



Observational Study

Colonoscopy plays an important role in detecting colorectal neoplasms in patients with gastric neoplasms

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Abstract

BACKGROUND

Gastric cancer (GC) and colorectal cancer (CRC) are the fifth and third most common cancer worldwide, respectively. Nowadays, GC is reported to have a potential predictive value for CRC, especially for advanced CRC.

AIM

To evaluate the necessity of colonoscopy for gastric neoplasm (GN) patients.

METHODS

Four databases, including PubMed, EMBASE, the Cochrane Library, and Ovid, were used to perform the search strategy on May 2, 2023. The prevalence of colorectal neoplasms (CRN) and baseline characteristics were compared between the neoplasm group and the control group. Continuous variables are expressed as the mean difference and standard deviation. Relationships of categorical variables in the two groups are expressed as odds ratios (OR) and 95% confidence intervals (95% CIs). Subgroup analysis according to different kinds of GNs was conducted for more in-depth analysis. The results of this study are represented by forest plots. Publication bias was evaluated by a funnel plot. All data analyses were performed by STATA SE 16.0 software.

RESULTS

A total of 3018 patients with GNs and 3905 healthy controls (age and sex matched) were enrolled for analysis. After comparing the prevalence of CRNs between the two groups, CRNs were detected significantly more frequently in GN patients than in controls (OR = 1.69, 95%CI = 1.28 to 2.23, $I^2 = 85.12\%$, $P = 0.00$), especially in patients with GC (OR = 1.80, 95%CI = 1.49 to 2.18, $I^2 = 25.55\%$, $P < 0.1$).

Moreover, other risk factors including age (OR = 1.08, 95%CI = 1.00 to 1.17, $I^2 = 90.13\%$, $P = 0.00$) and male sex (OR = 2.31, 95%CI = 1.26 to 4.22, $I^2 = 87.35\%$, $P = 0.00$), were related to the prevalence of CRNs. For patients in the GN group, body mass index (BMI, OR = 0.88, 95%CI = 0.80 to 0.98, $I^2 = 0.00\%$, $P = 0.92$) and smoking (OR = 1.03, 95%CI = 1.01 to 1.05, $I^2 = 0.00\%$, $P = 0.57$) were protective and risk factors for CRNs, respectively.

CONCLUSION

Patients are recommended to undergo colonoscopy when diagnosed with GNs, especially GC patients with a low BMI and a history of smoking.

Key Words: Gastric neoplasm; Gastric cancer; Colorectal neoplasm; Colonoscopy

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Core Tip: Gastric cancer (GC) is currently the fifth largest malignant tumor worldwide and the second largest cause of cancer-related deaths in the world. Synchronous and homologous neoplasms are common in gastric neoplasm (GN) patients, and the colorectal neoplasm (CRN) is the main neoplasm type. The prevalence of CRN in GN patients is a concern. Some studies reported that GN was not a risk factor for CRN. Therefore, the purpose of this pooling up analysis was to explore whether colonoscopy was needed for GN patients to detecting CRN. A total of ten case-control studies were included, involving 6923 patients. In conclusion, GN patients had higher risk of CRN, especially for GC patients. Therefore, colonoscopy was recommended when patients diagnosed with GN.

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INTRODUCTION

According to the International Agency for Research on Cancer, gastric cancer (GC) is the fifth most common cancer worldwide, accounting for 1.1 million new cancer cases[1,2]. *Helicobacter pylori* (*H. pylori*) infection is the greatest known risk factor for GC and shows a positive association with gastric polyps[3,4]. Gastric polyps are asymptomatic lesions found incidentally during endoscopy that may develop into GC. Gastric neoplasm (GN) is a general term for gastric adenoma and GC.

Similar to GC, colorectal cancer (CRC) is a gastrointestinal malignant disease that develops from colorectal polyps[5]. Early colorectal polyps can be removed under colonoscopy, which significantly decreases the incidence of CRC[6,7]. Some characteristics, including age, male sex, family history, obesity, and red meat intake, have been reported to have predictive value for colorectal neoplasms (CRNs) (including colorectal polyps and CRC)[8-10]. Therefore, regular colonoscopy in high-risk patients with CRN is important to improve their survival.

Recently, GN was also reported to have potential predictive value for CRN, especially for advanced CRN[11-15]. However, some other studies demonstrated that colonoscopy surveillance is not recommended for all GN patients[16-18]. Therefore, this study sought to investigate whether it is necessary for GN patients to receive colonoscopy.

