Eradication of Helicobacter pylori for the Prevention of Peptic Ulcer Rebleeding

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Keywords
Helicobacter pylori, peptic ulcer bleeding, H2 receptor antagonist, proton pump inhibitor, upper gastrointestinal hemorrhage, upper gastrointestinal bleeding.

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Abstract

Aim: To evaluate the effect of Helicobacter pylori eradication on ulcer bleeding recurrence in a prospective, long-term study including more than 400 patients.

Methods: Patients with peptic ulcer bleeding were prospectively included. H. pylori infection was confirmed by rapid urease test, histology or 13C-urea breath test. Several eradication regimens were used. Ranitidine 150 mg was administered daily until eradication was confirmed by breath test 8 weeks after completing eradication therapy. Patients with therapy failure received a second or third course of therapy. Patients with eradication success did not receive maintenance anti-ulcer therapy, and were controlled yearly with a repeated breath test.

Results: Four hundred and twenty-two patients were followed up for at least 12 months, with a total of 906 patient-years of follow up. Mean age was 59 years, and 35% were previous nonsteroidal anti-inflammatory drug (NSAID) users. Sixty-nine percent had duodenal, 24% gastric, and 7% pyloric ulcer. Recurrence of bleeding was demonstrated in two patients at 1 year (incidence: 0.22% per patient-year of follow up), which occurred after NSAID use in both cases.

Conclusion: Peptic ulcer rebleeding does not occur in patients with complicated ulcers after H. pylori eradication. Maintenance anti-ulcer (antisecretory) therapy is not necessary if eradication is achieved.

Upper gastrointestinal hemorrhage is a major cause of morbidity, mortality and medical care costs, with peptic ulcer being the most frequent source of bleeding [1]. It has been estimated that approximately 2–3% of duodenal ulcer patients who are not receiving antisecretory therapy are likely to develop hemorrhage during each year of follow-up study, giving a cumulative risk of hemorrhage after 5 years of approximately 10–14% [2]. Furthermore, patients whose ulcers have bled once have an increased risk of further rebleeding, compared with those with uncomplicated ulcer disease. Thus, among patients who present with a bleeding ulcer, approximately one-third will develop recurrent bleeding in the following 1–2 years, and 40–50% within the subsequent 10 years, if left untreated after ulcer is healed [3,4]. Furthermore, patients with bleeding ulcers account for an overall mortality rate that has remained around 5–10% for the past 50 years, despite improved medical and surgical treatments, the development of diagnostic and therapeutic endoscopy, and the availability of intensive care units [1].

Maintenance antisecretory therapy has been the standard long-term treatment for patients with bleeding ulcers to prevent recurrent bleeding, despite the fact that only two randomized studies have specifically examined such option in patients with peptic ulcer hemorrhage [5,6]. The first study found no significant difference in the rate of recurrent bleeding between ranitidine maintenance therapy and placebo, but the number of bleeding episodes was so small that a treatment benefit could not be demonstrated [5]; the second study reported significantly fewer episodes of hemorrhage among patients taking ranitidine maintenance antisecretory regimen when compared with placebo [6].

Helicobacter pylori infection is the main etiologic factor for peptic ulcer disease. However, although the role of this organism on noncomplicated peptic ulcer has been
definitely established [7], the precise relationship between *H. pylori* and complicated ulcer disease has hardly been studied [8]. *H. pylori* eradication has been demonstrated to dramatically reduce the rate of ulcer recurrence [9]. Therefore, it would seem logical to assume that *H. pylori* cure would also represent an effective strategy to prevent recurrence of ulcer bleeding. In 1994, the National Institutes of Health (NIH) Consensus Conference panel stated that, although preliminary studies indicate that cure of *H. pylori* infection prevents recurrent ulcer bleeding at rates equal to those of maintenance antisecretory therapy, until these studies can be confirmed, maintenance antisecretory “may be prudent” in such patients even after *H. pylori* eradication, in view of high risks associated with rebleeding [10]. Two years later, in 1996, the NIH Consensus Conference did not go any further, stating that “several trials indicate that *H. pylori* eradication also reduces the recurrence of ulcer complications, but the magnitude of this reduction remains to be firmly established” [11].

