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META-ANALYSIS

Helicobacter pylori infection and peptic ulcer disease in cirrhotic patients: An updated meta-analysis

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Abstract

BACKGROUND

Peptic ulcer (PU) is more prevalent in patients with liver cirrhosis. The role of *Helicobacter pylori* (*H. pylori*) infection in the pathogenesis of PU in patients with cirrhosis is still not elucidated.

AIM

To perform a meta-analysis on the prevalence of *H. pylori* infection and PU and their association in liver cirrhosis patients.

METHODS

We searched PubMed, EMBASE, Web of Science, Cochrane, CNKI, Wangfang, and CQVIP databases from inception to July 10, 2020. Odds ratio (OR) and 95% confidence interval (CI) were pooled using a random-effects model. The statistical heterogeneity among studies (I^2-index), subgroup analyses, regression analysis, sensitivity analysis, and the possibility of publication bias were assessed.

RESULTS

A total of 14 studies (13 cross-sectional studies; 1 cohort study) involving 2775 individuals (611 cases with PU and 2164 controls) were included in our meta-analysis. The prevalence of PU in patients with cirrhosis was 22%. The prevalence of *H. pylori* infection was 65.6% in cirrhotic patients with PU, and 52.5% in those without. The pooled overall OR was 1.73 (95%CI: 1.16-2.56, I^2 = 66.2%, P < 0.001, Z = 2.7, P_z < 0.05). We did not find the cause of heterogeneity in the subgroup analyses and meta-regression analysis except for one study. Funnel plot did not show significant publication bias. The results of Begg's test and Egger's test indicated no evidence of substantial publication bias (P_{Begg} = 0.732, P_{Egger} = 0.557).

CONCLUSION

There is a weakly positive association between *H. pylori* infection and PU in patients with liver cirrhosis. It is suggested that *H. pylori* infection may play a role

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in the pathogenesis of PU in liver cirrhotic patients.

Key Words: *Helicobacter pylori*; Peptic ulcer; Cirrhosis; Meta-analysis; Infection

Core Tip: Peptic ulcer (PU) is more prevalent in patients with liver cirrhosis than in the general population. What's more, cirrhotic patients with PU have a high risk of PU bleeding than the general population. So, if studies can prove that *Helicobacter pylori* (*H. pylori*) is also an independent risk factor for PU in patients with liver cirrhosis, the eradication of *H. pylori* can indirectly prevent PU bleeding in cirrhotic patients. This study showed that there is a weak positive association between *H. pylori* infection and PU in patients with liver cirrhosis.

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INTRODUCTION

Based on endoscopy screening, the prevalence of peptic ulcer (PU) in cirrhotic patients has been reported to be approximately 5%-20% compared to 2%-4% in the general population[1-5]. It has been shown that cirrhotic patients have a significantly higher risk of PU bleeding than the general population[6]. There are data indicating that upper gastrointestinal hemorrhage (UGIB) due to PU worsens the prognosis of cirrhotic patients. The morbidity and mortality of patients with liver cirrhosis and PUs are very high. Leontiadis *et al*[7] performed a meta-analysis on the effect of comorbidities on mortality in patients with PU bleeding and showed that the mortality rate of PU bleeding patients with liver diseases was 26.9% compared with the mortality rate of 6.3% among those who had no hepatic diseases[7,8]. In the general population, *Helicobacter pylori* (*H. pylori*) infection is central to the pathogenesis of PU. If studies can prove that *H. pylori* is also an independent risk factor for PU in patients with liver cirrhosis, the eradication of *H. pylori* can indirectly prevent PU bleeding in cirrhotic patients. Therefore, it is very important for cirrhotic patients that also have *H. pylori* infection to eradicate *H. pylori* in advance of developing PU, and the relationship between *H. pylori* infection and PU in liver cirrhosis is of great clinical significance. Whether patients with liver cirrhosis should be treated with anti-*H. pylori* drugs in advance has become a very important clinical problem. There is debate concerning the relationship between *H. pylori* infection and PU in patients with liver cirrhosis[5,9-21]. Some of the results suggest that *H. pylori* infection is not related to PU in liver cirrhosis, while others suggest that *H. pylori* infection is related or weakly related to PU in liver cirrhosis patients. Therefore, we summarized the articles published in recent years on the *H. pylori* and PU in patients with liver cirrhosis and performed a meta-analysis to assess the prevalence and the association between *H. pylori* infection and PU in patients with cirrhosis.

MATERIALS AND METHODS

Registration of review protocol

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, and the protocol for this meta-analysis is available on international prospective register of systematic reviews (PROSPERO; registration number CRD42020218033).

