Incidence of duodenal ulcers and gastric ulcers in a Western population: Back to where it started

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MJM Groenen, EJ Kuipers, BE Hansen, RJ Th Ouwendijk. Incidence of duodenal ulcers and gastric ulcers in a Western population: Back to where it started. Can J Gastroenterol 2009;23(9):604-608.

BACKGROUND/OBJECTIVES: As recently as 40 years ago, a decline in the incidence of peptic ulcers was observed. The discovery of *Helicobacter pylori* had a further major impact on the incidence of ulcer disease. Our aim was to evaluate the trends in the incidence and bleeding complications of ulcer disease in the Netherlands.

METHODS: From a computerized endoscopy database of a district hospital, the data of all patients who underwent upper gastrointestinal endoscopy from 1996 to 2005 were analyzed. The incidence of duodenal and gastric ulcers, with and without complications, were compared over time.

RESULTS: Overall, 20,006 upper gastrointestinal endoscopies were performed. Duodenal ulcers were diagnosed in 696 (3.5%) cases, with signs of bleeding in 158 (22.7%). Forty-five (6.5%) of these ulcers were classified as Forrest I and 113 (16.2%) as Forrest II. Gastric ulcers were diagnosed in 487 cases (2.4%), with signs of bleeding in 60 (12.3%). A Forrest 1 designation was diagnosed in 19 patients (3.9%) and Forrest 2 in 41 patients (8.4%). The incidence of gastric ulcers was stable over time, while the incidence of duodenal ulcers declined.

CONCLUSIONS: The incidence of duodenal ulcer disease in the Dutch population is steadily decreasing over time. Test and treatment regimens for *H pylori* have possibly contributed to this decline. With a further decline in the prevalence of *H pylori*, the incidence of gastric ulcers is likely to exceed the incidence of duodenal ulcers in the very near future, revisiting a similar situation that was present at the beginning of the previous century.

Key Words: *Duodenal ulcer; Endoscopy; Epidemiology;* Helicobacter pylori; *Peptic ulcer; Stomach ulcer*

L'incidence d'ulcères duodénaux et d'ulcères gastriques au sein d'une population occidentale : De retour à la case départ

HISTORIQUE ET OBJECTIFS : Il y a à peine 40 ans, on observait un fléchissement du nombre d'ulcères gastroduodénaux. Par ailleurs, la découverte de l'*Helicobacter pylori* a eu des conséquences importantes sur l'incidence des maladies ulcéreuses. Nous visions à évaluer les tendances dans l'incidence et les complications hémorragiques des maladies ulcéreuses aux Pays-Bas.

MÉTHODOLOGIE : Les auteurs ont analysé les données de tous les patients qui ont subi une endoscopie œsogastroduodénale entre 1996 et 2005, tirées de la base de données informatisée des endoscopies d'un hôpital de district. Ils ont comparé l'incidence d'ulcères duodénaux et gastriques, avec ou sans complications, au fil du temps.

RÉSULTATS : Dans l'ensemble, 20 006 endoscopies œsogastroduodénales ont été exécutées. Dans 696 cas (3,5 %), on a diagnostiqué un ulcère duodénal, lesquels comportaient des signes de saignements dans 158 (22,7 %) cas. Quarante-cinq de ces ulcères (6,5 %) étaient classés Forrest I et 113 (16,2 %), Forrest II. On a diagnostiqué des ulcères gastriques dans 487 cas (2,4 %), dont 60 (12,3 %) comportaient des signes de saignement. Dix-neuf patients (3,9 %) avaient une désignation Forrest I et 41 (8,4 %), une désignation Forrest II. L'incidence d'ulcères gastriques est demeurée stable au fil du temps, tandis que celle d'ulcères duodénaux a diminué.

CONCLUSIONS : L'incidence de maladies ulcéreuses duodénales au sein de la population hollandaise diminue régulièrement au fil du temps. Les tests et les posologies thérapeutiques du *H pylori* ont peut-être contribué à ce fléchissement. Étant donné le recul de la prévalence de *H pylori*, l'incidence d'ulcères gastriques est susceptible de dépasser celle des ulcères duodénaux dans un avenir très rapproché, ce qui nous ramènerait à une situation similaire à celle observée au début du siècle dernier.

