

Original Article

Meta analysis of the correlation between Helicobacter pylori infection and coronary heart disease

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Abstract: Objective: To investigate the relationship between Helicobacter pylori infection and coronary heart disease. Methods: Pubmed, Medline and Embase databases were retrieved by a computer. Studies published in English from January 2000 to June 2015 that reported on association between coronary heart disease and infection of helicobacter pylori were selected. Meta analysis was used to evaluate the combined OR value and the 95% confidence interval (95% CI) after merging. Results: There were 18 studies included in this Meta analysis, the combined OR was 1.64 and 95% CI was 1.22-2.23 that calculated by a random effect model. 12 studies on association between coronary heart disease and Helicobacter pylori infection were collected. The Meta analysis showed that there was a certain relationship between the coronary heart disease and Helicobacter pylori infection, and the combined OR was 1.96, 95% CI was 1.28-3.02. Conclusion: Infection with helicobacter pylori was associated with coronary heart disease. Therefore, health education should be strengthened to reduce the chance of helicobacter pylori infection and prevent the occurrence of coronary heart disease.

Keywords: Coronary artery disease, myocardial infarction, Helicobacter pylori, infection, Meta analysis

Introduction

Helicobacter pylori is a gram-negative, micro aerobic bacteria, which mainly exists in pylorus of the stomach. Most of the population in the world infected with Helicobacter pylori [1]. Previous studies have indicated that Helicobacter pylori can cause peptic ulcer disease, chronic gastritis and gastric malignant cancer etc. Other studies have reported that Helicobacter pylori infection may increase the incidence of other diseases besides gastrointestinal diseases, such as chronic obstructive pulmonary disease, diabetes mellitus and others [2, 3].

Coronary heart disease is a common cardiovascular disease, whose occurrence of myocardial infarction and heart failure is one of the leading causes of death in the world. It is known that coronary atherosclerosis can cause coronary heart disease and myocardial infarction. In the formation and development of atherosclerotic

plaque, the plaque might be instable and ruptured that easily cause myocardial infarction. Moreover, there is a study shows that chronic bacterial infection and inflammation is one of the main factors in the development of atherosclerotic plaque [4].

Currently, many studies have revealed the effects of Helicobacter pylori in the occurrence of myocardial infarction, but the results are controversial. Based on these studies, we performed a meta-analysis to elucidate the relationship between Helicobacter pylori and the risk factors of the occurrence of myocardial infarction on coronary heart disease.

Materials and methods

Bibliography retrieval

We used Helicobacter Pylori, Coronary Heart Disease, Myocardial infarction, Atherosclerosis as the subject words to search relevant studies in Pubmed, Medline and Embase, and selected

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Table 1. 18 included literatures on the relationship between Helicobacter pylori infection and myocardial infarction

First author	Year and country	Age (case group)	Sample size MI / non-MI	Control group	Research type	Quality score
Galante	2000 Italy	63.3	63/61	Patient	Cross-sectional study	7
Kahan	2000 Sweden	66.4	100/100	Not clear	Cross-sectional study	7
Gunn	2000 UK	65.1	342/214	Not clear	Cross-sectional study	6
Zhu	2001 USA	69.5	167/723	Patient	Prospective study	6
Ridker	2001 USA	57.8	445/445	Not clear	Prospective study	6
Kinjok	2002 Japan	63.9	618/967	Not clear	Cross-sectional study	6
Witherell	2003 USA	55.2	121/204	Patient	Prospective study	7
Fraser	2003 New Zealand	Not clear	341/831	Not clear	Cross-sectional study	6
Ozdogru	2007 Turkey	Not clear	163/163	Patient	Cross-sectional study	6
Nikolopoulou	2008 Greece	63.2	138/49	Health	Cross-sectional study	7
Jafarzadeh	2010 Iran	54.6	60/60	Healthy	Cross-sectional study	7
Guan	2010 China	57.3	102/150	Patient	Cross-sectional study	7
Nakic	2011 Croatia	64.7	100/93	Healthy	Not clear	6
Khodaii	2011 Iran	53.1	500/500	Not clear	Cross-sectional study	6
Padmavati	2012 India	46.8	110/108	Not clear	Cross-sectional study	7
Schöttker	2012 Germany	Not clear	154/8482	Not clear	Prospective study	6
Ikeda	2013 Japan	57.0	106/212	Not clear	Prospective study	6
Shrikhande	2014 India	Not clear	261/261	patient	Cross-sectional study	7

