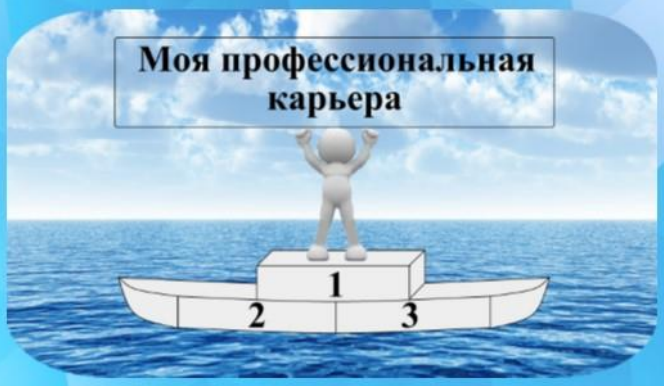

Научно-образовательный электронный журнал

ОБРАЗОВАНИЕ И НАУКА В XXI ВЕКЕ

Выпуск №24 (том 2)
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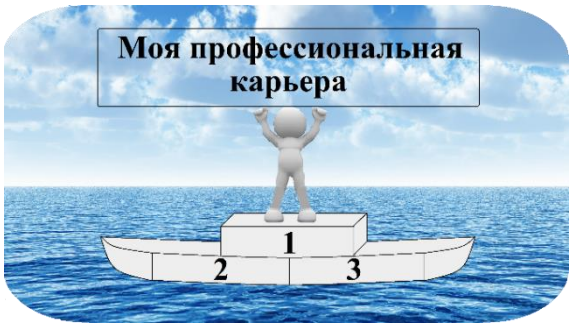

Международный научно-образовательный электронный журнал
«ОБРАЗОВАНИЕ И НАУКА В XXI ВЕКЕ»

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Сборник содержит научные статьи отечественных и зарубежных авторов по экономическим, техническим, философским, юридическим и другим наукам.

Миссия научно-образовательного электронного журнала «ОБРАЗОВАНИЕ И НАУКА В XXI ВЕКЕ» состоит в поддержке интереса читателей к оригинальным исследованиям и инновационным подходам в различных тематических направлениях, которые способствуют распространению лучшей отечественной и зарубежной практики в интернет пространстве.

Целевая аудитория журнала охватывает работников сферы образования (воспитателей, педагогов, учителей, руководителей кружков) и школьников, интересующихся вопросами, освещаемыми в журнале.

Материалы публикуются в авторской редакции. За соблюдение законов об интеллектуальной собственности и за содержание статей ответственность несут авторы статей. Мнение редакции может не совпадать с мнением авторов статей. При использовании и заимствовании материалов ссылка на издание обязательна.

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Название публикации: «THE ROLE OF HELICOBACTER PYLORI IN CARDIOESOPHAGEAL CANCER»

Abstract. Esophageal cancer ranks the eighth in the world's cancer incidence and the sixth in the global cancer death cause. There are two major histological subtypes of the esophagus: esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC). ESCC and EAC have different geographic and demographic models. ESCC has a high incidence in many developing countries.
The most important risk factors in Western countries are smoking and habitual consumption of alcohol. In developed countries such as North America, Australia, and Europe, esophageal adenocarcinoma has become the main subtype of esophageal cancer; its major risk factors include chronic gastroesophageal reflux disease, obesity, and smoking. Esophageal cancer is mainly a disease of the male population over 55 years of age. Men get sick more often than women on average 5-10 times. The peak incidence occurs at the age of 55-60 and older, with people over 70 accounting for about 40 percent of cases. The highest incidence is observed in the so-called "Central Asian zone of esophageal cancer", which includes the Caspian coast, Central Asian republics, Mongolia and northwestern China. In the Russian Federation, the incidence of esophageal cancer is growing steadily. In 2017, the absolute number of cases amounted to 8220 cases, compared with 2010 this figure has doubled. The highest incidence of esophageal cancer is in China, Iran, the states of Central and Central Asia - about 100 people per 100 thousand of the population fall ill there every year. In the regions with the lowest level (Armenia, Mali, Israel, Vietnam) this indicator is almost 100 times lower and amounts to

approximately 1.7-2.2 cases per 100 thousand population per year.
Differences in the incidence of esophageal cancer reach 15 times between individual countries. The highest rates are found in the male population of