MATERIALS AND METHODS

Study population and data collection

This current analysis was conducted by the PRISMA statement[19].

Search strategy

Two items including colonoscopy and GN were used for searching articles studying on the necessity of colonoscopy for GN patients. The text words of colonoscopy included colonoscopy, colonoscopies, and colonoscopic. The text words of GN included GC, gastric carcinoma, GNs, stomach cancer, stomach carcinoma, and stomach neoplasms. The search scope was limited to titles, abstracts, and author keywords. Only English was allowed.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Patients were divided into the GN group (gastric adenoma or cancer) and the control group; and (2) prevalence of CRN (colorectal adenoma, polyp or cancer) was reported. The exclusion criteria were as follows: (1) No comparison or insufficient data; and (2) the study types were conferences abstract, trail, review, meta-analysis, case report, letters to the editor, or comments.

Study selection

Eligible studies were searched in four databases including PubMed, EMBASE, the Cochrane Library, and Ovid. After conducting the search strategy, duplicates records were removed at first. Then, records in ineligible study types were excluded. Finally, full-texts were screened and studies were selected according to the inclusion and exclusion criteria.

Data collection

Baseline information of included studies and patients were collected for analysis. As for included studies, author, year, country, study date, study type, sample size, patients in the study group, evaluation of outcomes, conclusion, and the Newcastle-Ottawa Scales (NOS) score were collected. As for patients, age, sex, body mass index (BMI), diabetes, hypertension, alcohol, and smoking were collected. Moreover, for patients with CRNs, size, location, pathology, and number of CRN were also collected. Variables including age, male, BMI, smoking, drinking, and diabetes were collected to find whether there was a potential predictive value for CRNs in the whole patients and in the GN patients.

Quality Assessment

We used NOS score to assess the quality of included studies[20]. All the studies were case-control studies, which were assessed in selection, comparability and exposure. Nine score was regarded as high-quality, eight or seven score was regarded as median-quality, and lower than seven score was regarded as low-quality.

Statistical analysis

Continuous variables were expressed as mean difference (MD) and standardized deviation (SD), and the relationship of categorical variables in two groups were expressed as odds ratios (ORs) and 95% confidence intervals (95% CIs). All the variables were pooled up for a pooling up analysis using the random-effects model and DerSimonian-Laird method. When $P < 0.1$, the results was considered statistically significant. The chi-squared test and the I^2 value were used to evaluate the statistical heterogeneity[21,22]. When the $I^2 < 30\%$, the statistical heterogeneity was considered non-important. When the $I^2 = 30\%-60\%$, the statistical heterogeneity was considered moderate. When the $I^2 > 60\%$, the statistical heterogeneity was considered substantial. The funnel plot was used to evaluate the publication bias. STATA SE V16.0 software was used for data analysis.

RESULTS

Study selection

There were 871 studies after conducting the search strategy in four databases (223 studies in PubMed, 527 studies in EMBASE, 78 studies in the Cochrane Library, and 43 studies in Ovid). Duplicate records and records in ineligible study type were removed by Endnote software, and the left 63 records were ready for screening. Excluded for seven studies without unavailable full-text, 56 studies were carefully selected by two authors according to the inclusion and exclusion criteria. Finally, this current analysis enrolled ten studies (Figure 1).

Baseline information of included studies

Except for one study conducting in Japan, the other nine studies were conducted in Korea. The ten included studies were all case-control studies, and five were retrospectively conducted, the other five were prospectively conducted. As for patients in the case group, four studies reported GN, three studies reported GC, two studies reported early GC (EGC), and the other one reported early GN (EGN). After receiving colonoscopy, CRNs including colorectal adenoma, high-risk adenoma, cancerous adenoma, and CRC were reported. More information including author, year, study date, patients, conclusion, and the NOS score were shown in Table 1.

Baseline characteristics of the GN group and the control group

After comparing the baseline characteristics between the GN group and the control group, we found that patients with GNs had lower BMI (MD = -0.38, 95% CI = -0.73 to -0.03, $I^2 = 8.00\%$, $P = 0.03$). There was no significant difference in age, sex, diabetes, hypertension, alcohol, and smoking ($P > 0.1$). As for patients who were detected to have CRNs in the two groups, there was no significant difference in size, location, pathology, and number > 3 ($P > 0.1$, Table 2).