articles published in English from January 2000 to June 2015. We carefully examined relevant literature references, and suitable researches were also included in this study.

Literature selection

Inclusion criteria: the research design was a case control study to discuss the relationship between Helicobacter pylori infection and myocardial infarction. Literature exclusion criteria: quality evaluation literature; duplicate reports; research information which is too little to obtain the required information; research that cannot provide 95% CI or OR values directly or indirectly; review literature, case reports, comments and other literatures.

Literature quality evaluation is separately listed. The quality of the included literature was evaluated by Newcastle-Ottawa Scale and the score was in the range of 0-9. The higher the score is, the higher the quality of the literature is. The literatures over 7 points are considered to be "high quality" research.

Data extraction

Two researchers independently read and extract the following data: the first author, pub-

lication year, country, average age, sample size and study type etc. In addition, two researchers cross-checked the experimental results of the literatures and discussed to decide whether to include those debatable researches or not.

Statistical treatment

Man5.2 Rev Software supplied by software Cochrane was used to collect statistical data and carry out Meta analysis. Meta analysis of the relationship between Helicobacter pylori infection and Myocardial infarction used odd ratio (OR) as the effect index, and calculated the combined OR and its 95% CI by using fixed effect model and random effect model. We used chi-square test to evaluate whether there was heterogeneity among the researches; I^2 test was used to evaluate the size, $I^2 > 50\%$ means heterogeneity exists. If there is no statistical heterogeneity between the studies, we use fixed effects model, otherwise we use random effects model, at the same time, draw forest plots. A funnel plot was used to analyze the publication bias of the included studies. And the sensitivity analysis was used to test the reliability of the results.

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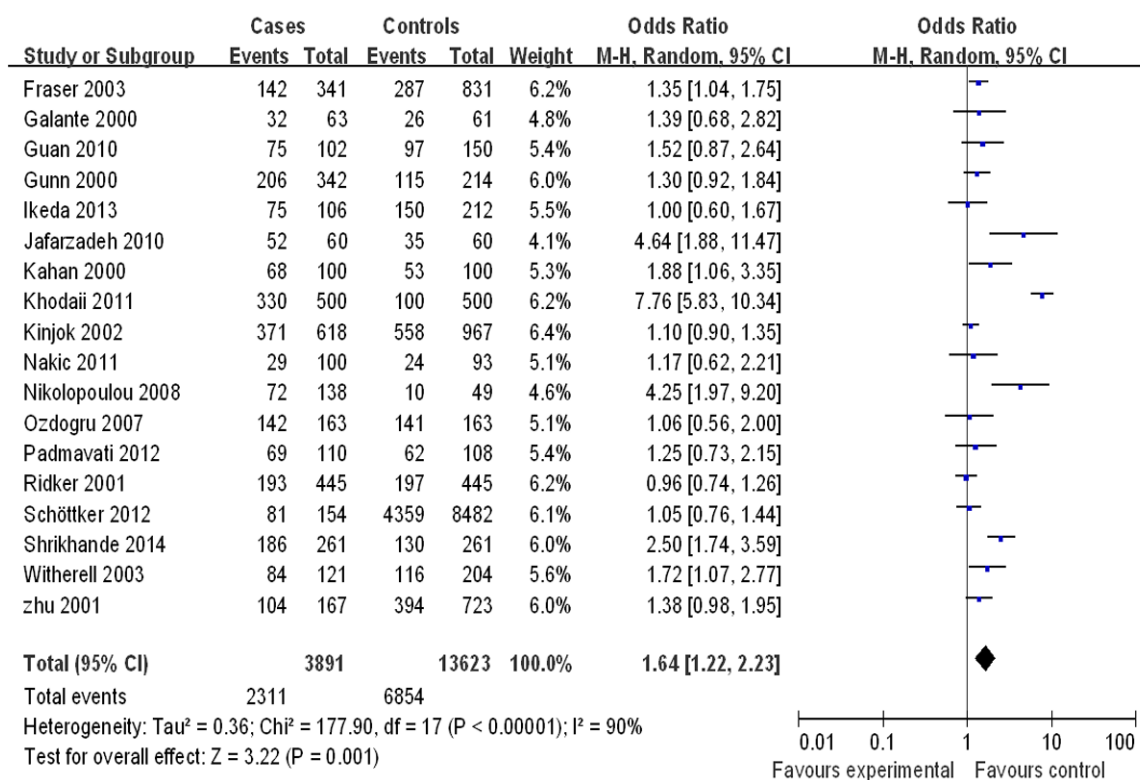


