H. Pylori Associated with Better Outcomes in Gastric Cancer

BY ED SUSMAN

SAN FRANCISCO—It may seem counterintuitive, but it appears that gastric cancer patients who are found to be infected with ulcer-causing *Helicobacter pylori* have longer survival after surgery than patients without the infection, researchers reported here at the Gastrointestinal Cancers Symposium (***Abstract 137***).

"Despite similar disease presentation, preoperative *H. pylori* infection was independently associated with improved overall survival, particularly in Stage 3 disease," said Lauren Postlewait, MD, a resident in general surgery and a fellow in surgical oncology at Emory University.

She and her coauthors reported that the 104 patients with *H. pylori* infection following gastric cancer surgery achieved a median overall survival of 84 months compared with 44 months for the 455 patients who did not have *H. pylori* infection at the time of presentation.

"When we do stage-specific analysis, that difference is most prominent in Stage 3 gastric cancer," she said in an interview at her poster presentation. In comparing the 247 patients who presented with a diagnosis of Stage 3 gastric cancer, the overall survival was 44 months for individuals who were infected with *H. pylori* compared with 25 months for patients who did not have *H. pylori*.

Disease-specific survival among these Stage 3 gastric cancer patients was 45 months for those with *H. pylori* infection and 27 months for patients without.

Postlewait reported that for the 168 patients presenting with Stage 1 gastric cancer, the median overall survival has not been reached for either group and in the 136 patients who presented with Stage 2 gastric cancer the median overall survival has not been reached among patients with *H. pylori* infection and is 46 months among patients without the infection.

Patients with or without *H. pylori* infection had no differences in adverse pathologic factors including positive margin, high-grade cancer, lymph node metastases, or advanced stage.

"Our thought going into this project was that we knew *H. pylori* was a cause of gastric cancer, but not all gastric cancers are secondary to *H. pylori* infection," she explained. "We thought that patients with *H. pylori* infections might do better with gastric cancer because the cancer would be detected earlier since they would be symptomatic. But it ends up that is not the case.

"Our results showed that people who present with or without *H. pylori* have pretty much the same stage cancer when they present. It almost looks identical. So the patients didn't present earlier, but they did do better."

Ed Susman

LAUREN POSTLEWAIT, MD: "We need to examine further the interaction between *H. pylori* and tumor immunology and genetics to better understand the relationship between *H. pylori* and survival in gastric cancer."

Reasons Unknown

Why the patients with *H. pylori* then did better is a question she admitted she could not answer. But she did speculate that it might have something to do with the immune system reaction to the infection.

"There have been studies showing that there is a differential immune response in the tumor microenvironment with and without *H. pylori* infection. So we think *H. pylori* stimulates this immune response, which might prevent tumor progression."

She said the theory is that *H. pylori* ramps up an immune response and

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> "It could be that gastric cancer that occurs in an environment where *H. pylori* is not present is very different from gastric cancer that develops when *H. pylori* is present."

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in the sinful sense, and a balanced view of life with common sense are at odds.

End-of-Life Care

However, in medicine one of the saddest examples of a close-minded view are physicians who manage end-of-life care badly.

For the most part, oncologists today know when a cancer is incurable and, further, when there is no likely treatment that will extend the patient's life with reasonable quality. Still, there are those who continue offering yet another chemotherapy regimen that will not work because "you never know"—a stupid, bogus way to escape responsibility.

And there are those who continue useless therapy because the family insists; if that is how it works, what do they need a doctor for? They might as well go to Mexico for coffee enemas (no kidding!).

These physicians have failed to take seriously and be open-minded to convincing data showing that when the cancer is no longer curable or even responsive to any anti-cancer therapy, a strong effort in supportive care by experts can make whatever time the patient has more tolerable, comfortable, and rewarding by providing time under good conditions to visit with family and friends, and get all affairs in order without rushing, often in their own homes. Studies have shown that these patients usually live longer than those given ineffective chemotherapy and, without question, have a much better quality of life.