Over the past decades, important changes have occurred in the epidemiology of ulcer disease. The peak incidence was seen among individuals born at the end of 19th century. The peak for duodenal ulcers followed the gastric ulcer peak, with a 10-year to 20-year lag (1). As recently as 40 years ago, a decline in the incidence of peptic ulcers was suggested, based on a cohort analysis (2) showing that the mortality due to peptic ulcers decreased in successive birth cohorts. This observation was supported by decreasing hospitalization rates for peptic ulcers in the Unites States as well as in many European countries over the past decades (3,4).

The discovery of *Helicobacter pylori* in the early 1980s as a major cause of peptic ulcer disease had a significant impact on the treatment of ulcer disease. The significance of the discovery led to the award of the 2005 Nobel Prize in Medicine to Robin Warren and Barry Marshall. *H pylori* eradication therapy was proven to cure patients with previous chronic, recurrent ulcer disease. Further research into the epidemiology of *H pylori* infection showed that the prevalence of this bacterium was decreasing over time in recent decades, presumably as a result of improvements in living conditions (5,6). A recent Asian study (7) showed that the prevalence of peptic ulcer disease – mainly duodenal ulcers – was reduced in association with a decreasing trend in the prevalence of *H pylori*, confirming that *H pylori* is especially involved in the development of duodenal ulcers.

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Received for publication August 19, 2007. Accepted January 31, 2009

With the decreased incidence of ulcer disease, the incidence of ulcer complications may have been affected as well. A recent study in the Netherlands (8) showed that the incidence of the most important complication, ulcer bleeding, remained stable in the period between 1993 and 2003, notwithstanding the decreasing incidence of peptic ulcers. Mortality and rebleeding rates for peptic ulcer bleeding did not change either. Investigators from England (9) reported that the incidence of gastric and duodenal ulcer hemorrhage increased, even among older patients. This rise was shown to be correlated with oral anticoagulants, nonsteroidal anti-inflammatory drugs (NSAIDs) and oral corticosteroid intake (10,11).

The introduction of an endoscopy database allowed for closer investigation of the incidence and epidemiology of gastric and duodenal ulcers, complication rates and classifications. We aimed to define changes in the incidence of gastric and duodenal ulcer disease, and its complications over a 10-year period in a large, uninvestigated, dyspeptic population in the Netherlands. Moreover, use of the database enabled us to describe a more detailed incidence of ulcer complications over time in a large group of peptic ulcer patients for the first time, with the use of the 'Forrest' classification (12).

METHODS

All gastrointestinal endoscopies performed between June 1996 and January 2006, at the Ikazia Hospital (Rotterdam, The Netherlands), were evaluated. The Ikazia Hospital is a district hospital with an open-access endoscopy unit, where approximately 40% of the patients are referred by general practitioners. The large percentage of referrals by general practitioners from both the urban agglomeration and rural sites makes the investigated population a cross-section of the Dutch population. In July 1995, a computerized endoscopy report system, Endobase III, developed by Olympus Software (Olympus, Japan), was introduced. From June 1996 to present, each gastrointestinal endoscopy performed in the centre was recorded with this system. Four experienced endoscopists performed all endoscopy procedures recorded in the database, which enabled standardized methods for report writing (13). All data were labelled with a specific gastrointestinal endoscopic terminology code, which is an extension of the *International Classification of Diseases – 10th Revision* (ICD-10) (14).

All codes in the database starting with 'K25' and 'K26', coding for gastric and duodenal ulcer, respectively, were included in the present study. Furthermore, a search for the word "ulcer" in all reports of upper gastrointestinal endoscopies in the database was performed. These reports were reviewed for the diagnosis of gastric and duodenal ulcers. Many patients with a gastric ulcer underwent a follow-up gastroscopy a few weeks later. These follow-up endoscopies were excluded from the analysis; consequently, all included cases were newly diagnosed ulcers in a previously uninvestigated dyspeptic population.

Patient characteristics such as age, sex and indication for endoscopy were retrieved from the database. Furthermore, the Forrest classification and *H pylori* status were investigated. All of the ulcers detected were classified according to the Forrest classification (12). From 2001 to present, the Endobase III program enabled entering the Forrest classification into the database, and was completed for all peptic ulcers. Ulcer cases entered before 2001 were reclassified using the Forrest classification based on the reports and available endoscopic images.

