The effects of the presence of Helicobacter pylori (Hp) and the eradication therapy of Helicobacter pylori on the progress and complications of GERD were examined under four main headings.

**DOES THE PRESENCE OF HELICOBACTER PYLORI AFFECT THE PREVALENCE, SYMPTOM SCORES, SEVERITY, AND RELAPSE OF REFLUX?**

Helicobacter pylori infection has been thought to play a facilitating role for the development of GERD by causing a reduction in the lower esophageal sphincter (LES) pressure, an increase in the transient relaxation of the lower esophageal sphincter, hypergastrinaemia, and a delay in gastric emptying. On the other hand, it has been suggested to be protective from GERD because it leads to a reduction in acid secretion and provides acid neutralization due to the gastritis type it creates. With the implementation of eradication therapies, a decrease has occurred in the prevalence of H. pylori; however, the frequency and complications of GERD have increased. This result supports the view that H. pylori may be protective from GERD. In an epidemiological study, the prevalence of H. pylori was reported to be lower in GERD than the non-reflux group (32.8% vs. 49.5%; OR: 0.58) (1). The first clinical trials showed that the presence of H. pylori reduced the need for proton pump inhibitor (PPI) (2). When compared in terms of maintaining symptomatic and endoscopic remission, H. pylori eradicated (Hp negative, Hp-) GERD patients were indicated to need a higher dose of PPI than patients that had H. pylori (Hp positive, Hp+) (3). Subsequently, it was shown that erosive esophagitis developed more frequent in patients treated with H. pylori eradication compared to Hp+ patients (4). It was reported in another study that reflux esophagitis recovered synchronous in patients who underwent eradication therapy due to peptic ulcers (5). In epidemiological studies, it was seen that there were differences between the East and the...
West; but there was an inverse relationship between \textit{H. pylori} prevalence and GERD when all the proportions were evaluated together (1).

In order to search for the answers to this controversial question, when the keywords “Gastroesophageal reflux disease [MeSH Terms]” AND “Helicobacter pylori [MeSH Terms]” were entered, a total of 293 studies were found in the systematic literature review written in English on adult subjects. Of these, 17 randomized controlled studies, consistent with the criteria, and 4 meta-analyses (covering also 17 randomized controlled studies) were evaluated. A meta-analysis, by Cremonini et al. (6), that involved 14 case-control studies and 10 clinical trials, analyzed the effect of \textit{H. pylori} eradication among participants in terms of “de novo” reflux development and progression in the existing symptoms of reflux. It was identified that eradication therapy increased new reflux development 3.25 times (95% CI 2.09-5.33), rebound reflux development increased 2.39 times (95% CI 1.75-3.34), and new or rebound reflux development increased 2.54 times (95% CI 1.92-3.37). Despite this meta-analysis that states the presence of \textit{H. pylori} is protective against the development of GERD, other studies have not reached this conclusion. In the meta-analysis, by Yaghoobi et al. (7), that involved five cohort studies and 7 randomized controlled trials (RCTs), all \textit{H. pylori}+ and non-GERD patients were compared by receiving placebo vs. eradication therapy in terms of new reflux symptoms and/or reflux esophagitis development. Cohort studies and RCTs were assessed separately; the odds ratio was found as 1.22 (95% CI 0.89-1.69) for the risk of symptomatic GERD development in RCTs, 1.11 (95% CI 0.81-1.53) for the risk of erosive esophagitis development, and 1.37 (95% CI 0.89-2.12) for the risk of GERD development in cohort studies (7). In another meta-analysis, 11 RCTs were evaluated. GERD and non-GERD groups were initially included in this study; the group in which eradication was applied and \textit{H. pylori} persistent groups were examined in terms of the development of symptomatic reflux and/or erosive esophagitis. As a result, no difference was detected between the two groups in terms of symptomatic reflux, heartburn, and erosive esophagitis frequency. They were indicated as odds ratio: 0.88 (95% CI 0.63-1.23), 0.79 (95% CI 0.54-1.15), and 0.97 (95% CI 0.67-1.40), respectively (8). Finally, in the meta-analysis by Saad et al. (9) of 10 RCTs, the group of \textit{Hp} therapy vs. placebo and the group in which a successful \textit{Hp} was applied vs. persistent group were compared among themselves in terms of the development of symptomatic reflex and erosive esophagitis, and similar conclusions were reached: The odds ratio was found as 0.81 (95% CI 0.56-1.71) for the development of symptomatic reflux and as 1.13 (95% CI 0.72-1.78) for the development of erosive esophagitis. Moreover, a decrease in the rate of symptomatic reflux was found in the group with successful \textit{Hp} eradication in comparison to the persistent group (13.8% vs. 24.9%; OR: 0.55; 95% CI 0.35-0.87) (9).