It is very hard to tell a family that there is no effective therapy remaining for their mother or father (or their child—I had to do this many times). Some parents of children with cancer understand that extending life a few weeks with suffering is harder to bear than supportive therapy at home with all the comforts that can be applied. It is the doctor's responsibility to help families understand that extending useless therapy, often in a hospital or even an ICU, can be, as one patient told me, "torture worse than death."

Supportive-care programs for end-of-life cancer patients are multiplying in this country and provide pain control, and a variety of social and medical services to ease the patient's final journey. Prof. Matthew Loscalzo at City of Hope, Dr. Jimmie Holland at Memorial Sloan Kettering, and other pioneers in the field have helped build these programs and train others to practice this "new" specialty.

Just a bit more open-mindedness would be a great asset for physicians who manage patients with cancer. If, God forbid, I had an incurable cancer, I would prefer to go home and have the needs of my last days managed by these experts.

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that immune system action may also take out cancer cells.

"Another theory is that the way that the cancer actually develops is impacted *by H. pylori.* Maybe gastric cancer that occurs in an environment where *H. pylori* is not present is very different from gastric cancer that develops when *H. pylori* is present.

"In studies looking at microsatellite instability and gastric cancer in *H. pylori,* there are indications that patients with *H. pylori* are much more likely to have tumors with microsatellite instability compared with those who don't have *H. pylori* infection," Postlewait continued. "And patients who have tumors with microsatellite instability tend to do better."

She said all these theories merit further study, but that the study itself doesn't really touch on possible reasons for the results. "We need to examine further the interaction between *H. pylori* and tumor immunology and genetics to better understand the relationship between *H. pylori* and survival in gastric cancer."

Asked for his perspective, Robert Mayer, MD, the Stephen B. Kay Family Professor of Medicine and Faculty Associate Dean of Admissions at Harvard Medical School and Dana-Farber Cancer Institute, said that the most likely reason for the differences in outcome is probably that there are two different types of gastric cancer: "The types of cancer seen with *H. pylori* infection are typically based on inflammation in the stomach, and these tumors are less aggressive than the stomach cancer that is now more prevalent in the United States. This cancer is more diffuse and is more aggressive than the cancers that arise with *H. pylori*."

Mayer, an *OT* Editorial Board member, explained that before the year 1930, stomach cancer was the number one cancer in the United States, but it has now fallen to number 12. Worldwide, though, stomach cancer is the number two killer. The advent of refrigeration and better protection of food supplies have greatly reduced the *H. pylori* infection rate, he said.

> The theory is that *H. pylori* ramps up an immune response and that immune system action may also take out cancer cells.

Study Details

For the study, Postlewait and colleagues reviewed the U.S. Gastric Cancer Collaborative database, which includes all patients who underwent resection of gastric cancer from 2000 to 2012 at seven academic institutions.

Of the 965 patients in the database, 559 met the criteria for inclusion in the study; and of that group, 18.5 percent tested positive for *H. pylori* infection. The median time for follow-up was 49.8 months.

The majority of the patients were men (313, or 56% of the total); the average age of the patients was 64.6; and their average body mass index was 25.8 kg/m^2.

Patients with *H. pylori* infection were more likely to receive adjuvant radiation therapy—34.7 percent of those without *H. pylori* infection compared with 47 percent of those with infection. However, in the multivariate analysis, radiation therapy did not retain its significance.

The only significant factor that affected overall survival in the study appeared to be infection with *H. pylori.* "In our data we don't have information on who was later treated for *H. pylori* and who was not," Postlewait said. "But the assumption is that everyone was treated. Patients with *H. pylori* are at risk for ulcer disease as well as gastric cancer, so I certainly think *H. pylori* should still be treated."

The symposium is co-sponsored by the American Gastrointestinal Association Institute, the American Society of Clinical Oncology, the American Society for Radiation Oncology, and the Society of Surgical Oncology.