Data sources and search strategy

PubMed, EMBASE, Web of Science, Cochrane, CNKI, Wangfang, and CQVIP data-

bases were electronically searched from inception to July 10, 2020 without language restrictions. The search terms were as follows: ("*H. pylori*" OR "*Campylobacter pylori*" OR "*H. pylori*" OR "HP" OR "*Helicobacter spp.*" OR "*H. pylori*") AND ("liver cirrhosis" OR "cirrhosis" OR "cirrhosis hepatis" OR "cirrhosis, liver" OR "cryptogenic liver cirrhosis" OR "dietary cirrhosis" OR "dietary liver cirrhosis" OR "hepatic cirrhosis" OR "postnecrotic liver cirrhosis" OR "Fibrosis, Liver" OR "Liver Fibrosis") AND ("ulcer" OR "peptic ulcer" OR "duodenal ulcer" OR "Curling ulcer" OR "stomach ulcer" OR "gastric ulcer"). Both Medical Subject Heading and free words were used. We also reviewed references from relevant original papers and review articles to identify further eligible studies not covered by the original database research. This review was performed according to the guidelines for meta-analyses and systematic reviews of observational studies[22].

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Cross-sectional, case-control, or cohort studies published as original articles that explored the association between PU and *H. pylori* in cirrhotic patients; (2) *H. pylori* infection had to be confirmed by at least one positive test as follows: Serological testing (using *H. pylori* immunoglobulin G enzyme-linked immunosorbent assays), 13C-labeled or 14C-labeled urea breath test (UBT), rapid urease test (RUT), histology, or fecal antigen test; (3) Cirrhosis had to be diagnosed by histology, or by clinical, analytical, and imaging (mostly ultrasonography) methods; etiology and Child-Pugh score were specified; (4) The diagnosis of PU was obtained by endoscopy; and (5) All the studies included a control group.

Criteria for exclusion were as follows: (1) Letters, abstracts, case reports, animal studies, editorials, reviews, and meta-analyses; (2) Irrelevant literature and duplicate studies; and (3) The lack of data made it impossible to derive an exact number of patients with or without *H. pylori* and with or without PU by endoscopy.

Two investigators (Ding HG and Wei L) independently screened the titles and abstracts of all studies identified using the previously described search criteria to identify studies meeting the inclusion criteria. Each study meeting the requirements of the inclusion criteria then underwent an independent full-text review by both investigators. Disagreements about the inclusion of studies between investigators were resolved by discussion.

Data extraction and quality assessment

We extracted the following data from each study: (1) Study characteristics, including the name of the first author, publication year, country of publication, study design, and sample size; and (2) The number of positive/negative *H. pylori* infections in the PU with liver cirrhosis group, the number of positive/negative *H. pylori* infections in the control group, method of detection of *H. pylori* infection, method of detection of liver cirrhosis, and case/control ratio. We assessed the quality of each study according to the Agency for Health care Research and Quality (AHRQ), which is a validated scale for cross-sectional studies[23].

Data synthesis and analysis

We used STATA version 12.0 software (Stata Corporation, College Station, TX, United States) to perform meta-analyses. Odds ratio (OR) with 95% confidence interval (CI) was pooled to describe the ratio of the prevalence of *H. pylori* infection in cirrhotic patients with and without PU. Heterogeneity was assessed by Chi-square-based Q test and I^2 index was used to evaluate the statistical heterogeneity between the studies[24]. The significance for the Q test was defined as P value < 0.1. Heterogeneity was classified as follows: I^2 value of 0%-25% indicated no heterogeneity, 26%-50% indicated low heterogeneity, 51%-75% indicated moderate heterogeneity, and 76%-100% indicated high heterogeneity. A fixed effect model was used when I^2 value was < 50%, and a random effect model was used when I^2 value was > 50%[24]. Subgroup analysis and regression analysis were performed to explore sources of heterogeneity. The forest plot was used to assess the relationship between *H. pylori* infection and PU in cirrhotic patients. The funnel plot and Begg's and Egger's tests were used to investigate publication bias. $P < 0.05$ was considered statistically significant.

