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Clinical Significance and Outcome of Gastric Mucosal Erosions: A Long-Term Follow-Up Study

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Our purpose was to evaluate the long-term clinical significance of gastric erosions. A series of 117 patients with gastric erosions without peptic ulcer disease, and matched controls were studied in 1974–1979. All available subjects were reinvestigated 17 years later, including detailed clinical history and laboratory analysis. At follow-up, erosions were still more prevalent (39%; 20/50) in the erosion group than in the controls (11; 7/66). In *Helicobacter pylori*–positive participants, peptic ulcer or a scar was more common in the erosion group (17%; 9/52) than in controls (5%; 3/66). Overall malignancy rate was higher in controls (15%; 17/117) than in erosion group (5%; 6/117; $P = .025$), but no other differences were seen between the groups or related with current erosion. We conclude that a significant proportion of gastric erosions are chronic or recurrent but mostly without serious complications. However, *H. pylori*–positive patients with erosions have significant risk to develop a peptic ulcer.

KEY WORDS: gastric erosions; long-term; follow-up; *Helicobacter pylori.*

Gastric erosions are a common finding in both dyspeptic patients and in asymptomatic volunteers (1). Clinically, the most obvious importance of gastric erosions is that they may bleed. They are the cause of upper gastrointestinal bleeding in up to 16–23% of patients studied for bleeding (2, 3). Erosions can be short term, recurrent, or chronic (4–7). Except for a bleeding tendency, gastric erosions are considered harmless. However, being a destructive and inflammatory process, chronic or recurrent erosions in gastric mucosa might be associated with clinically important local, distant, or systemic complications. Nevertheless, recent scientific research has largely ignored chronic gastric erosions and no long-term endoscopic follow-up studies of the clinical significance of these lesions have been published.

In the present study, we examined erosion patients and their controls after a mean follow-up of 17 years to determine the long-term clinical significance and outcome of erosions. The relationship of the type and location of erosion with recurrence or persistence and the occurrence of local complications, such as ulcers or tumors, was analyzed. The association of erosions with abdominal symptoms and the basic blood chemistry was also analyzed to evaluate their significance in terms of experienced morbidity and systemic effects, respectively. Finally, we looked for associations between erosions and overall mortality and cancer morbidity.

MATERIAL AND METHODS

Patients. Patients were recruited from among those referred for elective gastroscopy for primary endoscopic evaluation of their abdominal symptoms from September 1, 1974 to

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August 31, 1979. The whole series consisted of 3837 patients (2080 men and 1757 women). Gastric erosions were diagnosed in 404 patients. The patients who had erosions concurrent with peptic ulcer disease ($n = 129$), a gastrointestinal disease requiring specific or urgent treatment ($n = 16$) or some serious disease ($n = 21$) were excluded. Another 121 patients had to be excluded because of inadequate cooperation, poor tolerance of gastroscopy, and difficulties in attending the follow-up examination or refusal to attend further examinations. Hence, 287 patients were excluded from the original series, leaving 117 patients (63 men and 54 women of mean age 48.9 $\pm$ 10.7 years) with erosion as the predominant finding. These 117 patients were included in present the study and invited for a reexamination in 1996. The same patients have been included in our two previous reprots (8, 9).

Controls. For each patient, a control of the same age ($\pm$5 years) and gender (except 1 woman instead of a man) was drawn prospectively from patients undergoing gastroscopy electively in the same department during 1979–1981 and not diagnosed as having gastric erosions, peptic ulcer disease, or any other severe disease of the gastrointestinal tract or other organs requiring immediate treatment. The control group consisted of 117 patients (62 men and 55 women of mean age 50.5 $\pm$ 12.1 years).

Endoscopy. Upper gastrointestinal endoscopy was done during both visits. The erosions were classified according to the dominant type as follows (8): type I, complete erosion—erosion elevated above the surrounding mucosa and surrounded by a marginal wall; type II, incomplete erosion—erosion located on even mucosa and often surrounded by a reddish margin; or type III, hemorrhagic-erosive gastritis—several small hemorrhagic erosions on even mucosa. All other endoscopic findings were also recorded according to a protocol. Two biopsies were taken from the greater curvature of the antrum and the corpus.

Helicobacter pylori. *H. pylori* infection was diagnosed from biopsy specimens taken at both visits from the antral and body mucosa using Giemsa and hematoxylin–eosin staining.

Symptoms and Other Clinical Data. At both visits, all patients were interviewed by one of the investigators and pertinent anamnestic and clinical data from the local hospital were recorded using a questionnaire. A routine clinical abdominal status was taken and written down.