Prevalence of CRN between the GN group and the control group

The prevalence of CRN was pooled, and it was found that the detection of CRN was significantly more in the GN group than the control group (OR = 1.69, 95% CI = 1.28 to 2.23, $I^2 = 85.12\%$, $P = 0.00$, Figure 2).

Subgroup analysis based on different kinds of GNs

Subgroup analysis according to patients with different kinds of GNs was conducted. The results showed that GC patients (OR = 1.80, 95% CI = 1.49 to 2.18, $I^2 = 25.55\%$, $P < 0.1$) had a higher prevalence of CRN compared to patients with EGC (OR = 1.73, 95% CI = 0.60 to 4.95, $I^2 = 90.92\%$, $P > 0.1$) or EGN (OR = 1.60, 95% CI = 0.99 to 2.23, $I^2 = 85.12\%$, $P > 0.1$, Figure 3).

Risk factors for CRN in the whole group (including control) and in the GN group

As for the whole patients included in this study, the analysis showed that age (OR = 1.08, 95% CI = 1.00 to 1.17, $I^2 =$

Table 1 Baseline characteristics of included studies

Ref.	Country	Study date	Study type	Patients	Patients in the study group	Evaluation of outcomes	Conclusion	NOS
Chung <i>et al</i> [16], 2017	Korea	January 2009-December 2012	Retrospective case-control study	402	EGC	Colorectal neoplasm and advanced polyps	Colonoscopy plays an important role with respect to the detection of synchronous advanced colorectal neoplasm in patients with EGC	7
Imai <i>et al</i> [11], 2017	Japan	January 2010-December 2012	Retrospective case-control study	390	EGC	High-risk adenomas	Patients with EGC had a significant risk for colorectal cancer	6
Joo <i>et al</i> [12], 2010	Korea	January 2002-December 2008	Retrospective case-control study	372	GN	Adenomatous and cancerous colon polyps	Endoscopists should consider performing routine fiberoptic colonoscopy in patients undergoing endoscopic removal of GNs	7
Kim <i>et al</i> [13], 2022	Korea	January 2015-December 2016	Prospective case-control study	220	EGN	Colorectal adenoma	More stringent colonoscopy surveillance should be considered in elderly patients with EGN	6
Kim <i>et al</i> [17], 2013	Korea	September 2005-August 2010	Prospective case-control study	832	Gastric adenoma or cancer	Colorectal adenoma or cancer	Screening colonoscopy should be considered for gastric adenoma or cancer patients	8
Koh <i>et al</i> [20], 2022	Korea	January 2010-July 2018	Retrospective case-control study	1505	Gastric adenoma or cancer	Adenoma and cancerous colon polyps	Patients with GN are regarded as a high-risk group for colorectal cancer and are recommended for screening colonoscopy at the time of diagnosis	8
Lee <i>et al</i> [14], 2011	Korea	October 2008-September 2010	Prospective case-control study	214	GN	Colorectal neoplasm and high-risk colorectal neoplasm	A screening colonoscopy should be considered in patients with EGN undergoing endoscopic submucosal dissection	6
Lee <i>et al</i> [15], 2011	Korea	July 2005-June 2010	Retrospective case-control study	369	GC	Colorectal neoplasms	Patients with stomach cancer should be regarded as a high-risk group for colorectal neoplasms, and colonoscopy should be recommended for screening	7
Park <i>et al</i> [31], 2010	Korea	November 2004-October 2006	Prospective case-control study	1629	GC	Colorectal neoplasia including colorectal cancer and adenoma	There is a higher prevalence and risk of colorectal cancer in patients diagnosed with GC	9
Yoo <i>et al</i> [32], 2013	Korea	January 2009-December 2010	Prospective case-control study	990	GC	Colorectal neoplasm	Preoperative colonoscopy is strongly indicated in patients with GC	8

GC: Gastric cancer; EGC: Early gastric cancer; GN: Gastric neoplasm; EGN: Early gastric neoplasm; NA: Not applicable; NOS: Newcastle-Ottawa Scales.

