Coexistent duodenal ulcer among patients with gastric carcinoma

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To examine the prevalence of coexistent duodenal ulcers among patients with gastric carcinoma in an otherwise intact stomach, we surveyed 604 endoscopically and pathologically diagnosed gastric carcinoma patients and thoroughly inspected their duodenums. Twenty-two (3,6%) of them had either active ulcers or scars in the duodenum. This prevalence was significantly less than that among 99 (16,4%) of 604 age- and gender-matched controls with endoscopically confirmed duodenal ulcers ($P < 0,0001$). Almost one-half of patients with coexistent cancer and duodenal ulcer experienced no change in abdominal symptoms when gastric cancer was diagnosed. Barium meal study appeared not to be sensitive enough to diagnose the coexistent ulcers. However, the nature of the lesions, including disease location, macroscopic appearance, chance of early cancer and metastasis, was no different in 22 patients with coexistent cancer and duodenal ulcer than in 582 patients with cancer alone. The present study suggests that although duodenal ulcer is unlikely to be a predisposing factor for gastric cancer, thorough screening by means of endoscopy is necessary in dyspepsic ulcer patients since duodenal ulcer and gastric cancer are not incompatible.

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Duodenal ulcer (DU) and gastric carcinoma (GC), both very common upper gastro-intestinal diseases, are extremely different with regard to gastric acid secretion in that DU is characterised by hypersecretion and GC by hyposecretion.[1,2] Although patients undergoing gastrectomy for peptic ulcer are often predisposed to GC later on, the probability of both diseases occurring concurrently in the same patient with an intact stomach is small.[3-6] Since this coexistence was first noted in 1916, 236 cases have been reviewed by Lewis and Woods.[7] Norfleet and Johnson[8] added another 77 cases in 1989. In Asia, Lee *et al.*[2] reported on 2 out of 715 DU patients who developed GC in the follow-up period of 9 - 23 years. We present our experience of such a coexistence and try to evaluate its significance in this community.

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Materials and methods

The subjects studied were 731 GC patients who had been endoscopically and pathologically diagnosed; data on them were obtained from a review of 47 896 endoscopies in the previous 4 years (July 1987 to June 1991). We excluded 127 GC patients of whom 103 had an occlusive pyloric tumour which precluded thorough inspection of the duodenum, 14 had a stump carcinoma and 10 a recurrent tumour. Six hundred and four GC patients (male/ female: 524/80, mean age: 65,8 ± 9,5 years) with intact stomachs and well-visualised duodenums were enrolled in the present study. Twenty-two individuals fulfilled the definition of coexistent GC and DU in an intact stomach. Their histories and clinical parameters were reviewed. The macroscopic appearance of GC was based on Borrmann's classification (as cited in Borchard[9]). The disease location was assessed either by means of endoscopy, barium meal examination or an operative procedure. Lesions situated at or above the gastric angle were considered 'at body', otherwise they were termed 'at antrum'. 'Diffuse type' referred to those where there was GC in both areas. Early GC was diagnosed according to the Japanese criteria.[10] Metastasis of GC was judged to have taken place if the resected lymph node showed GC cells or the presence of a metastatic lesion in a distal organ with various images. Ulcers were either active or healed. The former were ulcer craters shown endoscopically whereas the latter were characterised by the disappearance of any ulcer crater with only white or red scars remaining. Serum pepsinogen I levels (normal: 50 - 150 ng/ml) were determined by the SB-PEPSI radio-immunoassay kits (International CIS, France.) In order to study the significance of prevalence, we enrolled another 604 subjects as a control group within the same study period (July 1987 to June 1991) irrespective of whether they had histories of peptic ulcer. These controls were not included in the original 47 892 endoscopic records, and voluntarily received paid physical check-ups which included upper gastro-intestinal endoscopy as a routine procedure. Each GC patient was consecutively matched with an age- and gender-comparable control subject. The endoscopic findings of the controls were recorded. All data were expressed as means ± SD. The chi-square test was used for the comparison of percentage difference. The unpaired Student's *t*-test was used to compare numerical differences. Statistical significance was accepted at $P < 0,05$.

Results

Of the 604 GC patients, 22 (3,6%) were found to have DU after a thorough examination of the duodenum. Among the 604 age- and gender-matched controls, DUs were seen in 99 (16,4%) subjects. The difference in prevalence was significant ($P > 0,0001$). In none of the control subjects did GC and DU occur concurrently. Among male GC patients, 3,8% (20/524) exhibited a coexistent DU; this was significantly less than the DU prevalence (87/524) among cancer-free male control subjects ($P < 0,01$). The different prevalences were also observed among female individuals (2,5% *v.* 15%, $P < 0,01$). Only 8 (36,4%) patients with coexistent GC and DU had an active ulcer while healed scars were seen in the remainder. Meanwhile active ulcers existed in 49 (49,5%) cancer-free controls; the difference was not significant. The most notable symptoms of patients with coexistent GC and DU were dyspepsia (77,3%) and upper gastro-intestinal bleeding (22,7%). Compared with their initial ulcer symptoms, 6 (27,3%) patients experienced different symptoms when they became dyspeptic, 12 (54,5%) patients did not notice any change when they developed dyspepsia, whereas the data on the remaining 4 patients were unknown. The ulcer history of patients with coexistent GC and DU, previously confirmed either by barium meal examination or endoscopy, could be traced among 15 (68,2%) patients. Surprisingly, none of these patients ever underwent an upper gastro-intestinal examination before the occurrence of malignancy within the last 2 years. However, only 30% (6/20) of patients with coexistent GC and DU had been simultaneously diagnosed as having DU on barium meal examination when GC had been established. Serum pepsinogen I levels were determined among 12 patients with coexistent GC and DU; 4 (33,3%) had low levels (< 50 ng/ml). Table I summarises the pathological findings in patients either with coexistent GC and DU or with GC alone. The distribution and macroscopic appearance of GC among both groups were not different. Although early cancer seemed to be more common in patients with coexistent GC and DU, the difference was not significant.

