Original Article
CD14 gene-159C/T polymorphism and coronary artery disease: a meta-analysis involving 4467 subjects

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Abstract: Background: The cluster of differentiation antigen 14 (CD14) gene-159C/T polymorphism has been implied to be associated with coronary artery disease (CAD) susceptibility. However, the separate studies results are still conflicting between each other. Objective and methods: To investigate the relationship between *CD14* gene-159C/T polymorphism and CAD, a meta-analysis including 4467 subjects from 7 individual studies was performed. The random or fixed effect models were used to evaluate the pooled odds ratios (ORs) and their corresponding 95% confidence intervals. Results: There was a significant association between *CD14* gene -159C/T polymorphism and CAD in the whole population under allelic (OR: 1.280, 95% CI: 1.000-1.630, *P*=0.05), recessive (OR: 1.760, 95% CI: 1.120-2.750, *P*=0.01), homozygous (OR: 1.693, 95% CI: 1.008-2.843, *P*=0.046), and additive genetic models (OR: 1.278, 95% CI: 1.000-1.633, *P*=0.050). No significant association was found between them under dominant (OR: 0.580, 95% CI: 0.310-1.110, *P*=0.10) and heterozygous genetic models (OR: 1.334, 95% CI: 0.870-2.045, *P*=0.186). In the subgroup analysis, a significant association was detected in Chinese population (*P*<0.05), while there was no significant association in the Caucasian subgroup (*P*>0.05). Conclusions: *CD14* gene -159C/T polymorphism was significantly associated with CAD susceptibility, particularly in the Chinese population. The person with T allele of *CD14* gene -159C/T polymorphism might predispose to CAD. There was no distinct association between them in the Caucasian subgroup.

Keywords: *CD14*, -159C/T, polymorphism, coronary artery disease

Introduction

Coronary artery disease (CAD) is one of the main diseases threatening human health and contributing to human death. Atherosclerosis is the pathological foundation of CAD. Many hazards as inflammation, infection, and autoimmunity could lead to CAD. Hence, CAD is considered as a kind of inflammation disease. The inflammation reaction in the coronary artery atherosclerosis plaque leads to the intima damage, plaque rupture, and acute cardiac ischemia. The clinical practice has also shown that some inflammation markers could serve as the cardiovascular events predisposing predictors. Meanwhile, CAD has the heredity tendency and the heredity variation of the inflammation system might lead to the increased CAD risk [1]. The cluster of differentiation antigen 14 (CD14) is a multiple function inflammation cytokine which is mainly produced by mature mononuclear macrophage. CD14 plays a key role in the process of inflammation, immunity and atherosclerosis which is closely associated with cardiovascular disease [2].

CD14 acts as the receptor of lipopolysaccharide (LPS) which is the cytoderm ingredient of gram-negative bacteria. CD14 is one member of the glycoprotein family of the cell surface. With the help of LPS binding protein, CD14 could combine with LPS which lead to the cell activation, the pro-inflammatory cytokines release and the coagulator synthesis. The atherosclerosis formation was thus accelerated [3]. *CD14* gene, located in 5q23-31, spans 3.9 kb which encodes the 55 KD glycoprotein with 375 amino acids. In *CD14* gene -159C/T polymorphism, the -159th base cytosine (C) in the upstream of *CD14* gene promoter region is replaced by thymine (T). The position -159 is close to a DNA element binding to nuclear protein which is involved in promoter activation. Hence, *CD14* gene -159C/T polymorphism mi-

CD14 gene -159C/T polymorphism and CAD

Table 1. Characteristics of the investigated studies of the association between the *CD14* gene -159C/T polymorphism and coronary artery disease (CAD)

Author	Year	Country	Ethnicity	CAD			Control			Matching criteria	Sample size (CAD/control)
				CC	CT	TT	CC	CT	TT		
Li Y [6]	2005	China	Asian	24	75	63	54	89	53	Age, sex, ethnicity	162/196
Chen F [12]	2006	China	Asian	10	52	46	23	61	34	Age, sex, BMI, ethnicity	108/118
Wei YS [13]	2006	China	Asian	47	128	71	39	139	80	Age, sex, ethnicity	246/258
Li L [14]	2007	China	Asian	29	95	69	47	124	54	Age, sex, ethnicity	193/225
Liu XQ [7]	2010	China	Asian	10	65	25	103	133	44	Age, sex, ethnicity	100/280
Koch W [5]	2002	German	Caucasian	505	888	398	88	177	75	Age, sex, ethnicity	1791/340
Haberbosch W [15]	2009	German	Caucasian	65	92	41	71	131	50	Age, sex, ethnicity	198/252

Abbreviations: CAD, coronary artery disease; BMI, body mass index; Polymerase chain reaction-restriction fragment length polymorphism genotyping method and Case-control study design were adopted in the above studies.

ght influence the transcription and expression level of *CD14* gene. In 1999, Baldini et al reported that in an Arizona population, the TT homozygotes of *CD14* gene -159C/T polymorphism had significantly higher soluble CD14 (sCD14) levels than did both CC and CT genotypes carriers (P=0.01). They concluded that *CD14* gene -159C/T polymorphism played a significant role in regulating circulating sCD14 levels [4].

Although many researches on the relationship between *CD14* gene-159C/T polymorphism and CAD have been conducted so far, the individual studies results were still inconsistent. In 2002, Koch et al found no significant difference between *CD14* gene -159C/T genotype distributions of control and CAD patients and they concluded that the *CD14* gene -159C/T polymorphism was not related to CAD in an American population [5]. However, in 2005, Li et al found that the T allele of the *CD14* gene -159C/T polymorphism might be a risk factor for CAD in a Chinese population [6]. Analogously, in 2010, Liu et al also obtained the same conclusion in another Chinese population [7].

In the present study, a meta-analysis involving 2798 CAD patients and 1669 controls from 7 separate studies was performed to estimate the relationship of *CD14* gene -159C/T polymorphism and CAD.