90.13%, $P = 0.00$) and male ($OR = 2.31$, 95%CI = 1.26 to 4.22, $I^2 = 87.35\%$, $P = 0.00$) were independent risk factors for CRN. Other variables including BMI, smoking, drinking, and diabetes had no predictive value ($P > 0.1$). As for patients in the GN group, the analysis showed that BMI ($OR = 0.88$, 95%CI = 0.80 to 0.98, $I^2 = 0.00\%$, $P = 0.92$) was a protective factor and smoking ($OR = 1.03$, 95%CI = 1.01 to 1.05, $I^2 = 0.00\%$, $P = 0.57$) was a risk factor for CRN. Other variables including age, male, and drinking had no predictive value ($P > 0.1$, Table 3)

Publication bias

The funnel plot was used for evaluating the publication bias. The plot was not relatively symmetrical, and four plots were outside the 95% CIs, which meant that the results were affected by some publication bias (Figure 4).

Sensitivity analysis

This study evaluated the sensitivity by duplicate analysis of excluding each study at a time. The results of every time analysis were not significantly different, which meant that the results were relatively robust.

DISCUSSION

The current analysis included 6923 patients and found that GN patients had a higher risk of CRN, especially GC patients. Moreover, age and male sex were found to be independent risk factors for CRN in all patients, and BMI and smoking were protective and risk factors in GN patients, respectively.

Table 2 Baseline characteristics of the gastric neoplasm group and the control group

Characteristics	Studies	Patients (GN group/control group)	Odds ratio/mean difference (95%CI)	Heterogeneity
Age	9	2888/3645	0.73 (0.25, 1.21); $P = 0.77$	$I^2 = 0.00\%$; $P = 0.00$
Sex				
Female	10	Reference	Reference	Reference
Male	10	3012/3776	1.01 (0.91, 1.12); $P = 0.85$	$I^2 = 0.00\%$; $P = 1.00$
BMI	6	2100/2857	-0.38 (-0.73, -0.03); $P = 0.03$	$I^2 = 8\%$; $P = 0.03$
Diabetes	8	2181/2847	1.08 (0.86, 1.34); $P = 0.51$	$I^2 = 35.08\%$; $P = 0.15$
Hypertension	3	494/494	0.93 (0.68, 1.27); $P = 0.64$	$I^2 = 18.56\%$; $P = 0.29$
Alcohol	7	1273/1526	0.99 (0.71, 1.38); $P = 0.94$	$I^2 = 75.73\%$; $P = 0.00$
Smoking	8	1816/2612	1.32 (0.89, 1.95); $P = 0.17$	$I^2 = 86.15\%$; $P = 0.00$
Colorectal neoplasms				
Size	2	807/897	1.69 (0.77, 2.61); $P = 0.22$	$I^2 = 33.22\%$; $P = 0.00$
Location				
Rectum	5	Reference	Reference	Reference
Colon	5	841/915	1.02 (0.59, 1.77); $P = 0.94$	$I^2 = 75.16\%$; $P = 0.00$
Pathology				
Tubular adenoma	4	Reference	Reference	Reference
Tubulovillous/villous adenoma	4	1066/941	0.54 (0.03, 10.69); $P = 0.68$	$I^2 = 97.24\%$; $P = 0.00$
Serrated adenoma	4	1066/941	0.23 (0.03, 2.03); $P = 0.19$	$I^2 = 83.15\%$; $P = 0.00$
Adenocarcinoma	4	1066/941	3.15 (0.25, 39.30); $P = 0.37$	$I^2 = 71.58\%$; $P = 0.01$
Number > 3	2	460/460	1.50 (0.95, 2.36); $P = 0.11$	$I^2 = 0.00\%$; $P = 0.08$

GN: Gastric neoplasm; BMI: Body mass index; 95%CI: 95% confidence intervals.

Table 3 Risk factors for colorectal neoplasms among the whole group (including control) and the GN group