Figure 1. Meta-analysis of literatures regarding the relationship between Helicobacter Pylori infection and myocardial infarction by random-effect model.

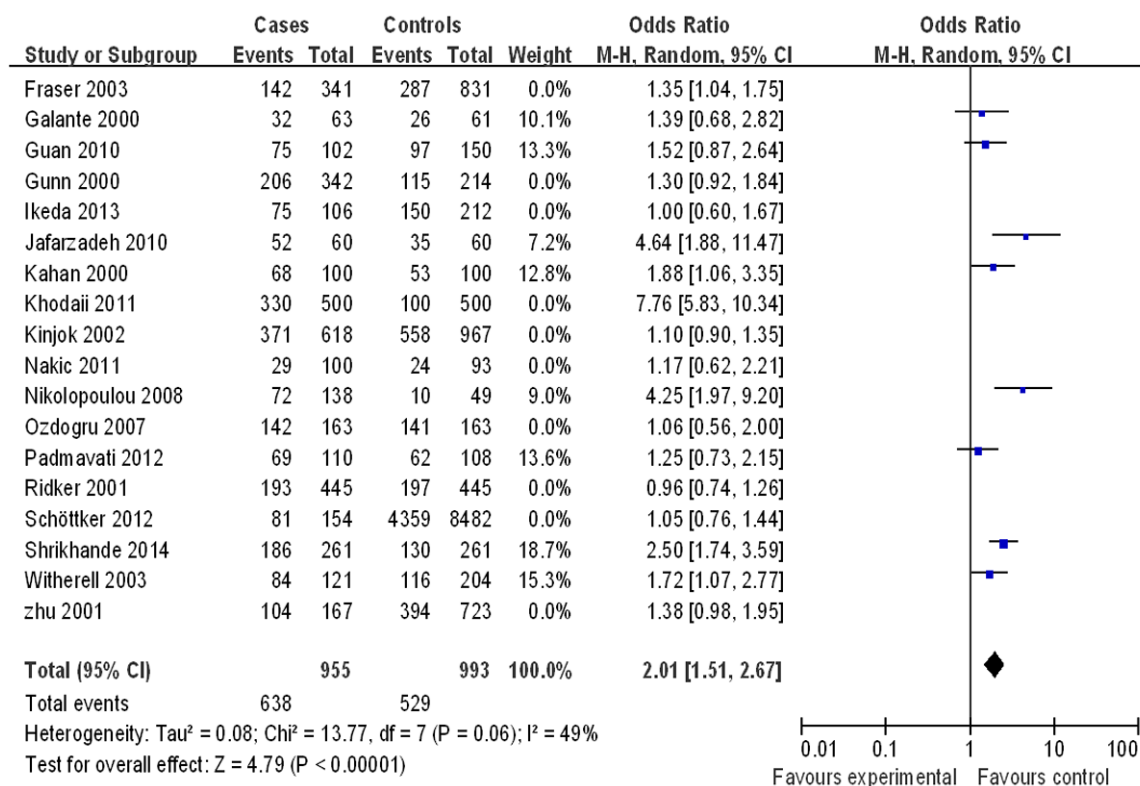


Figure 2. Meta-analysis of high quality literatures regarding the relationship between Helicobacter pylori infection and myocardial infarction by random-effect model.

