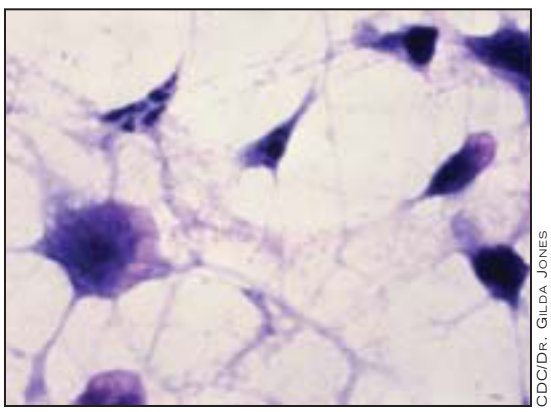
Simple Rule Predicts *C. difficile* Recurrence

BY ROBERT FINN

Many patients with *Clostridium difficile* infection experience repeated bouts of the illness, and a rule has been developed to accurately predict a patient's risk of recurrence, reported Dr. Mary Y. Hu and her colleagues.

The simple prediction rule takes into account a patient's age, use of antibiotics, and severity of disease. The researchers showed that the rule has a diagnostic accuracy of 72%.

These factors had been shown previously to be significant independent predictors of recurrent *C. difficile* diarrhea, wrote Dr. Hu of Harvard Medical School, Boston, and her colleagues. A fourth independent predictor—the serum level of antitoxin A IgG—appeared to reduce the accuracy of the rule (Gastroenterology 2009 April [doi:10.1053j.gastro.2008.12.038]).



CDC/Dr. Gilda Jones

A simple new rule can be used to predict recurrence of *C. difficile* infection, which can cause repeated bouts of diarrhea.

The investigators derived the rule from a study of 63 patients hospitalized with *C. difficile* infection between January and May 1998, and validated it with data collected prospectively from 64 patients hospitalized between December 2004 and May 2006.

The rule assigns 1 point to each of the following three characteristics: age greater than 65 years, disease judged to be severe or fulminant in intensity, and additional antibiotic use after the discontinuation of therapy for *C. difficile* infection. In the validation group, recurrence occurred in 7 of 19 patients scoring 2 points or higher (37%) but in 6 of 45 patients scoring 0 or 1 (13%).

In the validation cohort, the sensitivity of the rule was 54%, the specificity was 77%, the positive predictive value was 37%, and the negative predictive value was 87%. The diagnostic accuracy was 72%. This compared favorably to the original derivation cohort, in which the rule's diagnostic accuracy was 77%.

They also tested a combined rule that assigned an additional 2 points to a serum antitoxin A IgG level less than 1.29 ELISA units. With a threshold of 4 points or above, this combined rule appeared promising among the derivation cohort: Of these patients, 16 had antitoxin A IgG data available. Of those, all eight patients in the high-risk group had recurrent *C. difficile* infection, while only one of the eight patients in the low-risk group had recurrence. In this analysis, the sensitivity of the rule was 89%, specificity was 100%, and diagnostic accuracy was 94%. This rule proved to be far less predictive in the validation cohort, in which 26 patients had antitoxin A IgG data available. Infection recurred in 3 of 6 patients in the high-risk group and 5 of 20 patients in the low-risk group. This translates to a sensitivity of 38%, specificity of 83%, and diagnostic accuracy of 69%.

The researchers advanced several hypotheses for the disappointing performance of the combined rule, including few serum samples available for antibody measurement and variations in the timing of antibody measurement. Also, the epidemiology of *C. difficile* infection changed between 1998 and 2004-2006.

The three-factor prediction rule for recurrence was "simple, reliable, and accurate," according to the investigators. "This rule is valuable in clinical practice as it defines a high-risk population in whom awareness of the risk can facilitate more prompt recognition, diagnosis, and treatment of recurrent [*C. difficile* infection]. These patients are also most likely to benefit from interventions to prevent recurrence, such as infection control precautions [or] prudent use of antibiotics."

