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Peptic ulcer complications requiring surgery: What has changed in the last 50 years in Turkey

STOMACH DUODENUM

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ABSTRACT

Background/Aims: The incidence and prevalence of peptic ulcer disease has decreased in recent years, but it is not so easy to make the same conclusion when complications of peptic ulcer are taken into consideration. The aim of this study is to determine the time trends in complicated peptic ulcer disease and to state the effects of H2 receptor blockers, proton pump inhibitors (PPI), and *H. pylori* eradication therapies on these complications.

Materials and Methods: This study retrospectively evaluated the patients who were operated on for complications (perforation, bleeding, and obstruction) of peptic ulcer for the last 50 years. Patients were grouped into four groups (G1-G4) according to the dates in which H2 receptor blockers, PPIs, and eradication regimens for H. pylori were introduced The time periods that were studied were: (G1) 1962-1980, (G2) 1981-1990, (G3) 1991-1997, and (G4) 1998-2012.

Results: In total, 2953 patients were operated on for complications of peptic ulcer disease, of which 86% of the patients were male. In G1, perforation and obstruction were significantly the most frequent complications ($p<0.001$), followed by bleeding. In groups G2 and G3, obstruction was still the most frequent complication requiring surgery ($p<0.001$). In G2 and G3, obstruction was followed by perforation and bleeding, respectively. In G4, perforation was significantly the most frequent complication ($p<0.001$).

Conclusion: From 1962 to 1990 obstruction was the most common complication requiring surgery. In the last decade, perforation became the most common complication. In contrast to reports in the literature, bleeding was the least common complication requiring surgery in Turkey.

Keywords: Peptic ulcer, bleeding, obstruction, perforation

INTRODUCTION

The incidence and prevalence of uncomplicated peptic ulcer (PU) disease have decreased in recent years, most probably because of the identification and availability of treatment for *Helicobacter pylori* infection (1-3). It is not so easy to make the same conclusion when complications (bleeding, perforation, and obstruction) of PU are taken into consideration. The few studies that have examined the time trends in the incidence of PU hemorrhage reported no significant change during the last decade (4). Lassen et al. (2) and Bardhan et al. (5) noted a decrease in the annual incidence of PU perforation over the past decade A study of emergency admission due to PU complications reported that admission due to hemorrhage and perforation remained relatively steady (6). Interestingly, Lee and Sarosi (7) reported that while the rate of elective surgery for PU disease has been declining steadily over the past 3 decades, the rate of emergency ulcer surgery has risen by 44%. So, while time trends in the incidence and prevalence of uncomplicated PU disease are showing a steady decrease, time trends in complicated PU are still challeng-

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ing. This means that surgeons are likely to have to manage the emergent complications of PU disease.

The aim of this study is to determine the time trends in complicated (perforation, obstruction, and bleeding) PU disease and to state the effects of H_2 receptor blockers, proton pump inhibitors (PPIs), and *H. pylori* eradication therapies (HET) on these complications using data from a large-volume reference hospital in Turkey. To our knowledge, this is the first study analyzing data on this subject for the last 50 years (1962-2012).

MATERIALS AND METHODS

This study was carried out according to the Helsinki Declaration criterias and ethics committee aproval was taken. This study retrospectively evaluated patients who were operated on for complications (perforation, bleeding, and obstruction) of PU for the last 50 years in a high-volume reference hospital. Data were collected mainly from operating room records and personal files of the patients. Complication types were collected in a database. Patients were grouped into four groups (G1-G4) according to the dates in which H_2 receptor blockers, (Cimetidine; S. Doğu Drugs, Inc, İstanbul, Turkey), proton pump inhibitors (PPI) (Omeprazol; Sandoz Drugs, Inc, İstanbul, Turkey), and eradication regimens (Helipak; Abbott Laboratory, Inc, İstanbul, Turkey), for *H. pylori* were introduced in Turkey. The H_2 receptor blockers were introduced in Turkey in the beginning of 1980 for the treatment of PU disease and were followed by PPIs in the late 1980s (8). Eradication regimens for *H. pylori* were introduced in Turkey in 1998 (9). The time periods that were studied were: (G1) 1962-1980, (G2) 1981-1990, (G3) 1991-1997, and (G4) 1998-2012, in accordance with the introduction dates of the therapeutic regimen types.