Table 1. The relationship between \textit{H. pylori} eradication therapy and the development of symptomatic reflux disease and erosive esophagitis

<table>
<thead>
<tr>
<th>Author/Journal/Year</th>
<th>Study Design</th>
<th>Comparison Groups</th>
<th>“Outcome Measure”</th>
<th>“Outcome Pattern”</th>
<th>Results (OR)</th>
</tr>
</thead>
</table>
| Cremonini et al. (6), Aliment Pharmacol Ther, 2003 | Meta-analysis (14 case control 10 RCT) | *HpE tx+ vs. tx- , *Successful HpE tx vs. Hperf | Endoscopic esophagitis and reflux symptoms | Denovo/recurrent reflux development and worsening of existing symptoms of reflux disease/progression | Denovo: 3.25 (95% CI 2.09-5.33) 
Rebound: 2.39 (95% CI 1.75-3.34) 
Denovo + Rebound: 2.54 (95% CI 1.92-3.37) |
| Yaghoobi et al. (7), Am J Gastroenterol, 2010 | Meta-analysis (5 cohort study 7 RCT) | All cases Hp+ and GERD(-) | Erosive esophagitis or reflux symptoms | Denovo reflux symptoms or the development of reflux esophagitis | Symptomatic GERD for RCT: 1.22 (95% CI 0.89-1.69) 
Endoscopic GERD for RCT: 1.11 (95% CI 0.81-1.53) 
GERD for cohort study: 1.37 (95% CI 0.89-2.12) |
| Quian et al. (8), Helicobacter, 2011 | Meta-analysis (11 RCT) | Baseline patients with and without GERD | Symptomatic reflux disease, erosive esophagitis | Development or progression denovo and recurrent reflux disease | Incidence of symptomatic reflux: 0.88 (95% CI 0.63-1.23) 
Incidence of heartburn: 0.79 (95% CI 0.54-1.15) 
Incidence of erosive esophagitis: 0.97 (95% CI 0.67-1.40) |
| Saad et al. (9), Scand J Gastroenterol, 2012 | Meta-analysis (10 T) | *HpE tx vs placebo , *Successful HpE tx vs. unsuccessful HpE tx | Symptomatic reflux disease and erosive esophagitis | Recurrent reflux disease and erosive esophagitis | Development of symptomatic reflux: 0.81 (95% CI 0.56-1.71) 
Development of erosive esophagitis: 1.13 (95% CI 0.72-1.78) |

\textit{HpE} tx: \textit{H. pylori} eradication therapy, \textit{Hperf}: \textit{H. pylori} persistent
A subgroup analysis was made in these four meta-analyses in terms of the disease groups in which Hp eradication was performed, the rate of GERD development after Hp eradication was found higher in the group that was given eradication therapy due to peptic ulcers than the group that was given eradication therapy due to functional dyspepsia (6,7) [In the study of Yaghoobi et al. (7), OR: 1.26, 95% CI 0.88-1.80 for RCT and OR: 2.04, 95% CI 1.88-3.85 for cohort studies and in the study of Cremonini et al. (6) OR: 1.79; 95% CI 1.26-2.54] was detected.

According to the existing data, there is no relationship between GERD and H. pylori presence. Successful eradication therapy does not have an impact on the emergence or exacerbation of GERD. However, the development of GERD after eradication can be considered in patients with peptic ulcers. All the data of the above-mentioned studies are summarized in Table 1 and Table 2.