Table I. Comparison between patients with GC alone and those with coexistent GC and DU

	GC alone ($N = 582$)		GC + DU ($N = 22$)		
	No.	%	No.	%	Significance
Male/female ratio	6,5:1		10:1		NS
Age (years) (mean ± SD)	66,0 ± 9,6		64,7 ± 9,8		NS
GC location					
Body	288	49,5	14	63,6	
Antrum	165	28,4	5	22,7	NS
Diffuse	129	22,1	3	13,7	
Borrmann type					
I	70	12,0	3	13,7	
II	164	28,2	5	22,7	NS
III	193	33,2	11	50,0	
IV	155	26,7	3	13,6	
Early cancer	63	16,3*	5	27,8†	NS
Metastasis	375	68,2‡	12	60,0	NS
Successful resection	386	66,3¶	18	81,8	NS

Diffuse tumour involving both body and antrum; NS: not significant.
* 63 cases in 386 resectable tumours.
† 5 cases in 18 resectable tumours.
‡ Excluded 32 patients who refused operation.
¶ Excluded two patients with co-existent GC and DU who refused operation.

Discussion

A true measurement of DU prevalence among the age- and gender-matched general population is very difficult. Therefore, we enrolled some consecutive volunteers as controls, despite their initial motivations for a paid physical check-up. We did not exclude those subjects shown either to be dyspeptic or to have histories of peptic ulcer, since this exclusion would have led to an underestimation of the

Table II. Clinical features of GC patients with coexistent DU

	Lewis and Woods[7]	Norfleet and Johnson[8]	Present study
Patients (No.)	238	30	22
Average age (range)	52,3 (25 - 78) (128)*	53 (32 - 85)	64,7 (35 - 78)
Sex ratio: M/F	4,21 (152)*	3,29	10,0
Change of ulcer symptoms (%)			
Definite	33 - 50 (94)*	23,3	27,3
None	33	46,7	54,5
Not given	17-30	30,0	18,2
Gastric acid (No.)			
Present	60 (80)*	11	8
Low	20 (80)*	2	4
Not given	—	17	10
GC location (%)			
Body	27	50	63,6
Antrum	46	43,3	22,7
Diffuse	18	—	13,7
Unspecified	9	6,7	—
DU diagnosis (No.)			
Endoscopy		16	22
Radiography		14	6
Blood type (No.)			
O		6	10
A		2	6
Not given		22	—
Ulcer activity (%)			
Active	33 (21)*		36,4
Healed scars	67 (21)*		63,6

Diffuse: tumour involving both body and antrum.
*Number in parenthesis represents number of patients with data provided.

DU prevalence. That DU and GC rarely coexist in the same subject with an intact stomach has been confirmed by several observations. Firstly, patients with gastric ulcer have the same chance as the general population have of developing GC, whereas in DU patients the chance is reduced to 20 - 25% of normal expectation.[2,11] Secondly, if the coexistence of GC and DU is a chance finding, the expected prevalence of DU must be the same in both GC patients and the general population. The present study indicated a strikingly lower prevalence of DU among GC patients than in cancer-free controls. This result is very similar to the prevalence of surgically confirmed DU among 33 individuals out of 971 GC patients.[4] Long-term observations also confirm the rarity of coexistent DU among GC patients.[6,12] Thirdly, the prevalences of coexistent GC among DU patients in various surveys usually range between 0,06% and 1,2%, markedly lower than the believed DU prevalence in the general population.[6,13-15] Duodenal ulcer seems to offer a low risk for development of GC.

Table II summarises the clinical features of coexistent GC and DU patients in the literature as a comparison with our study. With regard to their initial ulcer episodes, most patients do not experience any change in abdominal symptoms. Coexistent ulcers among these patients may show either active craters or healed scars. It is therefore difficult to know whether to ascribe the common presenting symptoms such as bleeding, dyspepsia and loss of body weight to the ulcer itself or to the concurrent GC.[7,16,17] Our results and those of others indicate that barium meal evaluation is not a sensitive modality for the assessment of this coexistence.[7,18] Whether a dominant malignancy may shift the attention of radiologists remains uncertain. Nevertheless, DU and GC are not incompatible; diagnosis of one lesion does not guarantee the absence of another.[19] It has been speculated that a high rate of acid secretion decreases GC risk while low acid secretion increases this risk.[6,7,11] In fact, some patients with coexistent GC and DU have normal acid secretion; this appears to negate the theory that acid inhibits subsequent malignancy.

Currently, the pathogenesis of DU is closely linked to infection with *Helicobacter pylori* in the gastric mucosa.[20,21] Even long-term *H. pylori* infection causing chronic gastritis could be a risk factor for subsequent GC.[21] However, the actual role of *H. pylori* infection among those patients with coexistent GC and DU remains unknown. The present study suggests that DU probably offers little chance of the patient's developing GC whereas thorough endoscopic screening is necessary for ulcer patients shown to have dyspepsia or other related symptoms, since DU and GC are not incompatible.

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