Materials and methods

Publication search and inclusion criteria

The electronic databases including China National Knowledge Infrastructure, China Bio-

logical Medicine Database, Embase, PubMed, and Web of Science were retrieved by using the terms as *"CD14"*, *"-159C/T"*, "polymorphism" and "coronary artery disease". The last research was updated on April 22, 2015 with the publication years ranging from 2005 to 2010.

The included studies should follow such major criteria as the follows: a) Assessment of the association of *CD14* gene -159C/T polymorphism and CAD. b) CAD was diagnosed as at least one coronary artery stenosis was no less than 50% by coronary angiography. The control group was the healthy population in the corresponding period without coronary artery stenosis through coronary angiography. c) The studies should be case-control or cohort studies published officially. d) The genotype member of the control group in the individual studies should follow the Hardy-Weinberg equilibrium (HWE).

Data extraction

The studies data was extracted based on a standard protocol. Three investigators performed the meta-analysis; two of whom searched out the individual studies duplicately, and the third investigator served as the arbitrator to settle the disagreement between the two investigators and reach an agreement finally. The present meta-analysis excluded the studies that did not meet the major selection criteria, that were repeated publications, or that supplied inadequate data. If similar data appeared in different papers by the same authors, the data was only used once. The following items as publication year, the first author's name, ethnicity, country, matching cri-

Table 2. Summary of meta-analysis of association between the *CD14* gene -159C/T polymorphism and coronary artery disease (CAD)

Genetic model	Pooled OR (95% CI)	Z value	*P* value	Study number	CAD size	Control size	$P_{\text{heterogeneity } (I^2\%)}$
Allelic genetic model	1.280 (1.000-1.630)	1.96	0.05*	7	2798	1669	<0.00001* (83.2%)
Chinese subgroup	1.470 (1.080-1.990)	2.45	0.01*	5	809	1077	0.0004 (80.6%)
Caucasian subgroup	0.950 (0.830-1.090)	0.74	0.46	2	1989	592	0.83 (0%)
Recessive genetic model	1.760 (1.120-2.750)	2.46	0.01*	7	2798	1669	<0.00001* (84.2%)
Chinese subgroup	2.220 (1.240-4.000)	2.67	0.008*	5	809	1077	<0.0001* (83.6%)
Caucasian subgroup	1.030 (0.800-1.320)	0.23	0.82	2	1989	592	0.84 (0%)
Dominant genetic model	0.580 (0.310-1.110)	1.65	0.10	7	2798	1669	<0.00001* (91.5%)
Chinese subgroup	0.400 (0.170-0.970)	2.03	0.04*	5	809	1077	<0.00001* (90.8%)
Caucasian subgroup	1.280 (1.000-1.620)	2.00	0.046*	2	1989	592	0.45 (0%)
Homozygous genetic model	1.693 (1.008-2.843)	1.99	0.046*	7	2798	1669	<0.00001* (82.9%)
Chinese subgroup	2.276 (1.138-4.552)	2.33	0.020*	5	809	1077	<0.00001* (81.9%)
Caucasian subgroup	0.916 (0.690-1.217)	0.60	0.546	2	1989	592	0.921 (0%)
Heterozygous genetic model	1.334 (0.870-2.045)	1.32	0.186	7	2798	1669	<0.00001* (80.3%)
Chinese subgroup	1.717 (0.936-3.152)	1.75	0.081	5	809	1077	<0.00001* (79.9%)
Caucasian subgroup	0.841 (0.666-1.062)	1.45	0.146	2	1989	592	0.616 (0%)
Additive genetic model	1.278 (1.000-1.633)	1.96	0.050*	7	2798	1669	<0.00001* (83.2%)
Chinese subgroup	1.466 (1.079-1.991)	2.45	0.014	5	809	1077	<0.00001* (80.6%)
Caucasian subgroup	0.949 (0.825-1.091)	0.74	0.462	2	1989	592	0.833 (0%)

*$P \leq 0.05$. Abbreviations: CAD, coronary artery disease; CI, confidence interval; OR, odds ratio; CAD size, the total number of CAD cases; control size, the total number of control group; Allelic genetic model, T allele distribution frequency; recessive genetic model, TT vs. CC+CT; Dominant genetic model, CC vs. TT+CT; Homozygous genetic mode, TT vs. CC; Heterozygous genetic model, CT vs. CC; Additive genetic model, total T allele vs. total C allele.

teria, number of genotypes, and total number of cases and controls should be displayed in the data.

Statistical analyses

There were six genetic models as the allelic (T allele distribution frequency), recessive (TT vs. CC+CT), dominant (CC vs. TT+CT), homozygous (TT vs. CC), heterozygous (CT vs. CC), and additive (T vs. C) genetic models in the current meta-analysis. The association of *CD14* gene -159C/T polymorphism and CAD was compared by the odds ratios (ORs) and their corresponding 95% confidence intervals (CIs). The Chi-square-based Q-tests was adopted to calculate the heterogeneity among the studies with significance set at $P < 0.05$ level [8]. If there was heterogeneity among the individual studies, the random-effect model (DerSimonian and Laird method) would be adopted [9]. Or else, the fixed-effect model was used (the Mantel-Haenszel method) [10]. The pooled OR was estimated by Z test and significance was set at $P < 0.05$ level.

Fisher's exact test was used to evaluate the HWE and significance was set at $P < 0.05$ level. The funnel plot was adopted to assess the potential publication bias. Egger's linear regression test on the natural logarithm scale of the OR was used to evaluate the funnel plot symmetry with significance set at $P < 0.05$ level [11]. The Stata 12.0 software was used to perform the statistical analyses (StataCorp, College Station, TX, USA).