Variables	Studies	Participants (GN group/control group)	Odds ratio (95%CI)	Heterogeneity
Whole group				
Age	6	1735/1956	1.08 (1.00, 1.17); $P = 0.04$	$I^2 = 90.13\%$; $P = 0.00$
Male	5	1625/1846	2.31 (1.26, 4.22); $P = 0.01$	$I^2 = 87.35\%$; $P = 0.00$
BMI	3	944/1165	1.04 (0.82, 1.32); $P = 0.73$	$I^2 = 0.00\%$; $P = 0.44$
Smoking	2	237/367	1.16 (0.70, 1.91); $P = 0.57$	$I^2 = 0.00\%$; $P = 0.72$
Drinking	2	237/367	1.23 (0.79, 1.92); $P = 0.97$	$I^2 = 0.00\%$; $P = 0.35$
Diabetes	2	293/293	1.16 (0.40, 3.36); $P = 0.79$	$I^2 = 76.42\%$; $P = 0.04$
GN group				
Age	4	933/1063	2.17 (0.91, 5.17); $P = 0.08$	$I^2 = 83.37\%$; $P = 0.00$
Male	4	933/1063	1.85 (0.88, 3.90); $P = 0.10$	$I^2 = 68.71\%$; $P = 0.02$
BMI	3	438/568	0.88 (0.80, 0.98); $P = 0.02$	$I^2 = 0.00\%$; $P = 0.92$
Smoking	3	438/568	1.03 (1.01, 1.05); $P = 0.02$	$I^2 = 0.00\%$; $P = 0.57$
Drinking	2	237/367	1.36 (0.71, 2.62); $P = 0.36$	$I^2 = 0.00\%$; $P = 0.79$

GN: Gastric neoplasm; BMI: Body mass index; 95%CI: 95% confidence intervals.

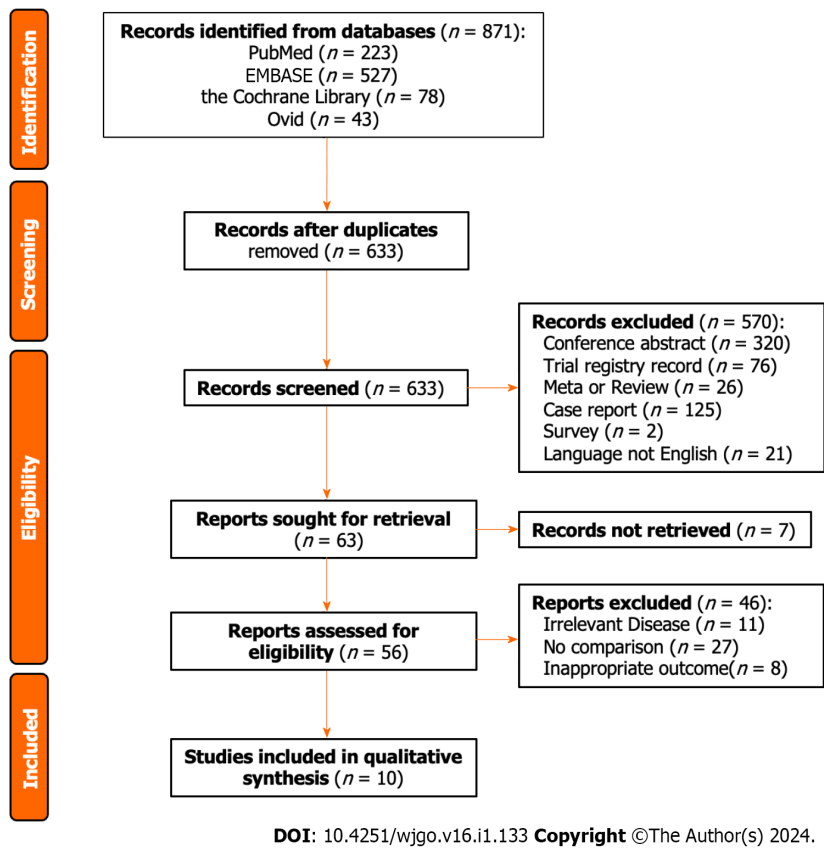


Figure 1 Flowchart of article selection.