Statistical analysis

Data analysis was performed by using SPSS for Windows, version 17 (SPSS, Chicago, IL, USA). Whether the distributions of continuous variables were normal or not was determined by the Shapiro-Wilk test. The Levene test was used for the evaluation of homogeneity of variances. Data were shown as mean±standard deviation or median (min-max), where applicable.

The differences between groups were compared by using student's t- or Mann-Whitney U-test, where appropriate. Categorical data were analyzed by Pearson's chi-square test; a p value of less than 0.05 was considered statistically significant.

RESULTS

In the last 50 years, 2953 patients were operated on for complications of PU disease, of which 86% of the patients were male. The mean age of the patients was 39.71 years. The number of patients operated on for perforation, bleeding, and obstruction were 1350, 198, and 1405, respectively. Breaking the mean age and sex data down by groups, the mean age was 38.84±12.05 (SD), and 92.4% of the patients were male in G1. In G2, the mean age was 39.23±12.00 (SD), and 77.4% was male.

Table 1. Frequencies of complications according to time period

	G1 (1962-1980)	G2 (1981-1990)	G3 (1991-1997)	G4 (1998-2012)
Perforation	689 (44.8%)	344 (41.0%)	101 (34.4%)	216 (77.1%)
Bleeding	135 (8.8%)	19 (2.3%)	13 (4.4%)	31 (11.1%)
Obstruction	715 (46.4%)	477 (56.7%)	180 (61.2%)	33 (11.8%)
Total	1539	840	294	280

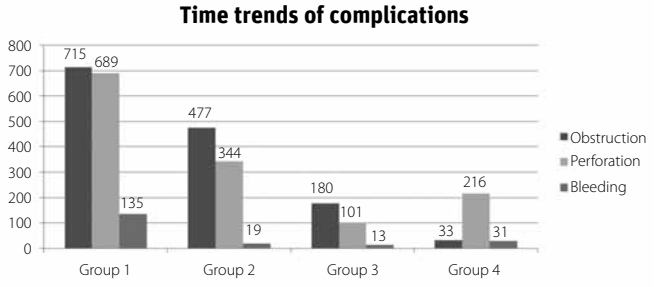

Figure 1. Time trends of complications.

In G3, the mean age was 39.41±18.96 (SD), and 81.3% was male. In G4, the mean age was 44.45±16.28 (SD), and 87.9% was male. The frequencies of the complications according to the time periods are given in Table 1. In G1, perforation and obstruction were significantly the most frequent PU complications (p<0.001), followed by bleeding. In groups G2 and G3, obstruction was still the most frequent complication requiring surgery (p<0.001). In G2 and G3, obstruction was followed by perforation and bleeding, respectively. In G4, perforation was significantly the most frequent complication (p<0.001). This was followed by obstruction and bleeding, respectively, with no significant difference between obstruction and bleeding. Time trends of PU complications are given in Figure 1. There was a significant decrease (p<0.001) in the total number of PU complications requiring surgical therapy by time period until 1998. After this time, there was no significant decline (p:0.559) in the total number of PU complications. Between the G1 and G2 time periods and between G2 and G3, there was a significant decline in the frequency of perforation (both p<0.001). Between the G3 and G4 time periods, there was a significant rise in the perforation rate (p<0.001). For the bleeding complication, there was a significant decline in rates between time periods G1 and G2 and between time periods G2 and G3, but in the G4 time period, the proportion of bleeding cases was significantly increased according to the G3 time period (p<0.05). Obstruction rates decreased dramatically and significantly over the time from G1 to G4 (p<0.001).

