Labs Predict IBD Response to Therapy

BY ROBERT FINN

Algorithms based on common laboratory values outperformed expensive metabolite testing in determining which patients with inflammatory bowel disease are likely to respond to thiopurine therapy, Dr. Akbar K. Waljee and his colleagues reported.

Thiopurines are known to be effective immunomodulators in patients with inflammatory bowel disease (IBD) who have failed 5-aminosalicylic acid therapy. The problem is that thiopurines have a narrow therapeutic index, and individuals vary widely in how they metabolize these agents.

Experienced clinicians can use inexpensive complete blood count and standard blood chemistry values to balance efficacy and risk in individual patients, but this takes expert judgment, and there are no established algorithms.

A more reproducible approach is to measure the metabolites 6-thioguanine (6-TGN) and 6 methylmercaptopurine (6-MMP). Unfortunately, monitoring these metabolites is expensive, and the sensitivity and specificity of this approach are only 62% and 72%, respectively.

In an effort to resolve this dilemma, Dr. Waljee and his colleagues from the University of Michigan, Ann Arbor, used a machine learning technique to tease out the most accurate algorithms based on CBC and blood chemistries (Clin. Gastroenterol. Hepatol. 2010 [doi:10.1016/j.cgh.2009.09.031]).

The investigators used data collected in 774 cases from 346 individuals who were seen at the University of Michigan between May 2004 and August 2006. To be included in the study, the patients had to have had thiopurine metabolite analysis, CBC, and a comprehensive chemistry panel within the same 24-hour period.

Using a randomly selected 70% of the cases, investigators used a statistical technique called the "random forest" method to derive the most accurate algorithms based on data from the CBC and chemistry panels. They then tested that algorithm on the remaining 30% of the cases, comparing the accuracy to that of thiopurine metabolite analysis.

Their primary outcome measure was the area under the receiver operating characteristic curve (AuROC), a standard measure of accuracy.

The random forest algorithm differentiated clinical response from nonresponse with an AuROC of 0.856, compared with 0.594, for 6-TGN levels, a difference that was highly statistically significant.

The most important independent variables in differentiating responders from nonresponders were neutrophil count, alkaline phosphatase, red-cell distribution width, age, and white blood cell count.

The investigators also derived a random forest algorithm that would predict patient nonadherence, and another that would predict which patients were likely to have unfavorable pharmacodynamic responses to thiopurine therapy. Both of those algorithms proved to be significantly better than thiopurine metabolite analysis.

They also developed a simple prediction rule that was reasonably accurate at differentiating responders from nonresponders. Patients with a ratio of mean corpuscular volume (MCV) to white blood cell count (WBC) of 12 or more had a 67% likelihood of having a clinical response, while those with a ratio less than 12 had a 35% likelihood of having a clinical response. This simplified algorithm was significantly worse than the more complex algorithm, but it was still significantly better than metabolite analysis.

The investigators disclosed that the Regents of the University of Michigan, along with several of the study's coauthors, have applied for a patent on the application of machine learning to the prediction of clinical response to thiopurines. ■

Colon Ca Rates Lower After Specialist Screen

BY DENISE NAPOLI

Canadian patients whose previous negative colonoscopies were performed by gastroenterologists are less likely to have subsequent colorectal cancer than are patients whose screens were done by other specialists, including general surgeons, Dr. Linda Rabeneck and her colleagues reported.

Despite previous studies finding a significantly decreased risk of colorectal cancer (CRC) even 10 years following a negative colonoscopy, "a small but clinically meaningful number of incident CRCs occur," wrote Dr. Rabeneck of the University of Toronto (Clin. Gastroenterol. Hepatol. 2010 March [doi:10.1016/j.cgh.2009.10.022]).

These cancers could include missed lesions because of poor bowel preparation, suboptimal colonoscopy technique, incomplete polypectomy, or even truly new cancers, the authors write. However, "The issue of whether endoscopist characteristics, including colonoscopy volume and specialty, are important in this context has not been previously addressed in a large-scale …population-based study that reflects usual clinical practice."

Dr. Rabeneck and her colleagues studied 110,402 Ontario residents aged 50-80 years who had a negative complete colonoscopy between Jan. 1, 1992, and Dec. 31, 1997. Participants had no history of colorectal cancer, no past di-agnosis of inflammatory bowel disease, and no colonic resection within 5 years of the index colonoscopy.