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THE EFFECTIVE PHYSICIAN

Managing Crohn's Disease 2009

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Crohn's disease has an estimated incidence of 5/100,000 U.S. residents and prevalence roughly 10 times that number. This systemic disease with primarily gastrointestinal manifestations is responsible for significant morbidity and incurs surgical and medical costs of approximately $2 billion annually in this country. The Practice Parameters Committee of the American College of Gastroenterology published revised guidelines for management in January 2009.

Conclusions

Onset of disease is usually insidious, with chronic diarrhea, nausea, abdominal pain, weight loss, and fever as common presenting symptoms. Other inflammatory bowel diseases, idiopathic intestinal diseases, and irritable bowel syndrome are the principal differential diagnostic possibilities for gastrointestinal Crohn's disease. Extraintestinal symptoms are common, and gastrointestinal adenocarcinoma risk is increased in patients with long-standing disease.

Crohn's disease usually has a chronic relapsing course. Less than 5% of patients have continuous disease activity, and 13% have no relapses after the initial exacerbation. A patient who is in remission for 1 year has an 80% chance of remaining in remission for an additional year; however, those with active disease in the past year have a 70% chance of recurrent symptomatic flare in the following year.

Gastrointestinal and respiratory infections, cigarette smoking, and use of NSAIDs have been implicated in initiating or exacerbating Crohn's disease. The contribution of stress is controversial.

Crohn's disease is not "curable" with currently available treatments; common treatment goals include inducing and maintaining symptomatic control, improving quality of life, and minimizing complications. Achieving short- and long-term mucosal and histologic healing is a newer goal of treatment.

Fistulas develop in 20%-40% of patients over a lifetime of disease, with enterocutaneous fistulas most common. Although fistulas may close spontaneously or with treatment, recurrence is common.

Implementation

Endoscopy with tissue biopsy and radiographic studies—based on an individual patient's presentation—are required to make the diagnosis of Crohn's disease. Several genetic mutations have been associated with the development of Crohn's disease but have not proven clinically useful to date.

The presence of fecal leukocytes and elevated serum markers for inflammation are useful in confirming intestinal inflammation but are not specific for a particular disorder. The presence of antibodies against *Saccharomyces cerevisiae,* antineutrophil cytoplasmic antibodies, and others support the diagnosis of Crohn's disease but are not sufficiently sensitive or specific to be diagnostic. There is no single standard for determination of disease activity.

Mesalamine and antibiotics (including antimycobacterial regimens) have not been demonstrated to be more effective than placebo for luminal Crohn's disease. Controlled-release oral budesonide is recommended for primary treatment of mild to moderate ileal and right colonic Crohn's disease.

Patients with moderate to severe Crohn's disease flares should be treated initially with 40-60 mg of oral prednisone daily until symptoms are controlled (usually 7-28 days). Parenteral methotrexate and anti–tumor necrosis factor monoclonal antibodies are effective for steroid-refractory Crohn's disease.

Azathioprine and 6-mercaptopurine are effective in maintaining steroid-induced remission; however, over 50% of patients treated acutely with steroids will develop steroid dependence or resistance.

Imaging to assess for obstruction or abscess, supportive care (including hydration, adequate nutrition, transfusion if required, nasogastric suction and bowel rest for bowel obstruction, and other interventions as needed), and hospitalization are required for patients with severe and/or fulminant exacerbations.

Parenteral corticosteroids are recommended for initial treatment of patients with severe or fulminant Crohn's disease. Parenteral cyclosporine and tacrolimus may be considered for those patients who do not respond to injectable steroids. Most patients will require maintenance therapy with an alternate immunomodulator.

Acute abscess formation and perianal abscesses require surgical drainage. Perianal complications without abscess formation may respond to metronidazole (with or without ciprofloxacin), and other antibiotics and immunomodulators have been evaluated in small studies.

Maintenance treatment to reduce relapse, maintain remission, and improve patient quality of life after induction treatment is recommended for many patients. Sulfasalazine and mesalamine have not been shown to be consistently effective for maintenance. The regimen chosen will often depend on the patient's specific disease pattern, what agent the exacerbation responded to, and the completeness of response. Smoking cessation remains a consistent factor in reducing the risk of recurrence.

Reference

Lichtenstein GR, et al. Management of Crohn's disease in adults. Am. J. Gastroenterol. 2009;104:465-83.

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