**Does the Risk of Atrophic Gastroitis Increase in the Presence of Helicobacter pylori in GERD Patients Using Long-Term PPI? Does Helicobacter pylori Eradication Affect the Risk in These Patients?**

Proton pump inhibitor (PPI) treatment alters the distribution of H.pylori in the stomach and causes corpus-fundus dominant gastritis with decrease in gastric acid secretion. While the annual development of atrophy was 10.9% in H.pylori + patients using PPI, this rate was found 0.9% in H.pylori - patients (10). In another study including patients not using a PPI, while this rate was 1.8% in H.pylori + cases, it was found 0.3% in H.pylori - cases (11). A search was made by entering the keywords “proton pump inhibitors [MeSH Terms]” AND “atrophy gastritis [MeSH Terms]” OR “Helicobacter pylori [MeSH Terms]” in the PubMed search, and a total of 7 RCTs were found qualified enough to answer the question above. While the groups that were taking PPI and underwent anti-reflux surgery (ARS) were compared in three of these studies, the groups in which H.pylori eradication was and was not received were compared in the others. In the RCT of Kuipers et al. (12), PPI therapy was given to 105 patients with GERD and ARS was applied in 72 patients. At the end of the 84-month follow-up, while the rate of atrophic gastritis development for H.pylori + cases was 31% in the omeprazole arm, it was found 3% in the ARS arm. In H.pylori- cases, whereas the same rate was 4% in those using omeprazole, it was found to be 0% in the ARS arm. In the study of Lundell et al. (13), 155 patients in whom GERD was proven endoscopically were given omeprazole and ARS was applied in 155 patients. At the end of a 36-month follow-up, a mild progression was seen in glandular corpus atrophy in H.pylori+ patients, and similar results were observed in the two arms in term of intestinal metaplasia. In the study of Lundell et al. (14) in 2006, omeprazole was administered in 98 of a total of 215 GERD patients, and ARS was applied in 117. It was shown that glandular atrophy developed in 5 of the 13 H.pylori+ patients using omeprazole and in 3 of the 12 patients who underwent ARS at the end of a 84-month follow-up. In the prospective randomized case-control study of Schenk et al. (15), 57 H.pylori+ and 26 H.pylori - GERD patients receiving omeprazole vs. placebo were followed for 12 months after eradication therapy; the rate of atrophy in corpus was observed not to have changed in the eradication arm. In another prospective double-blind RCT, omeprazole vs. placebo treatment was given to patients with 15 GERD with H.pylori+ omeprazole vs. eradication therapy was applied to another patients with 15 GERD with H.pylori+ patients, and patients with 11 GERD without H.pylori were received placebo as a control group. Whereas a slight atrophy in corpus occurred in 5 of the 11 patients who completed a one-year follow-up in the omeprazole arm, atrophy was seen in none of the 8 patients to whom eradication therapy was given (p=0.02) (16). In the RCT of Kuipers et al. (17) involving 231 H.pylori + GERD patients, omeprazole was given to 120 patients and H.pylori eradication therapy was applied to 111 patients; maintenance therapy was provided with omeprazole for 24 months. Atrophy in corpus was observed to regress in the eradication arm compared to the H.pylori + omeprazole arm (p=0.001), and no change occurred in intestinal metaplasia. In the study by Yang et al. (18), which involved 325 GERD patients (105 H.pylori + were given eradication treatment, 105 H.pylori + were followed without treatment, and 115 H.pylori - were in the control group) who were followed up24-month period after eradication therapy or placebo, the prevalence of atrophic gastritis was found to be 5.4% in the H.pylori eradication arm, 15.7% in the arm without treatment, and 0% in the control group. Intestinal metaplasia was reported as 19.4% in eradica-

---

### Table 2. The comparison between the group with successful H. pylori eradication therapy and persistent groups in terms of symptomatic reflux disease and erosive esophagitis incidence

<table>
<thead>
<tr>
<th>Author/Publication date</th>
<th>incidence of symptomatic reflux esophagitis</th>
<th>incidence of endoscopic erosive esophagitis</th>
<th>Incidence of GERD according to disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaghoobi et al. (7) 2010</td>
<td>1.22* (0.88-1.69)</td>
<td>1.17 (0.89-2.12)</td>
<td>Peptic Ulcer 0.12* (0.08-1.80)</td>
</tr>
<tr>
<td>Quiat et al. (8) 2011</td>
<td>0.88 (0.63-1.23) 0.79 (0.54-1.15) 0.97 (0.67-1.40)</td>
<td></td>
<td>Functional Dyspepsia 0.84** 0.44-1.58</td>
</tr>
<tr>
<td>Saad et al. (9) 2012</td>
<td>0.81 (0.56-1.17) 1.13 (0.72-1.78)</td>
<td>1.0 (0.7-1.42) 0.93 (0.32-2.74) 2.57 (0.64-10.22)</td>
<td>GERD 1.29 (1.26-2.54) 2.28 (1.15-2.54)</td>
</tr>
<tr>
<td>Cremonini et al. (6) 2003</td>
<td>1.34 (1.15-1.55)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*data of RCT ** data of cohort study
tion arm, as 36.2% in the arm without treatment, and as 2% in 
*H. pylori*- control arm. In all studies, an increase in corpus gastritis