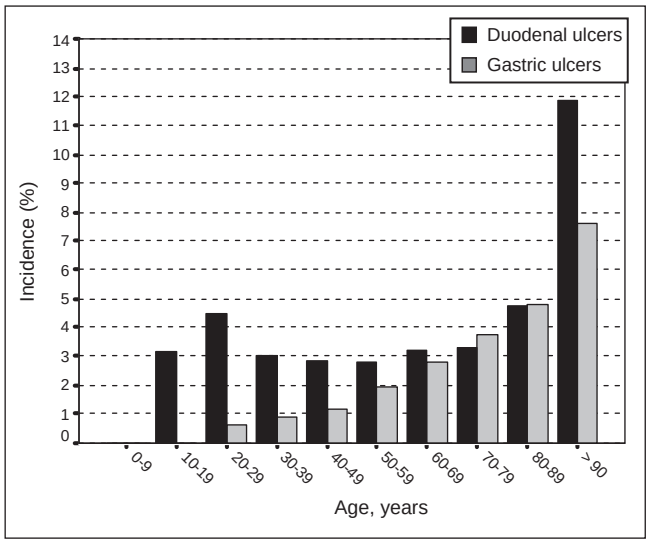

Figure 1) *Age-related proportion of patients with ulcer disease*

H pylori status was based on gastric biopsy specimens assessed with a rapid urease test (*Campylobacter*-like organism [CLO] test).

Data were analyzed with SPSS version 11.5 (SPSS Inc, USA). Regression analysis of ulcer incidence over time (years) was plotted against the observed incidence of ulcers in percentage per year. Data are described by mean ± SD or 95% CIs. A $P<0.05$ (based on a two-sided test) was considered to be statistically significant. Student's *t* test and linear regression analysis were used to compare groups and linear relations.

RESULTS

In total, the data from 20,006 upper gastrointestinal endoscopies were accessible for analysis, of which 10,784 (53.9%) were performed in women. The mean (± SD) age of the patients was 55.6±17.9 years. The total number of endoscopies performed yearly increased gradually over the 10 years, from 1800 to 2200 per year.

Duodenal ulcers were found in 696 of the investigated patients (3.5%) and gastric ulcers in 487 patients (2.4%). The majority of ulcer patients were men, who comprised 57.6% of duodenal ulcer and 51.5% of gastric ulcer patients.

Duodenal ulcer patients were significantly younger than gastric ulcer patients. The mean age of duodenal ulcer patients was 57.4 years (95% CI 55.9 years to 58.9 years), gastric ulcer patients had a mean age of 66.3 years (95% CI 64.9 years to 67.7 years; $P<0.001$). The distribution with respect to age group is shown in Figure 1. From 1996 to 2006, the mean age of the ulcer patients increased: for duodenal ulcer patients by 0.992 years per year (95% CI 0.44 to 1.4; $P<0.001$) and for gastric ulcers patients by 0.274 years per year, a difference that was not statistically significant (95% CI –0.34 to 0.89) (Figure 2).

Classification according to the Forrest system (Table 1) demonstrated that gastric ulcers showed signs of bleeding (Forrest 1 and 2) less frequently than duodenal ulcers ($P<0.001$). Ulcers classified as Forrest 3 (ie, no signs of recent bleeding) were seen in 77.3% of the duodenal ulcer cases and 87.1% of the gastric ulcer cases. Active bleeding (Forrest 1) was seen in 6.5% of all duodenal ulcers and 3.9% of all gastric ulcers, and