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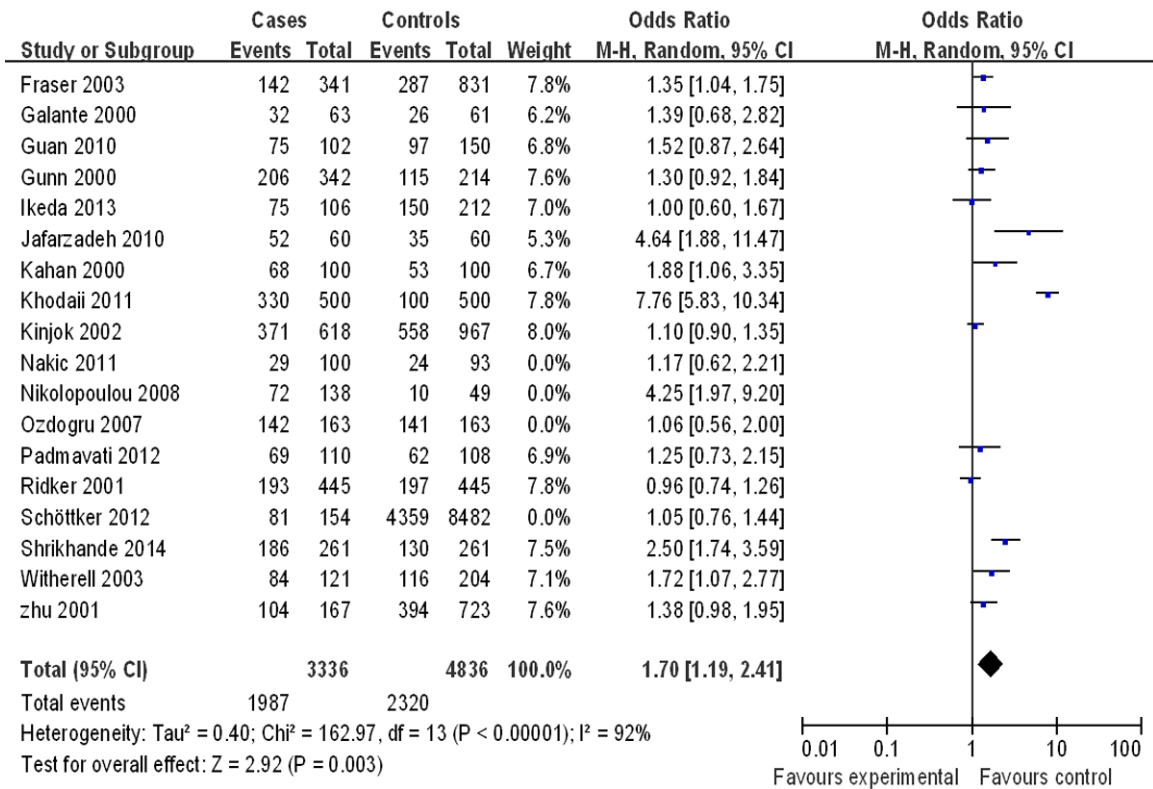


Figure 3. Meta-analysis of literatures regarding the relationship between Helicobacter pylori infection and myocardial infarction.