At both visits, we evaluated and inquired about the type and duration of abdominal pain as described (9). At the follow-up visit, the type of dyspepsia (reflux/ulcus/motility/nonspecific) was inquired about in detail (10). A patient history of diseases was recorded at each visit. Specifically, clinically identified gastrointestinal diseases, including gastrointestinal bleeding during the follow-up period, gastric, or other abdominal surgery, were recorded.

At both visits, the use all medication for abdominal diseases or symptoms was inquired about. The time of the most recent use of nonsteroidal anti-inflammatory drugs (NSAID) was registered (<24 hours, or 1–3, 4–7, or >7 days before endoscopy). Drugs for other diseases and the use of possible *H. pylori* eradication treatments were recorded. Family history of gastric cancer, gastric or duodenal ulcers and other gastrointestinal diseases in first-degree relatives was registered.

Blood Chemistry. Erythrocyte sedimentation rate, leukocyte count, serum C-reactive protein, hemoglobin, creatinine, alanine aminotransferase, and alkaline phosphatase were measured at both visits by routine methods.

Occurrence of Malignancies, Mortality, and Causes of Death. Data were obtained from Statistics Finland (Helsinki, Finland). Data on the occurrence of malignant diseases was obtained from the Finnish Cancer Registry (Helsinki, Finland).

Statistical Analysis. The statistical analysis was made using statistical software in a personal computer (SPSS for Windows Release 11.5.1, SPSS Inc., Chicago, Illinois, USA). The χ^2 test and Fischer's 2-sided exact test were used. A probability of $P < .05$ was considered statistically significant in the 2-tailed tests. Kaplan-Meier log-rank test was used to calculate mortality and malignancy data.

Ethical Considerations. The study was approved by the Ethical Committee of the Medical Faculty of the University of Oulu.

RESULTS

The 117 patients and 117 controls in the original series were included in the analysis of mortality and the occurrence of malignant tumors. At the follow-up visit in 1996, 54 (46% of the original series; 30 men and 24 women of mean age 62.6 $\pm$ 8.4 and 64.8 $\pm$ 8.0 years, respectively) of the 117 erosion patients studied in 1974–1979 were available for an interview, clinical assessment, and routine blood tests. The mean follow-up times were 18.8 years for the patients and 16 years for the controls. Of the erosion patients not available for follow-up, 27 had died and 36 were unable to attend. In the control series, 70 (60% of the original series, 39 men and 31 women of mean age 60.8 $\pm$ 8.8 years and 64.1 $\pm$ 9.9 years, respectively) of the 117 controls were available for an interview, clinical assessment, and routine blood tests in 1996. Of the original controls, 26 had died and 21 were unable to attend. Two patients and 3 controls refused endoscopy. Finally, 52 patients and 67 controls could be reexamined endoscopically at follow-up.

Endoscopic Findings

One person in the control group had been gastrectomized (for gastric cancer) and was excluded from the analysis of the occurrence of erosions. Of the 52 patients in the erosion group, 20 (39 %) had gastric erosions on follow-up endoscopy. The type of erosion seen at follow-up was most often similar than in the primary visit 18 years earlier, but in a remarkable proportion (30%) the type had changed (Table 1). Of the controls, 11% (7/66) had gastric erosion at the follow-up endoscopy ($P = .001$ compared to the erosion group).

At follow-up, patients with erosion had an active peptic ulcer or the scar of a healed peptic ulcer (17 %; 9/52) more often as compared to the control group (5 %; 3/66; $P = .031$). There were no other significant differences between the patient and the control groups concerning other endoscopic findings (Table 2).

TABLE 1. EVOLUTION OF GASTRIC EROSIONS IN EROSION PATIENTS AND CONTROLS

First Visit Erosion Status	*Follow-Up Visit Erosion Status*					
	Erosion Any Type n *(%)*	*Type I* n *(%)*	*Type II* n *(%)*	*Type III* n *(%)*	*No Erosion* n *(%)*	*Total*
Patients (any type erosion)	20 (38)	6 (12)	11 (21)	3 (6)	32 (62)	52
Type I	6 (60)	4 (40)	1 (10)	1 (10)	4 (40)	10
Type II	14 (35)	2 (5)	10 (25)	2 (5)	26 (65)	40
Type III	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	2
Controls (no erosion)	7 (11)	2 (3)	5 (8)	0 (0)	59 (89)	66

Note. Erosion patients have been grouped according to the type of erosion at the initial visit.