Results

Studies and populations

Fifteen manuscripts were searched out by the retrieval process, among which seven papers followed the inclusion criteria. Among the eight excluded studies, five papers were reviews, and three manuscripts were not involved with *CD14* gene -159C/T polymorphism or CAD. No study was rejected for deviating from the HWE. All of information was extracted from 2798 CAD cases and 1669 controls (**Table 1**) [5-7, 12-15]. Two countries were involved in the current

CD14 gene -159C/T polymorphism and CAD

Study or Subgroup	Coronary artery disease Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI
1.1.1 Chinese population						
Wei YS 2006	270	492	299	516	14.9%	0.88 [0.69, 1.13]
Liu XQ 2010	115	200	221	560	13.4%	2.08 [1.50, 2.88]
Li Y 2005	201	324	195	392	14.0%	1.65 [1.22, 2.23]
Li L 2007	233	386	232	450	14.4%	1.43 [1.09, 1.88]
Chen F 2006	144	216	129	236	12.3%	1.66 [1.13, 2.43]
Subtotal (95% CI)		**1618**		**2154**	**69.0%**	**1.47 [1.08, 1.99]**
Total events	963		1076			
Heterogeneity: Tau² = 0.10; Chi² = 20.65, df = 4 (P = 0.0004); I² = 81%						
Test for overall effect: Z = 2.45 (P = 0.01)						
1.1.2 Caucasian population						
Koch W 2002	1684	3582	327	680	16.3%	0.96 [0.81, 1.13]
Haberbosch W 2009	174	396	231	504	14.6%	0.93 [0.71, 1.21]
Subtotal (95% CI)		**3978**		**1184**	**31.0%**	**0.95 [0.83, 1.09]**
Total events	1858		558			
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		**5596**		**3338**	**100.0%**	**1.28 [1.00, 1.63]**
Total events	2821		1634			
Heterogeneity: Tau² = 0.09; Chi² = 35.69, df = 6 (P < 0.00001); I² = 83%						
Test for overall effect: Z = 1.96 (P = 0.05)						
Test for subgroup differences: Chi² = 6.41, df = 1 (P = 0.01), I² = 84.4%						

Odds Ratio IV, Random, 95% CI

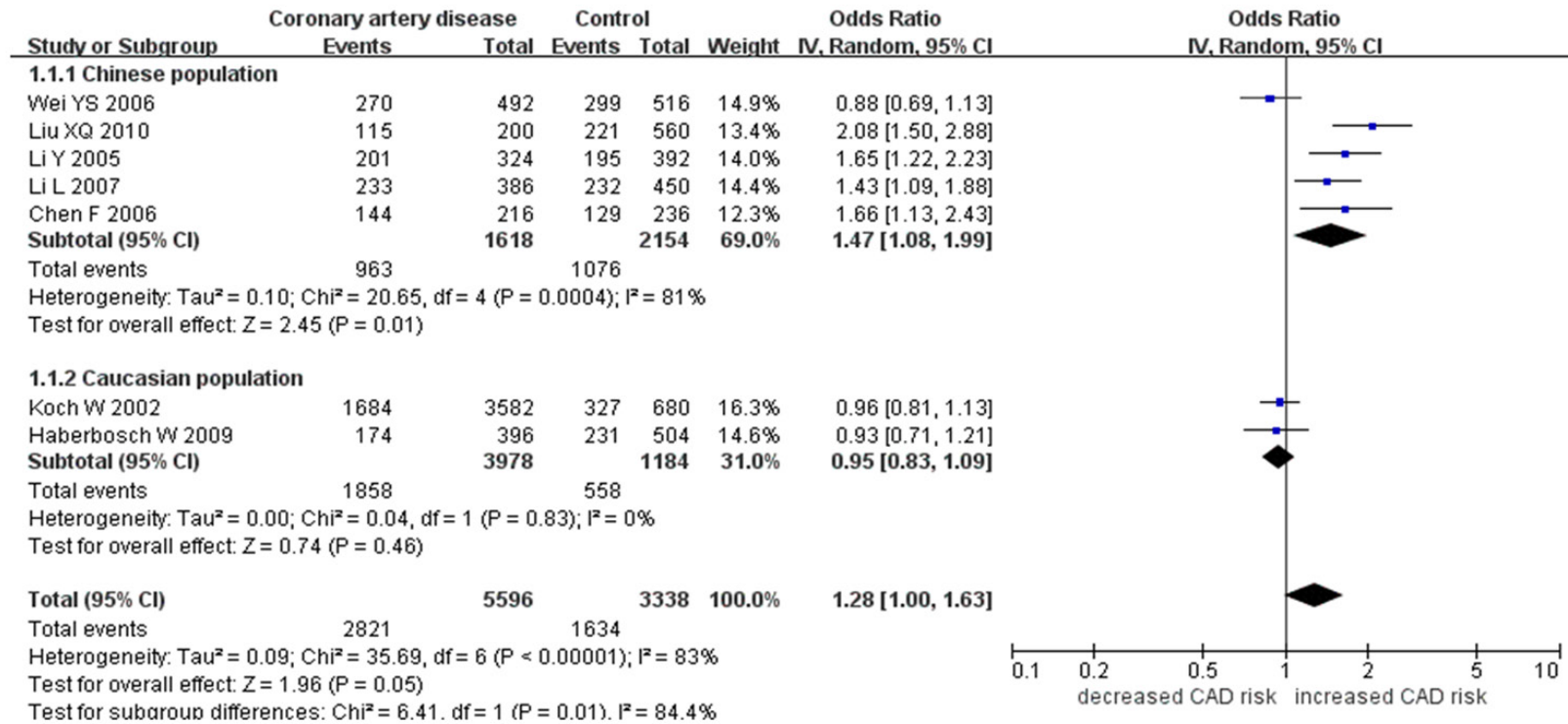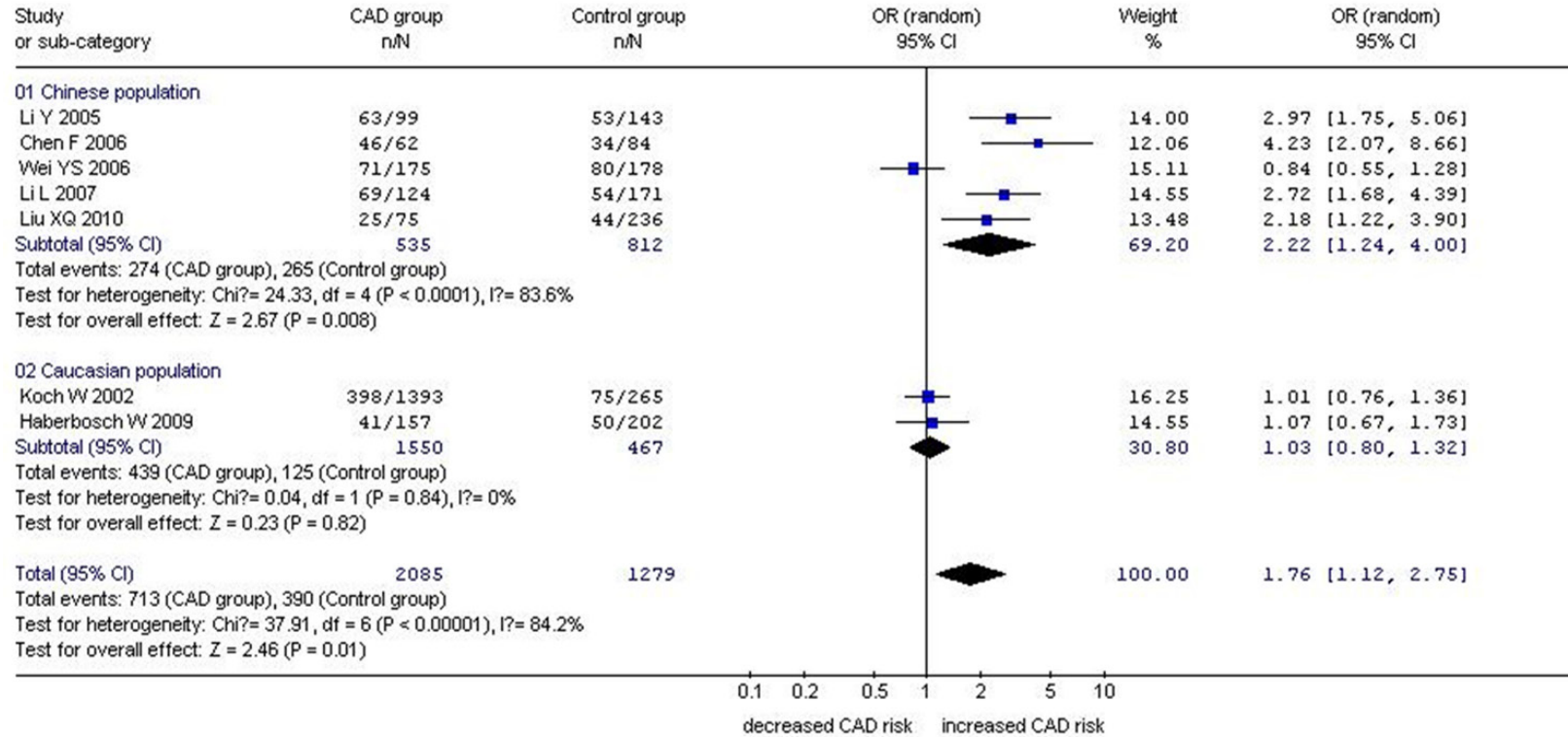0.1 0.2 0.5 1 2 5 10
decreased CAD risk   increased CAD risk

