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Research Article

Is There An Association Between Angiotensin II Type 1 Receptor A1166C Gene Polymorphism and Renal Scarring Susceptibility?

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Abstract

Relationship between Angiotensin II Type 1 Receptor (AT1R) A1166C gene polymorphism and renal scarring risk is still controversial. This meta-analysis was performed to evaluate the association of AT1R A1166C gene polymorphism and renal scarring risk susceptibility. A predefined literature search and selection of eligible relevant studies were performed to collect data from electronic databases of PubMed, Embase and Cochrane Library. Three literatures were identified and included for the analysis of the relationship between AT1R A1166C gene polymorphism and renal scarring risk. We found that AT1R A1166C gene polymorphism was not associated with renal scarring susceptibility using the comparison of patients with scarring vs patients without scarring (C: OR=1.33, 95%CI: 0.83-2.13, *P*=0.23; CC: OR=1.71, 95%CI: 0.22-13.56, *P*=0.61; AA: OR=0.69, 95%CI: 0.39-1.21, *P*=0.20). Furthermore, AT1R A1166C gene polymorphism was also not associated with renal scarring risk using the comparison of patients with scarring vs healthy control. In conclusion, AT1R A1166C gene polymorphism was not associated with renal scarring risk susceptibility. However, more studies should be performed in the future.

Introduction

Renal scarring, a serious complication, often occurs with chronic pyelonephritis in the presence of Vesicoureteral Reflux (VUR) [1]. Urinary Tract Infection (UTI) is the most common factor associated with VUR, and it is a pre-requisite for formation of further renal scarring that may cause later problems, such as hypertension, chronic renal failure and, in most cases, end-stage renal disease. UTI, along with other etiologic factors including VUR, is important in the pathogenesis of scarring [2].

Angiotensin II Type 1 Receptor (AT1R) is the primary pathogenic effector for angiotensin II, and it is a member of the G-protein coupled receptor super family expressed in most tissues, where receptor activation leads to vasoconstriction, water retention and vascular smooth muscle cell proliferation and hypertrophy [3,4]. AT1R signaling is well known for causing tissue damage, such as cardiovascular system, kidneys and retina [5]. AT1R A1166C gene polymorphism, an important mutation of AT1R, might be implicated in the etiology of renal scarring susceptibility and had been investigated in numerous epidemiologic studies. However, the available evidence reported to date is weak, due to sparseness of data or disagreements among studies. There was no meta-analysis to explore the association of AT1R A1166C gene polymorphism with renal scarring risk. We performed this meta-analysis to investigate the relation between AT1R A1166C gene polymorphism and renal scarring susceptibility.

Materials and Methods

Search strategy

The relevant studies were screened from the search engines of PubMed, Cochrane Library and CBM-disc (China Biological Medicine Database) on March 1, 2015. The following terms in English were used in PubMed and Cochrane Library to complete the search: "Renal scarring", "Angiotensin II type 1 receptor", "AT1R", "A1166C". We also extended search spectrum to the "related articles" and the bibliographies of all retrieved studies (Figure 1).

Inclusion criteria

(1) A case–control study; (2) the outcome had to be renal scarring; (3) there had to be at least two comparison groups (renal scarring group *vs* control group).

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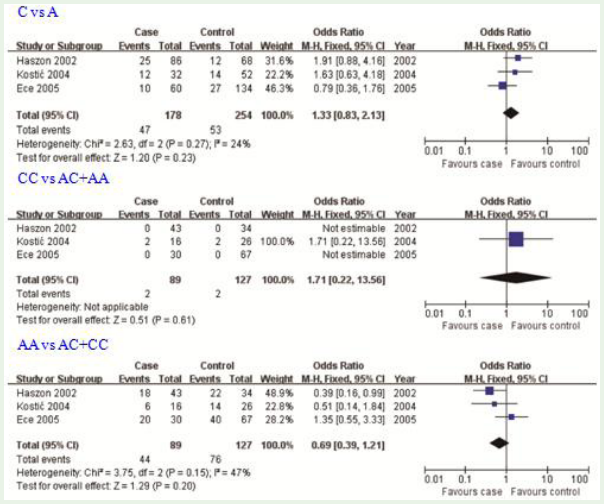

Figure 1: Relationship between AT1R A1166C gene polymorphism and risk of renal scarring (Patients with scarring vs Patients without scarring).

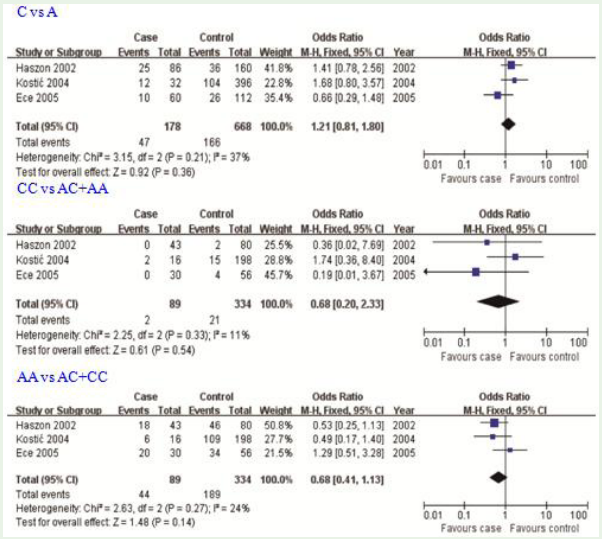

Figure 2: Relationship between AT1R A1166C gene polymorphism and risk of renal scarring (Patients with scarring vs Healthy control).