Turkmenistan, Kazakhstan and Kyrgyzstan (8-16 per 100,000), relatively rarely in Armenia, Mali, Israel, Vietnam (1.7-2.2). The average position is occupied by the incidence rate in Russia (7.0 and 1.1 in men and women, respectively). On the territory of Russia, the lowest indicators are in the North Caucasus (75-79 rank places); the highest - in Yakutia (29.6 - for men) and Tuva (9.7 - for women). In the structure of the morbidity of the population of most countries of the world, more than half of malignant formations occur in the digestive system, Uzbekistan is, unfortunately, no exception. The peculiarities of the national diet suggest the frequent consumption of very hot tea during the day, a large amount of fatty foods, the distribution of the daily ration mainly in the morning and late evening hours, due to national customs. This leads to a decrease in the secretory function of the stomach, and therefore, predominantly to the intestinal type of digestion, leading to atrophic changes and widespread cancer of gastroenterological localization among the indigenous population. In the structure of cancer incidence in Uzbekistan, esophageal cancer is 3.8% in men and 3.7% in women.

Keywords: Helicobacter Pylori, Cardioesophageal cancer, Proinflammatory genotypes

Introduction

Gastoesophageal junction (CEJ) cancer, especially adenocarcinoma of the CEJ, represents a solid tumor entity with a rapidly increasing incidence in Western countries during recent decades [25,10]. Being anatomically associated with esophageal cancer and gastric cancer, CEJ cancers, which are predominantly considered to be adenocarcinomas, are increasingly being considered as a distinct tumor entity. They have a constellation of risk factors that are distinct from those for esophageal and gastric cancers, with a certain genetic configuration and principally tailored therapeutic approaches. In Western countries, where the highest incidence of CEJ cancer is found, a limited level of centralization leads to difficulties in recruitment for prospective studies. In Asian countries, especially in Korea and Japan, the incidence of CEJ cancer is not high compared with gastric cancer, for which a large number of clinical trials have been performed, and the surgical treatment is highly standardized [41,25].

According to the Cancer Register of the Republican Cancer Research Center in Uzbekistan, cancer esophagus (15.1%) has a significant role in the incidence of cancer, along with breast cancer (20.4%), neoplasms of the cervix (13.1%), stomach

(8.5%), ovaries (5.4%), lungs (4.1%), lymphoma (4 , 1%), lips, oral cavity, pharynx (3.3%),
central nervous system (3.1%), rectum (2.8%), bones and soft tissues (2.7%), skin (2,
5%), colon (2.4%), leukemia (2.4%), kidney (1.9%), bladder (0.85%), larynx (0.78%). Mortality from esophageal cancer in 2019 averaged 1.1% [49]

Helicobacter pylori is a common bacterium in the upper digestive tract, which infects about half of the world [12] Marshall and Warren first reported the cultivation of Helicobacter pylori from human gastric mucosa in 1983 [6]. The International Agency for Research on Cancer and the World Health Organization believed that Helicobacter pylori is a carcinogen of gastric cancer. However, some studies have shown that Helicobacter pylori infection is negatively correlated with some diseases. The primary pathogenic role of *H. pylori* in peptic ulcer formation is supported by robust evidence [33], and *H. pylori* was recognized as a true class I carcinogen for gastric cancer by the International Agency for Research on Cancer and the World Health Organization in 1994 Helicobacter pylori infection appeared to have a "protective effect." Since the 20th century, the prevalence of Helicobacter pylori hasdeclined in Western countries; At present, the relationship between Helicobacter pylori and esophageal squamous cell carcinoma has not been clearly explained; the evidence of its protective or harmful effects on esophageal adenocarcinoma is still contradictory. In recent years, articles on the relationship between Helicobacter pylori and esophageal cancer have been published in succession; new data can be used to further analyze the relationship between Helicobacter pylori and esophageal cancer [38].

