Risk Reduction and the GI Tract: From Theory to Reality
Held on May 18, 2003, Orlando, Florida

The Measurement and Expression of Risk: An Overview

Interpreting risk and presenting it to patients in an appropriate manner requires an understanding of the different measures commonly used to express risk. Very different perspectives can emerge from an evaluation of risk, depending upon the measure chosen.

“Relative risk and absolute risk are based on the same numbers, but they can have a very different impact, depending on the way the risks are presented,” said Robert S. Sandler, MD, MPH, Professor of Medicine and Epidemiology at the University of North Carolina, Chapel Hill. “As long as you’re aware of that when you read the medical literature and when you counsel your patients, you won’t be misled.”

The field of medicine employs a variety of measures to express risk. One of the simplest approaches is to use a map that reflects areas of high and low incidence of a particular disease. Such maps are useful for hypothesis generation but not for making decisions regarding individual patients.

Time trends also can produce interesting observations. Just as risk maps, however, time trends reveal information that may not be particularly useful in the clinical setting. Dr. Sandler offered esophageal adenocarcinoma as an example.

“Between 1977 and 1997, esophageal adenocarcinoma increased 400% or fourfold (Gut. 2002;50:368-372),” he said. “That sounds very alarming, but the problem with that statistic is that we don’t have a good sense of the magnitude of the problem. The American Cancer Society estimates that there will be 13,900 new cases of esophageal cancer in 2003 (Cancer Facts and Figures, 2003), and perhaps 60% will be adenocarcinoma. That means there will be about 8,300 new cases of esophageal adenocarcinoma in the United States this year.”

Describing risk in terms of risk over time takes on more meaning for the individual patient. For example, a 50-year-old man has a 1-in-1,000 chance of developing esophageal cancer within the next 10 years and an 8-in-1,000 chance of having his lifetime (Survey Epidemiology and End Results Cancer Statistics Review, 1973-1999).

Absolute vs. Relative
Risk over time or incidence can be used to determine either the absolute risk or relative risk. An example presented was a study of ulcer-related hospitalization among users and nonusers of nonsteroidal antiinflammatory drugs (NSAIDs) (Am J Epidemiol, 1995;141:339-348). The incidence among nonusers was 4.2 per 1,000 persons, compared to 16.7 per 1,000 in users of NSAIDs.

“People who take NSAIDs are four times more likely to be hospitalized with ulcer disease than those who don’t take them,” said Dr. Sandler. “That’s relative risk.”

The relative risk or odds ratio. Another term that is frequently used to express risk is odds ratio, which is equivalent to relative risk but is calculated in a retrospective manner.

Risk can also be expressed as the relative risk increase or relative risk decrease. In the study of ulcer-related hospitalization, NSAID users had a 75% increase in relative risk, compared to nonusers. “The problem with relative risk is that we don’t have a denominator,” said Dr. Sandler. “For example, if the baseline risk of a disease is low, a 75% increase is not very much. If on the other hand, the baseline risk in the population is high, then a 75% increase might be something of major public health importance. We can’t determine the impact by looking at a relative measure.”

Excess risk or attributable risk is useful in that it assigns risk to a specific behavior or other factor. In the example of ulcer-related hospitalization, the excess risk in NSAID users compared to nonusers was 12.5 per 1,000, which is the attributable risk—that is, the risk that is attributable to use of NSAIDs. Attributable risk also can be used to calculate the number needed to harm (NNH) and number needed to treat (NNT). Treating 80 patients with NSAIDs would be expected to lead to one hospitalization (NNH). Alternatively, use of a drug to prevent ulcer-related hospitalization attributed to NSAIDs would require treatment of 80 patients (NNT) to prevent one hospitalization.

Influence on Decision-Making
How risk is presented can greatly influence decisions associated with that risk. In one study, hospital administrators were presented with identical information about cardiac rehabilitation and colorectal polyps and cancer, as reviewed by Dr. C. Richard Boland. The role of Helicobacter pylori infection in gastric cancer is reviewed by Prof. Joseph J.Y. Sung. The data show a strong association between infection and increased cancer risk, but the potential value of H. pylori eradication therapy and when this should be undertaken remains to be demonstrated in ongoing clinical trials.

