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¹ Clinical manifestation, lifestyle, and treatment patterns of chronic erosive gastritis: A multicenter real-world study in China

Yang YY *et al.* A real-world study of CEG

Abstract

BACKGROUND

Although chronic erosive gastritis (CEG) is common, its clinical characteristics have not been fully elucidated. The lack of consensus regarding its treatment has resulted in varied treatment regimens.

AIM

To explore the clinical characteristics, treatment patterns, and short-term outcomes in CEG patients in China.

METHODS

We recruited patients with chronic non-atrophic or mild-to-moderate atrophic gastritis with erosion based on endoscopy and pathology. Patients and treating physicians completed a questionnaire regarding history, endoscopic findings, and treatment plans as well as a follow-up questionnaire to investigate changes in symptoms after 4 wk of treatment.

RESULTS

Three thousand five hundred sixty-three patients from 42 centers across 24 cities in China were included. Epigastric pain (68.0%), abdominal distension (62.6%), and postprandial fullness (47.5%) were the most common presenting symptoms. Gastritis was classified as chronic non-atrophic in 69.9% of patients. Among those with erosive lesions, 72.1% of patients had lesions in the antrum, 51.0% had multiple lesions, and 67.3% had superficial flat lesions. In patients with epigastric pain, the combination of a

mucosal protective agent (MPA) and proton pump inhibitor was more effective. For those with postprandial fullness, acid regurgitation, early satiety, or nausea, a MPA appeared more promising.

CONCLUSION

CEG is a multifactorial disease which is common in Asian patients and has non-specific symptoms. Gastroscopy may play a major role in its detection and diagnosis. Treatment should be individualized based on symptom profile.

Key Words: Chronic erosive gastritis; Symptom; Endoscopic findings; Treatment pattern; Real-world

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Core Tip: This multicenter study is the first real-world observational study to explore lifestyle characteristics, symptoms, endoscopic findings, treatment patterns, and short-term outcomes in patients with chronic erosive gastritis in China. Our findings suggest that it is a multifactorial disease influenced by lifestyle, obesity, infection, emotion, and mood. Epigastric pain, abdominal distension, and postprandial fullness were the most common initial symptoms, which are non-specific. Therefore, gastroscopy may be valuable for detection and diagnosis. Individualized treatment based on symptom profile is crucial.

INTRODUCTION

Chronic gastritis is a common illness that affects billions of individuals worldwide^[1,2]. Among the different types, chronic erosive gastritis (CEG) is the most common. In 2014, the Chinese Chronic Gastritis Research group conducted a nationwide multicenter study that enrolled 8892 patients with chronic gastritis from 33 centers across 10 cities; 49.4% of patients were diagnosed with superficial gastritis and 42.3% with erosive gastritis, which indicated that chronic superficial gastritis and CEG are the most common endoscopic findings in Chinese patients^[3]. Although CEG does not carry a risk of cancer, it causes histological changes in the gastric mucosa and various gastrointestinal (GI) symptoms that may result in decreased quality of life.

According to the Sydney System for the classification of gastritis, chronic gastritis can be divided into non-atrophic and atrophic types based on endoscopic and pathological evaluations^[4]. The topographical patterns of chronic gastritis range from antrum-predominant to corpus-predominant gastritis or pangastritis^[5]. Erosive gastritis is defined as any type of gastritis accompanied by erosions in the mucosa, which are identified as either flat or minimally depressed white spots surrounded by a reddish area that may be accompanied by superficial bleeding or small nodules with central umbilication that mimics octopus suckers^[6]. In general, erosive gastritis involves inflammatory mucosal damage that can lead to ulceration or bleeding^[7,8]. Although gastric carcinogenesis and peptic ulcers have attracted considerable research attention over the past decade, few studies have focused on CEG.

