Inflammatory bowel disease: a systematic review on the value of diagnostic testing in primary care


CRD summary
This review concluded that calprotectin and ultrasonography showed consistent and promising findings for diagnosis of inflammatory bowel disease, but none of the studies were performed in primary care. These conclusions should be interpreted with some caution due to the limitations in the search, methodological limitations of the included studies and clinical heterogeneity between studies.

Authors' objectives
To summarise the available evidence on diagnostic tests available to primary care physicians for the evaluation of adult patients with abdominal symptoms in whom inflammatory bowel disease is part of the differential diagnosis.

Searching
PubMed and EMBASE were searched to February 2009. Some details of the search were reported and included use of a methodological filter; exact search terms were not reported. Reference lists of retrieved studies and relevant reviews and commentaries were screened. The review was restricted to studies reported in English, Dutch, German and French. Although not explicitly stated, it appeared that the review was restricted to published studies.

Study selection
Diagnostic cohort or case-control studies that assessed the accuracy of clinical signs and symptoms (alone or in combination), blood or faecal tests or abdominal ultrasonography for diagnosis of inflammatory bowel disease (included Crohn's disease and ulcerative colitis) in adults with non-acute abdominal symptoms in primary care or outpatients were eligible for inclusion. Studies in which the prevalence of inflammatory bowel disease was more than 25% were excluded. Case-control studies had to include control patients with a diagnosis of irritable bowel syndrome or in whom organic gastrointestinal disease was excluded. Studies had to use colonoscopy, histology, barium enema and/or clinical follow-up as the reference standard and report sufficient information to construct a 2x2 table of test performance.

Studies were conducted mostly in outpatient gastroenterology or radiology departments. Some studies assessed only Crohn's disease, some studies assessed both Crohn's disease and ulcerative colitis and five studies assessed inflammatory bowel disease without distinguishing exact aetiology. Prevalence of inflammatory bowel disease ranged from 2% to 25%. Tests evaluated included symptoms, blood or faecal tests and abdominal ultrasonography. None of the studies assessed physical signs. Nine studies used a minimum of colonoscopy plus histopathology or a clinical follow-up of at least one year as the reference standard.

One reviewer screened the titles and abstracts and a second reviewer checked those selected by the first reviewer as potentially relevant. Two reviewers screened full-text studies; disagreements were resolved by a third reviewer.

Assessment of study quality
Two reviewers independently assessed study quality using the 11-item Cochrane adaptation of the QUADAS tool.

Data extraction
Two reviewers independently extracted data to populate 2x2 tables of test performance. Estimates of sensitivity and specificity with 95% confidence intervals were calculated.

Methods of synthesis
For tests evaluated by four or more studies and where clinical and statistical heterogeneity could be ruled out, the bivariate model was used to estimate summary sensitivity and specificity together with 95% CIs. Sources of heterogeneity were considered (setting, disease prevalence, diagnosis and four of the QUADAS items). Subgroup
analyses based on these features were conducted if each subgroup included data from at least two studies. Pooled estimates were calculated where subgroups were assessed in four or more studies and data were relatively homogenous; otherwise, ranges in sensitivity and specificity were reported.

**Results of the review**

Twenty-four studies (n=5,516 participants) were included in the review: 13 diagnostic cohort studies, 10 nested case-control studies and one study that used both designs. The QUADAS items on which studies scored poorly were patient spectrum, appropriate reference standard and differential verification bias. Time between index test and reference standard and withdrawals were poorly described.

**Symptoms (11 studies):** None of the symptoms (diarrhoea, abdominal pain, blood in stools, weight loss) frequently associated with inflammatory bowel disease showed both good sensitivity and specificity; there was considerable heterogeneity across studies. Other symptoms were evaluated only in a small number of studies. Symptom-based criteria showed better accuracy, but estimates were variable. Kruis criteria (threshold <44) were assessed in three studies that showed high sensitivity (94% to 100%) but variable specificity (17% to 69%). Rome criteria showed lower sensitivity (68% to 89%) and better specificity (50% to 76%).

**Blood and faecal tests (13 studies):** Accuracy of C-reactive protein (four studies) was very variable. Sensitivity ranged from 55% to 100% and specificity ranged from 42% to 90%. Sensitivity of erythrocyte sedimentation rate (three studies) ranged from 56% to 78% and specificity ranged from 75% to 96%. Calprotectin (nine studies) showed consistently high sensitivity (range 84% to 100%) and specificity (range 71% to 100%), except for two studies that showed lower sensitivity (61% and 64%). Lactoferrin showed good accuracy (three studies). Sensitivity ranged from 78% to 100% and specificity ranged from 75% to 100%.

**Abdominal ultrasonography (four studies):** Summary sensitivity was 73% (95% CI 65% to 80%) and summary specificity was 95% (95% CI 91% to 97%).

Results of tests evaluated in single studies and subgroup analyses were reported.

**Authors’ conclusions**

Calprotectin and ultrasonography showed consistent and promising findings, but none of the studies were performed in primary care.

**CRD commentary**

The review addressed a broad question. Inclusion criteria were defined clearly. The literature search was restricted to two databases, incorporated a methodological filter, was restricted to studies in certain languages and appeared to be restricted to published studies; therefore, it was likely that relevant studies were missed. Appropriate steps were taken to minimise bias and errors at all stages of the review process. Study quality was assessed with appropriate criteria and the results of the assessment were clearly reported and considered in the analysis. The methods of analysis were appropriate and included some investigation of heterogeneity, although the large number of results presented made it difficult to identify the most important information.

The authors’ conclusions are supported by the results, but should be interpreted with some caution due to limitations in the search, methodological limitations of the included studies and clinical heterogeneity between studies.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated a need for high-quality cohort studies in consecutive patients with gastrointestinal symptoms in primary care. Tests should be standardised (assessment of symptoms included).

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