWE). Compared with the II genotype, the DD frequency of ACE I/D polymorphism among cases was significantly different from controls (DD versus II: OR=2.94; 95% CI=1.61-5.42; p<0.05). In addition, compared with the I allele, the D allele among cases was significantly associated with psoriasis risk (D versus I: OR=1.61; 95% CI=1.21-2.21; p<0.05). In conclusion, the current study showed that ACE I/D polymorphism may influence the risk of psoriasis in a Chinese Han population.**

**Keywords:** Psoriasis; Angiotensin-converting enzyme; Polymorphism.

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## Introduction

Psoriasis is a dynamic systemic disease that can have a profound effect on a patient's self-esteem [1]. It characterized by a chronic, autoimmune, and complex genetic disorder [2]. The burden of the disease is not limited solely to the skin, with an estimated 30% patients developing psoriatic arthritis, which in its most aggressive form can cause permanent joint damage [3].

Angiotensin-converting enzyme (ACE) is a key player in the renin-angiotensin system (RAS). ACE levels in plasma and tissue are under genetic control [4]. Rigat et al. found that approximately 50% of ACE plasma level variability was associated with I/D gene polymorphism [4]. ACE D allele carriers have higher ACE plasma [5] and tissue [6] levels compared with those with ID and II genotypes. The role of ACE I/D polymorphism in psoriasis has not been determined. Thus, in this study, we aimed to analyze ACE I/D polymorphism for the association with the risk of psoriasis in a Chinese Han population.

## Methods

### *Study subjects*

A total of 161 patients and 256 healthy controls were enrolled for this case-control study. Individuals who came to the hospital for routine physical examination were recruited as health controls. The characteristics of each subject, including age and gender, were collected via a questionnaire. For patients, the clinical features were collected from the patients' medical records. The study protocol was approved by the Institutional Review Boards of the hospital.

### *Genotyping*

DNA was extracted from whole blood samples by salting out method. Target DNA regions of the ACE gene were amplified by allele-specific polymerase chain reaction. The sequence of primers used for amplification of ACE was 5'-CTGGAGACCACTCCCATCCTTTCT-3' (forward) and 5'-GATGTCGCCATCACATTCGTCAGAT-3' (reverse). Amplification of the I allele is sometimes suppressed in ID genotype samples giving rise to mistyping of ID as DD in approximately 5 % of cases. To avoid such mistyping, samples of the DD genotype were subjected to a second independent PCR with primers that recognize an insertion-specific

sequence: 5'-TGGGACCACAGCGCCCGCCACTAC-3' (forward) and 5'-TCGCCAGCCCTCCCATGCCCATAA-3' (reverse). The reaction mixture consist of template DNA 3 µl, each of primer 1 µl, primers (i-Taq) 5 µl, and distilled water14 µl. Procedure consisted of initial denaturation at 94°C for 5 min, then denaturation at 94°C for 35 s, annealing at 56°C for 40 s, and extension at 72°C for 1 min, repeated for 35 cycles, and followed by a final extension at 72°C for 8 min.

### *Statistical analysis*

All statistical analyses were performed by the Statistical Package for Social Sciences for Windows software (Windows version release 18.0; SPSS, Inc., Chicago, IL, USA). The frequencies of allele and genotype in cases and controls were calculated by gene counting method. Differences between cases and controls in demographic characteristics and frequencies of genotypes were evaluated by using chi-square ($\chi^2$) test. Hardy-Weinberg equilibrium (HWE) was also tested by a chi-square ($\chi^2$) test. Differences were considered significant when $P<0.05$.

## Results

A total of 161 cases (72 men and 89 women; mean age, 43.8 ± 5.5 years) and 256 controls (119 men and 137 women; mean age, 42.1 ± 6.9 years) were included in the study. The demographic data of all participants are summarized in Table 1. There was no significant difference in age ($p>0.05$) and sex ($p>0.05$) between cases and controls. For the family history, 104 (64.4%) patients had family history. Most of the patients (66.2%) had psoriasis area and severity index less than 20.

***Table 1.*** *Clinical characteristics of the psoriasis patients (cases) and controls.*

| Characteristics | Case (%) | Control (%) | P value |
|---|---|---|---|
| Age | 43.8 ± 5.5 | 42.1 ± 6.9 | >0.05 |
| Gender | | | |
| Female | 89 (55.6%) | 137 (53.7%) | >0.05 |
| Male | 72 (44.4%) | 119 (46.3%) | |
| Family history | | | |
| Yes | 104 (64.4%) | | |
| No | 57 (35.6%) | | |
| PASI | | | |
| >20 | 54 (33.8%) | | |
| <20 | 107 (66.2%) | | |

PASI: Psoriasis Area and Severity Index

The genotype distributions of the polymorphism in cases and controls are presented in Table 2. The observed frequencies of all tested genotypes in controls did not deviate from Hardy-Weinberg equilibrium (HWE). Compared with the II genotype, the DD frequency of ACE I/D polymorphism among cases was significantly different from controls (DD versus II: OR=2.94; 95% CI=1.61-5.42; $p<0.05$). In addition, compared with the I allele, the D allele among cases was significantly associated with psoriasis risk (D versus I: OR=1.61; 95% CI=1.21-2.21; $p<0.05$).

***Table 2.*** *Genotype distribution and allele frequencies of ACE I/D polymorphism between psoriasis patients (cases) and controls.*

| | Case (%) | Control (%) | OR (95%CI) | P value |
|---|---|---|---|---|
| Genotype | | | | |
| II | 55 (34.2%) | 119 (46.5%) | 1 (Ref.) | |
| ID | 71 (44.1%) | 111 (43.4%) | 1.34 (0.85-2.04) | >0.05 |
| DD | 35 (21.7%) | 26 (10.1%) | 2.94 (1.61-5.42) | <0.05 |
| Allele | | | | |
| I | 181 (56.2%) | 349 (68.2%) | 1 (Ref.) | |
| D | 141 (43.8%) | 163 (31.8%) | 1.61 (1.21-2.21) | <0.05 |

## Discussion

In the present study the possible association between ACE I/D polymorphism and the risk of psoriasis was investigated. Compared with the II genotype, the DD frequency of ACE I/D polymorphism among cases was significantly different from controls. In addition, compared with the I allele, the D allele among cases was significantly associated with psoriasis risk. Thus, the results of the current study demonstrated that ACE I/D polymorphism significantly increased the risk of psoriasis in the Chinese population.

Genetic factors play important role in the development of psoriasis. Rajesh et al. indicated that TNFα gene -238G/A polymorphism increases the risk of developing psoriasis vulgaris among Indians [7]. Zablotna et al. suggested that the -2518 A/G MCP-1 and -403 G/A RANTES promoter gene polymorphisms may be risk factors for psoriasis [8]. Izmirli et al. found a correlation between methylenetetrahydrofolate C677T polymorphism and psoriasis among the southern Turkish population [9]. Shi et al. demonstrate a significant association between the CARD14 rs11652075 polymorphism and psoriasis [10].

ACE I/D polymorphism also played a critical role in the development of other diseases. Kang et al. indicated that the insertion/deletion polymorphism of the ACE gene may be associated with susceptibility to COPD in the Asian population [11]. He et al. suggested that genetically-reduced serum ACE activity might be a causal risk factor for obstructive sleep apnea syndrome (OSAS) [12]. Pabalan et al. found that carriers of the ACE II genotype appear to be protected from gastric cancer [13-25].

In conclusion, the current study showed that ACE I/D polymorphism may influence the risk of psoriasis in a Chinese Han population.

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