was observed in the 
*H. pylori*+ groups using long-term PPI.

In light of this data, long-term use of PPI therapy in

*H. pylori*+ patients can lead to the development of corpus predominant gastritis. The application of eradication therapy can prevent the development and progression of gastric atrophy and intestinal metaplasia (Table 3).

**Table 3.** The application of eradication therapy can prevent the development and progression of gastric atrophy and intestinal metaplasia

<table>
<thead>
<tr>
<th>Author/ Publication date</th>
<th>Study Design</th>
<th>Group of Patient</th>
<th>Methods of Treatment</th>
<th>Hp + / -</th>
<th>Fw-up period (month)</th>
<th>Results</th>
<th>Corpus Gastritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuipers et al. (12) NEJM, 1996</td>
<td>RCT</td>
<td>GERD</td>
<td>105 OMP 72 ARS</td>
<td>OMP 59/105 ARS 31/72</td>
<td>84</td>
<td>rate of AG for Hp+ group - OMP 31% (18/59) - ARS 3% (1/31) rate of AG for Hp - group - OMP 4% (2/46) - ARS 0%</td>
<td>Increased</td>
</tr>
<tr>
<td>Lundell et al. (13) Gastroenterology, 1999</td>
<td>RCT</td>
<td>GERD</td>
<td>155 OMP 155 ARS</td>
<td>OMP 40/155 ARS 53/155</td>
<td>36</td>
<td>Similar results in terms of IM Hp+ patients in both arms slight progression in the corpus glandular atrophy in Hp+ patients</td>
<td>Minimal increased</td>
</tr>
<tr>
<td>Schenck et al. (15) Gut, 2000</td>
<td>RCT</td>
<td>GERD</td>
<td>57 Hp+ 26 Hp-</td>
<td>HpE vs. Hp placebo followed by maintenance with OMP Hp+/-: 24 Hp+/-: 33 Hp-: 26</td>
<td>12</td>
<td>Decreased in antral atrophy in HpE tx group but no change corpus atrophy</td>
<td>Increased</td>
</tr>
<tr>
<td>Moayyedi et al. (16 Helicobacter, 2000</td>
<td>RCT</td>
<td>GERD</td>
<td>OMP vs Placebo15 OMP vs HpE bx 15 Hp – control11</td>
<td>Completed follow-up n=11 n=8 n=12</td>
<td>12</td>
<td>OMP: 5/11 minimal corpus atrophy HpE tx: 0/8 no atrophy (p=0.02)</td>
<td>Increased</td>
</tr>
<tr>
<td>Kuipers et al. (17) Gut, 2004</td>
<td>RCT</td>
<td>GERD</td>
<td>231 Hp + GERD 120 OMP vs. 111 HpE No control Hp-</td>
<td>Maintenance therapy with OMP for 2 years</td>
<td>24</td>
<td>HpE vs Hp+ OMP rate of antral IM and AG: no change rate of corpus atrophy: decrease (p=0.001) rate of IM in corpus: no change</td>
<td>Increased</td>
</tr>
<tr>
<td>Lundell et al. (14) APT 2006</td>
<td>RCT</td>
<td>GERD</td>
<td>215</td>
<td>98 OMP 117 ARS</td>
<td>OMP 39/98 ARS 53/117</td>
<td>84</td>
<td>Number of patients (Hp+): completed follow-up OMP: 13 ARS: 12 Glandular atrophy: 5/13 vs 3/12</td>
</tr>
<tr>
<td>Yang et al. (18) Am J Gastroenterol 2009</td>
<td>RCT</td>
<td>GERD</td>
<td>105 HpE bx 105 HpE bx - 115 Hp ( ) control group</td>
<td>After eradication or placebo therapy on-demand or continue PPI therapy</td>
<td>Completed follow-up n=83 n=83 n=100</td>
<td>24</td>
<td>Prevalence of expanded corpus atrophy HpE bx: 5.4% (5/93) Hp+ without treatment: 15.7% (13/83) Hp – control: 0% IM HpE: 19.4% (18/93) Hp+ without treatment: 36.2% (30/83) Hp+ control: 2% (2/100)</td>
</tr>
</tbody>
</table>

