

Inflammatory Bowel Disease

DIAGNOSING CROHN DISEASE AND ULCERATIVE COLITIS WITH ANTI-SACCHAROMYCES CEREVISIAE (ASCA) AND ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA)

Introduction

- Inflammatory bowel disease (IBD) is a general term used to describe diseases that cause inflammation of the intestines. Crohn disease (CD) and ulcerative colitis (UC) are the two major IBDs. In Crohn disease, inflammation usually occurs in the lower part of the small intestine (distal ileum), but may affect any part of the digestive tract. The inflammation in Crohn disease extends deep into the affected tissue, in contrast to ulcerative colitis, which causes inflammation and ulcers in the top layers of the lining of the colon and rectum. Inflammation in Crohn disease is asymmetrical and segmental, with areas of both healthy and diseased tissue, in contrast to ulcerative colitis where inflammation is symmetrical and uninterrupted from the rectum proximally.¹⁻³
- Both Crohn disease and ulcerative colitis are chronic, they affect men and women approximately equally, and they are most common in northern Europe and North America. Approximately 20 percent of individuals with Crohn disease have a blood relative with some form of IBD. The onset of Crohn disease is usually between the ages of 15 and 30 with a second smaller peak of incidence between the ages of 50 and 70. Over the past decade, several reports have noted an increase in the prevalence of Crohn disease in various geographic regions.⁴⁻⁷ Although there are many theories concerning the cause of Crohn disease and ulcerative colitis, none have been proven. Since many of the symptoms of Crohn disease and ulcerative colitis are similar, diagnosis is often difficult, time consuming, and invasive.¹⁻³ Approximately 10-12 percent of cases are not initially classifiable and are referred to as "indeterminate colitis." Over time, about half of these patients are eventually classified as CD or UC.⁸⁻¹⁰

Anti-Saccharomyces cerevisiae Antibodies (ASCA) IgG and IgA

- Anti-*Saccharomyces cerevisiae* antibodies (ASCA) have been found to be significantly more prevalent in patients with Crohn disease compared to patients with ulcerative colitis or healthy controls.⁸⁻¹⁴ These antibodies, which can include antibodies in both the IgG and IgA classes, appear to be directed against mannose sequences in the cell wall mannan of *Saccharomyces cerevisiae*.^{14,15} The presence of IgG or IgA ASCA has been shown to have a high specificity for Crohn disease. One report found that the presence of both IgG and IgA ASCA was 100 percent sensitive for Crohn disease.⁸ Detection of ASCA may be of value in differentiating Crohn disease from ulcerative colitis in some patients.⁸⁻¹⁰
- A subgroup of Crohn disease patients does not appear to have ASCA antibodies. Whether these individuals form a subgroup of patients with specific clinical characteristics is unknown at present. The ASCA IgG and IgA assays utilized at ARUP are the only commercial ASCA assays to be approved by the FDA for *in vitro* diagnostic use.¹⁶ These assays have been subjected to extensive FDA review and are produced under strict FDA and GMP guidelines.

Anti-Neutrophil Cytoplasmic Antibodies (ANCA) IgG

- Anti-neutrophil cytoplasmic antibodies (ANCA) that demonstrate atypical perinuclear staining (atypical pANCA; classic perinuclear pattern on ethanol-fixed human neutrophils, but absent on formalin-fixed neutrophils) are found in 70 percent of patients with UC, but only 20 percent of patients with CD.¹⁷⁻¹⁹
- The ANCA immunofluorescence antibody (IFA) assay utilized at ARUP employs ethanol and formalin-fixed human neutrophils and has been approved by the FDA for *in vitro* diagnostic use. This ANCA IFA system has been widely used for many years and is considered the "gold standard" for detection of these antibodies. ANCA systems that replace formalin-fixed neutrophils with an enzyme (DNase) digest step are not used outside the group that developed this patented method.¹⁶ This ANCA DNase method has not been approved by the FDA and no external independent publications exist that validate this method.

OmpC IgA

The OmpC IgA assay is promoted by one laboratory as a way to detect patients with Crohn disease that are ASCA negative in their hands. To date, there have been no external independent publications supporting this claim; therefore, the clinical utility of this assay remains questionable. Increasing the sensitivity of the ASCA assays employed likely results in no need for OmpC IgA, as yet unproven in the diagnosis of IBD.¹⁶ At this time, studies are being conducted at ARUP to investigate the clinical utility of OmpC IgA, but again, there is no outside laboratory validation of the medical usefulness of this patented but non-FDA approved assay in the diagnosis and differentiation of the various forms of IBD.

Clinical Significance and Appropriate Use of Test

When used in conjunction with clinical findings, the ASCA and ANCA assays aid the physician in the diagnosis and differentiation of Crohn disease and ulcerative colitis in patients previously diagnosed as having inflammatory bowel disease.

Laboratory Diagnosis

The presence of ASCA and the absence of ANCA support the diagnosis of Crohn disease. ASCA IgG antibodies are found in 80 percent of CD patients and 20 percent of UC patients, whereas ASCA IgA antibodies are found in 35 percent of CD patients, but less than 1 percent of UC patients. Small bowel Crohn disease is present in almost all patients with IgG and IgA to ASCA that do not have an atypical pANCA. Atypical pANCA is found in 70 percent of UC patients, but in only 20 percent of patients with CD. There is no outside validation for the use of the ANCA DNase method and OmpC IgA for IBD, nor is there FDA approval of these procedures. In contrast, the assays utilized at ARUP are the only FDA-cleared assays for use in IBD diagnosis.

Methodology

The ASCA IgG and IgA assays (test numbers 0050562 and 0050563) are performed using partially purified *S. cerevisiae* antigen and enzyme immunoassay (EIA) technology (these assays have been approved by the FDA for in vitro diagnostic use). The ANCA IgG assay (0050811) is performed using ethanol and formalin-fixed neutrophils from normal human donors and indirect fluorescent antibody (IFA) technology (this assay has been approved by the FDA for in vitro diagnostic use).

References

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Test Information

0050567

Inflammatory Bowel Disease Differentiation Profile

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.