DISCUSSION

The wide usage of PIPs for PU treatment and the introduction of eradication therapies for *H. pylori* have decreased the incidence of non-complicated PU disease all over the word. From the point of PU complications the results are somewhat controversial. Lee et al. (7) reported that the rate of elective surgery for

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PU disease has been declining steadily over the past 3 decades, but during this same period, emergency ulcer surgery rose by 44%. About 50% of the patients who are admitted to tertiary care hospitals with upper gastro-intestinal bleeding have PU bleeding (10). Incidence rates of PU complications reported in the literature are somewhat conflicting. Hemorrhage is more common than perforation (11). The few studies that have examined time trends in the incidence of PU bleeding reported no significant change during the last decade (4).

In our study, the results are somewhat controversial. Until the eradication therapies for *H. pylori* began to be used widely in Turkey (from 1998 to 2012), PU bleeding was the least frequent PU complication (p<0.001). After eradication therapies were introduced, perforation and obstruction were still more common than bleeding, but there was no significant difference between bleeding and obstruction (Figure 1). The introduction of H_2 receptor blocker therapies after 1980 facilitated a sharp and significant decline in bleeding (p<0.001), but PPI therapies did not supplement this decline significantly (p:0.289). In the time period (1998-2012), when eradication therapies were used in addition to PPIs, bleeding did not decrease; indeed its frequency was increased significantly (p<0.05). Despite new improved therapeutic modalities, this unexpected rise in bleeding may be due to other reasons; for example, *H. pylori* may not be the predominant etiologic factor in patients who experience complications requiring surgery (12,13). During the last decade, PU bleeding did not significantly change (2,5,14), but the incidence increased in patients older than 75 years of age (15). In last decade, usage of non-steroidal anti-inflamatory drugs (NSAID) also increased, especially in the increasing elderly population (16,17). The use of NSAIDs is associated with an increased risk of bleeding ulcers (18,19). In Turkey, life expectancy is also increasing by time. There is no evidence-based report available showing increasing use of NSAIDs in Turkey, but most probably there is a parallel increase with the increasing elderly population. This may explain the rise in bleeding complications in the last 2 decades in Turkey. Despite this increase, bleeding was the least common PU complication in our study.

Peptic ulcer perforation still remains a dangerous surgical condition, associated with high morbidity and mortality, and is not be underestimated (20). Perforation occurs in 2%-10% of PU patients and accounts for more than 70% of deaths associated with PU disease (21,22). PU perforation used to be a disorder mainly of younger patients (predominantly males), whereas the current peak age is 40-60 years (23). Our results correlate with this report. The mean age of the patients was 46.45, and 88.6% of the patients were male in the period (last 2 decades) when perforation showed a peak in incidence. In our study, from 1962 to 1998 perforation was the second most common PU complication. In G1, the percentage of perforation was less than that for obstruction, but there was no significant difference (p:0.488). In G2 and G3, perforation was significantly the second most common complication (p<0.001). In G4 (1998-2012), perforation significantly became the most common PU complication requiring surgery (p<0.001). Introduction of H_2 receptor blockers and later PPI usage caused a significant decrease (p<0.001) in frequency of perforation complications, but after 1998, there was a significant (p<0.001) increase in the frequency of perforation. It seems that *H. pylori* eradication did not show a positive preventive effect on this complication.This may be due to an increase in the use of aspirin and/or NSAIDs and *H. pylori* may not be the predominant etiologic factor Two studies comparing the dates 1993, 2002, 1990-1994 and 1995-2002 noted a decrease in the annual incidence of perforation over time (2,5). The compared time periods in our study were somewhat similar to those used in these studies, and in our study, we also noted a decrease in the percentage of perforation. A study of emergency admissions due to PU complications from Poland between 1996 and 2001 reported that admissions due to perforation remained constant during this period (6). In contrary to the result of this report, in our study there was a sharp rise in the number of surgical therapies required due to perforation.