Do Host Genes Matter?

Esophageal adenocarcinoma has risen at an alarming rate in Western countries over the past few decades. This rise has not been met with any substantial improvement in treatment, making this cancer among the deadliest. It is likely that prevention offers the most credible strategy to defeat this cancer. As such, it is imperative to understand the basic pathogenesis of this condition and its precursors. The classic risk factors for this cancer include gastroesophageal reflux disease (GERD), smoking, obesity and a diet low in fresh fruit and vegetables [41].

More recent work suggests that *Helicobacter pylori* infection, especially with more virulent cagA-positive strains, decreases the risk of esophageal adenocarcinoma.[5]. The mechanism of this protective effect is not clear but it has been postulated that it may be due to *H pylori*-induced gastric atrophy and hypochlorhydria, both of which reduce acid exposure of the lower esophagus.[8]There is, therefore, an emerging

consensus that pathologic changes at the gastroesophageal junction are determined to a large extent by the gastric pathophysiologic phenotype .

There are 3 main gastric phenotypes that result from chronic *H pylori* infection: (1) the commonest by far is a mild pangastritis that does not affect gastric physiology and is not associated with significant human disease, (2) a corpus-predominant gastritis

associated with multifocal gastric atrophy, hypochlorhydria, and increased risk of gastric cancer (the gastric cancer phenotype), and (3) an antral-predominant gastritis associated with high gastric acid secretion and increased risk of duodenal ulcer disease (the DU phenotype).[42]. The cause of these divergent clinical outcomes is most likely a combination of host genetic, bacterial, and environmental factors[2]. Proinflammatory polymorphisms in the interleukin-1 beta gene (*IL1-B*) and tumor necrosis factor alpha gene (*TNF-A*) increase the risk of gastric atrophy, hypochlorhydria, and gastric cancer.[18]. IL-1_ in particular is very relevant in this context because it is a very potent inhibitor of gastric acid secretion.[19].Recent work by Waghray et al showed that IL-1_ promotes gastric atrophy through suppression of sonic hedgehog [46] and this contributes to loss of the parietal cells capacity to secrete hydrochloricacid.[45]. TNF- is also an acid inhibitor, albeit weaker than IL-1_.

It is tempting to speculate that the gastric cancer phenotype with its low acidity and association with acidreducing and atrophy-inducing proinflammatory*IL-1_* and *TNF-_* genotypes is protective against GERD and adenocarcinoma, but is there any evidence for this? At least 2 studies have addressed the role of these polymorphisms in reflux disease. GERD patients to 285 controls in Brazil and showed that the proinflammatory*IL-1B*-31 C/C and *IL-1RN**2*2 genotypes were associated inversely with GERD in *H pylori*– positive individuals.[40]. In these subjects, cagA-positive status, *IL-1B* and *IL-1RN* proinflammatory genotypes, and the degree of corpus gastritis were negatively associated with GERD. They also demonstrated that the severity of the disease was inversely associated with the number of *IL-1B* and *IL1-RN* proinflammatory alleles. The second study by Ando et al examined 208 *H pylori*–positive and 112 *H pylori*–negative Japanese subjects and reported that infected subjects were less likely to report GERD symptoms and to have endoscopic evidence of erosive esophagitis. [3]. Interleukin 1B proinflammatory genotypes protect against gastro-oesophageal reflux disease through induction of corpus atrophy [12]. Furthermore, *H pylori*–positive subjects were more likely to have corpus gastric atrophy than *H pylori*– negative subjects. Among *H pylori*–positive patients, those without erosive oesophagitis or GERD symptoms were significantly more likely to