Helicobacter pylori

At the first visit, the *H. pylori* status of 1 patient could not be assessed because of inadequate histologic sections and insufficient material for additional sections. At the first visit, the *H. pylori* positivity rate was similar in the whole erosion group (60%; 70 of 116) and in the controls (65%; 76 of 117; P = NS), and it was also true among those subjects available in follow-up studies (erosion group 65%; 32 of 49; controls 73%, 46/63; P = NS). Two patients in the erosion group and 3 controls were on anticoagulant therapy at the follow-up visit and no biopsies for *H. pylori* diagnosis could be taken. At the follow-up visit, 58% (29/50) of the patients in the erosion group and 52% (33 of 63; P = NS) of the controls were *H. pylori* positive. In the erosion group, the proportion subjects with erosions at the follow-up visit were similar in *H. pylori*-positive (according to first visit data; 41%; 13/32) and -negative (35%; 6/17; P = NS) subjects. Similarly, in the control group, the erosion rate at follow-up was not related to the presence (15%; 7/46) or absence of *H. pylori* (0%; 0/17; P = NS). With the exception of 1 control, all persons with duodenal or gastric ulcer or scar were *H. pylori* positive.

Symptoms and Other Clinical Data

At the first visit, upper abdominal pain was more common in the erosion group (100%; 54/54) than in the controls (91%; 64/70; $P = .035$). At the follow-up visit, 70% (37/53) of the patients in the erosion group and 70% (49/70) of the controls had dyspepsia or upper abdominal pain. Presence or type of erosions at follow-up showed no relation with symptoms.

Use of NSAIDs

The use of NSAIDs within 1 week before the first visit was more common in the erosion group (41%; 22/54) than in the control group (23%; 16/70; $P = .049$), but at the follow-up, the rate of use was similar in both the erosion (57%; 27/47) and the control groups (58%; 38/66). Neither was there any correlation with concurrent erosions. Most of patients of the erosion group with concurrent ulcer or scar at the follow-up visit (67%, 6/9) had recently used NSAIDs.

Surgical Operations and Other Diseases

Rate of gastric surgery was similar in both groups; 6% (3/54) of the patients in the erosion group and 1% (1/69) of controls having undergone gastric surgery (P = NS). One control patient had a fatal hemorrhage of gastric ulcer. Rheumatoid arthritis was more prevalent in the control group (10%; 7/69) than in the erosion group (0%; 0/54; $P = .018$), but none had erosions at the follow-up visit. No other significant differences were observed in the occurrence of other diseases. No significant differences emerged between the groups regarding diseases in close relatives.

Blood Chemistry

No significant differences were seen in laboratory parameters, including the blood hemoglobin concentration

TABLE 2. UPPER GASTROINTESTINAL ENDOSCOPY FINDINGS AT THE FOLLOW-UP VISIT

Finding	*Erosion group*	*Controls*
Active GU	3	0
Active DU	2	2
GU scar	2	0
DU scar	5	1
Esophagitis	8	4
Polyp	5	7
Operated stomach	5	5
Duodenitis	5	3
Loose hiatus	2	5
Hiatal hernia	1	2
Gastric retention	1	2
Esophageal heterotopy	2	0
Antral deformation	1	2

Note. Only the diagnoses with more than 1 case have been included. One patient could have one or more endoscopic findings. There were single cases of each of the following: gastric cancer (control); Barrett esophagus (1 patient, 1 control), submucosal tumor (1 patient, 1 control), Schatzki's ring (patient), pylorus stenosis (patient), antral nodularity (1 patient), angiodysplasia (1 control), candidal oesophagitis (1 patient), and a prepyloric prominent fold (1 patient). *Abbreviations:* GU, gastric ulcer; DU, duodenal ulcer.

between the erosion patients and controls in either visit, or between subjects with or without current erosion at the follow-up visit.

Occurrence of Malignancies, Mortality, and Causes of Death

The incidence of malignancy during the 16 years of follow-up was significantly lower in the erosion group (5%; 6/117) than the controls (15%; 17/117; $P = .0247$). There were 3 cases of lung cancer, 1 of kidney cancer, and 1 of prostate cancer in the erosion group; 1 patient had both a gastric carcinoid tumor and esophageal cancer. In the control group, there were 4 cases of breast cancer, 3 rectal, 2 uterine, 1 gastric, 1 lung, 1 ovarian, 1 prostate, 1 kidney, 1 skin, and 1 central nervous system cancer, as well as 1 unspecified carcinoma. Smoking habits did not correlate with the incidence of malignancy.

During the 16 years of follow-up, 19% (22 of 117) of the patients and 22% (26 of 117) of the controls died ($P =$ NS). Malignancy was the reason for 2 deaths (9%) in the patient group and 6 (23%) in the control group ($P =$ NS). Gastrointestinal hemorrhage caused 1 death in the control group.