Whether the pathogenesis of erosive gastritis involves elevated production of gastric acid or is related to weakened mucosal defenses has been debated for decades^[6,9]. Although *Helicobacter pylori* (*H. pylori*) infection^[1,10], stress^[11], and obesity^[7] are potentially correlated with CEG incidence, further evidence is needed. Furthermore, the impact of medications such as non-steroidal anti-inflammatory drugs (NSAIDs) and warfarin on CEG remains unclear^[12,13]. CEG risk factors, presentation, endoscopic and histopathological findings, therapeutic options, and treatment effects remain largely controversial. As a result, treatment practices vary. This study was conducted to aid in

understanding the clinical and lifestyle ¹ characteristics, treatment patterns, and short-term outcomes of CEG in Chinese patients.

MATERIALS AND METHODS

Patient selection

This real-world, multicenter, prospective, observational cohort study was conducted in 42 participating centers in 24 cities in China from April 2019 to December 2019. The study flow chart is shown in Figure 1.

Patients aged 18 to 70 years with a diagnosis of ¹ chronic non-atrophic or mild-to-moderate atrophic gastritis with erosions based on both endoscopic and pathological evaluations were eligible for inclusion. We excluded patients with any of the following criteria: (1) Chronic atrophic gastritis with intraepithelial neoplasia; (2) other mucosal lesions, such as gastric ulcers; (3) diagnosis of dementia, delirium, severe mood disturbance, or other mental disorder; (4) diagnosis of severe cardiac or cerebrovascular disease; (5) malignancy that required ongoing treatment; (6) history of subtotal gastrectomy; (7) history of previous endoscopic procedure such as endoscopic submucosal dissection or endoscopic mucosal resection; (8) pregnancy; or (9) any other condition that was considered unsuitable for the study. Erosive gastritis was determined by endoscopy according to the Sydney System and 2017 Chinese consensus on chronic gastritis^[14]. ⁴ All patients provided written informed consent. The study protocol was approved by the ethics committees of all participating institutions (Clinical registration number: ChiCTR2100047690).

Study design

Patients were asked to complete the first part of a baseline questionnaire, which contained questions regarding lifestyle, other medical conditions, medications, and major GI symptoms and their severity, with the help of physicians. Each symptom was graded as 0 (non-existent), 1 (mild and occasional), 2 (obvious and frequent, partially disturbing daily life), or 3 (severe, disturbing daily life). Physicians then independently

completed the second part of the questionnaire, which contained information regarding endoscopy findings and treatment. Four weeks later, patients completed a follow-up questionnaire, which contained questions regarding medication compliance and major GI symptoms and their severity with the help of medical assistants, either in the clinic or by telephone interview.

Clinical effect evaluation

The severity of symptoms was scored at the time of enrollment and during follow-up. Symptoms included epigastric pain, abdominal distension, postprandial fullness, early satiety, acid regurgitation, nausea, belching, vomiting, and others. Clinical effectiveness of treatment was defined as a decrease in symptom score. Participants were categorized into four groups according to treatment strategy: Mucosal protective agent (MPA), proton pump inhibitor (PPI), MPA + PPI, and MPA + PPI + prokinetic drug (PD).

Statistical analysis

Categorical variables are presented as absolute values with relative frequencies. Comparisons of categorical variables were performed using the chi-square test or Fisher's exact test as appropriate. Odds ratios (ORs) with 95% confidence intervals (95% CIs) were calculated using logistic regression and adjusted for age and sex. Statistical analyses were performed using SAS software version 9.3 (SAS Institute Inc., Cary, NC, United States). All tests were two-sided. $P < 0.05$ was considered significant.

RESULTS

Physician characteristics

A total of 111 physicians were randomly selected from a panel of gastroenterologists from the participating centers. Sixty-one (55.0%) were men and fifty (45.0%) were women. The demographic distribution of each participating center is shown in Supplementary Figure 1.

Patient characteristics

The data of 3563 patients were included for analysis. Patient demographics are shown in Supplementary Figure 1. Patients aged between 40 and 60 years comprised 52.7% of the patients and 49.5% were men. Few patients reported comorbidities, although 310 (8.7%) had a family history of malignancy (Table 1).