have corpus atrophy than subjects with erosive esophagitis or GERD symptoms. Among *H pylori*–positive patients, subjects homozygous for the proinflammatory allele *IL-1B*-511T had a significantly lower risk of erosive oesophagitis and GERD symptoms compared with those homozygous for the -511C allele [35]. The authors concluded that a proinflammatory*IL- 1B* genotype was associated with increased risk of atrophy and decreased risk of GERD in *H pylori*– infected subjects in Japan. These data indicate that, in some genetically predisposed subjects, *H pylori* infection may protect against GERD through induction of gastric atrophy. Thus, these 2 studies clearly show that host genetic factors interact

with *H pylori* infection leading to onset of gastric atrophy and protection against GERD. The crucial question that remains is whether this protection extends to esophageal and junctional adenocarcinomas [26].

In this issue of, Whiteman et alattempted to answer this crucial question.[47]. They hypothesizedthat the association between *H pylori* infectionand the risk of adenocarcinomas of the esophagus and esophagogastric junction is modified by polymorphismsin the proinflammatory genes *IL-1B* and *TNF-A* that regulategastric acid secretion. As mentioned, this hypothesisassumes that a proinflammatory genetic makeup thatreduces acid secretion would protect *H pylori*–infectedsubjects from developing esophageal and junctional adenocarcinoma,cancers that most likely develop after decadesof acid-induced damage to the lower esophagus.Thus, one would expect that such infected and “protected”subjects would have the so-called gastric cancerphenotype, which is characterized by hypochlorhydriaand gastric atrophy, whereas subjects who develop theseproximal cancers are either free of *H pylori* infection or, ifinfected, have a normal or high gastric acid capacity [20,26]. Theauthors set out to answer this question with a sound andadequately powered epidemiologic design. They studied*IL-1B* and *TNF-A* polymorphisms but, unfortunately, not*IL-1RN*. The latter has consistently been shown to be anexcellent genetic marker for IL-1_ levels and function,and most of the genetic studies executed out in Caucasiansfound positive associations with proinflammatoryconditions when other markers were negative. As it turnedout, the authors found no evidence that polymorphisms in*IL-1B* or *TNF-A* modified the association between *H pylori*and esophageal or junctional adenocarcinomas. They concludedthat *H pylori* infection is associated inversely withrisks of these 2 cancers, but the reduction in risk was similaracross subgroups of potential modifiers, including the hostgenes studied.We need to consider potential explanations for these negative findings [15,18]. The simplest to exclude are genotyping errors that might have affected the results. All SNPs were in Hardy-Weinberg equilibrium, suggesting no major genotyping

problems. The 1 slight anomaly is in the degree of linkage disequilibrium between the *IL-1B*-31 and -511 loci, particularly in the controls. In other published reports, the 2 loci are in near total linkage disequilibrium, whereas in this study there seems to be a slight discrepancy. This may reflect population admixture (highly unlikely in this nearly homogeneous Caucasian population), genotyping error, or a genuine difference. It is unlikely that this small discrepancy could explain the negative findings of this study [7,19,22].

The second crucial factor to consider is the prevalence of *H pylori* infection, particularly in the control population. This clearly has to be high enough to allow a demonstration of the interaction with the host genes. The reason for this is that, in

Western populations,*H.pylori*infection is actually more likely to induce a mild pangastritis or an antral predominant gastritis that is either associated with normal or increased acid output and certainly with little or no gastric atrophy. Relatively few subjects develop the corpus-predominant gastric cancer phenotype.[37].It is therefore difficult to demonstrate a modifying effect of host genes that interact with aninfection if the prevalence of this infection is very low. So what was the prevalence of *H pylori* in this Australian population? As it turned out, it was quite low at 23%. This is much lower than most populations studied so far and certainly lower than the Brazilian and Japanese populationscited (62.9% and 65%, respectively[47]. Furthermore, the difference in *H pylori* prevalence between those with the cancer outcome versus those without was alsosmall (13% vs 23%). It is clear, therefore, that despite an adequate design with good numbers for cancer subjects and controls, the low prevalence of the infection was a major obstacle. Serologic diagnosis of the infection is bound to misclassify some subjects but this would impact equally on all participants, especially in the absence of major gastric atrophy [30,42].