Figure 1. Forest plot of CAD associated with *CD14* gene -159C/T polymorphism under an allelic genetic model (distribution of T allelic frequency of *CD14* gene -159C/T polymorphism).
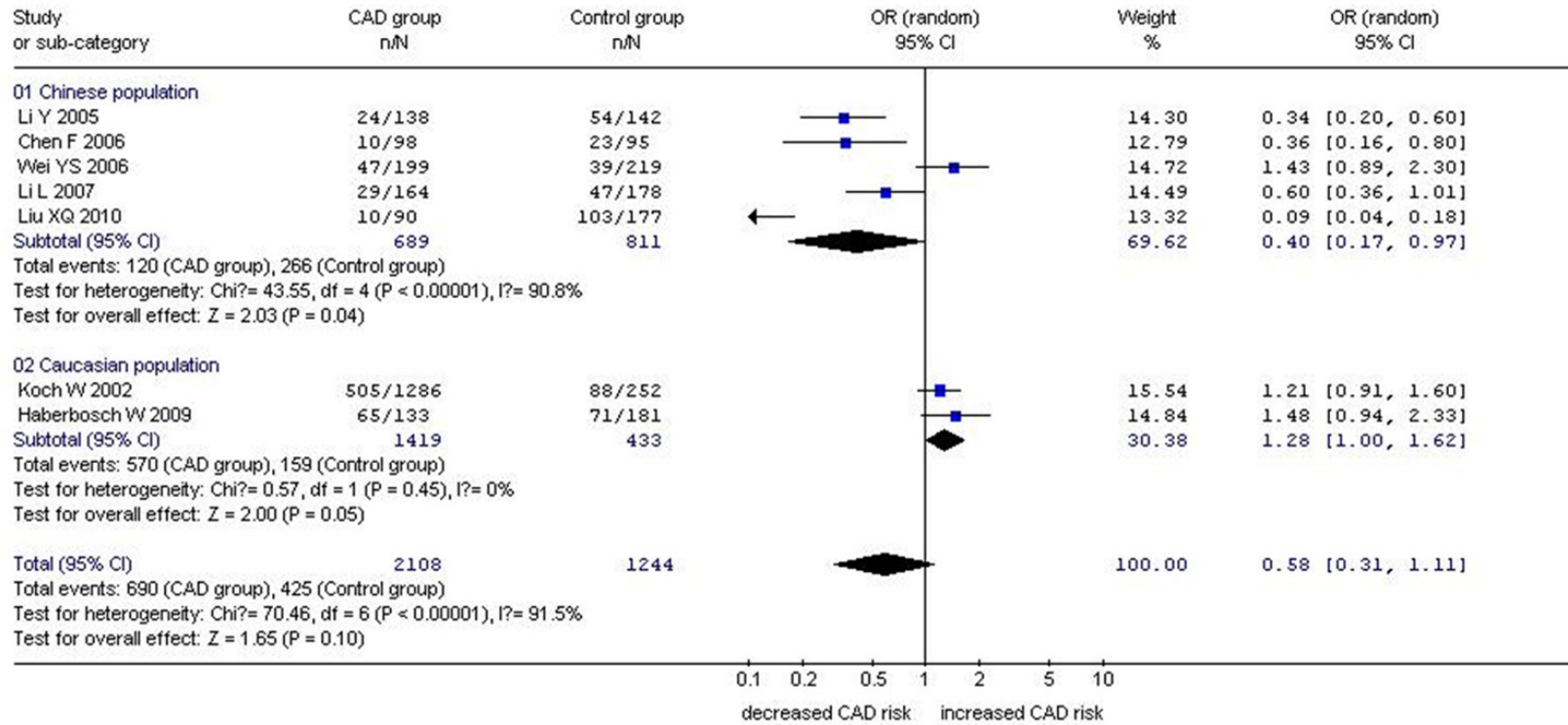
CD14 gene -159C/T polymorphism and CAD