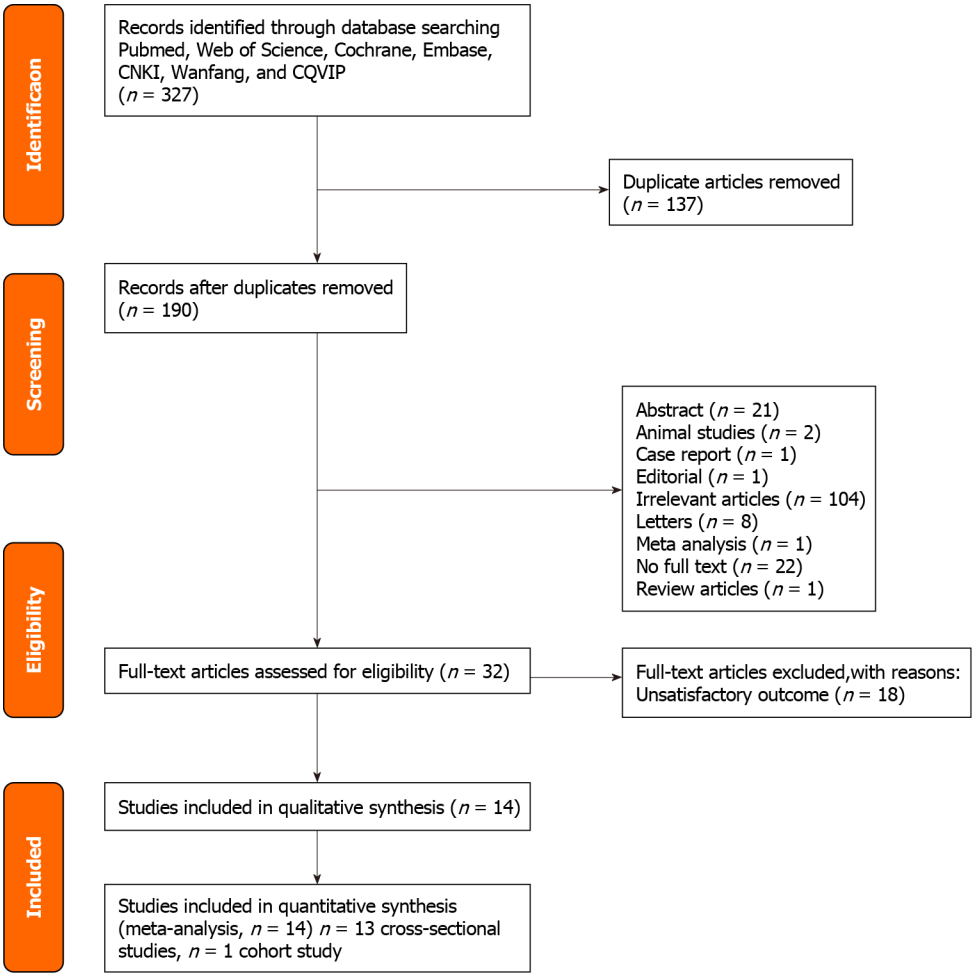

Figure 1 Flow diagram of the literature search and PRISMA.

RESULTS

Data search and study characteristics

The initial database search identified 327 records. After removing 137 duplicates, 190 records remained. Of these 190 studies, 176 were excluded. Thus, 14 studies were included in the meta-analysis. A flow diagram of the literature search is shown in Figure 1. The main characteristics of the 14 studies are summarized in Table 1. A total of 14 studies involving 2775 individuals were included in our meta-analysis[5,9-21]. These studies were published between 1994 and 2019. Our meta-analysis contained 13 cross-sectional studies and 1 cohort study[19]. Figure 2 shows the results of quality assessment according to the AHRQ.

Prevalence of H. pylori infection in cirrhotic patients with and without PU

The prevalence of PU in patients with cirrhosis was 22%. The prevalence of *H. pylori* infection in cirrhotic patients with PU was 65.6%, and the prevalence in those without PU was 52.5%. Figure 3 shows the forest plot and pooled estimates of *H. pylori* infection for cirrhotic patients with and without PU in the 14 studies (involving 2775 middle-aged individuals, 611 cases with PU, and 2164 controls). The pooled overall OR was 1.73 (95%CI: 1.16-2.56, I^2 = 66.2%, P < 0.005, Z = 2.7 P_z < 0.05). This result suggests that patients with *H. pylori* infection were 1.73 times more likely to develop PU than those without.

Given the heterogeneity in the results, we carried out subgroup analyses and meta-regression of the studies according to the publication year, location, diagnosis of *H. pylori*infection, sample size, case/control ratio, diagnosis of *H. pylori* infection, diagnosis of liver cirrhosis, and language. Unfortunately, we did not find the cause of the heterogeneity in the subgroup analyses and meta-regression analysis. The results of the subgroup and meta-regression analyses are shown in Table 2. Notably, the prevalence of *H. pylori* infection in cirrhotic patients with and without PU was

Table 1 Main characteristics of included studies in the meta-analysis

Study	Area	Study type	Peptic ulcer (Hp+/Hp-)	Prevalence	Non-ulcer (Hp+/Hp-)	Prevalence	D of Hp	D of LC
Wu *et al*[11], 1995	Asia	Cross-sectional	23/6	82.1%	59/32	64.8%	ELISA	Ultrosound
Kim *et al*[13], 2008	Asia	Cross-sectional	24/46	34.3%	76/142	34.9%	Multiple	Multiple
Siringo *et al*[12], 1997	Europe	Cross-sectional	39/2	95.1%	78/34	69.4%	ELISA	Multiple
Kirchner *et al*[10], 2011	Europe	Cross-sectional	11/7	61.1%	65/27	70.7%	ELISA	Multiple
Voulgaris *et al* [16], 2019	Europe	Cross-sectional	9/10	47.4%	45/36	55.6%	Multiple	Multiple
Wang *et al*[15], 1997	Asia	Cross-sectional	12/18	40.0%	7/12	36.8%	Multiple	Multiple
Chen *et al*[17], 1994	Asia	Cross-sectional	14/17	45.2%	33/44	42.9%	ELISA	Multiple
Chen *et al*[18], 1995	Asia	Cross-sectional	9/7	56.3%	18/16	52.9%	RUT	Multiple
Yeh *et al*[19], 2001	Asia	Cohort	26/19	57.8%	31/33	48.4%	UBT	Multiple
Hu *et al*[20], 2002	Asia	Cross-sectional	86/8	91.5%	373/189	66.4%	Multiple	Multiple
Tuo *et al*[21], 2000	Asia	Cross-sectional	29/45	39.2%	143/279	33.9%	Multiple	Multiple
Calvet *et al*[14], 1998	Europe	Cross-sectional	14/6	70.0%	79/91	46.5%	Multiple	Multiple
Zullo *et al*[9], 1999	Europe	Cross-sectional	51/9	85.0%	84/82	50.6%	Multiple	Multiple
Tsai[5], 1998	Asia	Cross-sectional	54/10	84.4%	46/20	69.7%	Multiple	Multiple