The third explanation is that the gastric phenotype was not assessed in this study, and this clearly reduced the ability to offer a mechanistic insight into the associations between host genotype and clinical outcome. There were no gastric biopsies to map out the type of gastritis, its severity and the presence of atrophy. The study did not report on serologic surrogate markers of atrophy, such as pepsinogen I levels or pepsinogen I/II ratios. This would have given some insight into gastric pathophysiology and this might have informed the statistical analyses a little better. One has to acknowledge, however, that such a study where biopsies are obtained from different parts of the stomach in addition to the primary tumor would only be meaningful if the controls also had a similar mapping of gastric inflammation and

atrophy. For such large-scale epidemiologic studies, this is quite a difficult prospect and is not feasible [15,20]

With combined estimates of more than 1.6 million new cases and more than 1 million related deaths in 2018, cancers of the stomach and esophagus (gastroesophageal cancer), which include esophageal squamous cell carcinoma (SCC), proximal esophagogastric junction adenocarcinomas (esophageal and gastric cardia adenocarcinomas), and distal gastric adenocarcinoma, remain important worldwide public health concern.25 The incidence of GEJ adenocarcinoma has notably risen in Western countries, and population analyses in the United States have reported a nearly 2.5-fold increased incidence since the 1970s.[9,10]

H. pylori is able to survive and multiply in the acidic gastric environment, which is hostile to the growth of most bacteria. When intraluminal acidity diminishes as a result

of gastric atrophy, *H. pylori* is less able to colonize the stomach, possibly because of competing organisms. *H. pylori* characteristics that permit gastric colonization include microaerophilism for survival within the mucous gel, spiral shape, flagella for motility within this viscous layer, and urease activity, which generates ammonium ions that buffer gastric acidity [22,25]. Although most organisms appear to be free-living in the mucous layer, smaller numbers appear to be adherent to the mucosal epithelial cells. Organisms may be found at the luminal surface of the gastric mucosa and also deeper within gastric glands. *H. pylori* localizes almost exclusively in association with gastric- type epithelium. Affected gastric epithelium may be in the gastric antrum or fundus or may be ectopic in the duodenum or in the esophagus. In contrast, *H. pylori* does not colonize intestinal epithelium, even when present in the stomach. Several important *H. pylori* adhesins have been identified, including the outer membrane proteins BabA (which binds to fucosylated Lewis b receptor on gastric epithelial cells), SabA (which binds to sialyl Lewis X receptors), HopQ (which binds to carcinoembryonic antigen- related cell adhesion molecules), AlpA, and AlpB [32,39].

Risk factors of esophageal cancer

Demographics. It has been reported that there is an increased risk of esophageal adenocarcinoma diagnosis for persons older than 50 years, but no trend was found for an increased magnitude of risk beyond age 50 years.[7]. Racially white individuals have a 2-fold risk of developing esophageal adenocarcinoma than Hispanics, and a 3e4-fold increased risk when compared with Blacks.[20].A prevalence study

performed in the United States on Barrett's esophagus through the use of an endoscopy indicated that its prevalence among non-Hispanic whites was 6.1%, compared to 1.7% among Hispanics and 1.6% among Blacks. Therefore, much of the differences in cancer risk attributable to race ethnicity may be the reason for the differences in the risk of being diagnosed with Barrett's esophagus.[1]. Additionally, the male/female ratio of Barrett's esophagus patients is about 2:1. However, the incidence rate of esophageal adenocarcinoma shows a 38-fold increase in males over females, which may suggest that men are not only more likely to develop Barrett's esophagus, but also once they have it, may b more likely to then have their diagnosis progress to cancer.[13].