I hope that physicians will find these articles informative and applicable to their clinical practice.
Prevention of Dyspepsia, Ulcers, and Complications: Appropriate Use of PPIs to Minimize GI Mucosal Injury

Currently, there are no definitive answers to the questions regarding the most effective ways to minimize gastrointestinal (GI) risk in patients who require regular treatment with nonsteroidal anti-inflammatory drugs (NSAIDs). Use of a selective cyclooxygenase-2 (COX-2) inhibitor (coxib) alone or combining a proton pump inhibitor (PPI) with a nonselective NSAID offer effective treatment strategies for many patients. However, high-risk patients may require even greater protection provided by combination therapy with a PPI plus a coxib.

“No NSAID is entirely safe. The [GI] risk is not reduced to zero, even with a selective COX-2 inhibitor,” said David J. Bjorkman, MD, MSPH, SM(Epid), Professor of Medicine at the University of Utah, Salt Lake City. “Thus, we are left with some very challenging problems with no current solutions.”

“What we can do is extrapolate from the data we have and use appropriate clinical judgment,” he added. “In the appropriate patient who has a very high [GI] risk, we have to use our best judgment. In some cases, it may be decided that a PPI combined with a coxib is appropriate. However, we still need more data on this approach.”

Scope of the NSAID Problem

Multiple problems are posed by regular NSAID use. Notably, NSAIDs are the most commonly prescribed class of medications in the world, with more than 100 million prescriptions written each year in the United States alone. The number of people who use NSAIDs daily is estimated to be 1 in 7 (Ann Intern Med. 1998;129:151-158; N Engl J Med. 1999;341:2159-2169).

NSAID-related gastrotoxicity has a wide clinical scope that encompasses everything from dyspepsia to death. Between 15% and 25% of NSAID users develop dyspepsia, which leads to a discontinuation or change in medication in 10% of patients. Gastric ulcers occur in 15% to 20% of patients who chronically use NSAIDs, and duodenal ulcers occur in 5% to 8%. The risk of GI complications increases fourfold in NSAID users, compared to non-users (Ann Intern Med. 1993;119:287-262, Lancet. 1994:343:1075-1078, Ann Intern Med. 1995;123:241-249).

The risk of bleeding ulcers, GI-related hospitalization, serious complications, and need for surgery is all substantially increased by chronic NSAID use. Minimizing this risk begins with identification of factors associated with increased risk of NSAID complications. Among these factors are concurrent use of multiple NSAIDs (including aspirin and over-the-counter NSAIDs), higher NSAID doses, concomitant use of anticoagulants and corticosteroids, older age, and a history of complications with NSAIDs.

“One we identify patients at highest risk, we must then try to stratify patients according to their degree of risk and compare them to those who have not risk factors,” said Dr. Bjorkman. “When we identify a patient at high risk of developing a complication, we should try to avoid NSAID use if possible.”

Evaluating Protection Strategies

In many instances, avoidance of NSAIDs is not an option. In such cases, one potential treatment strategy includes use of a PPI, an H2-receptor antagonist, or a prostaglandin analog. Use of a coxib provides another therapeutic approach. Patients at highest risk may warrant dual protection with a coxib and a prophylactic agent for the gastric mucosa.

While PPIs and H2-receptor antagonists both heal ulcers, PPIs are more effective (N Engl J Med. 1998;338:727-734, Arch Intern Med. 2000;160:1455-1461). The PPI lansoprazole and the prostaglandin analog misoprostol achieve similar rates of ulcer prevention (Arch Intern Med. 2002;162:169-175). However, misoprostol is associated with side effects that many patients find difficult to tolerate, and the need for four-times-daily dosing can reduce compliance. Although strong data are not available on prevention of GI complications among NSAID users, one study showed that lansoprazole can prevent complications in patients taking low-dose aspirin (N Engl J Med. 2002;346:2033-2038).

Development of coxibs is based on the working hypothesis that this class of drugs achieves the same antiinflammatory effect as NSAIDs but reduces the associated risk of ulcers and other GI complications. Results of a large, randomized clinical trial of rofecoxib provided support for this hypothesis, although GI risk was not completely eliminated (N Engl J Med. 2000;343:1520-1528). Limited data suggest that similar risk reduction may be achieved with a coxib alone or combined with a conventional NSAID plus a PPI (Gastroenterology, 2001;120:A104, N Engl J Med. 2002;347:2104-2110).