Cross-sectional studies (n = 13); Cohort study (n = 1). Hp: *Helicobacter pylori*; LC: Liver cirrhosis; UBT: Urea breath test; RUT: rapid urease test; ELISA: Enzyme linked immunosorbent assay; D: Diagnostic method.

consistent in most subgroups examined.

We performed a sensitivity analysis using the one-study removed (leave-one-out) approach to examine the influence of each study on the overall effect size. As shown in Figure 4, through sensitivity analysis, we found one study may be the source of the statistical heterogeneity. The pooled I^2 was 56%, and the OR was 1.55 (95%CI: 1.07-2.23, I^2 = 56%, P = 0.007, Z = 2.35, P_z = 0.02).

We used a funnel plot to qualitatively detect publication bias, and Egger's and Begg's tests were used to quantify publication bias. The funnel plots were almost symmetric (Figure 5A). The results of Begg's test and Egger's test indicated no evidence of substantial publication bias (P_{Begg} = 0.732, P_{Egger} = 0.557) and are shown in Figure 5B.

H. pylori infection in cirrhotic patients with and without duodenal or gastric ulcer

We also performed two other analyses of *H. pylori* infection in cirrhotic patients with and without duodenal or gastric ulcer diseases. The results showed that *H. pylori* was essentially equally associated with duodenal and gastric ulcer in cirrhotic patients. Figure 6 shows that the OR was 1.83 (95%CI: 1.25-2.67, I^2 = 0.0%, P = 0.454, Z = 3.11, P_z = 0.002) for duodenal ulcer and 1.89 (95%CI: 1.06-3.35, I^2 = 42.8%, P = 0.105, Z = 2.16, P_z = 0.031) for gastric ulcer. These two results are basically consistent with the previous results of liver cirrhosis with PU.

Table 2 Subgroup analyses and meta-regression

Subcategory	Random-effects model				Meta-regression		
	n	OR (95%CI)	*P* value	I^2	Ajusted-R^2	*P* value	χ^2
Year	14	1.73 (1.16-2.56)	< 0.01	66.20%	4.64%	0.241	33.29%
Before 2000	8	2.19 (1.31-3.67)	0.039	52.60%			
After 2000 (2000)	6	1.34 (0.75-2.38)	0.02	73.50%			
Area	14	1.73 (1.16-2.56)	< 0.01	66.20%	-5.48%	0.467	36.82%
Asia	9	2.19 (0.81-5.97)	0.001	79.0%			
Europe	5	1.67 (0.56-4.97)	0.09	74%			
Study type	14	1.73 (1.16-2.56)	< 0.01	66.20%	-14.28%	0.817	39.89%
Cross-sectional study	13	1.75 (1.14-2.70)	< 0.01	68.7%			
Cohort study	1	1.46 (0.68-3.14)					
Diagnosis of Hp	14	1.73 (1.16-2.56)	< 0.01	66.20%	-13.83%	0.935	39.73%
ELISA	4	1.52 (0.62-3.74)	0.036	64.80%			
Multiple	8	1.95 (1.12-3.39)	0.003	75.30%			
RUT	1	1.14 (0.35-3.78)					
UBT	1	1.46 (0.68-3.14)					
Diagnosis of liver cirrhosis	14	1.73 (1.16-2.56)	< 0.01	66.20%	-11.75%	0.817	39.01%
Ultrasound	1	1.43 (0.51-3.98)					
Multiple	13	1.75 (1.15-2.67)	< 0.01	68.70%			
Case/control ratio	14	1.73 (1.16-2.56)	< 0.01	66.20%	-14.36%	0.787	39.92%
≥ 0.3	9	1.80 (1.11-2.90)	0.009	60.60%			
< 0.3	5	1.59 (0.73-3.47)	0.001	77.90%			
Sample size	14	1.73 (1.16-2.56)	< 0.01	66.20%	5.11%	0.24	33.12%
≥ 100	12	1.89 (1.23-2.91)	< 0.01	68.70%			
< 100	2	0.87 (0.40-1.88)	0.5611				
Language	14	1.73 (1.16-2.56)	< 0.01	66.20%	-7.60%	0.439	37.56%
English	12	1.59 (1.05-2.42)	0.005	58.7%			
Chinese	2	2.55 (0.58-11.14)	0.001	90.6%			

UBT: Urea breath test; RUT: Rapid urease test; ELISA: Enzyme linked immunosorbent assay; Hp: *Helicobacter pylori*; CI: Confidence interval; OR: Odds ratio.