Smoking. Smoking is a risk factor associated with both Barrett's esophagus and esophageal adenocarcinoma. It has been reported that current smokers have an increased risk of esophageal adenocarcinoma, as compared to nonsmokers [odds ratio (OR)Z1.96; 95% confidence interval (CI), 1.64e2.34] [14]. Sex and duration of smoking cessation are also associated as risk factors of esophageal adenocarcinoma. Men with a history of smoking had a slightly higher risk of esophageal adenocarcinoma (ORZ2.10; 95%

CI,1.71e2.59) than women (ORZ1.74; 95% CI, 1.21e2.51). Persons who had quit smoking cigarettes for 10 years still had an increased risk of esophageal adenocarcinoma when compared to those who had never smoked (ORZ1.72; 95% CI, 1.38e2.15). Continuing to smoke also enhances the risk of Barrett's esophagus progressing to cancer.[26].Smoking was also a major cause in ESCC, where the OR was

2.9 (95% CI, 2.1e4.1); the OR in men was higher than in women (4.0 vs. 2.7, respectively). A current smoker has more risk than an ex-smoker. Total packs per year smoked was also correlated with increasing risk of ESCC. For those who smoked > 30 packs per year, the OR was 4.1 (95% CI, 2.7e6.2), and the rate was higher in men than in women (5.5 vs. 4.0, respectively)[38].

Alcohol consumption. Ethanol was metabolized by alcohol dehydrogenase and formed acetaldehyde. Acetaldehyde interacted with DNA and produced DNA adducts to induce gene mutation. Thus, alcohol is one of the risk factors for the development of upper aerodigestive tract cancer.[44].The average weekly alcohol intake exceeded 170 g, and the OR was significantly increased in ESCC patients but not in esophageal adenocarcinoma patients. The OR was upregulated in men and women with ESCC who consumed more than 210 g and 70 g per week, respectively[39].

Gastroesophageal reflux disease. GERD is one of the important risk factors for both Barrett's esophagus and esophageal adenocarcinoma. Approximately 10% of patients diagnosed with GERD will develop Barrett's esophagus.[22]. Patients experiencing recurrent heartburn or regurgitation have an approximately 5-fold increased risk to progress to esophageal adenocarcinoma, when compared to those without GERD-related symptoms.[13].

Obesity and body composition. Obesity is a risk factor toward developing esophageal adenocarcinoma. Both body mass index (BMI) and increased abdominal obesity are also associated with cancer risk. It has been reported that a BMI higher than 25 was associated with an increased risk of esophageal adenocarcinoma in both males (ORZ2.2; 95% CI, 1.8e2.7) and females (ORZ1.9; 95% CI, 1.5e2.5).[16]. The risk was also increased at greater BMI levels. Obese males and females had a higher risk of esophageal adenocarcinoma (ORZ2.4; 95% CI, 1.9e3.2 and ORZ1.9; 95% CI, 1.5e2.5, respectively) than did overweight males and females (ORZ1.8; 95% CI, 1.5e2.2 and ORZ1.5; 95% CI, 1.1e2.2, respectively). These reports suggest a dose response between the risk of esophageal adenocarcinoma and an increased BMI (p trend <0.001)[27].However, a high BMI level significantly decreased the risk of ESCC [adjusted relative risk (RR) for top vs. bottom quintile of BMI was 0.38; 95% CI, 0.23e0.62]. The adjusted RR was 0.67 (95% CI, 0.49e0.93) for BMI 25e29.9, and 0.47 (95% CI, 0.24e0.94) for BMI 30. Unlike BMI, blood pressure had a positive correlation with risk in ESCC. Higher mid blood pressure was correlated with an increased risk of ESCC. The adjusted RR for ESCC was 2.60 (95% CI 1.54e4.39) for top versus bottom quintile of mid blood pressure.[34]. Alcohol consumption has been identified as a risk factor in ESCC, and it could also cause hypertension. Thus, alcohol consumption was a confounder that could induce both hypertension and ESCC. Persistent *H. pylori* infection is believed to promote the development of gastric cancer through the development of atrophic gastritis and decrease in gastric acid secretion. However, it has a suppressive effect on GERD, Barrett's esophagus, Barrett's esophageal adenocarcinoma, and GEJ adenocarcinoma.