There were very few studies that examined the time trends in the incidence of obstruction due to PU. It was reported that obstruction was the least (12.9%) specific cause of PU disease in patients requiring surgery (12). Recently, acquired gastric outlet obstruction is more commonly related to malignancy than to ulcer disease (24). In their cohort study, comparing the results of 1977 with 1989 Makela et al. (25) reported that before and after the introduction of H_2-receptor antagonists, operations performed for obstruction did not increase, varying from 0.8 to 2.2 per 10^5 individuals over the study. In our study the results are different. In G1 (before introduction of H_2-receptor blockers), the differences were not significant, but obstruction was the leading cause of PU complication requiring surgery. After the introduction of H_2-receptor blockers and PIP (1981-1990, 1991-1997), obstruction was significantly the most common cause of surgery (p<0.001). After eradication therapies for *H. pylori* were introduced, the frequency of obstruction dramatically and significantly decreased, but it remained the second most common complication. Time trends in obstruction requiring surgery showed a continuous and significant (p<0.001) decline in frequencies by time from 1962 to 2012. An explanation of this decline may be that all kinds of anti-ulcer treatments, especially the eradication of *H. pylori*, have preventive effects on obstruction formation in PU disease patients.

Our study admittedly has its limitations. First, the hospital catchment population is not known exactly; so the results can not be extrapolated to the population as a whole. In addition, this study examined only surgically treated complications, whereas endoscopically treated complications were excluded.

In the last 50 years, the introduction of several new anti-ulcer medications and *H. pylori* eradication has caused a significant decrease in the total number of surgically treated obstruction,

perforation, and bleeding cases. Before and after H_2 receptor blockers, andeven after the introduction of PPIs, obstruction was the most common PU complication requiring surgery. In the last decade, after the introduction of eradication regimens for *H. pylori*, perforation became the most common PU complication requiring surgery. In contrast to reports in the literature, bleeding was the least common complication requiring surgery in Turkey. Despite the declining prevalence of PU in recent years, complications arising from PU remain a substantial healthcare problem.