“It is important to remember that use of a safer NSAID reduces but does not eliminate the risk to the gastric mucosa,” said Dr. Bjorkman. “To date, there are no strong data supporting a definitive choice among the various strategies available to reduce NSAID-related GI risk. In the absence of data from head-to-head clinical trials, physicians must exercise their best clinical judgment for each patient,” he concluded.

Gastroesophageal Reflux Disease: Could Early Intervention Reduce the Risk of Progression to Cancer?

Epidemics of obesity and gastroesophageal reflux disease (GERD) appear to have contributed substantially to a dramatic rise in the incidence of esophageal cancer. Both conditions confer a significant increase in the risk for esophageal cancer (Surg Oncol Clin N Am. 2002;11:235-256) and, in all likelihood, are interrelated.

Both obesity and reflux disease drive the continued and increased incidence of esophageal adenocarcinoma. This increase will inevitably persist because it is driven by these very strong contributing factors in the general population,” said Brian J. Reid, MD, PhD, Head of the Seattle Barrett’s Esophagus Study at the Fred Hutchinson Cancer Research Center in Seattle, Wash. “Excessive weight probably exerts its effect, in part, by causing reflux.”

Evidence of the contributions of obesity and GERD to esophageal cancer has come from the observation that adenocarcinoma constituted 5% of all esophageal cancer 30 years ago. Today more than 60% of esophageal cancers are adenocarcinomas. The increased prevalence of esophageal adenocarcinoma has coincided with epidemics of obesity and GERD in the United States. Being in the top quartile for excess weight increases the risk for esophageal adenocarcinoma by sixfold. Chronic, long-term symptoms of reflux, a significant risk factor for esophageal cancer, increase the risk of adenocarcinoma by 16-fold (Surg Oncol Clin N Am. 2002). Moreover, being overweight is associated with abnormalities in the p16 and p53 tumor-suppressor genes and flow cytometry of Barrett’s esophagus, which, in turn, are associated with development of esophageal cancer (Cancer Epidemiol Biomarkers Prev. 2002;11:745-752).

Role of Proton Pump Inhibitor Therapy

Treatment of GERD with a proton pump inhibitor (PPI) may play a role in reducing the risk for esophageal adenocarcinoma, although definitive data are not yet available. Compared with H2-receptor antagonists, PPIs have been shown to be more effective in controlling symptoms (Gastroenterology. 2000;119:680-690). Use of PPIs also reduces bile reflux, another risk factor for esophageal cancer, through a volume effect in the stomach. However, conclusive data do not exist to show that PPI treatment leads to regression of Barrett’s epithelium or prevention of dysplasia (Gut. 2000;46:144-146).

A study of the use of the PPI lansoprazole to treat symptoms of Barrett’s esophagus has provided intriguing results. Patients underwent 24-hour pH monitoring while on lansoprazole therapy, and approximately 66% had normalization of esophageal acid exposure. Histologic patients, tissue analysis revealed a decline in cellular proliferation from 22% pretreatment to 5% posttreatment (Gastroenterology. 1999;117:327-335).

Dr. Reid stated, “There is no evidence for or against prevention of dysplasia in Barrett’s esophagus. PPIs are used as an adjunct to endoscopic ablative techniques. I don’t think we should consider regression of Barrett’s epithelium a strategy for prevention. Instead, we should strive to control the Barrett’s esophagus.”

Nonsteroidal Antiinflammatory Drugs and Cancer Prevention

Emerging epidemiologic evidence has begun to build a persuasive case in favor of the use of nonsteroidal antiinflammatory drugs (NSAIDs) for cancer prevention, including esophageal cancer. These observational data were recently augmented by preclinical evidence provided by an animal model of Barrett’s esophagus. Results demonstrated that NSAIDs and selective cyclooxygenase-2 inhibitors reduce the risk of progression of Barrett’s esophagus to esophageal adenocarcinoma (Gastroenterology. 2003;124:47-56, Gastroenterology. 2002;122:1101-1112).