Although several authors have administered *H. pylori* eradication treatment to patients with a history of peptic ulcer hemorrhage with the intention to prevent recurrence of bleeding, however, only few prospective studies have been performed, the number of patients included in these “eradication” studies has been small, and the follow up has been very limited [12,13]. Consequently, the true efficacy of *H. pylori* eradication for the prevention of recurrent bleeding from peptic ulcer is not well known [14].

With these antecedents, we aimed to verify the effect of *H. pylori* eradication on ulcer bleeding recurrence in a prospective, multicenter, long-term study including more than 400 patients and several years of follow up.

**Patients and Methods**

**Patients**

Consecutive patients with peptic ulcer bleeding and concomitant *H. pylori* infection were included in this prospective multicenter study. Ten Spanish university hospitals participated in the study. Patients were included if bleeding was severe enough to warrant hospitalization, if hematemesis or melena was evident, or if a drop in hemoglobin level of more than 2 g/dL occurred. The presence of an ulcer had to be documented endoscopically and no other potential bleeding source had to be found during initial evaluation. An ulcer was defined as a disruption in the mucosal continuity of > 5 mm with apparent depth. Stigmata of recent hemorrhage included adherent blood clot, visible vessel, or active bleeding. Informed consent was obtained from all patients.

Exclusion criteria were: 1, other lesions of the esophageal, gastric or duodenal mucosa different to ulcer and with stigmata of recent hemorrhage at endoscopy; 2, previous gastric surgery. 3, any severe underlying disease that would have had an impact on life expectancy during the study period or any condition associated with poor patient compliance, and 4, pregnant and breast-feeding women. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) or aspirin during the 7 days before the bleeding episode was evaluated by means of a specific questionnaire, but it was not considered as an exclusion criteria. Only *H. pylori*-positive patients were included in this prospective study (see “Diagnostic methods of *H. pylori* infection” section).

**Diagnostic Methods of *H. pylori* Infection**

At endoscopy, biopsies from the antrum were obtained, when possible, for rapid urease test and/or histologic study (hematoxylin and eosin stain). Due to the high specificity of these biopsy-based methods [15], patients with positive rapid urease test or histology were considered definitively infected, and were treated with *H. pylori* eradication regimen. However, as it has been reported that a negative rapid urease test (or a negative histology) is unreliable for exclusion of *H. pylori* infection during the acute phase of upper gastrointestinal bleeding [15], a $^{13}$C-urea breath test (see later for protocol details) was performed before the presence of the infection was ruled out. In addition, when biopsies were not feasible, $^{13}$C-urea breath test was also performed. If the infection was not demonstrated with the $^{13}$C-urea breath test, and this test was performed while the patient was taking proton pump inhibitors (PPIs), *H. pylori* still needed to be definitively excluded with a new breath test performed 2 weeks after stopping these drugs (H$_2$-antagonists was used for this period of time). In summary, patients were finally considered infected if rapid urease test, histology or any of the performed $^{13}$C-urea breath tests were positive.

**Therapy**

All *H. pylori*-positive patients received eradication treatment with 7- to 10-day twice-daily PPI-based regimens, including clarithromycin plus amoxicillin (or metronidazole in case of penicillin allergy). Afterwards, ranitidine 150 mg was administered daily until eradication was confirmed by $^{13}$C-urea breath test. Patients with therapy failure received a second course of therapy (with a quadruple combination of PPI, bismuth, tetracycline and metronidazole, or ranitidine bismuth citrate with these same antibiotics), or a third-line regimen (culture-based according to microbial sensitivity to antibiotics, or empirical levofloxacin- or rifabutin-based treatments).
Diagnostic Methods to Confirm *H. pylori* Eradication

*H. pylori* eradication was defined as a negative $^{13}$C-urea breath test (with citric acid and 100 mg of urea, as previously reported) [16] performed 8 weeks after completion of eradication treatment. The $^{13}$C-urea breath test was carried out by operators unaware of therapy and patients’ *H. pylori* status.