Study or sub-category	CAD group n/N	Control group n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
01 Chinese population					
Li Y 2005	63/99	53/143		14.00	2.97 [1.75, 5.06]
Chen F 2006	46/62	34/84		12.06	4.23 [2.07, 8.66]
Wei YS 2006	71/175	80/178		15.11	0.84 [0.55, 1.28]
Li L 2007	69/124	54/171		14.55	2.72 [1.68, 4.39]
Liu XQ 2010	25/75	44/236		13.48	2.18 [1.22, 3.90]
Subtotal (95% CI)	535	812		69.20	2.22 [1.24, 4.00]

Total events: 274 (CAD group), 265 (Control group)
Test for heterogeneity: Chi²= 24.33, df = 4 (P < 0.0001), I²= 83.6%
Test for overall effect: Z = 2.67 (P = 0.008)

02 Caucasian population					
Koch W 2002	398/1393	75/265		16.25	1.01 [0.76, 1.36]
Haberbosch W 2009	41/157	50/202		14.55	1.07 [0.67, 1.73]
Subtotal (95% CI)	1550	467		30.80	1.03 [0.80, 1.32]

Total events: 439 (CAD group), 125 (Control group)
Test for heterogeneity: Chi²= 0.04, df = 1 (P = 0.84), I²= 0%
Test for overall effect: Z = 0.23 (P = 0.82)

Total (95% CI)	2085	1279		100.00	1.76 [1.12, 2.75]

Total events: 713 (CAD group), 390 (Control group)
Test for heterogeneity: Chi²= 37.91, df = 6 (P < 0.00001), I²= 84.2%
Test for overall effect: Z = 2.46 (P = 0.01)

0.1 0.2 0.5 1 2 5 10
decreased CAD risk   increased CAD risk

Figure 2. Forest plot of CAD associated with *CD14* gene -159C/T polymorphism under a recessive genetic model (TT vs. CC+CT).

CD14 gene -159C/T polymorphism and CAD

Review: CD14 gene -159C/T polymorphism and coronary artery disease
Comparison: 01 CAD group versus control group
Outcome: 03 CC vs. TT+CT

Study or sub-category	CAD group n/N	Control group n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
01 Chinese population					
Li Y 2005	24/138	54/142		14.30	0.34 [0.20, 0.60]
Chen F 2006	10/98	23/95		12.79	0.36 [0.16, 0.80]
Wei YS 2006	47/199	39/219		14.72	1.43 [0.89, 2.30]
Li L 2007	29/164	47/178		14.49	0.60 [0.36, 1.01]
Liu XQ 2010	10/90	103/177		13.32	0.09 [0.04, 0.18]
Subtotal (95% CI)	689	811		69.62	0.40 [0.17, 0.97]
Total events: 120 (CAD group), 266 (Control group)					
Test for heterogeneity: Chi²= 43.55, df = 4 (P < 0.00001), I²= 90.8%					
Test for overall effect: Z = 2.03 (P = 0.04)					
02 Caucasian population					
Koch W 2002	505/1286	88/252		15.54	1.21 [0.91, 1.60]
Haberbosch W 2009	65/133	71/181		14.84	1.48 [0.94, 2.33]
Subtotal (95% CI)	1419	433		30.38	1.28 [1.00, 1.62]
Total events: 570 (CAD group), 159 (Control group)					
Test for heterogeneity: Chi²= 0.57, df = 1 (P = 0.45), I²= 0%					
Test for overall effect: Z = 2.00 (P = 0.05)					
Total (95% CI)	2108	1244		100.00	0.58 [0.31, 1.11]
Total events: 690 (CAD group), 425 (Control group)					
Test for heterogeneity: Chi²= 70.46, df = 6 (P < 0.00001), I²= 91.5%					
Test for overall effect: Z = 1.65 (P = 0.10)					