In Western countries, *H. pylori* infection rates in cardiac cancers were found to be considerably lower than those in the control group. However, in Asian countries where gastric cancer is common, *H. pylori* infection rates are high in both noncardiac and cardiac cancers, and *H. pylori* infection is considered a carcinogenic risk factor for both sites of cancer [32]In a comparison of *H. pylori* infection rates between GEJ adenocarcinoma and distal gastric carcinoma [31]the *H. pylori* infection rate in GEJ

adenocarcinoma was significantly lower, and the degree of histological gastritis in the gastric body was also significantly lower. In Asian countries, including Japan, where the incidence of gastric cancer is high, 2 types of GEJ adenocarcinoma have been reported: one that is not associated with *H. pylori* infection as in Western countries and another that is associated with *H. pylori* infection. McColl described the pathogenesis of GEJ adenocarcinoma in terms of gastric acid secretion and categorized it into 2 types: one that is associated with atrophic gastritis and low gastric acid secretion (similar to distal gastric cancers) and another type that is associated with excessive acid secretion with or without *H. pylori* infection (similar to esophageal adenocarcinomas) [35].

A large number of patients with chronic gastritis have undergone *H. pylori* eradication therapy in Asian countries, including Japan. It is important to determine whether the incidence of esophageal adenocarcinoma will increase after *H. pylori* eradication therapy, especially in the context of future trends of GEJ adenocarcinoma. Although there is currently no sign of an increase in the incidence of GEJ adenocarcinoma in post-eradication cases in Japan, there is only limited evidence on this issue. Take et al. [43] followed up 2,737 patients after *H. pylori* eradication therapy for an average of 7.1 years and found 2 cases of esophageal adenocarcinoma. They concluded that although the incidence of GEJ adenocarcinoma in patients after *H. pylori* eradication is higher than that in the general population, it is still very low. A previous study also found that the prevalence of esophageal adenocarcinoma is higher with persistent *H. pylori* infection than after eradication therapy, and a recent meta-

analysis suggested that *H. pylori* infection may reduce the risk of esophageal adenocarcinoma in the general population. However, these findings may be one-sided; the statement of "protection effect" may be overestimated [23]. At present, it is reasonable to assume that the widespread use of *H. pylori* eradication therapy for chronic gastritis will not directly lead to an increase in the incidence of esophageal adenocarcinoma and GEJ adenocarcinoma, although further studies are needed to clarify this important issue.

Conclusion. Esophageal cancer remains a significant cause of all cancerrelateddeaths worldwide. With a spiked increase in incidencebeing observed in certain Western countries, 3-yearsurvival rates have been shown at rates of 10-15%. Mostpatients have already manifested the advanced disease atdiagnosis and are therefore precluded from curative surgical resection. However, identification of reliablemarkers that could predict treatment outcome is stilllimited in the available medical research literature.

Thus,it is important to identify biomarkers that are able topredict any post-CCRT response in order to develop theproper treatment guidelines. We can then use these resultsto help reduce the currently high mortality rates byapplying the most beneficial treatment methods to patientsin the future. Esophageal cancer remains a lethal disease entity. The biologic characteristics of the disease have evolved from squamous cell carcinoma predominant disease to adenocarcinoma. Death rates and incidence continue to increase, especially with regard to adenocarcinoma. Recent advances in multimodality treatment show promise in improving outcomes and survival while decreasing morbidity. Proper staging and workup is vital to determine treatment strategies and goals. Once determined, a multidisciplinary approach should be employed for treatment and surveillance. Preferably, evaluation and treatment options for each patient with localized esophageal cancer should be discussed in a multidisciplinary treatment planning conference. In general, early stage T1 tumors are best managed by endoscopic modalities (superficial T1a lesions) or esophagogastrectomy (T1b) if possible. Lesions extending into and beyond the submucosa and those with nodal involvement seen on preoperative staging should be treated with combined multimodality therapy in a high volume cancer center. Unresectable disease or patients unfit for chemotherapy, radiation therapy, and/or surgery should be considered for palliation.

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