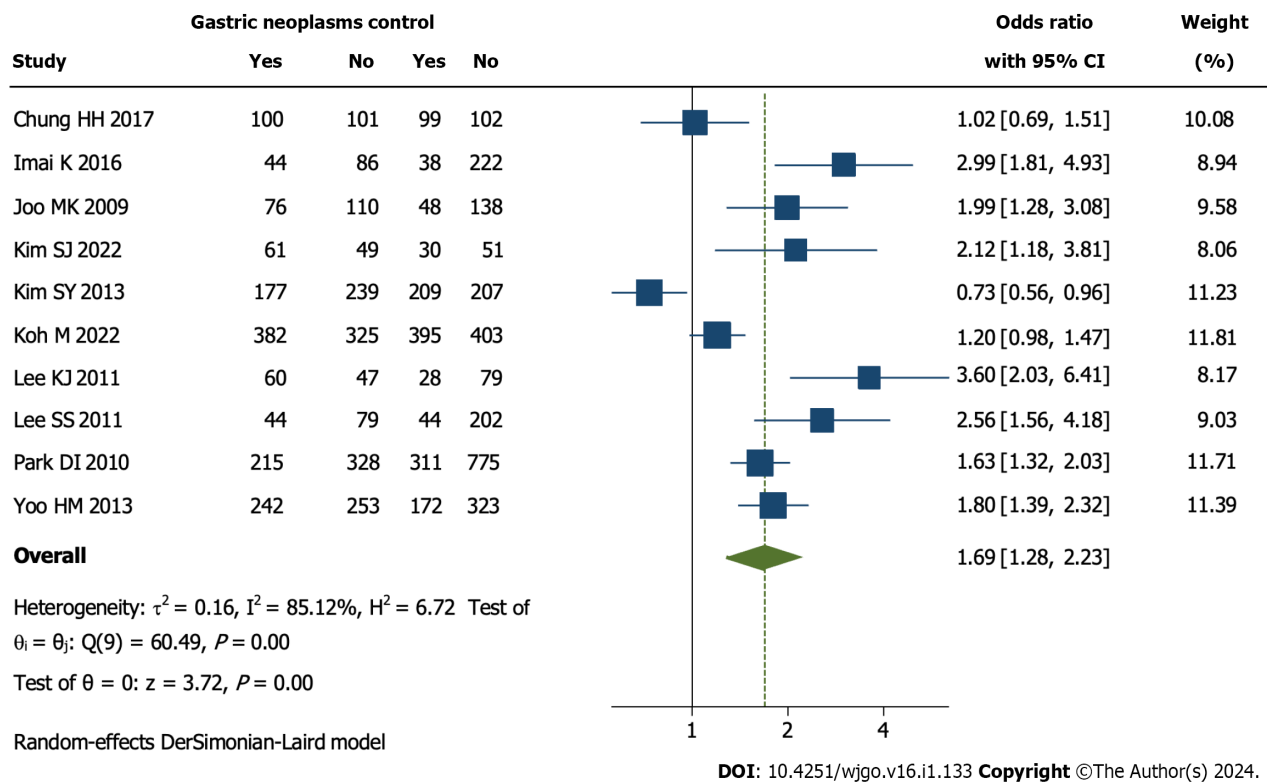


Figure 2 Prevalence of colorectal neoplasms in the gastric neoplasm group and the control group. 95%CI: 95% confidence interval.