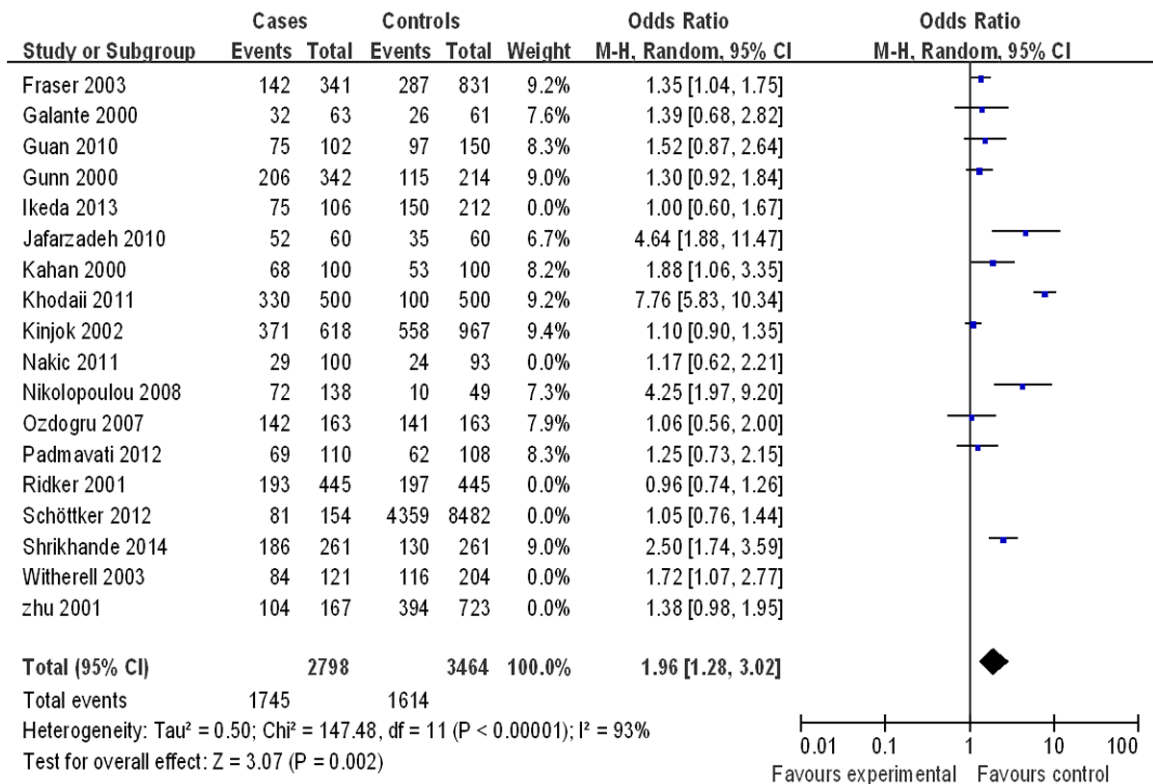


Figure 4. Meta-analysis of literatures regarding the relationship between CagA strain infection and risks of myocardial infarction.

