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Observational Study

Colonoscopy plays an important part in detecting colorectal neoplasm for patients with gastric neoplasm

Liu XR *et al.* Colonoscopy detects CRC in GC.

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

This study compared the prevalence of colorectal neoplasm in patients with gastric neoplasm and in healthy controls to evaluate the necessity of colonoscopy for gastric neoplasm patients.

METHODS

Four databases including PubMed, Embase, the Cochrane Library, and Ovid were used to performing search strategy on May 2nd, 2023. The prevalence of colorectal neoplasm and baseline characteristics were compared between the neoplasm group and the control group. Continuous variables were expressed as mean difference and standard deviation. The relationship of categorical variables in two groups were expressed as odds ratio and 95% confidence intervals. Subgroup analysis according to different kinds of gastric neoplasms were conducted for more in-depth analysis. The results of this

current study were represented by forest plots. Publication bias was evaluated by a funnel plot. All data analyses above were performed by STATA SE 16.0 software.

RESULTS

A total of 3018 patients with gastric neoplasm and 3905 healthy controls (age- and sex-matched) were enrolled for analysis. After comparing the prevalence of colorectal neoplasm between the two groups, colorectal neoplasm was detected significantly more frequently in gastric neoplasm patients than controls (OR=1.69, 95%CI=1.28 to 2.23, I^2=85.12%, P = 0.00), especially in patients with gastric cancer (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 (OR=2.31, 95%CI=1.26 to 4.22, I^2=87.35%, P = 0.00) were related to the prevalence of colorectal neoplasm. As for patients in the gastric neoplasm group, body mass index (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 colorectal neoplasm, respectively.

CONCLUSION

Patients are recommended to receive colonoscopy when diagnosed gastric neoplasm, especially GC patients with low body mass index 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.

INTRODUCTION

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

Similar to GC, colorectal cancer (CRC) is a gastrointestinal malignant disease which develops from colorectal polyps[5]. Early colorectal polyps can be removed under the colonoscopy, which significantly decrease the incidence of CRC[6-7]. Some characteristics including age, male sex, family history, obesity, and red meat intake have been reported to have a predictive value for colorectal neoplasm (CRN) (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 a potential predictive value for CRN, especially for advanced CRN[11-17]. However, some other studies demonstrated that colonoscopy surveillance was not recommended for all GN patients[18-20]. Therefore, this study attempts 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 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[21].

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 gastric cancer, gastric carcinoma, gastric neoplasms, 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 NC 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, BMI, diabetes, hypertension, alcohol, and smoking were collected. Moreover, for patients with CRN, 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 CRN in the whole patients and in the GN patients.

Quality Assessment

We used NOS score to assess the quality of included studies[22]. 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 (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[23-24]. 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 gastric cancer (EGC), and the other one reported early gastric neoplasm (EGN). After receiving colonoscopy, CRN 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 GN 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 CRN 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=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 higher risk of CRN, especially for GC patients. Moreover, age and male were found to be independent risk factors for CRN in the whole patients, and BMI and smoking were protective and risk factors in GN patients, respectively.

Other primary neoplasms are common in GN patients, with the incidence ranging from 3.4% to 42.2%[25-28]. CRN is the main neoplasm type of synchronous and homologous neoplasms[25-26]. Although early CRN and EGN share many similarities, they have different tumor immune signature and drug responses, which pose significant challenges for advanced CRN and GN[29-32]. Early detection of neoplasms is obviously an important way to improve patients' prognosis, therefore, regular medical checkups are needed for GN patients.

Several previous studies revealed an association between GN and CRN[11-20]. Imai K *et al* reported that EGC was a risk factor for CRC[11]. Some others demonstrated that GC patients were at high risk for not only CRC, but all CRNs[15-17]. Moreover, colonoscopy was thought to be considered in patients with benign GN[12-14]. However, both Chung HH *et al* and Koh M *et al* revealed that the prevalence of CRN was not significantly different between patients with and without GN[18-19]. Based on the above findings, our study was designed to address the current controversy and provide more valuable suggestions for GN patients.

Except for GN, *H. pylori* are also 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 immune signature by reducing T cells, pro-carcinogenic signal transducer and activator of transcription 3 (STAT3) signalling, and goblet cells, which

have an effect of pro-inflammatory and degrading microbial, then contributing to the neoplasm development[37-38]. Reducing the incidence of GN and CRN through the 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]. The mutations of hMSH2 and hMLH1 genes play an important part in the occurrence of GN and CRN, which mainly take part in the repair of base-pair mismatches during deoxyribonucleic acid (DNA) replication[39]. In addition, the same mutations in K-ras, p53, and adenomatous polyposis coli (APC) genes 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 this current analysis.

This study addressed a current pressing question and provided more reliable evidence for GN patients to receive regular colonoscopy. Since almost all the patients were Korean, the results were particularly applicable to Korea. Although there were important discoveries revealed by this study, there were some limitations. The results were limited in terms of region and ethnicity and there was some publication bias. Therefore, more prospective case-control studies conducting over the world were 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.

Research methods

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

Research results

Colorectal neoplasm was detected significantly more frequently in gastric neoplasm patients than controls.

Research conclusions

Gastric cancer patients were suggested to receive colonoscopy before surgery.

Research perspectives

This study first systematically reviewed the prevalence of colorectal neoplasms in patients with and without gastric neoplasms.

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