Data investigating the use of NSAIDs and esophageal cancer in humans also exist. In humans, NSAIDs have been shown to have no effect on the first step in Barrett’s [transit to cancer].

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Gastroesophageal Reflux Disease

The development of p16 lesions. Use of NSAIDs does reduce the association with p53 lesions to a level of about 0.3, compared to people who have never taken NSAIDs. (Cancer Epidemiol Biomarkers Prev. 2002;11:745-756).

The effect of NSAIDs on the

risk of esophageal cancer requires evaluation in randomized clinical trials. In the absence of definitive data for other thera-

pies, esophagectomy remains the only cure for high-grade esoph-
ageal dysplasia.

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SYMPOSIUM HIGHLIGHTS

The Natural History of Reflux Esophagitis: Does the Problem Start in Childhood?

S
ome prominent gastrointesti-
nal (GI) disorders better known for afflicting adults than children may, in fact, have their origins in childhood," said Benjamin D. Gold, MD, Associate Professor of Pediatrics at Emory University School of Medicine in Atlanta.

Gastroesophageal reflux disease (GERD), for example, appears to affect more children than previously thought. Furthermore, conditions such as erosive esophagitis and Barrett's esophagus were rarely a childhood condition, but more recently appear to be occurring in children with increasing frequency. Even esophageal adenocarci-

noma, once thought to be limited to adults, has now been docu-

mented in children.

“When we talk about reducing the risk or incidence of GI disor-

ders, we should consider the pos-

sibility that many of these diseases started in childhood. Early detec-

tion and early intervention in childhood may result in better outcomes,” said Dr. Gold.

Children have an increased frequency and duration of normal reflux until age 12, when values approach those of adults (J Pediatr Gastroenterol Nutr. 2001;32(suppl 2):S1-S31). Moreover, obesity, a risk factor for reflux in adults, also has reached epidemic proportions in children (JAMA.

2001;286:2845-2848). An obese child in the 85th percentile for weight at age 10 has more than a 12-fold increased risk of morbid obesity in adulthood (Br Med J. 2001;323:1280-1284. Gastroen-

terology. 1997;113:399-408).

Familial and Genetic Links

Familial clustering of GERD, hiatus hernia, esophagitis, Barrett’s esophagus, erosive esophagitis, and esophageal cancer strongly suggests a genetic predisposition that could be expressed as early as childhood. Occurrence of GERD is more frequent in certain racial and ethnic groups, providing further evidence of the influ-

ence of genetics and heredity. Authors of recent publications have proposed a genetic basis for a severe pediatric GERD pheno-

Studies of regurgitation symp-
toms in infants have yielded addi-
tional intriguing information about the potential progression of GERD from childhood to adult-

hood. Results have shown that the incidence of regurgitation declines among infants, as acid-

related signs and symptoms occur with increasing frequency after the first 12 months of life. More-

over, evidence from pediatric cohort studies has shown that the prevalence of heartburn in-

creases with age, escalating from 1.8% in children aged 3 to 9 years to more than 22% in indi-


“Maybe what we are observing is not necessarily a change in the condition but a change in the character of the condition,” said Dr. Gold. “We need improved, validated, age-specific symptom-assessment instruments to follow these conditions long term.”

Findings from another recent study suggest that many children with reflux will often have reflux in adults (J Pediatr Gastroenterol Nutr. 2002;35:334-338). History of childhood reflux symptoms was compared in adults with and without GERD. Significantly more adults with reflux reported childhood GERD symptoms. This study also demonstrated a signifi-
cant association between adult re-

flux and a childhood history in-


Complicated GERD is also occurring more often in pediatric populations. For example, one study showed that the incidence of Barrett’s esophagus increased from less than 2% in 1997 to 3.8% in 2000. In other studies, an in-

crease in the incidence and preva-

lence of erosive esophagitis and esophageal adenocarcinoma, once unheared of in children, has been documented in pediatric pop-

ulations (J Pediatr Gastroenterol Nutr. 1997;25:255-260; Gastroen-

terology. 2002;120:154; Gastroen-


Proton Pump Inhibitors: Safe and Effective in Children

Treatment of acid-related condi-
tions in pediatric populations suffers from a lack of definition based on valid case and control evaluations and a lack of placebo-controlled studies. As a result, much of the therapy in children is empiric. Two proton pump in-