OMP: omeprazol; ARS: anti-reflux surgery; HpE: *H. pylori* eradication therapy; IM: intestinal metaplasia; AG: atrophic gastritis

**DOES THE PRESENCE OF HELICOBACTER PYLORI AFFECT THE FREQUENCY OF BARRETT’S ESOPHAGUS (WITH OR WITHOUT DYSPLASIA)?**

The incidence of esophageal adenocarcinoma has been increasing gradually in developed countries over the last three decades. Barrett’s esophagus (BE) is a precancerous lesion for esophageal adenocarcinoma and the incidence is <2% in the general population (19). The relationship between *H. pylori* and BE development seems somewhat complicated. In the literature, there are studies that reach different results on this issue; in addition to the studies reporting that the presence of *H. pylori* is a risk factor for BE development, there are studies reporting that it does not influence the development of BE or it prevents BE development (20-29). In the study by Vaezi et al. (29), it was found that being infected with *H. pylori* had a protective effect for development of BE and its malignant complications. This effect was more apparent in the infection with the CagA+ (positive) strain. In the study by Thrift et al. (30), the risk of BE development was reported to be lower, 80% in *H. pylori*+GERD patients in comparison to *H. pylori* - reflux patients (OR: 2.6 vs. 8.24) (30).
In order to examine the subject, a search was made using the keywords “Barrett esophagus [MeSH Terms]” AND “Helicobacter pylori [MeSH Terms]” and a total of 176 trials were found. Two meta-analyzes among them were included in the evaluation. In the research of Fischbach et al. (31), 44 case-control studies and 5 cross-sectional studies were included in the evaluation. Whether the 
\textit{H.pylori} prevalence in patients with Barrett’s esophagus and protective effect of being infected with the CagA+ strain for BE was investigated. The presence of \textit{H.pylori} was shown to be protective for BE development (RR: 0.73, 95% CI 0.60-0.88) and this effect was higher in patients infected with the CagA+ strain (RR: 0.38, 95% CI 0.19-0.78). In the meta-analysis of Wang et al. (32), 12 case-control studies were evaluated. 550 BE patients were compared with 2979 volunteers consisting of healthy blood donors with normal endoscopic examination. While the \textit{H.pylori} prevalence was 42.9% (236/550) in the group of Barrett’s esophagus while it was found to be 43.9% (1308/2979) in healthy volunteers (OR: 0.74, 95% CI 0.40-1.37).

According to the available data, the presence of \textit{H.pylori} seems to be protective for BE development and this effect is more evident in CagA+ patients. This data is summarized in Table 4.

**Table 4.** The presence of \textit{Hp} seems to be protective from BE development and the protective effect is more evident in CagA+ patients

<table>
<thead>
<tr>
<th>Author/Publication date</th>
<th>Study design</th>
<th>Comparison groups</th>
<th>“Outcome measure”</th>
<th>Results</th>
<th>Results (RR/OR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fischbach et al. (31)</td>
<td>Meta-analysis (44 case control study)</td>
<td>H. pylori prevalence in control groups and with BE patients</td>
<td>H. pylori is protective for development BE and BE prevalence in cagA+ patients</td>
<td>RR: 0.73 (95% CI 0.60-0.88)</td>
<td>Homogeneous 4 studies were analyzed separately: RR: 0.46 (95% CI 0.35-0.60) cagA+ group; study: RR: 0.38 (95% CI 0.19-0.78)</td>
</tr>
<tr>
<td>Helicobacter, 2012</td>
<td>5 cross sectional study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang et al. (32)</td>
<td>Meta-analysis (12 case control study)</td>
<td>550 with BE patients and 2979 control groups (endoscopically normal blood donors)</td>
<td>Prevalence of \textit{H.pylori} 42.9% (236/550) vs. 43.9% (1308/2979)</td>
<td>OR: 0.74 (95% CI 0.40-1.37)</td>
<td></td>
</tr>
<tr>
<td>Am J Gastroenterol, 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 5.** The presence of \textit{Hp}, and especially the infection with the CagA+ strain, show a protective effect against esophageal adenocarcinoma. The relationship between \textit{Hp} and esophagus squamous cell cancer is not clear.