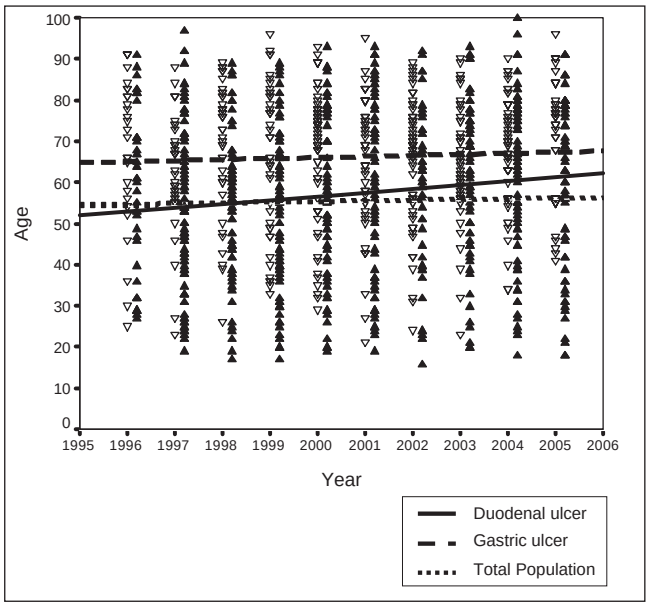

Figure 2) *Linear regression of mean age of duodenal and gastric ulcer patients in a 10-year period. The mean age of the duodenal ulcer patients increased by 0.992 years per year (95% CI 0.44 to 1.4) (P<0.001) compared with a nonsignificant increase of 0.274 years per year for gastric ulcer patients (95% CI −0.34 to 0.89)*

signs of bleeding (ie, a visible vessel [Forrest 2a], an overlying clot [Forrest 2b] or a hematin-covered base [Forrest 2c]) were diagnosed in 16.2% of the duodenal ulcers and 9.0% of the gastric ulcers.

Complicated ulcers, defined as Forrest 1 and 2, were more frequently seen in elderly patients, with a mean age of bleeding duodenal ulcer patients of 69.7 years (95% CI 66.8 years to 72.7 years) versus 54.3 years (95% CI 52.8 years to 55.9 years) for nonbleeding duodenal ulcer patients (P<0.001). For bleeding gastric ulcer patients, the mean age was 71.6 years (95% CI 67.6 years to 75.5 years), compared with 65.6 years (95% CI 64.1 years to 67.1 years) for uncomplicated ulcer disease (P=0.077). Of the patients with complicated ulcers, 60.4% with duodenal and 63.4% with gastric ulcers were older than 70 years of age. The sex distribution was not different for various Forrest-classified ulcers, nor was the sex distribution in patients with complicated ulcers different from that in patients with uncomplicated ulcers. For both groups, the majority of patients were men (57.7% and 54.5%, respectively; P=0.395).

In patients with complicated ulcer disease, *H pylori* infection was assessed in 22.6%, with a positive result in 37.1% of the tested patients.

The incidence of gastric ulcers remained stable over the 10-year observation period. In contrast, duodenal ulcers showed a decreasing incidence, with a linear regression coefficient of –0.169 (P=0.040) (Figure 3). This decline was due to a decline in the incidence of uncomplicated ulcers only. The incidence of complicated duodenal and gastric ulcers increased over this 10-year period, as shown in Figure 4. This increase was more dramatic for duodenal ulcers.

The CLO test performed on biopsy specimens taken during endoscopy for the presence of *H pylori* was completed in 20.5% of gastric ulcer patients and 36.4% of duodenal ulcer patients.

TABLE 1
Number and classification of duodenal and gastric ulcers

	Ulcers, n (%)	
Forrest classification	**Duodenal**	**Gastric**
1a	15 (2.2)	1 (0.2)
1b	30 (4.3)	18 (3.7)
2a	39 (5.6)	14 (2.9)
2b	37 (5.3)	7 (1.4)
2c	37 (5.3)	23 (4.7)
3	538 (77.3)	424 (87.1)
Total	696 (100)	487 (100)

Thirty-four per cent of the tested gastric ulcer patients and 56.5% of the tested duodenal ulcer patients were positive for *H pylori*. The overall incidence of CLO-positive tests declined significantly from 57.7% in the period between 1996 and 2000, to 45.1% in the period between 2001 and 2006 (P=0.02).