DISCUSSION

This is the first very long-term endoscopic follow-up study on the clinical significance of gastric erosions. The results of about 17 years follow-up show that the erosions are persistent or recurrent in more than one third of the cases, and one sixth of erosion patients show development of peptic ulcer. However, gastric erosions without concomitant peptic ulcer are not otherwise associated with an increased risk of local complications or other morbidity as compared to dyspeptic patients without erosions. Our results therefore support the view that gastric erosions are often a chronic or recurrent, but clinically largely not a dangerous condition, except for significant peptic ulcer risk.

Our finding of the high prevalence of persistent or recurrent erosions is in agreement with previous follow-up studies of shorter duration. Our previous results of up to 6 years' follow-up showed that erosions are detectable for years in 34% of cases (4). Freise *et al.* (5) observed 64 erosion patients for $4\frac{1}{2}$ years, and 50% showed no change in the extent of erosions, whereas in 20% the erosions disappeared completely. Franzin *et al*. (6) followed up 49 erosion patients, and in 29% the erosions disappeared totally within 2 years of follow-up. Walk (7) also conducted a long-term follow-up study, arriving at a similar conclusion, but with a radiologic method and in a small series of patients.

Bleeding is one of the most important complications of gastric erosions (2, 3), but in the earlier long follow-up studies, there is no information about occurrence of bleeding (4–6). In our series, erosion patients had no clinical history of gastrointestinal bleeding during the follow-up and no differences between the groups or between the patients with and without concurrent erosion were seen in blood hemoglobin concentration at the second visit, indicating that clinically significant bleeding is rare. However, there were no hemorrhagic erosions (type III) as the predominant erosion type in the subjects available for follow-up, and the long-term outcome of these lesions, possibly more prone to significant bleeding, remains unknown. Furthermore, the occurrence of slight or temporary bleeding cannot be excluded without constant monitoring for occult fecal blood.

The type of erosion seems to be mostly stable, with about 70% of erosions presenting with the original type. The erosion type had, however, changed in about 30% of the cases, but the numbers of cases are too small for any analysis of evolutionary sequences. In our earlier follow-up for a maximum of 6 years, the type of erosions changed in only about 5% of cases (4).

None of our subjects had peptic ulcer in the first visit; all such patients were excluded. Interestingly, at the follow-up, 17% (9/52) of patients in the erosion group had developed an active ulcer or scar. All of them were *H. pylori* positive and most (67%; 6/9) had recently used NSAID medication. Our figures agree with the results of Freise *et al*., who found that 25% of erosion patients presented with ulcer during four and a half years (5). These results indicate that erosions, especially in *H. pylori*-positive patients or in patients using NSAIDs, are associated with a significant risk of peptic ulcers. On the other hand, *H. pylori* infection showed no significant association with the presence of erosions, and the results do not support an important role of *H. pylori* in the pathogenesis of chronic or recurrent gastric erosions. However, initial exclusion of erosion patients presenting with concurrent peptic ulcer may have caused exclusion of erosions with more evident etiologic association with *H. pylori.* Another factor explaining the absence of association with *H. pylori* in our material might be the observed high prevalence of the infection without any difference between the groups, which is likely related to the high prevalence of the infection in the Finnish population almost 30 years ago. Our data favor eradication of *H. pylori* in patients with gastric erosions.

The relation of gastric erosions to symptoms is largely unknown. All patients and controls were originally examined for dyspeptic symptoms or upper abdominal pain. At the first visit, the patients had slightly more often

upper abdominal pain than controls. At the follow-up visit, prevalence of symptoms was similar; 70% of both the patients in the erosion group and the controls had symptoms. Neither was any differences seen in the pattern of symptoms between the groups or related to concurrent erosions at the follow-up visit. In a recent study, Lehmann *et al.* noted gastric erosions in 8% of asymptomatic volunteers (1). These observations indicate that although the gastric erosions may be asymptomatic or related with dyspeptic symptoms or pain, the symptom pattern does not help in identification of a subject with erosions or erosions with a tendency for chronicity or relapse.

We did not see any differences in overall mortality between the patients in the erosion group and controls after 17 years of follow-up. No deaths were related to gastric erosions. However, significantly fewer of the erosion patients had diagnosed malignancies compared to the controls. The types of malignancy were diverse in both groups without any characteristic pattern. The low number of patients limits drawing any conclusion about the clinical significance or mechanisms of the observed negative association between erosions and malignancy, although some protective effect of NSAID use in erosion patients may be a factor.

In conclusion, our long-term follow-up study shows that a significant proportion of gastric erosions are chronic or recurrent. Overall clinical history of the subjects indicates that occurrence of chronic or recurrent gastric erosions are a condition mainly without major local or systemic consequences. However, peptic ulcers develop in about 20% of patients with erosions, and these patients should be treated for potential causes, such as *H. pylori* infection or use of NSAIDs.

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