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Transforming growth factor-β1-509C/T polymorphism might be associated with chronic periodontitis risk.

Zhen-Hui Wei, Yuan-Hong Du*

Department of Stomatology, the 463rd Hospital of PLA, No.46 Xiaoheyan Road, Shenyang, Liaoning, PR China

Abstract

It is unclear whether there is significant association between TGF-β1-509C/T polymorphism and chronic periodontitis risk. Therefore, we performed this meta-analysis. We conducted a search through PubMed, Embase and the Web of Science. The associations between TGF-β1-509C/T polymorphism and chronic periodontitis risk as estimated using the OR and 95% CI. A total of 7 studies were included in this systematic review and meta-analysis. In the overall analysis, a significant association between the TGF-β1-509C/T polymorphism and chronic periodontitis risk was identified (OR=0.84; 95% CI, 0.71-1.00). When stratified by ethnicity, the TGF-β1-509C/T polymorphism showed a significant contribution to chronic periodontitis risk in the Asians (OR=0.80; 95% CI, 0.65-0.99). However, Caucasians with the TGF-β1-509C/T polymorphism did not show positive result (OR=0.94; 95% CI, 0.67-1.32). In the non-smoker subgroup, no significant association was detected (OR=0.83; 95% CI, 0.60-1.15). In conclusion, this study suggested that TGF-β1-509C/T polymorphism was associated with chronic periodontitis risk.

Keywords: TGF-β1, Chronic periodontitis, Polymorphism.

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Introduction

Chronic periodontitis is an inflammatory disease affecting tissues of the periodontium resulting in Clinical Attachment Loss (CAL) and bone loss [1]. The pathogenesis of periodontitis involves role play of cytokines, produced by host defence cells in reaction to antigenic stimuli, which have a wide range of overlapping functions [2].

Chronic periodontitis is multifactorial in nature with smoking, diabetes, and genetic polymorphism being some of the risk factors [3].

Transforming Growth Factor-β1 (TGF-β1) is a multifunctional cytokine with various effects on cell proliferation, differentiation, apoptosis, migration, inflammation, tissue repair, and immune responses [4]. Molecular biological evidence showed that polymorphisms in the TGF-β result in a T→C transition at nucleotide 869 in the region encoding the signal sequence [5].

Functional experiments indicated that T869C polymorphism can increase the expression of TGF-β1 mRNA by influencing the intracellular trafficking or exporting efficiency of the synthesized protein to the endoplasmic reticulum, resulting in the elevated serum TGF-β1 level [6].

It is unclear whether there is significant association between TGF-β1-509C/T polymorphism and chronic periodontitis risk [7-13]. Therefore, we performed this meta-analysis.

Materials and Methods

Publications search

We conducted a search using the terms "Transforming growth factor-β1", "TGF-β1", "chronic periodontitis", and "polymorphism" through PubMed, Embase, and the Web of Science. Only papers written in the English language were included. References from the identified studies were also investigated to identify additional studies.

Inclusion criteria

Studies included in the current meta-analysis met the following criteria: (1) Were case-control studies; (2) Assessed the association between TGF-β1-509C/T polymorphism and chronic periodontitis risk; (3) Had available genotype frequencies for calculating Odds Ratios (ORs) with their 95% Confidence Interval (CI).

Data extraction

The following information was extracted from each study: the first author, year, ethnicity, sample size and smoking.

Statistical analysis

The allele counting method was used to determine the allele frequencies of the genetic polymorphism. The associations between TGF-β1-509C/T polymorphism and chronic periodontitis risk as estimated using the OR and 95% CI.

Heterogeneity assumption was verified by χ^2-based Q-test and quantified using the I^2 value. The random-effects model (the Der Simonian and Laird method) was used. The Egger's linear regression test on a natural log scale of the OR was used to evaluate the funnel plot symmetry and the significance was set at P<0.05 level. Software's Stata 12.0 and Review Manager 5.0 were used to perform the statistical analyses (StataCorp, College Station, TX, USA).

Results

Characteristics of the studies

The characteristics of the studies are summarized in Table 1. Data was extracted from 899 cases and 866 controls. Three studies used Caucasians and four studies used Asians. Four studies used never smoking subjects.