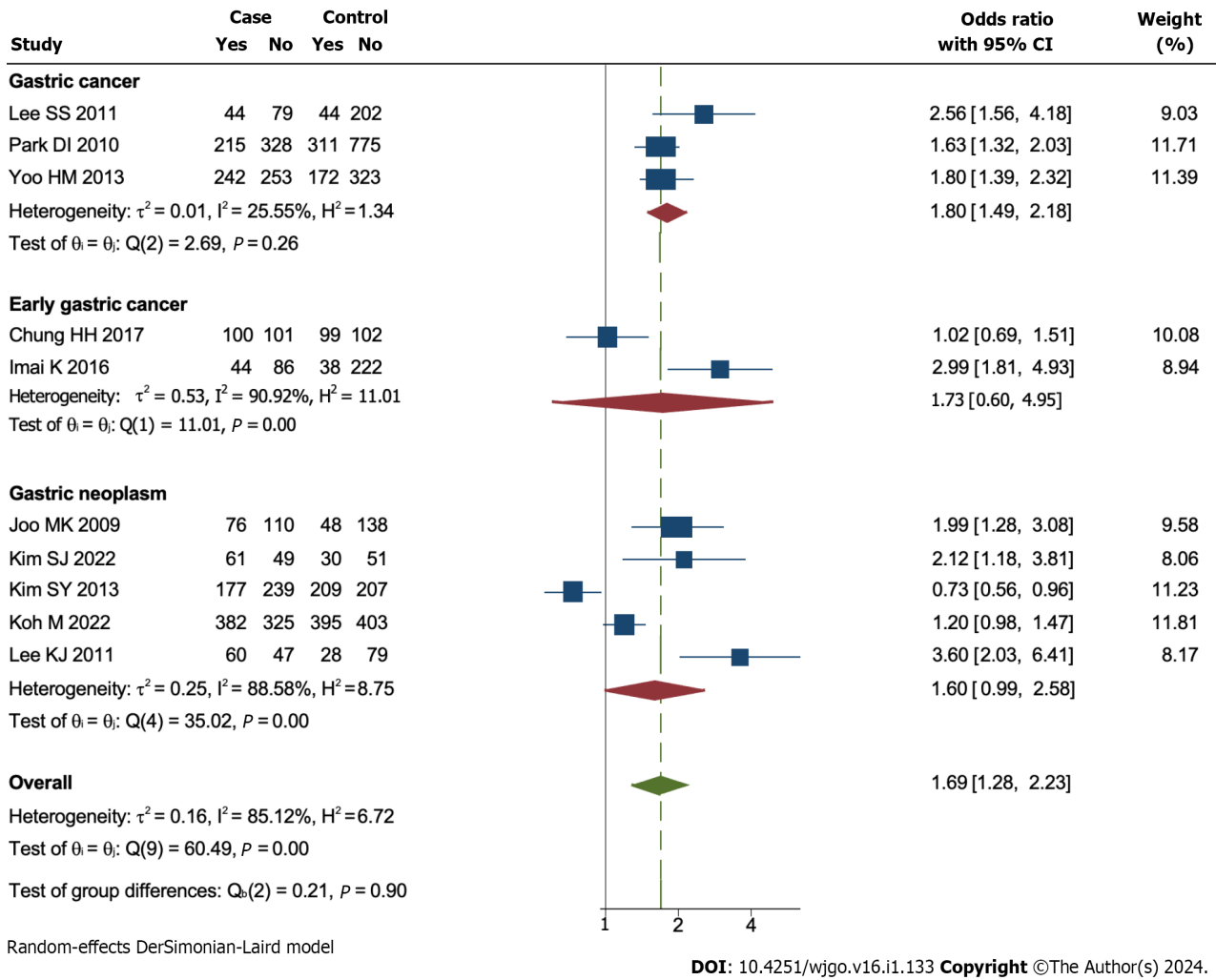


Figure 3 Subgroup analysis according to difference kinds of gastric neoplasms. 95%CI: 95% confidence interval.

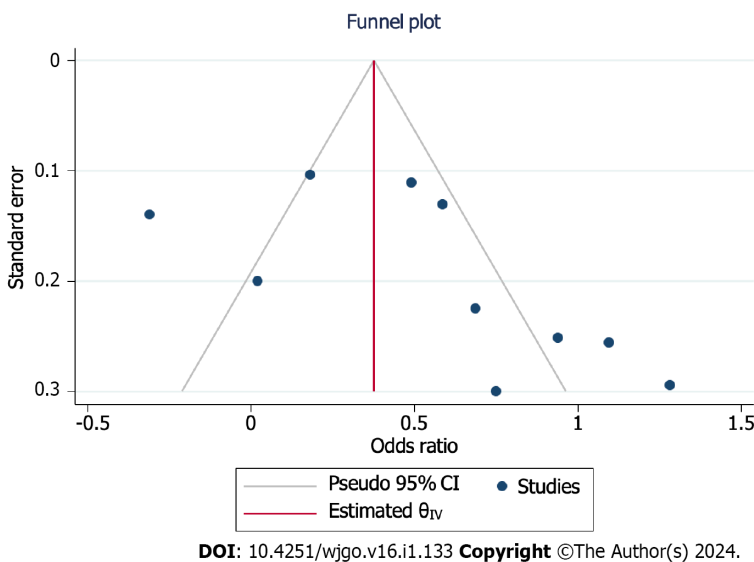


Figure 4 Funnel plot. 95%CI: 95% confidence interval.

Other primary neoplasms are common in GN patients, with the incidence ranging from 3.4% to 42.2% [23-26]. CRN is the main neoplasm type of synchronous and homologous neoplasms [23,24]. Although early CRN and EGN share many similarities, they have different tumor immune signatures and drug responses, which pose significant challenges for advanced CRN and GN [27-30]. Early detection of neoplasms is obviously an important way to improve patient prognosis; therefore, regular medical checkups are needed for GN patients.