Follow-up and Outcome Variable

Once *H. pylori* eradication was confirmed, ranitidine was stopped and patients entered the follow-up period. Patients with eradication success did not receive maintenance anti-ulcer therapy (ranitidine, PPIs, or other). Patients were carefully instructed to avoid taking NSAIDs during follow up. Nevertheless, in case of rebleeding, the use of NSAIDs during the last 7 days was evaluated by means of a specific questionnaire. All *H. pylori*-negative patients were followed with a clinical examination and a $^{13}$C-urea breath test every 12 months. During follow up, patients were requested to immediately report to the responsible physician any symptom or sign suggesting peptic ulcer rebleeding (hematemesis, melena, postural hypotension, pulse rate > 100 beats per minute, blood pressure < 100 mmHg). In case any of these signs were present, endoscopy was performed immediately.

The main outcome considered in this study was “incidence of peptic ulcer rebleeding”. Rebleeding during follow up was assessed with the same criteria used for initial evaluation (see previous discussions).

Statistical Analysis

For quantitative variables, mean and standard deviation were calculated. For categorical variables, percentages and corresponding 95% confidence intervals were provided. To take into account the follow-up time after *H. pylori* eradication, the risk of rebleeding was expressed as “yearly” recurrence of bleeding, per patient-year of follow up.

Results

A flow diagram of subject progress through the phases of the study is shown in Fig. 1. From the initial 450 patients with peptic ulcer bleeding, 427 (95%) were finally proved to be *H. pylori* positive, and 98.8% of them achieved *H. pylori* eradication success (after several eradication attempts). Therefore, 422 patients with acute hemorrhage secondary to gastroduodenal ulcer and previous *H. pylori* eradication were finally included in the prospective study and followed up for at least 12 months.

Mean age was $59 \pm 16$ years, 75% were males, and 27% were smokers. Thirty-five of the patients were previous NSAID or aspirin users. Among them, 69.3% had duodenal ulcer, 23.9% gastric ulcer, 0.5% both duodenal and gastric ulcer, and 6.3% pyloric ulcer. The antecedent of previous peptic ulcer bleeding was described by 14% of the patients.

One-hundred and eighteen patients (28%) were followed up for 1 year, 154 (36.5%) for 2 years, 129 (30.6%) for 3 years, 12 (2.8%) for 4 years, and 9 (2.1%) for 5 years; giving a total of 906 patient-years of follow up. The mean time of follow up was $26.4 \pm 11$ months. Two patients were lost to follow up at 1 year, one patient was lost at 2 years, and one more patient was lost at 3 years. Dropouts were considered as not having recurrent bleeding, as it is the most frequent outcome [12,13]. In addition, it seems to be exceptional that patients having recurrent bleeding are lost to follow up, as it is logical to assume that these patients will be finally included in the analysis.

Despite carefully instructing the patients to avoid taking gastroerosive drugs during follow up, NSAID and aspirin use was reported, respectively, by 4.3% and 2.4% of the patients. On the other hand, PPIs and H$_2$-antagonists were taken, respectively, by 8.3% and 1.2% of the patients during follow up.

Reurrence of *H. pylori* infection was confirmed in four patients at 1 year (incidence: 0.95% per patient-year of

![Figure 1](https://example.com/figure1.png)  
*Figure 1 Flow diagram of subject progress through the phases of the study.*  
*Patients with initial therapy failure received a second or third course of eradication therapy.*
follow up; 95% confidence interval, 0.37–2.41); none of these patients had recurrence of bleeding peptic ulcer.