Table 1. *Characteristics of the studies.*

First author	Race	Smoking	No. of cases	No. of control
de Souza	Caucasian	Never	50	37
Heidari	Caucasian	Never	100	100
Holla	Caucasian	Mixed	98	108
Komatsu	Asian	Never	113	108
Kobayashi 1	Asian	Mixed	117	108
Kobayashi 2	Asian	Mixed	319	303
Zhao	Asian	Never	102	102

Meta-analysis results

In the overall analysis, a significant association between the TGF-β1-509C/T polymorphism and chronic periodontitis risk was identified (OR=0.84; 95% CI, 0.71-1.00) (Figure 1). When stratified by ethnicity, the TGF-β1-509C/T polymorphism showed a significant contribution to chronic periodontitis risk in the Asians (OR=0.80; 95% CI, 0.65-0.99) (Table 2). However, Caucasians with the TGF-β1-509C/T polymorphism did not show positive result (OR=0.94; 95% CI, 0.67-1.32) (Table 2). In the non-smoker subgroup, no significant association was detected (OR=0.83; 95%CI, 0.60-1.15) (Table 2).

Publication bias among the eligible studies was assessed by the Egger's test, and there was no publication bias in this meta-analysis (P=0.59).

Table 2. *Meta-analysis results.*

	OR (95% CI)
Total Ethnicity	0.84 (0.71-1.00)
Asian	0.80 (0.65-0.99)
Caucasian	0.94 (0.67-1.32)
Smoking status	

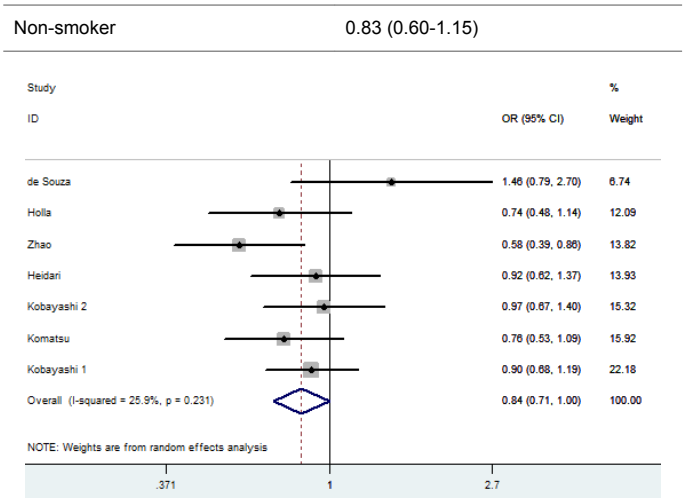

Figure 1. *The association between TGF-β1-509C/T polymorphism and chronic periodontitis risk.*

Discussion

A total of 7 studies were included in this systematic review and meta-analysis. In the overall analysis, a significant association between the TGF-β1-509C/T polymorphism and chronic periodontitis risk was identified. When stratified by ethnicity, the TGF-β1-509C/T polymorphism showed a significant contribution to chronic periodontitis risk in the Asians. However, Caucasians with the TGF-β1-509C/T polymorphism did not show positive result. In the non-smoker subgroup, no significant association was detected.

Lee et al. found a significantly lower circulating TGF-β1 level in SLE patients, and a significant association between TGF-β1+869 T/C polymorphism and RA development [14]. Qiao et al. found that patients with T2DM and those with albuminuria had increased serum and urine TGF-β1 levels [15]. Wang et al. suggested that TGFβ1 869C/T polymorphism was a risk factor of radiation pneumonitis [16]. Mao et al. indicated that T allele at the -509 T/C polymorphism may be an indicator of CKD risk in overall populations and Asians [17]. Zhang et al. suggests that donors or recipients with TGF-β1 rs1800469 polymorphism and donors with TGF-β1 rs1800470 polymorphism might be associated with reduced GVHD risk [18]. Deng et al. suggests that TGFβ1 T+869C and C-509T polymorphisms may not contribute to lung cancer risk [19].

There are some limitations that should be addressed. First, the number of studies that were included in this analysis was small, which could not provide sufficient statistical power. Second, although we employed a thorough literature search strategy to identify qualified studies, a few studies may not get involved in the meta-analysis. Third, our meta-analysis is based on unadjusted estimates because of a lack of original data.

In conclusion, this study suggested that TGF-β1-509C/T polymorphism was associated with chronic periodontitis risk.

Conflicts of Interest

The authors have declared that no competing interests exist.

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*Correspondence to

Yuan-Hong Du

Department of Stomatology

The 463rd Hospital of PLA

No.46 Xiaoheyan Road

Shenyang

Liaoning

PR China