DISCUSSION

The investigated population consisted of patients referred for endoscopy, for the most part based on either serious recurring complaints, alarming symptoms or older age, according to the 1996 Dutch General Practitioners' Guideline on Dyspepsia (15). Thus, the investigated population is not a cross-section of the total population and incidences from this investigation are not fully comparable with findings concerning total populations. Trends over time are, however, clear. We found a decreasing incidence of duodenal ulcers and a stable incidence of gastric ulcers. This suggests a further amplification of the trend observed from 1980 onward, implying a decreasing incidence of both gastric and duodenal ulcers, with only a slight decline for gastric ulcer incidence (8). Our data suggest that the former, albeit slighter, decline in gastric ulcer incidence has stopped by now, whereas duodenal ulcer incidence continues to decrease further. This will lead to a situation in which, similar to 100 years ago, gastric ulcers will become more common than duodenal ulcers, whereas for the past 100 years, duodenal ulcer disease has been more common than gastric ulcer disease in Western countries (1).

Other trends that we found were an increasing incidence of complicated ulcers for both duodenal and gastric ulcers, an increasing age at diagnosis for patients with duodenal ulcers and a declining incidence of *H pylori*-positive ulcers.

The overall decline of peptic ulcer disease is likely to be due to a combination of factors including the introduction of acid suppressive medication, a decreasing prevalence of *H pylori* in subsequent birth cohorts and the development of eradication treatment for *H pylori*-positive ulcer patients, which prevents chronic relapsing ulcer disease. The introduction of newer NSAIDs and a tendency for the prescription of lower doses of acetylsalicylic acid for patients with cardiovascular disease may also have contributed to the changing epidemiology of ulcer disease.

The Forrest classification can predict the risk of rebleeding from peptic ulcer disease and, therefore, is an important tool in the selection of patients for endoscopic treatment (16,17). In the present study, a minority (12.3%) of the gastric and 22.7% of the duodenal ulcers were complicated by bleeding. As in

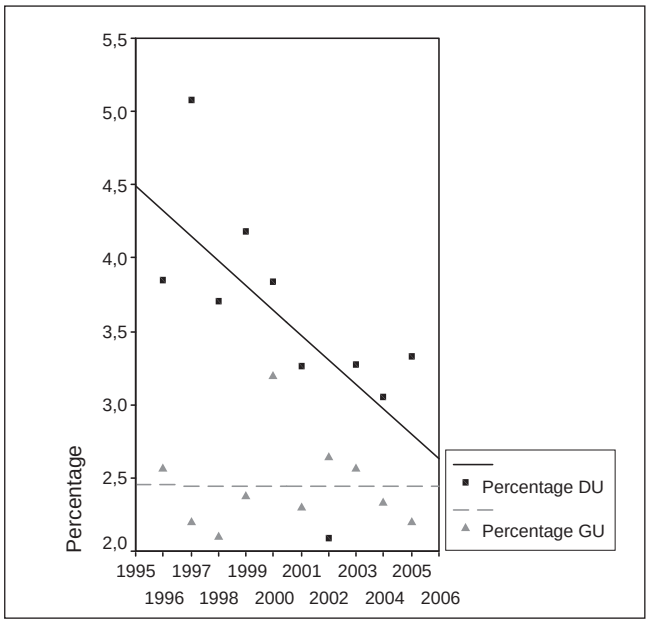

Figure 3) *Trends in the incidence of duodenal ulcer (DU) and gastric ulcer (GU) disease*

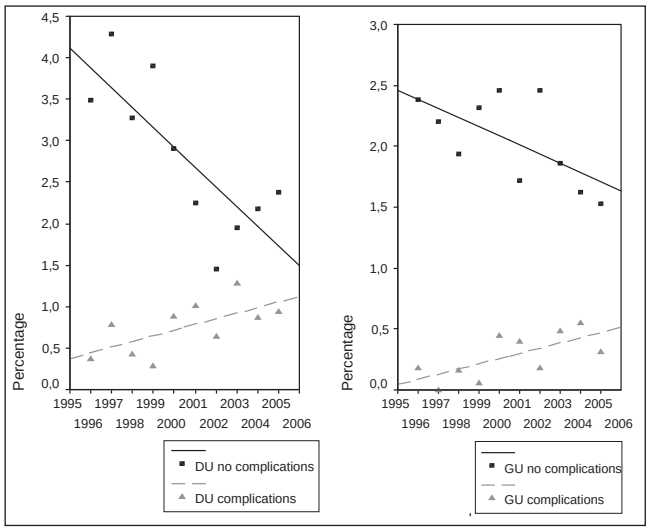

Figure 4) *Trends in the incidence of complicated and uncomplicated ulcers.* **Left panel:** *Duodenal ulcers (DU) without complications of bleeding (Forrest 3); DU with complications of bleeding (Forrest 1 and 2).* **Right panel:** *Gastric ulcers (GU) without complications of bleeding (Forrest 3); GU with complications of bleeding (Forrest 1 and 2)*

other studies (10), bleeding ulcers were more prevalent in older patients and in men.

