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

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 \textit{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 \textit{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 \textit{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-
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 criteria and ethics committee appraisal 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; SANDZ Drugs, Inc, İstanbul, Turkey), and eradication regimens (Helipak; Abbott Laboratory, Inc, Istanbul, 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.

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<th>Table 1. Frequencies of complications according to time period</th>
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<td>Perforation</td>
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**DISCUSSION**

The wide usage of PPIs for PU treatment and the introduction of eradication therapies for $H. pylori$ have decreased the incidence of non-complicated PU disease all over the world. From the point of PU complications the results are somewhat controversial. Lee et al. (7) reported that the rate of elective surgery for
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 significant changes 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-inflammatory 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 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 ever 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 H₂ receptor blockers, and even 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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**Author contributions:** Concept - H.G.; Design - Ş.K.; Supervision - T.K.; Resource - G.T.; Materials - H.G.; Data Collection\&or Processing - Ş.K.; Analysis\&or Interpretation - D.Ş.; Literature Search - G.O.; Writing - D.Ş.; Critical Reviews - H.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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**REFERENCES**


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]