Lifestyle

Two-thirds of patients (66.2%) had no history of smoking; 29.4% and 4.4% were current or former smokers, respectively. Half (50.1%) had no history of alcohol consumption, whereas 45.3% and 4.6% were current or former drinkers, respectively. Regarding dietary habits, 66% of patients ate a regular diet and 69.8% never drank coffee. Detailed dietary preferences are shown in Table 1. Almost half of patients (47.1%) slept ≥ 7 h per night on average and 32.8% reported irregular sleep (Table 1).

Medication

NSAIDs were the most commonly used medication (8.3%). Anticoagulation drugs and corticosteroids were used by 4.6% and 2.0% of patients, respectively (Table 1).

Stress and mood

A relatively high proportion of patients reported stress or mood issues: 27.3% of patients felt stressed, 10.8% of patients underwent major life events in the previous 6 months, 24.3% of patients felt depressed, and 31.9% suffered from anxiety (Table 1).

H. pylori infection

Among the 2922 patients who underwent *H. pylori* testing, 24.8% were positive (Table 1).

Initial symptoms and endoscopic findings

Data regarding initial symptoms and endoscopic findings were collected through history taking and gastroscopic reports. Eight major symptoms and their severity were evaluated. Symptom duration varied: 26.7% of patients had symptoms for less than 3 months and 34.7% had symptoms for more than 1 year (Figure 2A). The most common symptoms were epigastric pain, abdominal distension, and postprandial fullness. Symptoms and their severity were similar between non-atrophic gastritis patients and all patients (Figure 2, Supplementary Figure 2, Supplementary Tables 1 and 2). Among patients with erosions, 72.0% were diagnosed with chronic non-atrophic gastritis, 22.5% with chronic mild atrophic gastritis, and 5.5% with chronic moderate atrophic gastritis. Most patients had erosions in the gastric antrum. Slightly more than half (51.0%) had a single lesion and 67.3% had superficial flat lesions (Table 2).

Treatment patterns and efficacy

Treatment patterns are shown in Table 3. Lifestyle instructions without medication were prescribed in 10.3% of patients; 89% received a drug or drug combination. The most frequently used regimens were MPA + PPI (35.24%), MPA (12.27%), PPI (10.17%), and MPA + PPI + PD (9.45%). The effectiveness of these four treatment regimens against each symptom is shown in Table 4. Table 5 shows the same with patients stratified according to *H. pylori* status. Treatment effectiveness was generally lower in *H. pylori*-positive patients. Effectiveness was higher in the MPA group than the PPI group for postprandial fullness (48.7% vs 32.6%), early satiety (36.7% vs 18.2%), nausea (34.4% vs 18.8%), and epigastric pain (55.9% vs 47.7%). Effectiveness was higher in the PPI + MPA group than the PPI group for epigastric pain (66.7% vs 47.7%) and acid regurgitation (41.4% vs 31.4%). For abdominal distension and belching, effectiveness was highest in the PPI + MPA + PD group. Comparisons between groups after adjusting for sex and age are shown in Table 6.

DISCUSSION

Previous studies have suggested that erosions are common in chronic gastritis, especially Asian patients. In a multicenter chronic gastritis survey, 42.3% of patients were found to have CEG of varying severity^[3]. Another multicenter study conducted in France that enrolled 3287 patients with upper GI bleeding revealed that 11.8% of patients aged < 75 years and 13.9% of patients aged > 75 years had gastroduodenal erosions^[8]. However, there is currently insufficient data and evidence regarding CEG risk factors, symptoms, endoscopic and pathologic characteristics, and treatment strategies^[15]. As a result, treatment patterns vary extensively. Moreover, evidence regarding CEG treatment outcomes is limited, especially regarding symptom improvement. Therefore, we conducted this study, which is the first real-world observational and non-interventional study in China to explore lifestyle characteristics, symptoms, endoscopic findings, treatment patterns, and short-term outcomes in patients with CEG.