hibitors (PPIs), lansoprazole and omeprazole, are now approved by the U.S. Food and Drug Admin-

istration for use in children. A representative study of lansopra-

zole showed a 21% reduction in GERD symptoms after 2 weeks of treatment and an 80% reduction by 12 weeks (J Pediatr Gastroen-

terol Nutr. 2002;35(suppl 4):S300-S307). Similar effects have been observed with omeprazole (J Pe-

diatr. 2000;137:800-807). In addi-

tion, both PPIs have been shown to be highly effective in mucosal healing, resulting in up to 100% resolution of erosive esophagitis in children by 12 weeks of therapy (J Pediatr Gastroenterol Nutr. 2002;35(suppl 4):S300-S307; J Pediatr. 2000;137:800-807).

“PPIs clearly heal erosive esoph-


agitis in pediatric patients, includ-

ing disease that is refractory to H2-receptor antagonists and even surgery,” said Dr. Gold. “Resolution and improvement occur in the majority of GERD-related symptoms, with sustained mucosal healing. As maintenance thera-

pies, PPIs are safe in children for up to 2 years. Moreover, PPIs have demonstrated minimal side effects in children with short- or long-term use and don’t result in toler-

ance (i.e., tachyphylaxis) as do the H2-receptor antagonists.”

NEEDS ASSESSMENT

The spectrum of gastrointestinal risk encompasses a wide range of diseases and disorders. The conditions include mucosal injury induced by chronic treatment with nonsteroidal antiinflammatory drugs, gastroesophageal reflux disease, reflux esophagitis, Barrett’s esophagus, esophageal cancer, and gastric cancer. Each of the conditions affords potential opportunities for risk reduction. By recognizing the opportunities and intervening appropriately, clinicians can reduce the morbidity and mortality associated with gastrointestinal diseases and perhaps prevent many of their serious clinical consequences.

LEARNING OBJECTIVES

Upon completion of this continuing education activity, participants should be able to:

• Discuss different approaches to assessment and expression of gastrointestinal risk and to recognize the advantages and disadvantages of each approach.

• Understand the gastrointestinal risks associated with chronic antiinflammatory therapy and options for reducing the risks.

• Appreciate the factors associated with the increased prevalence of adenocarcinoma of the esophagus and recognize potentially beneficial strategies to reduce the cancer risk.

• Evaluate the evidence from studies of dietary interventions to reduce the risk of gastrointestinal cancer.

• Understand current evidence regarding the role of Helicobacter pylori eradication in the prevention of gastric cancer.

Faculty Disclosures

Faculty/authors must disclose any significant financial interest or relationship with proprietary entities that may have a direct or indirect relationship to the subject matter. They must also disclose any discussion of investigational or unapproved uses of products.

Dr. Boland is on the External Advisory Board of Exact Sciences, Inc. Dr. Gold is a consultant to TAP Pharmaceuticals, Inc. He discloses the unlabeled use of proton pump inhibitors (PPIs) in infancy and suprasphageal GERD. Dr. Hunt is a consul-
tant/speaker for TAP, ActoZenna, Merck, and Astra Pharma Inc. Dr. Reid has received grants from the U.S. National Insti-
tutes of Health, is a consultant to Strategic Consultants International, and has a financial interest in Epigenomics. He discloses the unlabeled use of PPIs for Barrett’s esophagitis. Dr. Bjorkman, Dr. Sandier, and Prof. Sung have nothing to disclose.
Aspirin, NSAIDs, and COX-2 Selective Inhibitors for Chemoprevention of GI Cancers

There is strong evidence that regular use of non-steroidal anti-inflammatory drugs (NSAIDs) reduces the risk of colon cancer. However, to justify using NSAIDs in light of their potential associated risks, there is still the challenge of identifying high-risk patients who will likely benefit the most from NSAID therapy.

Emphasis is now being placed on the need for improved patient selection for NSAID therapy due to results of recent studies demonstrating their variable effects on colon cancer risk. While some studies have shown dramatic risk reductions of 50% or more provided by NSAIDs, a meta-analysis of eight clinical trials showed an overall benefit of less than 25% (Ann J Gastroenterol. 2002;97:5232).