Several previous studies have revealed an association between GN and CRN. Imai *et al* [11] reported that EGC is a risk factor for CRC. Others have demonstrated that GC patients are at high risk for not only CRC but also all CRN [15,31,32]. Moreover, colonoscopy might be considered for patients with benign GN [12-14]. However, both Chung *et al* [16] and Koh *et al* [18] revealed that the prevalence of CRN was not significantly different between patients with and without GN. Based on the above findings, our study was designed to address the current controversy and provide more valuable suggestions for GN patients.

In addition to GN, *H. pylori* is thought to promote the development of CRN [33,34]. *H. pylori* can not only increase the risk of GN and GC by damaging the mucosal barrier but also affect intestinal mucosa through the secretion of gastrin [35,36]. Moreover, *H. pylori* can alter the immune signature by reducing T cells, pro-carcinogenic STAT3 signaling, and goblet cells, which have proinflammatory and degrading microbial effects, contributing to neoplasm development [37,38]. Reducing the incidence of GN and CRN through eradication of *H. pylori* has been demonstrated in both mice and humans [37].

Another hypothesis is associated with genetic alteration and microsatellite instability [39,40]. Mutations in the hMSH2 and hMLH1 genes, which mainly participate in repair of base-pair mismatches during DNA replication, play an important role in the occurrence of GN and CRN [39]. In addition, the same K-ras, p53, and APC genes mutations are detected in both GN and CRN [40]. These genetic correlations between CRN and GN support the higher risk of CRN in GN patients, as indicated in the current analysis.

This study addresses a current pressing question and provides reliable evidence for GN patients to receive regular colonoscopy. Since almost all the patients were Korean, the results are particularly applicable to Korea. Although there were important discoveries revealed by this study, there are some limitations. The results are limited in terms of region and ethnicity, and there is some publication bias. Therefore, more prospective case-control studies conducted worldwide are needed for further investigation.

CONCLUSION

Patients are recommended to receive colonoscopy when diagnosed with GN, especially those diagnosed with GC.

ARTICLE HIGHLIGHTS

Research background

Gastric cancer (GC) and colorectal cancer (CRC) are the fifth and third most common cancer worldwide, respectively. Nowadays, GC is reported to have a potential predictive value for CRC, especially for advanced CRC.

Research motivation

Colonoscopy is not commonly received by GC patients. Whether colonoscopy is necessary for GC patients is unclear.

Research objectives

The objectives of this study are patients diagnosed with gastric neoplasms (GNs).

Research methods

This study conducted a pooling-up analysis and subgroup analysis by STATA SE 16.0 software.

Research results

Colorectal neoplasm (CRN) was detected significantly more frequently in GN patients than controls.

Research conclusions

GC patients were suggested to receive colonoscopy before surgery.

Research perspectives

This study first systematically reviewed the prevalence of CRNs in patients with and without GNs.

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FOOTNOTES

Co-first authors: Xu-Rui Liu and Ze-Lin Wen.

Author contributions: Peng D conceived, designed and refined the study protocol; Liu XR and Wen ZL were involved in the data collection; Liu XR and Wen ZL analyzed the data; Liu XR and Wen ZL drafted the manuscript; All authors were involved in the critical review of the results and have contributed to, read, and approved the final manuscript. Liu XR and Wen ZL contributed equally to this work as co-first authors. The reasons for designating Liu XR and Wen ZL as co-first authors are threefold. First, the research was performed as a collaborative effort, and the designation of co-first authorship accurately reflects the distribution of responsibilities and burdens associated with the time and effort required to complete the study and the resultant paper. This also ensures effective communication and management of post-submission matters, ultimately enhancing the paper's quality and reliability. Second, the overall research team encompassed authors with a variety of expertise and skills from different fields, and the designation of co-first authors best reflects this diversity. This also promotes the most comprehensive and in-depth examination of the research topic, ultimately enriching readers' understanding by offering various expert perspectives. Third, Liu XR and Wen ZL contributed efforts of equal substance throughout the research process. The choice of these researchers as co-first authors acknowledges and respects this equal contribution, while recognizing the spirit of teamwork and collaboration of this study. In summary, we believe that designating Liu XR and Wen ZL as co-first authors of is fitting for our manuscript as it accurately reflects our team's collaborative spirit, equal contributions, and diversity.

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Informed consent statement: The data was accessed in the database and all patients signed informed consent.

Conflict-of-interest statement: The authors declare that there are no conflicts of interests.

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STROBE statement: The authors have read the STROBE Statement – checklist of items, and the manuscript was prepared and revised according to the STROBE Statement – checklist of items.

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