In regard to patient characteristics, CEG did not show a sex predominance. Furthermore, contrary to our expectations, more than half of the patients with erosions had no history of alcohol consumption or smoking, and more than 60.0% ate a regular diet and had normal or healthy diet preferences. However, a considerable proportion of patients exhibited mood problems. Specifically, 27.3% of patients felt stressed, 24.3% felt depressed, and 31.9% felt anxious, which suggested that mood disturbances may play a role in the development of erosions. Treatment of stress-induced gastritis and gastric ulcers in the intensive care unit setting has been discussed previously^[11]; however, the relationship between daily life stress and CEG has not been fully ascertained. Our results and those of previous studies suggest that CEG is a multifactorial disease which is influenced by lifestyle, obesity, infection, emotion, and mood. The correlation between a single factor, such as dietary habits, and disease incidence remains unclear and further studies are warranted.

The FUTURE study revealed that among patients with chronic symptomatic gastritis, 48.2% experienced heartburn, 68.0% had epigastralgia, and 67.5% had epigastric fullness. These were the most common symptoms^[16]. In our study, the most common

symptom was epigastric pain (68.0%), followed by abdominal distension (62.6%), postprandial fullness (47.5%), acid regurgitation (43.4%), belching (39.6%), early satiety (30.5%), nausea (26.7%), and vomiting (13.9%); most of these were mild or moderate in severity. To further clarify the symptom profile of erosive gastritis, we compared the ratios of different symptoms in all patients, which were comparable between those with chronic non-atrophic gastritis and those with chronic atrophic gastritis. Epigastralgia, epigastric burning, postprandial epigastric fullness, and early satiation are typical symptoms of functional dyspepsia^[17]. The symptoms of CEG are non-specific and similar to those of dyspepsia. Differentiating these two diseases is crucial. A recent meta-analysis indicated that the prevalence of functional dyspepsia is higher in Western countries than in Asian countries^[18]. Moreover, questions have been raised regarding the inconsistent symptom clusters for functional GI disorders in China^[19]. Thus, we speculate that the lack of consensus poses difficulties in identifying CEG, which may contribute to the disparate prevalence between Asian and Western countries. Previous studies have demonstrated that the prevalence of CEG is not considered low in China and other Asian countries, which suggests that gastroscopy for patients with the above symptoms may help physicians detect and diagnose CEG in Asian patients.

Current mainstream treatment options for CEG include lifestyle guidance, MPAs, PPIs, and other symptomatic treatments. Several studies have demonstrated that geranylgeranyl acetone treatment is more effective than cimetidine for chronic gastritis-associated erosions and petechial hemorrhage^[20]. In addition, rebamipide had a stronger suppressing effect on mucosal inflammation and provided greater symptom relief in CEG patients than sucralfate^[10]. Furthermore, famotidine is effective in relieving abdominal symptoms in chronic symptomatic gastritis^[16]. For *H. pylori*-associated gastritis, anti-*H. pylori* therapy is recommended and accepted by physicians^[21,22]. However, a significant number of patients in our study were not treated using anti-*H. pylori* regimens and *H. pylori*-positive patients consistently exhibited lower symptom relief rates. Treatment of CEG varies across different centers^[10,23], which is partially because of a lack of consensus and lack of treatment guidelines. However,

high-level evidence evaluating the efficacy of existing treatment regimens is currently limited. In our study, PPIs and MPAs were used by 69.9% and 66.8% of patients, respectively, and 31.6% received combination treatment. Further studies comparing relief of the various symptoms between PPI, MPA, PPI + MPA, and PPI + MPA + PD may provide valuable information for selecting the most appropriate drug regimen. If epigastric pain is the predominant symptom, a MPA + PPI may provide a better response than a PPI or MPA alone. If abdominal distension is the predominant symptom, MPA may provide a slightly superior response than PPI; however, combining the two did not offer an additional benefit. Nonetheless, adding a PD to a combination of an MPA and a PPI seemed to provide greater symptom relief. If postprandial fullness, early satiety, or nausea are the most notable symptoms, the use of an MPA may be the optimal choice. When symptoms are predominantly related to acid reflux, a PPI or PPI + MPA are more effective. For patients whose predominant complaint is dyspepsia, treatment with an MPA is recommended; adding a PD may provide a better response in some cases. Our results demonstrate that individualized treatment based on symptom profile is crucial for patients with CEG.