“Aspirin and NSAIDs are very effective in suppressing polyp formation and significantly reduce mortality due to colorectal cancer,” said C. Richard Boland, MD, Professor of Medicine and Chief of Gastroenterology at Baylor University Medical Center, Dallas. “However, these drugs have toxicities, and we don’t yet know what the risk-benefit ratio might be. Although colon cancer is very common, compared with other types of cancer, it still affects only about 5% of the population. The next step is to identify specific therapeutic approaches for patients at very high risk for cancer and to find the safest possible interventions for these patients who feel well and will not tolerate even minor side effects.”

Compelling Evidence

Multiple studies have demonstrated the ability of aspirin, NSAIDs, and selective cyclooxygenase-2 (COX-2) inhibitors to reduce the risk of colon cancer and colorectal polyp formation.

One early epidemiologic study showed a 40% reduction in the relative risk for mortality associated with colon cancer in people who reported taking 16 or more aspirins every month (N Engl J Med. 1991;325:1593-1596). These findings were consistent with another study in patients with rheumatoid arthritis. Of these patients, many were using aspirin or NSAIDs regularly, and results demonstrated a 56% reduction in the incidence of colorectal cancer (Clin Exp Rheumatol. 1996;14:551-553).

An early clinical trial involved use of the NSAID sulindac in patients with familial adenomatous polyposis (FAP). The results showed a 56% reduction in polyp number and a 65% reduction in polyp size. However, sulindac did not prevent the formation of new polyps, and a considerable number of patients developed peptic ulcers during treatment (Eng J Med. 1993;328:1313-1316).

Some evidence suggests aspirin may reduce polyp formation. These findings came from a study that was conducted in patients who had colorectal adenomas removed and were reevaluated by colonoscopy one year later. Investigators assessed aspirin use based on responses to a questionnaire. Regular aspirin use was associated with a 48% reduction in the relative risk for recurrent adenomas (J Natl Cancer Inst. 1993;85:912-916). It has also been reported recently that the relative risk of colorectal cancer among adenomatous polyps was 0.81 (CI = 0.69-0.96) in patients given 81 mg of aspirin daily, compared with those given placebo (N Engl J Med. 2003;348:891-899).

Moreover, the selective COX-2 inhibitor celecoxib demonstrated the ability to reduce total polyp burden by 31% in patients with FAP (N Engl J Med. 2000;342:1946-1952). Rofecoxib has shown similar efficacy in animal models of FAP, according to Dr. Boland.

Dr. C. Richard Boland

No Benefits From Dietary Intervention

Similar to many discoveries in medicine, the theory that aspirin and NSAIDs may impact colon cancer risk evolved almost inadvertently. Some of the earliest observational evidence came from trials of dietary intervention. The dietary strategies failed to reduce colon cancer risk; however, reviews of medication history showed consistent risk reductions among patients reporting regular use of aspirin or NSAIDs.

“Perhaps we can actually prevent cancer at a very early stage,” said Dr. Boland. “However, dietary interventions have not been effective when initiated in people who have adhered to a diet that pre-disposed them to cancer for 50, 60, or 70 years.”

Foods and nutrients associated with reduced colorectal cancer risk include folate, calcium, vitamin D, vitamin E, estrogens, omega-3 fatty acids, and low-fat/high-fiber foods, such as wheat bran, fruits, and vegetables.

Gastric Cancer and Helicobacter pylori: Can Eradication Therapy Reduce the Risk?

Initial results from ongoing clinical trials suggest that eradication of Helicobacter pylori infection favorably affects precursors of gastric cancer but may not prevent cancer.

Thus far, trials have shown that eradication of H. pylori infection can reduce the progression of gastric atrophy and intestinal metaplasia. However, available data on gastric cancer incidence show no difference between treated and placebo groups, with the possible exception of a subset of patients who did not have gastric atrophy or intestinal metaplasia at baseline.