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REFERENCES

1. Xia B, Xia HH, Ma CW, et al. Trends in the prevelence of peptic ulcer disease and Helicocayer pylori infection in family physician-referreduninvestigated dyspeptic patients in Hong Kong. Aliment Pharmacol Ther 2005; 22: 243-9. **[CrossRef]**
2. Lassen A, Hallas J, Schaffalitzky de Muck-adell OB. Complicated and uncomplicated peptic ulcers in a Danish county 1993-2002: A population-based cohort study. Am J Gastroenterol 2006; 101: 945-53. **[CrossRef]**
3. Everhart JE. Recent developments in the epidemiology of Helicobacter pylori. Gastroenterol Clin North Am 2000; 29: 559-78. **[CrossRef]**
4. Lau JY, Sung J, Hill C, Henderson C, Howden CW, Metz DC. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. Digestion 2011; 84: 102-13. **[CrossRef]**
5. Bardhan KD, Williamson M, Royston C, Lyon C. Admission rates for peptic ulcer in the Trent region, UK, 1972-2000. Changing pattern, a changing disease? Dig Liver Dis 2004; 36: 577-88. **[CrossRef]**
6. Bobrzynski A, Beden P, Budzynski A, Bielanski W, Plonka M, Konturek S. Incidence of complications of peptic ulcers in patients with Helicobacter pylori infection and/or NSAID use in the era of Hp eradiction. Med Sci Monit 2002; 8: 554-7.
7. Lee CW, Sarosi GA Jr. Emergency ulcer surgery. Surg Clin North Am 2011; 91: 1001-13. **[CrossRef]**
8. Kalafat H. Peptik ülserin cerrahi tedavisi. 2001 Gastarointestinal Sistem Hastalıkları Sempozyumu. 2001.p.119-31.
9. Uzunismail H. Helicobacter pylori eradikasyonunda proton pompa inhibitörlü birinci basamak tedavisi: Ülkemizde ve dünyada son durum. Endoskopi 2004; 15: 110-4.
10. Fallah MA, PrakashC, Edmunddowicz S. Acute gastrointestinal bleeding. MedClin North Am 2000; 84: 1183-208. **[CrossRef]**
11. Baron JH, Sonnenberg A. Publications on peptic ulcer in Britain, France, Germany and the US. Eur J Gastroenterol Hepatol 2002; 14: 711-5. **[CrossRef]**
12. Zelickson MS, Bronder CM, Johnson BL, et al. Helicobacter pylori is not predominant etiology for peptic ulcers requring operation. Am Surg 2011; 77: 1054-60.
13. Castillo-Rojas G, Ballesteros MA, Ponce de Leon S, Morales-Espinosa R, Cravioto A, Lopez-Vidal Y. Bleeding peptic ulcers and presence of Helicobacter pylori by various tests: A case-controlstudy. Eur J Gastroenterol Hepatol 2002; 14: 1113-8. **[CrossRef]**
14. van Leerdam ME, Vreeburg EM, Rauws EA, et al. Acute upper GI bleeding: Did anything change? Time trend analysis of incidence and outcome of acute upper GI bleeding between 1993/1994 and 2000. Am J Gastroenterol 2003; 98: 1494-99. **[CrossRef]**
15. Loperfido S, Baldo V, Piovesana E, et al. Changing trends in acute upper-GI bleeding: a population-based study. Gastrointestinal Endosc 2009; 70: 212-24. **[CrossRef]**
16. Nakashima S, Arai S, Mizuno Y, et al. A clinical study of Japanese patients with ulcer induced by low-dose aspirin and other non -steroidal anti-inflammatory drugs. Aliment Pharmacol Ther 2005; 21 Suppl 2: 60-6. **[CrossRef]**
17. Ootani H, Iwakiri R, Shimoda R, et al. Role of Helicobacter pylori infection and nonsteroidal anti-inflammatory drug use in bleeding peptic ulcers in Japan. J Gastroenterol 2006; 41: 41-6. **[CrossRef]**
18. Fujinami H, Kudo T, Hosokawsa A, et al. A study of the changes in the cause of peptic ulcer bleeding. World J Gastrointest Endosc 2012; 4: 323-7. **[CrossRef]**
19. Lanas A, García-Rodríguez LA, Arroyo MT, et al. Risk of upper gastrointestinal ulcer bleeding associated with selective cyclo-oxygenase-2 inhibitors, traditional non-aspirin non-steroidal anti-inflammatory drugs, aspirin and combinations. Gut 2006; 55: 1731-8. **[CrossRef]**
20. Conservative management of perforated peptic ulcer. Lancet 1989; 16: 1429-30.
21. Druart ML, Van Hee R, Etienne J, et al. Laparoscopic repair of perforated duodenal ulcer. A prospective multicenter clinical trial. Surg Endosc 1997; 11: 1017-20. **[CrossRef]**
22. Milosavljevic T, Kostić-Milosavljević M, Jovanović I, Krstić M. Complications of peptic ulcer disease. Dig Dis 2011; 29: 491-3. **[CrossRef]**
23. Betleff MJOE, Lange JF. Perforated peptic ulcer disease: A review of history and treatment. Gig Surg 2010; 27: 161-9.
24. Khuller SK, DiSario JA. Gastric outlet obstruction. Gastrointest Endosc Clin N Am 1996; 6: 585-603.
25. Makela JT, Kiviniem H, Ohtonen P, Laitinen SO. Factors that predict morbidity and mortality in patients with perforated peptic ulcer. Eur J Surg 2002; 68: 446-51.