Recurrence of bleeding was demonstrated in two patients, which occurred at 1 year (incidence: 0.22% per patient-year of follow up; 95% confidence interval, 0.06–0.8). Emergency endoscopic examination revealed a duodenal ulcer as the source of bleeding in the two patients (these two patients were the only ones that had an endoscopy performed during follow up). Rebleeding occurred after NSAID use in both cases. None of them were receiving concomitant PPIs for ulcer bleeding prophylaxis (NSAIDs were not prescribed by the corresponding physician, but was taken over the counter, and therefore the physician was unaware of this). One of these two patients was a 73-year-old, nonsmoker male. The other patient was a 78-year-old, nonsmoker male.

**Discussion**

The decision of whether maintenance antisecretory therapy must be continued or stopped in patients with a history of peptic ulcer hemorrhage and prior *H. pylori* eradication will depend on the true efficacy of *H. pylori* eradication for the prevention of recurrent bleeding. In the present study, recurrence of bleeding was demonstrated in only two of 422 patients after *H. pylori* eradication, giving a rebleeding incidence as low as 0.22% per patient-year of follow up, which argues against the necessity of prescribing maintenance antisecretory therapy in these cases. This figure is in agreement with that previously reported in the literature (Table 1) [17–46]. As the follow-up time markedly varied among studies, the risk of rebleeding is better expressed as “yearly” recurrence of bleeding. Thus,

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients</th>
<th>Mean follow up (months)</th>
<th>Rebleeding (%)</th>
<th>Follow up (patient-years)</th>
<th>Yearly rebleeding (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amendola et al. [17]</td>
<td>42</td>
<td>24</td>
<td>0 (0%)</td>
<td>84</td>
<td>0</td>
</tr>
<tr>
<td>Arkkila et al. [18]</td>
<td>176</td>
<td>12</td>
<td>2 (1.1%)</td>
<td>176</td>
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<tr>
<td>Bataga et al. [19]</td>
<td>–</td>
<td>12</td>
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<td></td>
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<tr>
<td>Capurso et al. [20]</td>
<td>83</td>
<td>36</td>
<td>3 (3.3%)</td>
<td>249</td>
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</tr>
<tr>
<td>Di Mario et al. [21]</td>
<td>40</td>
<td>21</td>
<td>0 (0%)</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>Fakhreih et al. [22]</td>
<td>61</td>
<td>12</td>
<td>3 (4.9%)</td>
<td>61</td>
<td>4.9</td>
</tr>
<tr>
<td>Gisbert et al. [23]</td>
<td>111</td>
<td>12</td>
<td>0 (0%)</td>
<td>111</td>
<td>0</td>
</tr>
<tr>
<td>Graham et al. [24]</td>
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<td>12</td>
<td>0 (0%)</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Huelin et al. [25]</td>
<td>80</td>
<td>18</td>
<td>1 (1.2%)</td>
<td>120</td>
<td>0.8</td>
</tr>
<tr>
<td>Jaspersen et al. [26]</td>
<td>24</td>
<td>12</td>
<td>0 (0%)</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Jaspersen et al. [27]</td>
<td>29</td>
<td>12</td>
<td>1 (3.4%)</td>
<td>29</td>
<td>3.4</td>
</tr>
<tr>
<td>Jensen et al. [28]</td>
<td>171</td>
<td>24</td>
<td>1 (0.6%)</td>
<td>342</td>
<td>0.3</td>
</tr>
<tr>
<td>Krimman et al. [29]</td>
<td>33</td>
<td>17</td>
<td>0 (0%)</td>
<td>47</td>
<td>0</td>
</tr>
<tr>
<td>Labenz et al. [30]</td>
<td>42</td>
<td>17</td>
<td>0 (0%)</td>
<td>59</td>
<td>0</td>
</tr>
<tr>
<td>Lai et al. [31]</td>
<td>41</td>
<td>53</td>
<td>2 (4.9%)</td>
<td>177</td>
<td>3.4</td>
</tr>
<tr>
<td>Lai et al. [32]</td>
<td>29</td>
<td>11</td>
<td>0 (0%)</td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td>Lee et al. [33]</td>
<td>92</td>
<td>15</td>
<td>0 (0%)</td>
<td>115</td>
<td>0</td>
</tr>
<tr>
<td>Liu et al. [34]</td>
<td>26</td>
<td>56</td>
<td>0 (0%)</td>
<td>121</td>
<td>0</td>
</tr>
<tr>
<td>Loperfido et al. [35]</td>
<td>38</td>
<td>24</td>
<td>0 (0%)</td>
<td>76</td>
<td>0</td>
</tr>
<tr>
<td>Macri et al. [36]</td>
<td>21</td>
<td>48</td>
<td>0 (0%)</td>
<td>84</td>
<td>0</td>
</tr>
<tr>
<td>Pamos et al. [37]</td>
<td>31</td>
<td>18</td>
<td>0 (0%)</td>
<td>46</td>
<td>0</td>
</tr>
<tr>
<td>Pazzi et al. [38]</td>
<td>39</td>
<td>47</td>
<td>4 (10.3%)</td>
<td>153</td>
<td>2.6</td>
</tr>
<tr>
<td>Pellicano et al. [39]</td>
<td>46</td>
<td>47</td>
<td>0 (0%)</td>
<td>180</td>
<td>0</td>
</tr>
<tr>
<td>Pica et al. [40]</td>
<td>6</td>
<td>12</td>
<td>0 (0%)</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Riemann et al. [41]</td>
<td>42</td>
<td>19</td>
<td>2 (4.8%)</td>
<td>66</td>
<td>3</td>
</tr>
<tr>
<td>Roikkas et al. [42]</td>
<td>13</td>
<td>12</td>
<td>0 (0%)</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Santander et al. [43]</td>
<td>84</td>
<td>12</td>
<td>2 (2.4%)</td>
<td>84</td>
<td>2.4</td>
</tr>
<tr>
<td>Sung et al. [44]</td>
<td>108</td>
<td>12</td>
<td>0 (0%)</td>
<td>108</td>
<td>0</td>
</tr>
<tr>
<td>Vcev et al. [45]</td>
<td>36</td>
<td>12</td>
<td>0 (0%)</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>Vergara et al. [46]</td>
<td>93</td>
<td>27</td>
<td>0 (0%)</td>
<td>209</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>1650</td>
<td>21 (1.3%)</td>
<td>2886</td>
<td>0.8</td>
<td></td>
</tr>
</tbody>
</table>