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      0.1   0.2   0.5   1    2    5   10
      decreased CAD risk    increased CAD risk
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Figure 3. Forest plot of CAD associated with *CD14* gene -159C/T polymorphism under a dominant genetic model (CC vs. TT+CT).
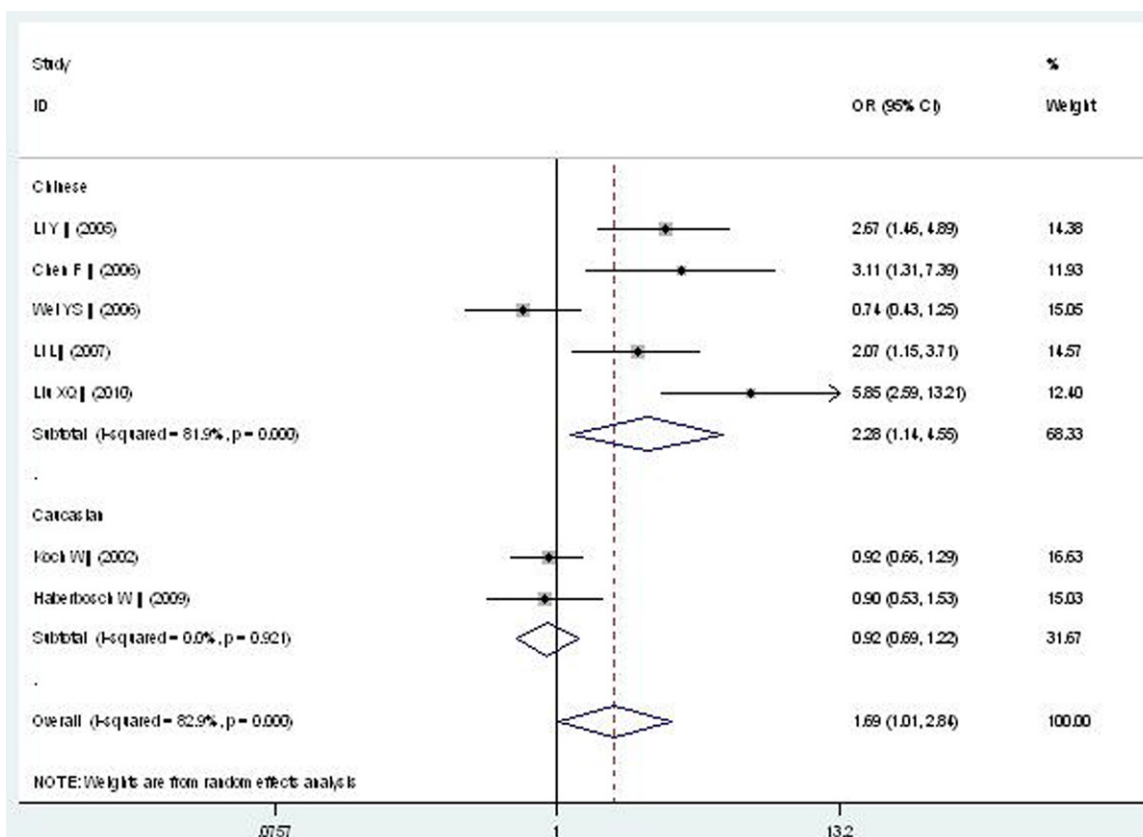
Figure 4. Forest plot of CAD associated with *CD14* gene -159C/T polymorphism under a homozygous genetic model (TT vs. CC).

meta-analysis as China and German. These populations belong to Chinese and Caucasian subgroups respectively. The Chinese subgroup includes 5 individual studies and the Caucasian subgroup consists of 2 individual studies.

Pooled analyses

There was a significant association between *CD14* gene -159C/T polymorphism and CAD in the whole population under allelic (OR: 1.280, 95% CI: 1.000-1.630, *P*=0.05), recessive (OR: 1.760, 95% CI: 1.120-2.750, *P*=0.01), homozygous (OR: 1.693, 95% CI: 1.008-2.843, *P*=0.046), and additive genetic models (OR: 1.278, 95% CI: 1.000-1.633, *P*=0.050). No significant association was found between them under dominant (OR: 0.580, 95% CI: 0.310-1.110, *P*=0.10) or heterozygous genetic model (OR: 1.334, 95% CI: 0.870-2.045, *P*=0.186).

In the subgroup analysis, a significant association between *CD14* gene -159C/T polymor-

phism and CAD was detected in the Chinese population under allelic (OR: 1.470, 95% CI: 1.080-1.990, *P*=0.01), recessive (OR: 2.220, 95% CI: 1.240-4.000, *P*=0.008), dominant (OR: 0.400, 95% CI: 0.170-0.970, *P*=0.04), homozygous (OR: 2.276, 95% CI: 1.138-4.552, *P*= 0.020), and additive genetic models (OR: 1.466, 95% CI: 1.079-1.991, *P*=0.014). However, there was no significant association between *CD14* gene -159C/T polymorphism and CAD under heterozygous genetic model (OR: 1.717, 95% CI: 0.936-3.152, *P*=0.081).