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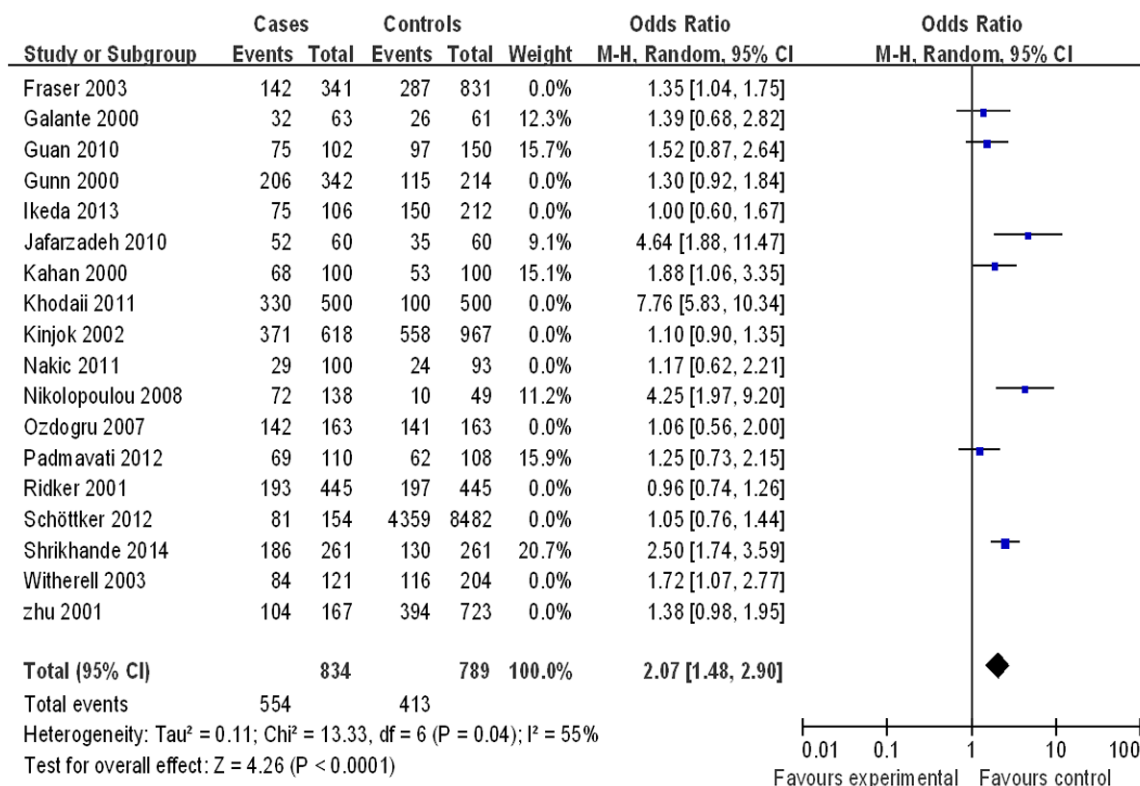


Figure 5. Meta-analysis of high quality literatures regarding the relationship of CagA strain infection and risks of myocardial infarction.

Result

Basic characteristics of the included literatures

A total of 240 articles were retrieved from the database, and 18 studies were included in this study. 6 of these studies were excluded because they could not be completely obtained. And the specific reasons for the 216 excluded studies were as follows: 106 of them were overviews, comments and case reports that without raw data. In addition, the 110 studies involves other subjects, such as animal studies, vitro studies and epidemiological studies, these are not the studies of the relationship between Helicobacter pylori infection and myocardial infarction. The basic characteristics and quality score of the 18 included articles are shown in **Table 1**.

Relationship between Helicobacter pylori infection and myocardial infarction

18 studies have reported the relationship between Helicobacter pylori infection and myo-

cardial infarction. The random effect model results show that the combined OR value was 1.64 (95% CI 1.22-2.23, P=0.001), see **Figure 1**. Excluding the studies with quality evaluation score less than 6, only 8 studies were included, the result shows that the combined OR value was 2.01 (95% CI 1.51-2.67, P<0.00001), see **Figure 2**. Meta analysis was conducted on the reported risk factors of myocardial infarction. The random effect model result shows that the OR value was 1.70 (95% CI 1.19-2.41, P=0.003), see **Figure 3**.

Relationship between CagA strain and myocardial infarction

Cross-sectional study reported the relationship between CagA strain infection and the risk of myocardial infarction. The combined OR 1.96 (1.28-3.02 P=0.002, 95% CI) was calculated by the random effect model, see in **Figure 4**. There were seven cross-sectional studies scored 7, with a combined OR of 2.07 (1.48-2.90 95% CI, P<0.0001), as shown in **Figure 5**. Due to lacking of data, the result of meta-analysis of the CagA strain subgroup could not be obtained.