“I believe that we have seen enough evidence to show that eradication of H. pylori infection does retard gastric atrophy and intestinal metaplasia,” said Joseph J.Y. Sung, MD, FRCPC, FRACP, FACC, Professor of Medicine at the Chinese University of Hong Kong. “However, we must await the results of the larger end point. There are no randomized studies suggesting that treatment of H. pylori infection reduces the incidence of gastric cancer.”

Significant Associations

Cohort and case-control studies have demonstrated a significant association between H. pylori infection and gastric cancer. Meta-analyses suggest that the cancer risk at least doubles in patients with H. pylori infection compared with patients without H. pylori infection (Ann Intern Med. 1988;109:347-353).


Moreover, the duration of H. pylori infection appears to influence gastric cancer risk. One recent study showed a substantially higher risk of gastric cancer among patients whose history of H. pylori infection extended beyond 10 years (Cancer Res. 2001;61:347-353). Despite the evidence implicating H. pylori infection in gastric cancer, intervention studies have yet to produce compelling evidence that eradication of the infection reduces the risk. To date, only one study has been completed and published (J Natl Cancer Inst. 2000;92:1881-1888). The trial evaluated H. pylori eradication therapy and various forms of antioxidant therapy used alone, but no additional benefit from combining these two approaches to treatment. According to Prof. Sung, “these findings remain difficult to explain.”

Limited Intervventional Data

Currently, at least 11 prevention studies are ongoing to evaluate interventions to prevent gastric cancer (five trials) and to target progression of gastric histology (six trials). Of these trials, two have preliminary data. Prof. Sung and colleagues have 5-year follow-up data on a Chinese cohort treated with H. pylori eradication therapy. One-year endoscopic and biopsy results showed a dramatic reduction in inflammation but no change in gastric atrophy or intestinal metaplasia (Gastroenterology. 2000;119:7-14). After 5 years, several cases of gastric cancer had developed in both the eradication therapy and placebo groups, but the between-group difference was not significant. However, patients randomized to eradication therapy had significant regression of gastric atrophy and intestinal metaplasia (Gastroenterology. 2002;122:A170). Five-year results from another ongoing Chinese trial also showed significant regression of gastric atrophy and intestinal metaplasia in patients treated with H. pylori eradication therapy. After 7 years of follow-up, seven cases of gastric cancer had occurred in the eradication therapy group versus none in the placebo group. When patients with gastric atrophy or intestinal metaplasia at baseline were excluded, there were no cases of gastric cancer in the eradication therapy group versus six in the placebo group, suggesting that eradication therapy might help prevent gastric cancer (Gastroenterology. 2002;122:A888).

“Perhaps we can actually prevent gastric cancer, but the H. pylori infection has to be treated early,” said Prof. Sung in conclusion.
HIGHLIGHTS OF A SYMPOSIUM:
Risk Reduction and the GI Tract: From Theory to Reality

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1. Which of the following statements best reflect(s) different approaches to characterization of risk?
   a. Relative risk is often used for impact.
   b. Absolute risk is useful for discussions with individual patients.
   c. Discussion of absolute and relative risk may provide the greatest clarity.
   d. All of the above
   e. None of the above
   4. Which of the following statements is/are true about the use of PPIs in patients with Barrett’s esophagus?
   a. PPIs effectively control symptoms and heal esophagitis.
   b. PPIs induce regression of Barrett’s epithelium and prevent dysplasia.
   c. PPIs reduce bile reflux.
   d. All of the above
   e. a and c

2. NSAID use increases the risk for which of the following?
   a. Peptic ulcer bleeding
   b. Hospitalization
   c. Serious gastrointestinal complications
   d. Gastrointestinal surgery
   e. All of the above

3. H2 receptor antagonists are:
   a. Equivalent to proton pump inhibitors (PPIs) for healing and preventing duodenal ulcers.
   b. Equivalent to PPIs for healing and prevention of gastric ulcers.
   c. Inferior to PPIs for ulcer healing and prevention.
   d. Superior to PPIs for healing duodenal but not gastric ulcers.
   e. a and b

5. Studies of Helicobacter pylori eradication have shown that eradication:
   a. Reduces the risk of gastric cancer.
   b. Retards glandular atrophy and intestinal metaplasia.
   c. Reduces the risk of colorectal cancer.
   d. Results in a paradoxical increase in gastric cancer risk.
   e. None of the above

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