DISCUSSION

The exact mechanism underlying the association between *H. pylori* infection and PU in patients with liver cirrhosis has not been fully elucidated. At present, there are some hypotheses. Since the PU prevalence is considerably higher in liver cirrhosis patients than in the general population, it is reasonable to postulate that there are "ulcerogenic mechanisms" specific to cirrhotic patients which may cause PU in the absence of *H. pylori* infection and which could additionally increase the ulcerogenic effects of *H. pylori* infection. Several possible ulcerogenic mechanisms have been suggested in cirrhotic patients: A decrease in gastric prostaglandin E2 levels, hypergastrinemia, portosystemic shunting allowing the ulcerogenic factors to escape hepatic clearance, and an impairment of gastric mucosal defense secondary to portal hypertension and congestive gastropathy which may make the mucosa more susceptible to damage from other agents or reduce its capacity to repair damage[25-31]. Taken together, the pathogenic mechanisms of PU in cirrhotic patients seems to be a multifactorial event, which may increase the ulcerogenic effects of *H. pylori* infection.

Figure 2 Quality assessment according to the Agency for Healthcare Research and Quality.

Our meta-analysis included 14 studies, of which 9 showed that there was no significant difference in the incidence of *H. pylori* infection in cirrhotic patients with or without PU[10-13,15-18,21]. The other five studies showed that *H. pylori* infection was positively or weakly correlated with PU in liver cirrhosis[5,9,14,19,20]. The results of the 14 studies showed that the incidence of liver cirrhosis complicated with PU was 22%, and the *H. pylori* infection rate of patients with liver cirrhosis complicated with PU was 65.6%. This study found that there was a weakly positive correlation between *H. pylori* infection and PU in patients with liver cirrhosis. In other words, *H. pylori* infection may be a reason why patients with liver cirrhosis are more likely to develop PU than the general population, and *H. pylori* may be one of the factors causing PU. However, because of the weak correlation and data from retrospective studies, more prospective studies are needed to evaluate the incidence of *H. pylori* infection in patients with liver cirrhosis complicated with PU in the future.

In 2002, Vergara *et al*[3] published a meta-analysis of the relationship between *H. pylori* infection and PU in patients with liver cirrhosis. The meta-analysis included seven studies, four of which suggested that *H. pylori* infection did not increase the risk of PU in liver cirrhosis, while three others suggested a positive or weak correlation[3]. That meta-analysis suggested that *H. pylori* infection increases the risk of PU in patients with liver cirrhosis. The OR was 2.70 (95%CI: 1.91–3.82), which is consistent with our collective results. And the meta-analysis of Vergara *et al*[3] showed that the relationship between *H. pylori* infection and PU in patients with liver cirrhosis does not seem to be as intense as in the general population. The reason may be that in most studies, *H. pylori* infection is diagnosed by serology. Although serology is the preferred technique in epidemiological investigation, its reliability is lower than that of other diagnostic tools such as histology or urea breath test, which affects the sample size of *H. pylori* positive cases to some extent. It increases the size of the sample needed to find an association, increases the risk of type-β error, and decreases the power of the estimated association.