This study is subject to several limitations. First, the absence of a control group comprising healthy individuals limits our capacity to robustly identify risk factors. Second, follow-up was only a month. While this timeframe is adequate for preliminary assessment of therapeutic responses, it is inadequate to provide a comprehensive understanding of long-term disease progression or sustainability of treatment effects. It is imperative for future studies to incorporate longer follow-up periods to thoroughly evaluate the long-term impact of treatment on symptoms, endoscopic findings, and histopathological changes and identify any late-onset adverse effects or diminished effectiveness.

CONCLUSION

We conducted the first ¹ multicenter real-world study to assess clinical characteristics, treatment patterns, and short-term outcomes in patients with CEG in China. The

development of CEG is likely a multifactorial process. ¹ Epigastric pain, abdominal distension, and postprandial fullness were the most common initial symptoms. CEG is relatively common in Asians and clinical symptoms are non-specific. Therefore, gastroscopy may be valuable for CEG detection and diagnosis. Our comparisons of symptom relief between different treatment strategies should provide useful information to fellow clinicians regarding treatment selection. Patients with acid reflux symptoms may respond best to a PPI or PPI + MPA, whereas an MPA may be more effective for those with dyspepsia; in some cases, combination therapy with a PD may also be effective. Patients testing positive for *H. pylori* experience better symptom relief when anti-*H. pylori* therapy is used. Taken together, our study highlights the need to individualize CEG treatment based on symptom profile.

ARTICLE HIGHLIGHTS

Research background

This multicenter observational study delves into chronic erosive gastritis (CEG) in China, a condition whose clinical characteristics and treatment approaches have been inadequately explored. It illuminates the commonality of CEG and its varied clinical presentations, emphasizing the necessity of a better understanding of its treatment patterns and short-term outcomes.

Research motivation

Addressing the pressing need for clarity in the clinical management of CEG, the study seeks to demystify the disease's symptomatology, lifestyle influences, endoscopic findings, and treatment efficacies. It aspires to enhance the understanding of CEG's multifactorial nature and guide more effective, personalized treatment strategies.

Research objectives

¹ To explore the clinical characteristics, treatment patterns, and short-term outcomes in CEG patients in China.

Research methods

Employing a prospective observational cohort approach, the study involved patients ¹with chronic non-atrophic or mild-to-moderate atrophic gastritis with erosions. It combined questionnaires, endoscopic and pathological evaluations, and follow-up assessments to evaluate treatment responses and lifestyle characteristics, offering a comprehensive view of CEG's clinical landscape.

Research results

The study reveals the predominance of symptoms like epigastric pain, abdominal distension, and postprandial fullness in CEG, with treatments like mucosal protective agents and proton pump inhibitors showing varying effectiveness. It underscores the non-specific nature of CEG symptoms and the importance of gastroscopy in diagnosis, especially in Asian populations.

Research conclusions

This investigation proposes new insights into CEG, highlighting its multifactorial etiology influenced by lifestyle, obesity, infection, and emotional factors. The study's findings advocate for individualized treatment strategies based on specific symptom profiles, enhancing treatment efficacy.

Research perspectives

Future research should focus on long-term outcomes of CEG treatments, the sustainability of therapeutic effects, and the identification of potential late-onset side effects. Extending the understanding of CEG's long-term progression and refining treatment approaches are crucial steps forward.

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Figure 1 Studyflow chart.

Figure 2 Initial symptoms and their severity. A: All patients ($n = 3563$); B: Chronic non-atrophic gastritis patients.

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