As the follow-up time markedly varied among studies, this factor needs to be taken into account. Thus, follow-up periods in each study, measured in patient-years, and respective yearly bleeding (in patient-years⁻¹), are also included in the Table.
mean incidence of peptic ulcer rebleeding calculated from studies where \textit{H. pylori} was eradicated and no maintenance antisecretory therapy was prescribed was only per patient-year of follow up (Table 1) [17–46]. In this respect, a recent \textit{Cochrane} systematic review and meta-analysis concluded that rebleeding was less frequent after \textit{H. pylori} eradication therapy than after non-eradication antisecretory therapy, with an odds ratio of about 0.20 [12,13]. This advantage is expressed by a number needed to treat with eradication therapy to prevent one episode of rebleeding of only 5 when compared with ulcer healing treatment alone, in agreement with the results of another meta-analysis [47]. Liu et al. [34] randomized consecutive patients with \textit{H pylori}-associated bleeding peptic ulcers, after successful \textit{H. pylori} eradication, to receive maintenance treatment with antacids, antisecretors, bismuth or placebo [34]. During a mean follow up of 56 months, there was no peptic ulcer recurrence among the three treatment groups, not even in the placebo group. Moreover, two recent randomized studies [32,39] have directly compared, after anti-\textit{H. pylori} therapy had been prescribed and eradication confirmed, long-term maintenance antisecretory therapy versus no treatment, reporting no differences in rebleeding rates, during a mean follow-up period of up to 47 months.