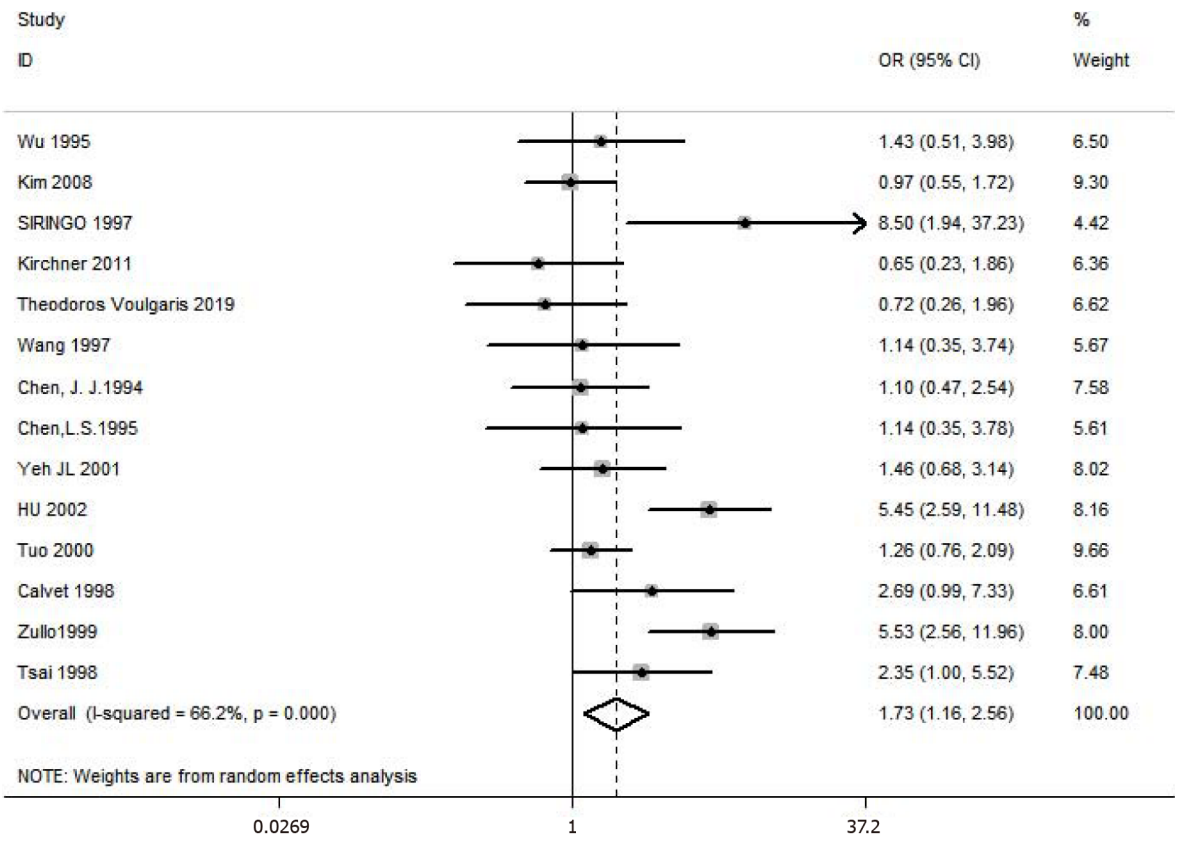

Figure 3 Forest plot and pooled estimates of *Helicobacter pylori* infection in cirrhotic patients with and without peptic ulcer. CI: Confidence interval; OR: Odds ratio.

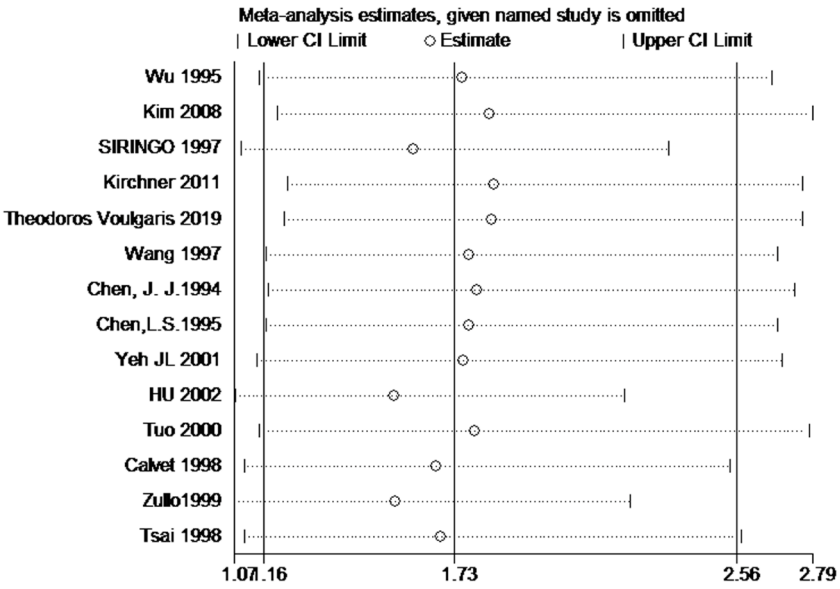

Figure 4 Sensitivity analysis by the one-study removed (leave-one-out) approach.

Our meta-analysis has some limitations. First and foremost, only the study of Voulgaris *et al*[16] had a prospective design, and most of original studies are retrospective or cross-sectional design, which can only at best demonstrate an association but not causality[16]. And the results of observational studies are generally more susceptible to bias and confounding factors than randomized studies. Furthermore, large-scale prospective studies verifying the causal relationship are needed. Second, the etiologies of liver cirrhosis are alcohol, viral hepatitis, cholestasis, nonalcoholic fatty liver disease, parasites, hepatic-venous outflow obstruction, *etc*. Most of the involving patients had some additional risk factors for PU, such as alcohol, non-