While we observed a decreasing incidence of ulcers, there was a rise in the proportion of complicated ulcers – an observation consistent with data presented in other studies (8,9). The incidence of complicated ulcers rose in both gastric and, to a greater extent, duodenal ulcers in the time period investigated (Figures 3 and 4). The decline in the incidence of duodenal ulcers, in particular, can be completely attributed to a decrease of uncomplicated Forrest 3 ulcers.

The changes in the proportional distribution of complicated versus uncomplicated ulcers in the investigated period may have been influenced by the more accurate description of ulcers in endoscopic reports in recent years. The endoscopy report program Endobase III enabled more detailed standardized report writing as a result of improvements in the program from 2001 onward. Consequently, the need for free text was minimized in the updated version of the program. This may have influenced the description of the ulcer classification. We support the suggestion from other publications showing a stable incidence or slight increase of ulcer bleeding compared with overall peptic ulcer disease. It was suggested that the use of NSAIDs are the main cause of this change (8,10,11). The high proportion of negative CLO tests in bleeding ulcers supports the hypothesis that bleeding ulcers are more often related to NSAID use, although it may also partly be due to the low sensitivity of the CLO test in patients with upper gastrointestinal bleeding (18). Adherence to guidelines to prevent NSAID-related upper gastrointestinal events is low in the Netherlands and in the United States (9,19). This may be an important factor in the opposite trends in the incidence of complicated versus uncomplicated peptic ulcer patients.

Both ulcer types show an increase in incidence rate with increasing age. Duodenal ulcers occur in our population at a younger age than gastric ulcers. The incidence of duodenal ulcers starts to rise at approximately 20 years of age, in contrast with 50 years of age for gastric ulcers. This again indicates an etiological factor for duodenal ulcers early in life, such as infection with *H pylori*. These findings are not completely comparable with other studies (10) that report an older age for duodenal ulcer patients than in the present study.

In 1996, an update of the 1993 Dutch General Practitioners Guidelines on Dyspepsia was published (15). In this guideline, it was advised to diagnose *H pylori* status by endoscopic biopsy because only *H pylori* infection in patients with ulcers should be treated. The role of *H pylori* in other dyspeptic symptoms was stated as unclear.

In 2004, a new multidisciplinary guideline for dyspepsia was published in the Netherlands by The Dutch Institute for Healthcare Improvement CBO and the Dutch General Practitioners Society (20). In this guideline, an *H pylori* test is recommended if there are persistent nonreflux-like complaints without alarming symptoms. If the test for *H pylori* is negative, treatment with proton pump inhibitors for two to four weeks is recommended. If symptoms persist or diagnostic certainty is desired, endoscopy is recommended. Because these guidelines were published in 2004, and the total number of endoscopies performed was still rising up to that year, these guidelines were not suspected to have influenced the incidence and complications of peptic ulcer disease in the present study. However, it is possible that noninvasive testing for *H pylori* and the use of trials of therapy for dyspeptic patients have had a significant effect on the rate of endoscopies performed in duodenal ulcer patients, resulting in an apparent decline in incidence.

A CLO test was performed only in a small proportion of the patients. Other tests such as the carbon-13 urea breath test or serology may have been used in patients included in the present study, particularly in cases of bleeding. However, those test results were not included in the endoscopy database and, thus, could not be analyzed in the present study.

CONCLUSION

The incidence of uncomplicated peptic ulcer disease, especially for duodenal ulcers, has declined in the Western population. This will soon bring us back to a situation in which gastric ulcers are more common than duodenal ulcers. However, the incidence of complicated ulcer disease is rising, which underlines the need to be more alert in providing patients using NSAIDs with adequate gastroprotection to prevent ulcer disease and its complications.

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