Exclusion criteria

(1) Review articles, editorials and case reports (2) Articles did not provide the detail genotype data; (3) Investigating the association of other genes with renal scarring. (4) Investigating the gene expression of AT1R to renal scarring. (5) Multiple publications of the same data from the same study group (Figure 2).

Data Extraction and Synthesis

The following information was extracted from each study independently by at least 2 investigators: first author's surname, year of publication, ethnicity of study population, and the number of cases and controls for A1166C genotype. Frequencies of C allele were calculated for case group and control group, from the corresponding genotype distribution. The results were compared and disagreements were resolved by discussion.

Statistical Analysis

Available data was entered into Cochrane Review Manager (RevMan, version 5) and analyzed. The pooled statistic was counted using the fixed effects model, but a random effects model was conducted when the *P* value of heterogeneity test was less than 0.1 [6,7]. Results were expressed with odds ratios (OR) for dichotomous data, and 95% Confidence Intervals (CI) were also calculated. $P < 0.05$ was required for the overall OR to be deemed statistically significant [8,9]. I^2 was used to test the heterogeneity between the included studies.

Results

Study characteristics

According to the inclusion and exclusion criteria, three articles [10-12] were identified for this meta-analysis of the association between AT1R A1166C gene polymorphism and renal scarring susceptibility. All the studies were conducted in Caucasian population. The data of our interest were extracted and shown in Table 1.

Association of the AT1R A1166C gene polymorphisms with renal scarring risk (patients with scarring *vs* patients without scarring): In this meta-analysis, no significant association between AT1R A1166C gene polymorphism and renal scarring susceptibility using the comparison of patients with scarring vs patients without scarring (C: OR=1.33, 95% CI: 0.83-2.13, *P*=0.23; CC: OR=1.71, 95% CI: 0.22-13.56, *P*=0.61; AA: OR=0.69, 95% CI: 0.39-1.21, *P*=0.20). (Table 2).

Table 1: Characteristics of the studies evaluating the effects of Angiotensin II Type 1 Receptor (AT1R) A1166C gene polymorphism on renal scarring risk.

First author, year	Ethnicity		Patients with scarring					Patients without scarring		
		CC	AC	AA	Total		CC	AC	AA	Total
Haszon 2002	Caucasian	0	25	18	43		0	12	22	34
Kostić 2004	Caucasian	2	8	6	16		2	10	14	26
Ece 2005	Caucasian	0	10	20	30		0	27	40	67
First author, year	**Ethnicity**		**Patients with scarring**					**Healthy control**		
		CC	AC	AA	Total		CC	AC	AA	Total
Haszon 2002	Caucasian	0	25	18	43		2	32	46	80
Kostić 2004	Caucasian	2	8	6	16		15	74	109	198
Ece 2005	Caucasian	0	10	20	30		4	18	34	56

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Table 2: Meta analysis of the association of AT1R A1166C gene polymorphism with risk of renal scarring.

Genetic	Studies	Q test	Model	OR	P
contrasts	number	P value	selected	(95%CI)	
Patients with scarring vs Patients without scarring					
C vs A	3	0.27	Fixed	1.33(0.83, 2.13)	0.23
CC vs AC+AA	3	-	Fixed	1.71(0.22, 13.56)	0.61
AA vs AC+CC	3	0.15	Fixed	0.69(0.39,1.21)	0.20
Patients with scarring vs Healthy control					
C vs A	3	0.21	Fixed	1.21(0.81, 1.80)	0.36
CC vs AC+AA	3	0.33	Fixed	0.68(0.20,2.33)	0.54
AA vs AC+CC	3	0.27	Fixed	0.68(0.41, 1.13)	0.14

Association of the AT1R A1166C gene polymorphisms with renal scarring risk (patients with scarring *vs* healthy control): In this meta-analysis, AT1R A1166C gene polymorphism was also not associated with the susceptibility of renal scarring using the comparison of patients with scarring vs healthy control (C: OR=1.21, 95%CI: 0.81-1.80, *P*=0.36; CC: OR=0.68, 95%CI: 0.20-2.33, *P*=0.54; AA: OR=0.68, 95%CI: 0.41-1.13, *P*=0.14; Table 2).

Discussion

We performed this investigation using meta-analysis method for the association of AT1R A1166C gene polymorphism with renal scarring susceptibility, three studies were recruited. Meta-analysis of multiple studies has a role in offering an association with such potentials and the results from meta-analysis might be more convincing compared with those from separate studies. In our meta-analysis, we found the difference of distribution of C allele, CC homozygous and AA genotype between patients with renal scarring group and patients without renal scarring group was not statistically different. Furthermore, we also found that the distribution difference of C allele, CC homozygous and AA genotype between patients with renal scarring group and healthy control group was also not statistically different. It seemed that AT1R A1166C gene polymorphism was not associated with the susceptibility of renal scarring.

In previous, there was no any meta-analysis to explore this relationship. Our meta-analysis reported firstly and included three studies for this meta-analysis. However, the number of included studies in our meta-analysis was small, and better designed studies should be performed in the further.

In our study, we might draw the conclusion that AT1R A1166C gene polymorphism was not associated with the susceptibility of renal scarring. However, these findings should be regarded cautiously because many other ingredients, such as heterogeneity of enrolled cases, limited statistical power, variable study designs and different interventions, were closely related to affect the results.

In conclusion, the results in our study supported that AT1R A1166C gene polymorphism was not associated with the susceptibility of renal scarring. However, more case-control association investigations on larger, stratified populations are required to further clarify the role of AT1R A1166C gene polymorphism in renal scarring susceptibility.

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