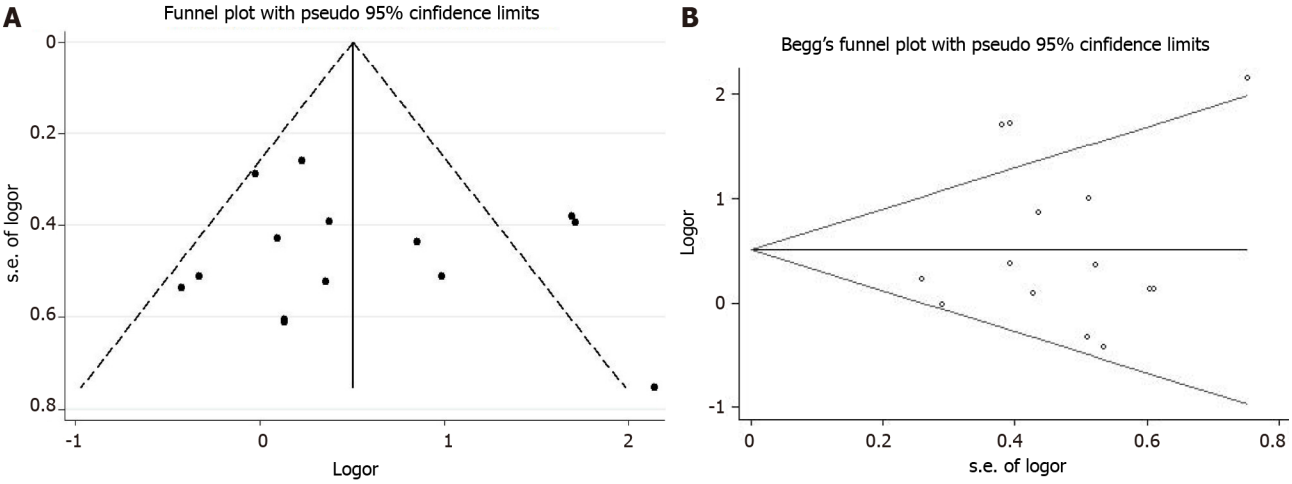

Figure 5 Funnel plot and Begg's funnel plot of association between *Helicobacter pylori* infection and peptic ulcer in patients with cirrhosis. A: Funnel plot; B: Begg's funnel plot.

steroidal anti-inflammatory drugs, antiplatelet medication, and anticoagulants. All these factors might affect the incidence of PU. Although viral hepatitis and alcohol abuse were the most common causes of the liver cirrhosis patients included, not all the studies have controlled the etiological effect of liver cirrhosis on the occurrence of ulcers. Third, patients with liver cirrhosis are mainly male, with low socioeconomic status, usually between 40 and 70 years old. Age and socioeconomic status may also be factors affecting the prevalence of PU in patients with liver cirrhosis. Fourth, in some studies, the severity of cirrhosis was scored according to the Child-Pugh classification, while in the other studies, the severity was classified by compensatory stage and decompensation stage. Fifth, the diagnosis of cirrhosis was based on elastography, liver biopsy, or a combination of clinical, biochemical, and imaging data. The diagnosis of *H. pylori* infection was based on serological test (enzyme linked immunosorbent assay), RUT, UBT, histology, or multiple means. These standards are not uniform, and these may be the root causes of bias. All of the above limitations should be considered or controlled in future research and study design. Sixth, there is a moderate heterogeneity in the overall results. Heterogeneity may reduce the reliability of our conclusions. However, we conducted numerous subgroup analyses, meta-regression analyses, and sensitivity analyses with the hope of detecting potential factors for such heterogeneities. Many results of subgroup analyses were consistent with overall results, indicating the robustness and reliability of our results.

Therefore, the relationship between *H. pylori* infection and PU in patients with liver cirrhosis is of great clinical significance. Future prospective studies and reliable clinical trial designs are of great importance to determine whether *H. pylori* is an independent risk factor for PU in liver cirrhosis. If studies can prove that *H. pylori* is also an independent risk factor for PU in patients with liver cirrhosis, the eradication of *H. pylori* can indirectly prevent bleeding in patients with liver cirrhosis complicated with PU. Therefore, it is very important for cirrhotic patients that also have *H. pylori* infection to eradicate *H. pylori* in advance. In addition, microbiome is booming, especially intestinal microbiome, and many studies describe the role of bacterial microbiome in *H. pylori*-associated diseases. Whether bacterial microbiome can be applied to cirrhotic patients with PU is a subject worth studying[32].

CONCLUSION

There is a weakly positive association between *H. pylori* infection and PU in patients with cirrhosis. It is suggested that *H. pylori* infection may increase the PU risk and play a role in the pathogenesis of PU in patients with cirrhosis. In the future, prospective studies and reliable experimental designs should be used to determine if *H. pylori* is an independent risk factor for PU in liver cirrhotic patients. If this link is confirmed in the near future, the eradication of *H. pylori* may become a new specific strategy to prevent PU bleeding.