Patients were followed up for colorectal cancer diagnosis from the date of the index negative colonoscopy through Dec. 31, 2006. During the study's 15-year follow-up period, colorectal cancer "was diagnosed in 1,596 persons, of whom 1,426 had the index colonoscopy in a hospital [86%], and 170 had the procedure in a private office/clinic," wrote the authors.

'Most general surgery trainees have 2 months of dedicated endoscopy training in their programs. Gastroenterology trainees have dedicated endoscopy training for a minimum of 16 months.'

Among patients who had colonoscopies performed in a hospital, 38% of endoscopists were general surgeons and 17% were gastroenterologists, with the remainder classified as "other": primarily internists, family physicians, and "general physicians." Regarding these hospital-based patients, the authors wrote: "For those who had their procedures performed by a general surgeon, the risk of incident CRC was increased by almost 40% (hazard ratio 1.389), compared with those who had their procedures performed by a gastroenterologist."

Patients whose hospital-based colonoscopies were performed by physicians classified in the "other" category (primarily internists) also were at higher risk for a subsequent colorectal cancer diagnosis (HR 1.275).

In the office-based setting, however, "in which only 14% of procedures were performed, and where only 8.1% of procedures were performed by a gastroenterologist …endoscopist specialty was not significantly associated with incident CRC." Nor was there any association between the volume of colonoscopies previously performed by the endoscopist and incident CRC in either setting, after adjustment for patient age, sex, and comorbidity.

The authors attempted to explain the disparate findings between the office and hospital settings by pointing out that patients seen in the private office/clinics were younger, more likely to be men, and had less comorbidity. Therefore, "It is likely that the procedures in the private office/clinics were technically easier to perform," they said.

"Most general surgery trainees have 2 months of dedicated endoscopy training in their programs. Gastroenterology trainees have dedicated endoscopy training for a minimum of 16 months during their programs," they added. "Having extensive formal training matters more when the procedures are more challenging to perform."

The authors reported no conflicts of interest related to this study. ■

Eosinophilic GI Disorder Rates Vary Widely

BY MIRIAM E. TUCKER

NATIONAL HARBOR, MD. — Eosinophilic esophagitis affects an estimated 52 per 100,000 Americans, while eosinophilic gastritis/colitis affects about 28 per 100,000, according to the results of the first nationwide study to investigate the disease burden of eosinophilic gastrointestinal disorders.

Previous epidemiologic studies of eosinophilic gastrointestinal disorders have been limited to specific regions of the country surrounding a tertiary referral center, with published estimates of eosinophilic esophagitis (EoE) ranging from 7.3 per 100,000 children in West Virginia (Am. J. Gastroenterol. 2007;102:2281-5) to 55 per 100,000 in Olmstead County, Minn. (Clin. Gastroenterol. Hepatol. 2009;7:1055-61).

The current study, conducted via an e-mail survey of pediatric and adult gastroenterologists, demonstrated wide variations in the rates of both EoE and eosinophilic gastritis/eosinophilic colitis (EG/EC) in different parts of the country, Dr. Wendy M. Book said at the annual meeting of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN).

Electronic surveys were e-mailed to all physician members of NASPGHAN (total 1,423), the American College of Gastroenterology (5,789), and the American Academy of Allergy, Asthma, and Immunology (3,621). The total response rate was 17%, including 866 allergy-immunology specialists, 333 pediatric gastroenterologists, and 602 adult gastroenterologists. Just over half (55%) practiced in urban settings, while 41% were suburban and 4% were rural. Fifty-nine percent were in private practice.

Analyses included only the gastroenterologists, in order to avoid possible duplication of patients. For EoE, the pediatric gastroenterologists reported seeing an average of 20.2 individual patients per year, while the adult gastroenterologists reported an average of 10.7 annually.

Based on those numbers and U.S. census data, Dr. Book said there are an estimated 158,705 patients with EoE in the United States, with a prevalence of 52.2 per 100,000 U.S. population. For EG/EC, the pediatric gastroenterologists reported seeing an average of 8.9 patients per year while the adult gastroenterologists reported 5.9/year, for an estimated 85,281, or 28.1/100,000, said Dr. Book, of the department of internal medicine at Emory University, Atlanta.

The disease burden of patients seen with EoE was highest in the U.S. Northeast, followed by the South, the Midwest, and the West.

Dr. Book is president of the nonprofit organization American Partnership for Eosinophilic Disorders (www.apfed.org). She stated that she had no relevant conflicts of interest. ■