In the Caucasian subgroup, no significant association was found between *CD14* gene -159C/T polymorphism and CAD under allelic (OR: 0.950, 95% CI: 0.830-1.090, *P*=0.46), recessive (OR: 1.030, 95% CI: 0.800-1.320, *P*=0.230), homozygous (OR: 0.916, 95% CI: 0.690-1.217, *P*=0.600), heterozygous (OR: 0.841, 95% CI: 0.666-1.062, *P*=0.146), and additive genetic models (OR: 0.949, 95% CI: 0.825-1.091, *P*=0.462). However, a significant association was only detected under a domi-
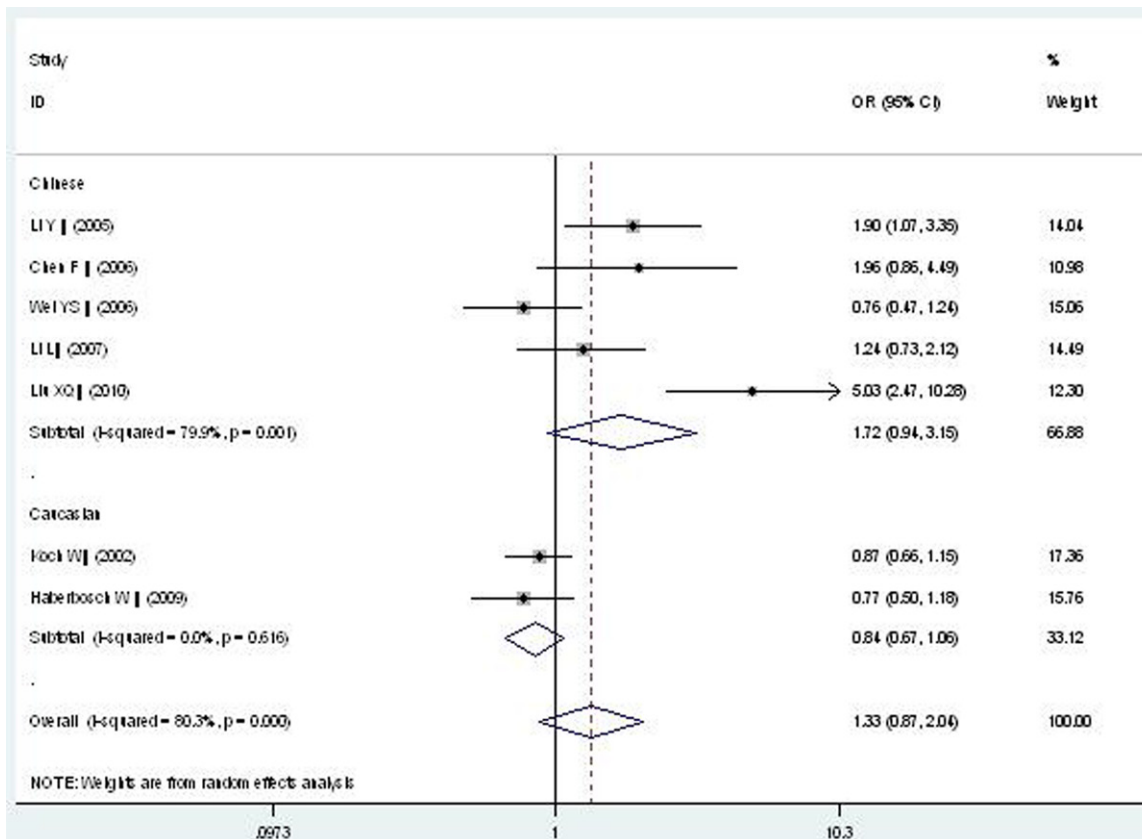
Figure 5. Forest plot of CAD associated with *CD14* gene -159C/T polymorphism under a heterozygous genetic model (CT vs. CC).

nant genetic model (OR: 1.280, 95% CI: 1.000-1.620, *P*=0.046) (**Table 2**; **Figures 1-6**).

There was significant heterogeneity in the whole population under all of the genetic models. In the subgroup analysis stratified by ethnicity, there was no heterogeneity in the Caucasian subgroup under all of the genetic models ($P_{heterogeneity}$>0.05, I^2=0%). However, the heterogeneity was reduced a little but still significant in the Chinese population under all of the genetic models ($P_{heterogeneity}$<0.0001, I^2: 79.9%-90.8%).

Bias diagnostics

The funnel plot and Egger's test were adopted to evaluate the publication bias among the individual studies. No visual publication bias was found in the Begg's funnel plot under the additive genetic model (**Figure 7**). In addition, no significant difference in the Egger's test yet, which indicated that publication bias did not exist in the present meta-analysis by using additive genetic model (T=2.48, P=0.056).

Discussion

In the present meta-analysis, a significant association was found in the whole population between *CD14* gene -159C/T polymorphism and CAD under allelic (OR: 1.28), recessive (OR: 1.76), homozygous (OR: 1.693), and additive genetic models (OR: 1.278). No significant association was found under a dominant (OR: 0.58) or heterozygous genetic model (OR: 1.334). In the subgroup analysis stratified by ethnicity, there was a more significant association in Asian subgroup than that in the whole population under allelic (OR: 1.47), recessive (OR: 2.22), dominant (OR: 0.40), homozygous (OR: 2.276), and additive genetic models (OR: 1.466). However, no significant association was detected in the Caucasian subgroup (*P*>0.05). In conclusion, it was indicated that the carriers with T allele of *CD14* gene -159C/T polymorphism might predispose to CAD, except in the Caucasian population. The negative conclusion in the Caucasian subgroup was possibly not only associated with the different race, but also with the few manuscripts, because
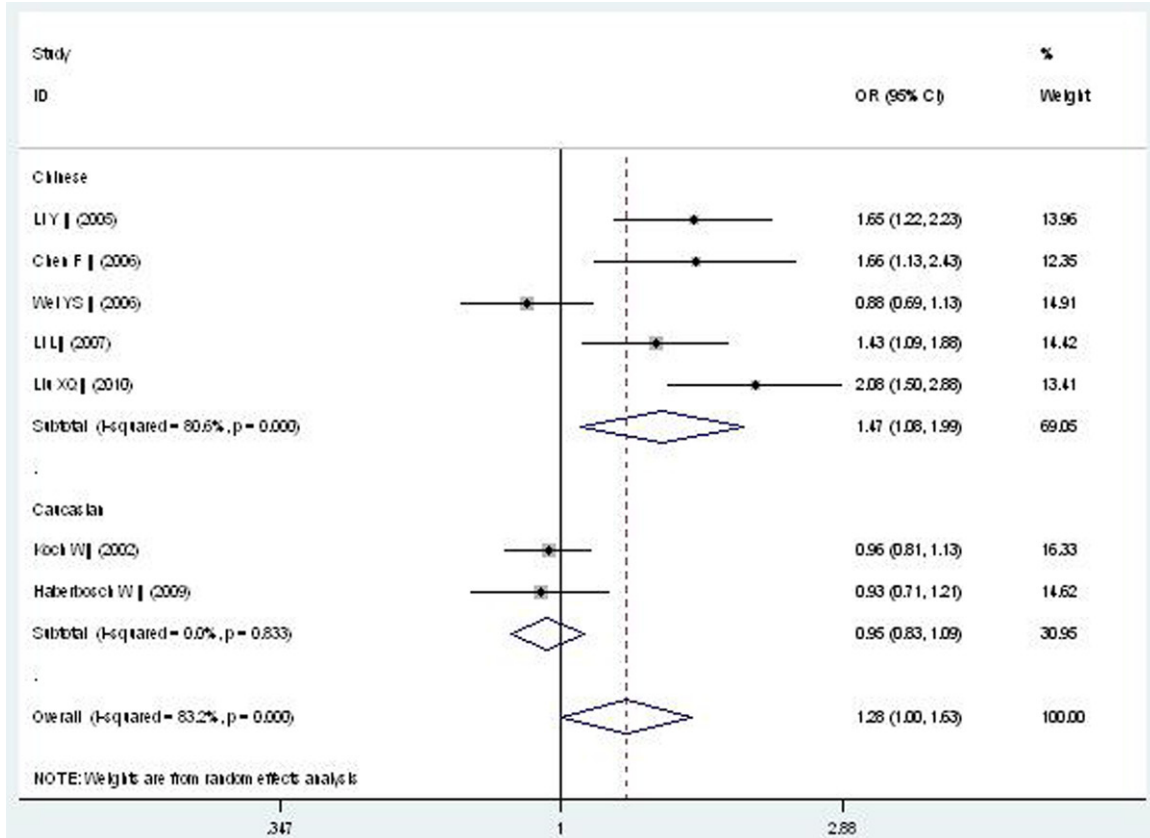
Figure 6. Forest plot of CAD associated with *CD14* gene -159C/T polymorphism under an additive genetic model (T vs. C).
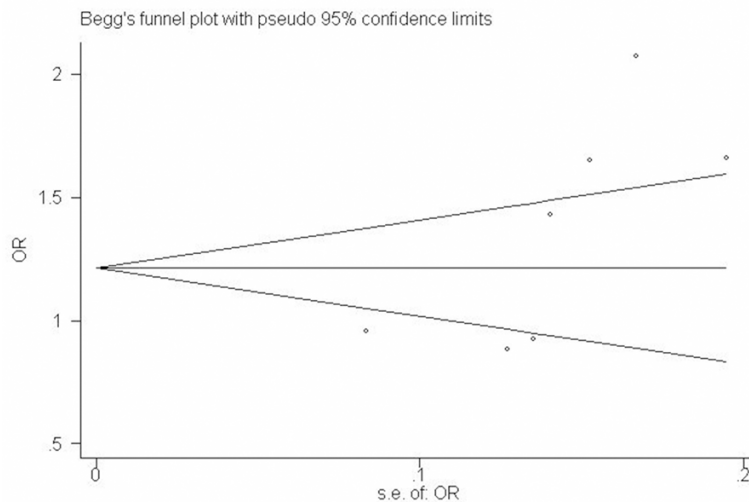
Figure 7. Begg's funnel plot for studies of the association of CAD associated with *CD14* gene -159C/T polymorphism under an additive genetic model (T vs. C). The horizontal and vertical axis correspond to the OR and confidence limits. OR: odds ratio; SE: standard error.