<table>
<thead>
<tr>
<th>Author/Publication date</th>
<th>Study design</th>
<th>Comparison groups</th>
<th>Outcome measure</th>
<th>Results</th>
<th>Results (RR/OR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Islami et al. (35)</td>
<td>Meta-analysis (19 study)</td>
<td>H.p+ vs. H.p- cagA+ vs. cagA-</td>
<td>Risk of Adeno Ca or Squamous Ca</td>
<td>H.pylori reduces the risk Adeno Ca, this phenomenon more pronounced rate in cagA+ Hp does not affect the risk of squamous Ca. No relationship with the cagA.</td>
<td>ADENO CA Overall OR: 0.56 (95% CI 0.46-0.68) cagA+ OR: 0.41 (95% CI 0.28-0.62) cagA- OR: 1.08 (95% CI 0.76-1.53) SQUAMOUS CA Overall OR: 1.1 (95% CI 0.78-1.55) cagA+ OR: 1.01 (95% CI 0.80-1.27) cagA- OR: 1.41 (95% CI 1-1.97)</td>
</tr>
<tr>
<td>Cancer Rev Pres 2008</td>
<td>Adeno Ca: 13 study; 848 patients/2890 control group Squamous Ca: 9 study; 921 patients/2743 control group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xie et al. (36)</td>
<td>Meta-analysis (27 study)</td>
<td>H.p+ vs. H.p- cagA+ vs. cagA- East/West study</td>
<td>Risk of Adeno Ca or Squamous Ca</td>
<td>Hp reduces the risk of adeno Ca Rate of H.p+ in Adeno Ca: 35.96% (479/1332) vs. 44% in control groups; 44% (2070/4705), OR: 0.71 (0.63-0.81) Hp generally does not risk of squamous Ca affect the cagA+ OR: 0.90 (95% CI 0.78-1.05) *East OR: 0.77 (95% CI 0.65-0.92) *West OR: 1.26 (95% CI 0.97-1.63)</td>
<td>Adeno Ca Overall OR: 0.59 (95% CI 0.51-0.68) Squamous Ca Overall OR: 0.83 (95% CI 0.63-1.03) Reduces the risk of squamous Ca CagA + Hp in Eastern studies</td>
</tr>
<tr>
<td>W J Gastroenterol, 2013</td>
<td>Adeno Ca: 15 study Squamous Ca: 16 study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In order to examine the subject, a search was made using the keywords “Barrett esophagus [MeSH Terms]” AND “Helicobacter pylori [MeSH Terms]” and a total of 176 trials were found. Two meta-analyzes among them were included in the evaluation. In the research of Fischbach et al. (31), 44 case-control studies and 5 cross-sectional studies were included in the evaluation. Whether the \textit{H.pylori} prevalence in patients with Barrett’s esophagus and protective effect of being infected with the CagA+ strain for BE was investigated. The presence of \textit{H.pylori} was shown to be protective for BE development (RR: 0.73, 95% CI 0.60-0.88) and this effect was higher in patients infected with the CagA+ strain (RR: 0.38, 95% CI 0.19-0.78). In the meta-analysis of Wang et al. (32), 12 case-control studies were evaluated. 550 BE patients were compared with 2979 volunteers consisting of healthy blood donors with normal endoscopic examination. While the \textit{H.pylori} prevalence was 42.9% (236/550) in the group of Barrett’s esophagus while it was found to be 43.9% (1308/2979) in healthy volunteers (OR: 0.74, 95% CI 0.40-1.37). According to the available data, the presence of \textit{H.pylori} seems to be protective for BE development and this effect is more evident in CagA+ patients. This data is summarized in Table 4.
The persistent *H. pylori* infection in GERD has been reported to be a risk factor for a subtype of esophageal squamous cell carcinoma (33). On the other hand, it has been suggested that the presence of *H. pylori* protects from the development of esophageal adenocarcinoma through various mechanisms (hypoaclidity, decrease in gastric ghrelin secretion, affected gastric and esophageal microbiota, and it leads to changes in gastric T-cell compartments) (34). In the search that was conducted to investigate this issue, the keywords “esophagus cancer [MeSH Terms]” and “Helicobacter pylori [MeSH Terms]” were used and of a total of 142 studies that were obtained. Two meta-analyses meeting the criteria were included in the assessment. The first meta-analysis was published in 2008 and it consisted of 19 studies. The majority of them were community-based and large-scale case-control studies; 13 of them include adenocarcinoma patients (848 patients/2890 control) and 9 of them include squamous cell carcinoma patients (921 patients/2743 control). The patients and controls in this study were grouped in terms of Hp positivity and Hp+ patients were also grouped in terms of CagA+/CagA- strains. It was shown that *H. pylori* positivity reduced the risk of adenocarcinoma [overall OR: 0.56 (95% CI 0.46-0.68)] and the protective effect was more evident in CagA+ cases [CagA+OR: 0.41 (95% CI 0.28–0.62) and CagA- OR: 1.08 (95% CI 0.76-1.53)]. However, the presence of *H. pylori* does not affect the risk of squamous cell carcinoma [Overall OR: 1.1 (95% CI 0.78-1.55)]. Similarly, it has also been found that being infected with CagA+ or CagA- strains does not have an association with the development of squamous cell carcinoma [overall OR: 1.1 (95% CI 0.78-1.55)] (35). In the meta-analysis by Xie et al. (36), a total of 27 community and hospital based studies (15 studies with adenocarcinoma and 16 with squamous cell carcinoma) were assessed. In this study as well, the relationship between the development of cancer in the esophagus and *H. pylori* was examined, and it was shown that *H. pylori* positivity reduced the risk of adenocarcinoma development [overall OR: 0.59 (95% CI 0.51-0.68)]. While the rate of *H. pylori* positivity was 35.96% (479/1332) in the group of adenocarcinoma, it was 44% (2070/4705) in the control group. Similar to the aforementioned meta-analysis, it was determined that the presence of *H. pylori* did not usually affect the risk of squamous cell carcinoma [Overall OR: 0.83 (95% CI 0.63-1.03)] and being infected with the CagA+ strain was shown in Eastern studies to reduce the risk of squamous cell carcinoma development more than in Western studies: Eastern CagA+OR: 0.77 (95% CI 0.65-0.92) and Western cagA+OR: 1.26 (95% CI 0.97-1.63).