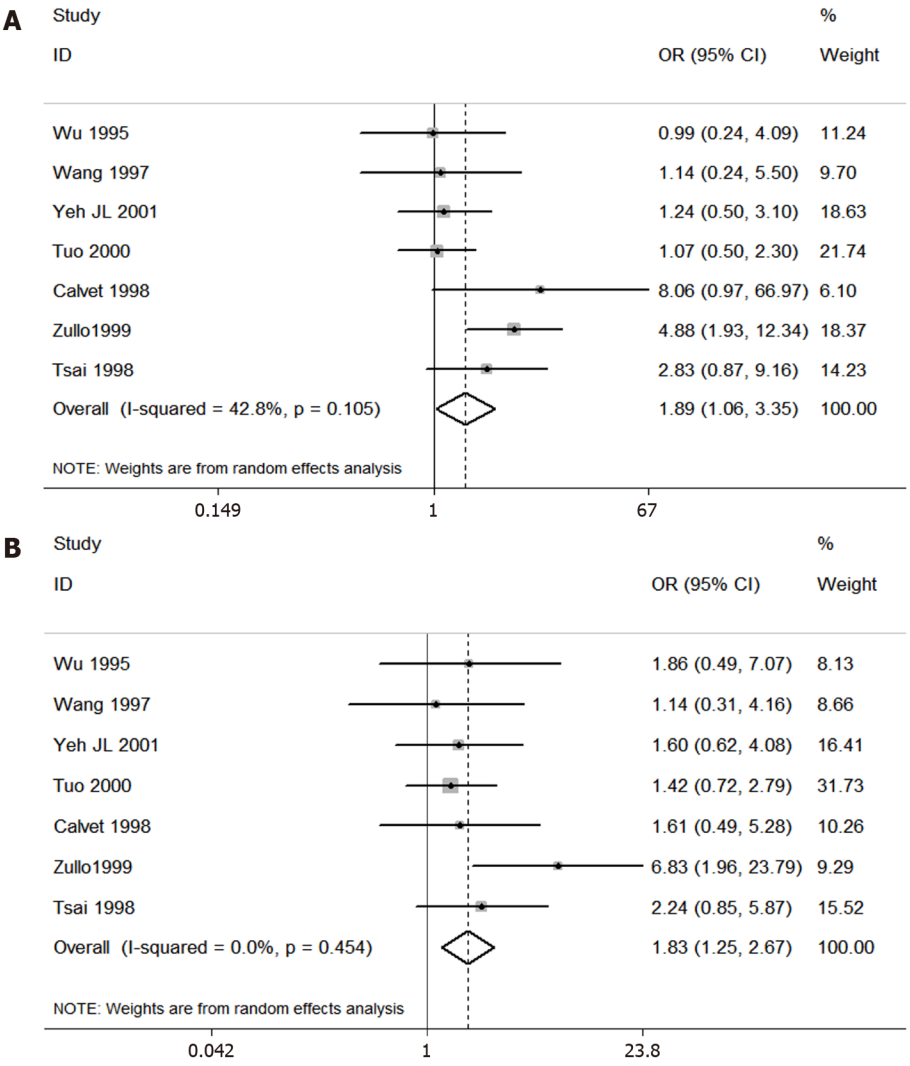

Figure 6 Forest plots and pooled estimates. A: Forest plot and pooled estimates of *Helicobacter pylori* (*H. pylori*) infection for cirrhotic patients with and without gastric ulcer; B: Forest plot and pooled estimates of *H. pylori* infection for cirrhotic patients with and without duodenal ulcer. CI: Confidence interval; OR: Odds ratio.

ARTICLE HIGHLIGHTS

Research background

Peptic ulcer (PU) is more prevalent in patients with liver cirrhosis than in the general population. What's more, cirrhotic patients with PU have a significantly higher risk of PU bleeding than the general population. The role of *Helicobacter pylori* (*H. pylori*) infection in the pathogenesis of PU in patients with cirrhosis is still not elucidated.

Research motivation

Why cirrhotic patients have a higher risk of peptic ulcer? Whether this is related to *H. pylori* infection? If studies can prove that *H. pylori* is also an independent risk factor for PU in patients with liver cirrhosis, eradication of *H. pylori* can indirectly prevent PU bleeding in cirrhotic patients. With these doubts and questions, we performed this meta-analysis.

Research objectives

To perform a meta-analysis on the prevalence of *H. pylori* infection and PU and their association in liver cirrhosis patients.

Research methods

We searched PubMed, EMBASE, Web of Science, Cochrane, CNKI, Wangfang, and CQVIP databases from inception to July 10, 2020. Odds ratio (OR) and 95% confidence interval (CI) were pooled with a random-effects model. The statistical heterogeneity

among studies (I^2-index), subgroup analyses, regression analysis, sensitivity analysis, and the possibility of publication bias were assessed.

Research results

The prevalence of PU in patients with cirrhosis was 22%. The prevalence of *H. pylori* infection was 65.6% in cirrhotic patients with PU, and 52.5% in those without. The pooled overall OR was 1.73 (95%CI: 1.16-2.56, I^2 = 66.2%, P < 0.001, Z = 2.7, P_z < 0.05). We did not find the cause of heterogeneity in the subgroup analyses and meta-regression analysis. We found that one study may be the source of the statistical heterogeneity through sensitivity analysis.

Research conclusions

There is a weakly positive association between *H. pylori* infection and PU in patients with liver cirrhosis.

Research perspectives

Prospective studies and reliable experimental designs should be further used to determine if *H. pylori* is an independent risk factor for PU in liver cirrhotic patients. If this link is confirmed in the near future, the eradication of *H. pylori* may become a new specific strategy to prevent non-variceal bleeding, especially PU hemorrhage in cirrhotic patients.

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