be further confirmed by more researches in the Caucasian subgroup in the future.

There was significant heterogeneity in the whole population under all of the genetic models. In the subgroup analysis stratified by ethnicity, the heterogeneity did not exist any longer in the Caucasian subgroup (P>0.05). However, the heterogeneity still existed in the Chinese population (P< 0.05).

CD14 receptor is the membrane glycoprotein with 365 amino acids. As the major LPS receptor, CD14 has the function of identifying initial immune system molecules. CD14 participates in the monocytes activation, the interaction of leukocyte and endothelial cells (ECs), apoptosis regulation of

only two researches were included in this subgroup. Hence, the current conclusion needs to

monocytes and ECs. Thus, CD14 plays a key role in the process of atherosclerosis and complications. CD14 could specially combine with LPS, then transfer the activation signal to the downstream pathway through the Toll like receptor 4 and bone marrow differentiation protein-2. By this way, the monocytes-macrophage system was launched and many pro-inflammation cytokines as tumor necrosisα, interleukin-1, interleukin-6 and so on were released. These cytokines have multi-functions in the process of mediating initial immune response and inflammation reaction which cause the histocyte damage, disturbance of immunologic function and vascular smooth muscle cells proliferation [16-18]. In addition, the combination of CD14 and LPS can induce the transcription of endothelial leukocyte adhesion molecule-1 and vascular cell adhesion molecule-1 which prompt the cell adhesion and signal transmission. Additionally, the CD14 and LPS could induce macrophagocyte and ECs to release the tissue factor with procoagulant activity and protease, thus facilitate the thrombus formation. Hence, CD14 is the key molecule in the systemic inflammatory response and atherosclerosis [19]. T allele of *CD14* gene -159C/T polymorphism can increase the CD14 level and prompt CAD progress by influencing *CD14* gene transcription and expression [20].

There was no internationally relevant meta-analysis on the association of CAD with *CD14* gene -159C/T polymorphism so far. However, there were some limitations in the current meta-analysis. The present meta-analysis still lack large-scale or prospective studies on the association of *CD14* gene -159C/T polymorphism and CAD. The death cases were not recruited in each individual study which might lead to the research results power insufficiency and reduce the current meta-analysis demonstration intensity. The internal CD14 level was influenced not only by the *CD14* gene -159C/T polymorphism, but also by other polymorphism as -260C/T gene polymorphism, and other environmental factors as hypertension, hyperlipemia, and diabetes mellitus [21]. CAD is a multiple gene inheritance disease and many micro-effect genes inevitably generate a general effect. Other genes polymorphisms as *intercellular adhesion molecule-1* gene E469K polymorphism, *methylenetetrahydrofolate re-*

ductase gene C677T polymorphism, *plasminogen activator inhibitor-1* gene 4G/5G polymorphism, *ATP-binding cassette transporter A1* gene R219K polymorphism, *apo A5* gene -1131T/C, FgB -455G/A, -148C/T, and *CETP* gene TaqIB polymorphisms might confer the risk to CAD [22-25].

Finally, *CD14* gene -159C/T polymorphism was significantly associated with CAD susceptibility, particularly in the Chinese population. The persons with the T allele of *CD14* gene-159C/T polymorphism might predispose to CAD. This conclusion might help us formulate a new CAD individual therapy strategy. Considering the above limitations, more studies on the association of *CD14* gene-159C/T polymorphism and CAD needed to be performed to further verify the ultimateness in the future.

Disclosure of conflict of interest

None.

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