Nevertheless, the prescription of \textit{H. pylori} eradication therapy does not always prevent recurrence of bleeding, and several explanations could be suggested for this. First, as antibiotic regimens are not 100% effective to treat \textit{H. pylori} infection, eradication failures may explain, obviously, some of the rebleedings. For example, in the study by Lai et al. [31], four of the six patients with a rebleeding episode in the eradication treatment group had failed to eradicate \textit{H. pylori} infection; and in the study by Vcev et al. [45], all the three patients with recurrence of bleeding had failed to eradicate \textit{H. pylori} infection with antibiotic therapy. Therefore, in case of initial eradication failures, re-treatment should be prescribed. In clinical practice, several studies have demonstrated that \textit{H. pylori} eradication can finally be achieved in almost all patients if several rescue therapies are consecutively given [48]. In the present study, patients with therapy failure received a second or even a third course of therapy and, finally, 99\% of the patients achieved \textit{H. pylori} eradication success and were included in the prospective study and followed up.

Second, as recurrence of \textit{H. pylori} infection seems to be an important cause of subsequent ulcer recurrence (and consequent rebleeding) [49], the study of incidence of the organism’s recurrence represents an important issue, as high reinfection rate offsets the expected beneficial effects of \textit{H. pylori} eradication [49]. In the previously mentioned \textit{Cochrane} meta-analysis [12,13], one of the patients who had recurrence of hemorrhage in the study by Lai et al. [31], had recurrence of \textit{H. pylori} infection at the time of rebleeding, while \textit{H. pylori} recurrence occurred in the two patients having recurrence of hemorrhage in the study by Santander et al. [43]. Other studies have also reported rebleeding only in patients with reinfection [27]. In our study, recurrence of \textit{H. pylori} infection was confirmed in four patients at 1 year (incidence: 0.95\% per patient-year of follow up), but none of these patients had recurrence of bleeding. Fortunately, recurrence of \textit{H. pylori} infection seems to be a relatively infrequent event in developed countries [49]. Nevertheless, in countries where the rate of reinfection is higher, rebleeding may be a relevant problem.

Third, NSAID intake probably explains a major percentage of rebleedings occurring despite \textit{H. pylori} eradication. The two rebleeding episodes in our study occurred after NSAID use, and none of them were receiving concomitant PPIs for ulcer bleeding prophylaxis. The use of NSAIDs at the time of rebleeding seemed to explain some of the episodes in two of the studies [31,41] included in the aforementioned \textit{Cochrane} meta-analysis [12,13] and also in other studies [25]. Although excluding from the analysis those patients with NSAID use would give us more strict data about the true role of \textit{H. pylori} eradication in the prevention of recurrent bleeding, in clinical practice a relevant group of patients will probably take these drugs. Due to the fact that clinical research, unlike basic science research, has clinical practicality as its foundation and not pure knowledge, we must probably accept the real results (including patients taking NSAIDs) as predictive of outcome for the population in question [50]. Nevertheless, the results of the present study emphasize the observation that \textit{H. pylori} eradication is of value in chronic NSAID users, but is insufficient to prevent NSAID-related ulcer disease and ulcer complications [51]. For instance, Chan et al. [52] showed that in \textit{H. pylori}-positive NSAID users who had bled from peptic ulcer, PPI maintenance was better than eradication treatment in preventing bleeding recurrence. As expected, in a similar high risk population, Lai et al. found that after treating \textit{H. pylori}, PPI maintenance was better than placebo in preventing NSAID ulcers [53] or aspirin-induced rebleeding [54]. Nevertheless, only two of the 28 patients using NSAIDs in our study had recurrent ulcer bleeding during a mean follow up of approximately 2 years, which represents a rebleeding rate of only 7\% per patient-year. This figure is considerably lower than that reported by Chan et al. [52], who observed that among NSAID users, the probability of recurrent bleeding for patients previously receiving eradication therapy was 19\% at 6 months (that is, approximately 36\% per year). Therefore, we may conclude that the rate of recurrent ulcer bleeding due to NSAIDs in our study was relatively low after successful eradication of \textit{H. pylori}.