In the light of the data presented, the presence of *H. pylori*, and especially the infection with the CagA+ strain, show a protective effect against esophageal adenocarcinoma. The relationship between *H. pylori* and esophage squamous cell cancer is not clear. The data is summarized in Table 5.

**RECOMMENDATIONS**

- There is no relationship between *H. pylori* and GERD (Level of evidence: 1a).
- *H. pylori* eradication does not have any effects in the emergence or exacerbation of GERD, except for patients with peptic ulcers (Level of evidence: 1a).
- Long-term use of PPI may have an impact on the development of atrophy and/or intestinal metaplasia in *H. pylori* positive patients; therefore, *H. pylori* eradication is recommended in patients that should use long-term PPI (Level of evidence: 1b).
- Barrett’s esophagus and esophageal adenocarcinoma are less frequent, especially in the presence of CagA positive *H. pylori* infections (Level of evidence: 3a).
- *H. pylori* screening and the eradication decision should be independent of GERD, except for patients that will use long-term PPI (Level of evidence: 5).

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

**REFERENCES**

4. Labenz J, Blum AL, Bayerdörffer E, Meining A, Stolte M, Börsch G. Curing Helicobacter pylori infection in patients with duodenal ulcer may provoke reflux esophagitis. Gastroenterology 1997; 112: 1442-7. [CrossRef]
Mungan and Pinarbaşı Şimşek. Gastroesophageal reflux disease and Helicobacter pylori

19. El-Serag HB, Mason AC, Petersen N, Key CR. Epidemiological differences between adenocarcinoma of the oesophagus and adenocarcinoma of the gastric cardia in the USA. Gut 2002; 50: 368-72. [CrossRef]