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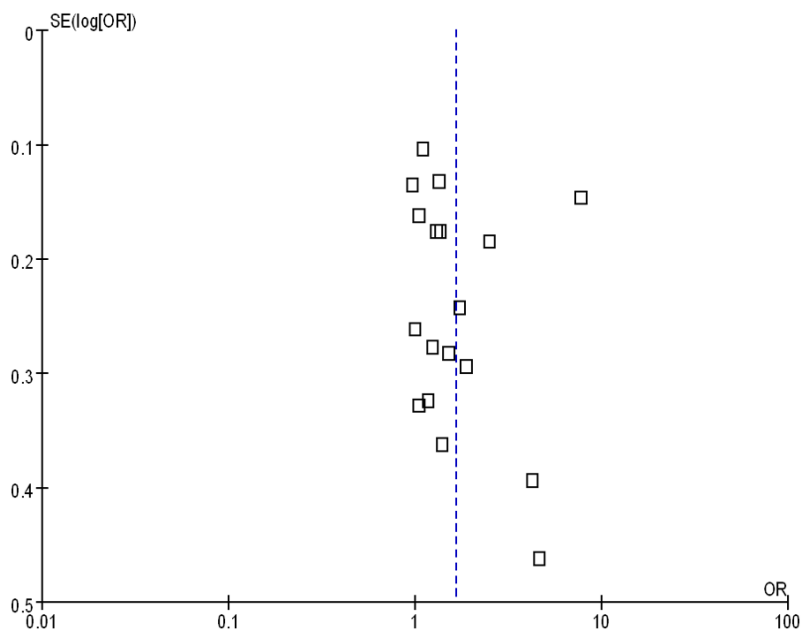


Figure 6. The inverted funnel plot of the relationship between Helicobacter pylori infection and coronary heart disease.

Analysis of publication bias

Taking the effect OR value as the horizontal coordinate, IgOR value standard error as the vertical coordinate, the inverted funnel plot of this study shows that the effect value is asymmetric distributed, this indicates that the included literatures have a certain publication bias, as shown in **Figure 6**.

Discussion

Since Meta analysis could comprehensively evaluate and quantitatively analyze the researches of same purpose, it can increase the statistical effect of the original researches and solve the problem of inconsistency among them. The relationship between Helicobacter pylori infection and myocardial infarction is still controversial. This study carried Meta analysis on this problem for the first time. Based on the results of this study, we believe that Helicobacter pylori infection can increase the incidence of myocardial infarction. In this study, the included literatures were all high quality with satisfactory scores (≥ 6 points). Meta analysis of the literatures scored 7 provided a more reliable result. In addition, the results obtained from the Meta analysis of the literatures scored 6 were not significantly different from those scored 7. Result of funnel plots showed that the

included literatures were asymmetric distributed, and a certain degree of publication bias existed. Studies have indicated that infection of Helicobacter Pylori with cytotoxin associated gene (CagA) can easily cause gastric cancer and duodenal ulcer [6]. The meta-analysis of CagA positive Helicobacter Pylori infection and myocardial infarction in this study showed that CagA positive virulence strains are associated with myocardial infarction. However, according to the present experimental data, the relationship between Helicobacter Pylori infection and coronary heart disease couldn't

be defined as caused by the infection of virulence strains of Helicobacter Pylori.

Now, there are 2 reasons to explain the relationship between Helicobacter Pylori infection and the risk of myocardial infarction. First, Reszka et al. [7] found that there were Helicobacter pylori DNA in the aortic tissue and atherosclerotic plaque of patients with ischemic heart disease, which is likely to show that Helicobacter Pylori plays a direct role in the pathogenesis of ischemic cardiomyopathy. Second, chronic Helicobacter Pylori infection may reduce serum high density lipoprotein level and increase triglycerides, and some clotting factors and inflammatory factors such as fibrinogen, prothrombin fragment, tumor necrosis factor, interleukin - 6 and interleukin - 8 in serum [8]. These may promote the occurrence and development of ischemic heart disease caused by Helicobacter Pylori infection.

In a word, the results of this meta-analysis indicated that there might be a link between the Helicobacter Pylori infection and the risk of myocardial infarction. Further studies are needed to identify the pathogenesis mechanism of coronary heart disease caused by Helicobacter Pylori infection.

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Disclosure of conflict of interest

None.

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