The protective effect of \textit{H. pylori} eradication on peptic ulcer rebleeding seems to be maintained at least in the
medium-term follow up, as rebleeding rates of 0% have been reported even after 24 months [17,35,36,39]. However, few large prospective studies evaluating peptic ulcer rebleeding after _H. pylori_ eradication exist, the number of patients included in these studies has been small, and the follow up has been relatively short. Thus, as summarized in Table 1, the follow-up period was limited to only 1 year in most studies. In this respect, it remains to be demonstrated that the beneficial effects of _H. pylori_ eradication are maintained in the future, mainly because, as previously mentioned, _H. pylori_ reinfection could be a problem in the long-term management. Our study is, at the best of our knowledge, the largest (in number of patients) and the longest (in patient-years of follow up) one performed up to now with the aim to evaluate the effect of _H. pylori_ eradication on ulcer bleeding recurrence, as 422 patients have been included for a total of 906 patient-years of follow up.

Several advantages are associated with _H. pylori_ eradication therapy, when compared with long-term maintenance antisecretory therapy, in patients with previous peptic ulcer bleeding. First, the first strategy is more effective than the second [12,13]. Furthermore, some data exist suggesting that continued administration of H₂-receptor antagonist leads to pharmacologic tolerance, with a decrease in its effect in controlling gastric acid secretion [55]. Second, one disadvantage of maintenance antisecretory therapy is the requirement for long-term compliance, which may not be sustained but wane, especially when symptoms are absent. Third, it is obvious that 7–10 days of antibiotic therapy is more convenient for the patients than many years of continuous antisecretory treatment. Finally, the cost of antibiotic therapy is lower than long-term management by antisecretory drugs, mainly because the financial outlay for medication in the former approach is not cumulative as with the latter [56,57]. Cost-effectiveness analysis comparing treatment of _H. pylori_ infection with other approaches to prevent recurrent ulcer hemorrhage demonstrated that treatment of _H. pylori_ infection was the least costly strategy unless the incidence of complicated recurrences after treatment was over 6%, or the cost of confirming eradication was over $US741 [47].

Although, based on aforementioned arguments, it seems logical to test all patients with peptic ulcer bleeding for _H. pylori_ infection, and to prescribe eradication therapy to _H. pylori_-positive patients, in clinical practice this strategy seems to have limited divulgence. Thus, it is disappointing that relatively few patients admitted to hospital with peptic ulcer hemorrhage appear to be tested for the infection or to be treated when present. In this respect, a recent study on a high number of such patients admitted to US hospitals found that only 56% were tested for _H. pylori_ infection or appropriately treated for it [58]. These discouraging results regarding the implementation of _H. pylori_ testing and treating have been confirmed in a review of case notes and endoscopy records of patients presenting to Auckland Hospital [59]. Finally, in another study aimed to investigate current management of ulcer hemorrhage in the Netherlands, it was found that _H. pylori_ eradication was confirmed by only 64% of the physicians [60]. In summary, it seems evident that management of patients with previous peptic ulcer hemorrhage is only partly in accordance with evidence-based medicine.

In summary, the conclusion of the present study is that rebleeding does not occur in patients with complicated ulcers after _H. pylori_ eradication. Consequently, all patients with peptic ulcer bleeding should be tested for _H. pylori_ infection, and eradication therapy should be prescribed to _H. pylori_-positive patients. It seems unnecessary to continue antisecretory maintenance therapy in patients with a history of peptic ulcer bleeding and prior _H. pylori_ eradication. Although further short-term trials of greater sample size would be useful, the main area of uncertainty is the assessment of the long-term beneficial results of _H. pylori_ eradication and the role of the factors that could explain recurrence of bleeding despite _H. pylori_ eradication success (especially NSAID use and _H. pylori_ reinfection).

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References


H. pylori and Peptic Ulcer Rebleeding

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