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Accuracy and cost of diagnostic strategies for patients with suspected Crohn's disease

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Abstract

Objective: To evaluate accuracy and cost of non-invasive diagnostic strategies including magnetic resonance imaging, intestinal ultrasonography, ileocolonoscopy and video-capsule endoscopy in suspected Crohn's disease.
Methods: A decision-analytic model was used to assess the costs in low (25%), intermediate (50%) or high (75%) pre-test probability of Crohn's disease. Based on the published accuracy of diagnostic modalities and Bayes' rule, we calculated post-test probability of Crohn's disease using different strategies, starting from ileocolonoscopy, ultrasonography or magnetic resonance. Each strategy was considered successful when post-test probability was >95% or <5%.
Results: With low pre-test probability, only ileocolonoscopy as the first investigation could exclude or confirm Crohn's disease while a normal ultrasonography may exclude Crohn's disease. With high pre-test probability, ileocolonoscopy or ultrasonography as the first test may confirm Crohn's disease, but at least 3 negative tests are required to exclude Crohn's disease.
The cost to diagnose one patient was cheapest utilising an ultrasonography-based strategy both in low (ultrasonography €1076; ileocolonoscopy €2005; magnetic resonance €4515) and high pre-test probability of Crohn's disease (ultrasonography €321; ileocolonoscopy €712; magnetic resonance €1412).
Conclusion: The accuracy and cost of these strategies depend on pre-test probability of Crohn's disease and vary according to the first test used. Ileocolonoscopy plus ultrasonography is the most accurate and less expensive initial diagnostic strategy.

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1. Introduction

Crohn's disease (CD) is a life-long inflammatory disease of unknown aetiology. Typically, the disease has its onset in the second and third decades of life with a heterogeneous clinical presentation. Symptoms in CD are non-specific and may include abdominal pain, diarrhoea, nausea and vomiting. Clinically it is often difficult to differentiate these symptoms from other gastrointestinal disorders, particularly irritable bowel syndrome (IBS) whose prevalence is reported 10 to 50 times more frequently than CD.[1–3] However, the incidence of inflammatory bowel diseases (IBD), in particular CD, is increasing around the world.[4] This may be due to the increased awareness of IBD by physicians and the public, greater access to colonoscopy, and the advancements in diagnostic methods, especially the radiological and endoscopic advancements in the investigation of the small bowel. Nevertheless, a single gold standard for the diagnosis of CD is still not available. Ileocolonoscopy with biopsies has been adopted by many physicians as the first line procedure of choice, but it may not be preferred as an initial investigation in some cases (e.g. paediatric patients) and may be limited by the rate of technical failures (5–15%) in intubating the ileum.[5,6] Irrespective of the findings at ileocolonoscopy, guidelines recommend further assessment of the gastrointestinal tract to completely examine the entire small bowel and the stomach[7,8] in order to diagnose and fully stage CD. Significant radiological advancements such as high resolution intestinal ultrasonography (IUS), computed tomography (CT)- and magnetic resonance imaging (MRI)-enteroclysis now allow for complete assessment of the small bowel. Additional endoscopic techniques such as video capsule endoscopy (VCE) and double balloon enteroscopy (DBE) are also used to image parts of the bowel that are not traditionally accessible with standard endoscopic techniques.

A definitive diagnosis of CD using invasive diagnostic procedures is essential to confirm the clinical suspicion of IBD, even in patients with high pre-test probability of organic disease prior to initiation of treatment. However, with increasing rates of IBD, combined with availability of new non-invasive diagnostic methods for assessment of the small bowel, there may be a paradoxical increase in the utilisation of new diagnostic modalities, even in patients with low pre-test probability of IBD. This has the potential to have unexpected economic consequences in the form of increased healthcare costs to both the individual and the healthcare system.

We developed a decision analytic model in order to estimate the accuracy of the most common non-invasive diagnostic strategies including MRI and transabdominal IUS, ileocolonoscopy and VCE and their combination, in order to diagnose CD. We also estimated the cost associated with each diagnostic strategy in patients at low, intermediate and high pre-test probabilities of CD.

2. Methods

2.1. Model design

A decision-analytic model, utilising the current guidelines of the European Crohn's and Colitis Organization,[8,9] was used to assess the accuracy and costs of obtaining a definite diagnosis of CD based on the clinical scenario of a patient undergoing evaluation of symptoms that suggest the presence of CD. Given the prevalence of CD is unknown in patients who present with clinical symptoms suggestive of the disease, we hypothesised 3 clinical scenarios: 1. A patient with low pre-test probability of CD, estimated to be no more than 25%. 2. A patient with an intermediate pre-test probability of CD, estimated to be 50%. 3. A patient with high pre-test probability, estimated to be at least 75%, according to previously published data.[10,11] The first scenario may be characterised by isolated or episodic diarrhoea and abdominal pain with normal or absent biochemical and faecal tests. The second may include a patient with abdominal pain and episodic diarrhoea and a first degree relative with known IBD, but normal or absent biochemical and faecal tests. The final scenario may be characterised a patient with chronic symptoms such as diarrhoea, abdominal pain, weight loss and positive biochemical tests (positive C-reactive protein or faecal calprotectin) along with negative stool cultures. These levels of pre-test probability were arbitrarily chosen. Although the use of non-invasive faecal markers of inflammation (e.g. faecal calprotectin) can set pre-test probabilities less that $<10\%$ and $>90\%$[12] there are significant rates of false negative results, especially for isolated small bowel CD, therefore they cannot be relied upon alone for a definitive diagnosis. We have deliberately excluded clinical scenarios suggestive of acute illness including infectious gastroenteritis, appendicitis and diverticulitis.

The investigations were analysed exclusively for their accuracy and costs to make a diagnosis of CD. In ileocolonoscopy it is the presence of ulcers or erosions, combined with nodular and hyperaemia and friability that confirm a diagnosis of CD. In MRI and IUS, diagnostic criteria of CD include increased bowel wall thickening, associated with creeping fat or changes in bowel pattern and vascularity. Assessment of disease extent, site of disease and abdominal complications (e.g. strictures, fistulae or abscesses) were therefore not considered.

The impact of biochemical diagnostic tests (e.g., C-reactive protein, blood cell count and faecal calprotectin) was not considered in the diagnostic strategies, but it was generically considered within the definition of pre-test probability of CD. Since the aim of this study was to suggest a cost-effective strategy to make a correct initial diagnosis in patients with suspected CD, not to determine the gold standard, we assessed conditional probabilities for a three-test sequence based on 3 different algorithms (Fig. 1). The first algorithm used ileocolonoscopy as the first examination, followed by bowel IUS or MRI then VCE. The second algorithm used IUS followed by ileocolonoscopy or MRI then VCE, the third algorithm used MRI followed by ileocolonoscopy or IUS. The conditional probabilities were calculated based on VCE always utilised as a final modality. This is due to the fact that VCE, depending on the individual centre and country, may be a very expensive investigation and not always available. However, the European Crohn's and Colitis Organization (ECCO) consensus guidelines have stated that in patients with suspected Crohn's disease and negative ileocolonoscopy, VCE may be the initial diagnostic modality for the evaluation of the small bowel.[13] Likewise, the International Conference on Capsule Endoscopy (ICCE) recommended that patients with suspected Crohn's disease should be selected to undergo VCE in high pre-test or moderate pre-test probability of CD, in particular if they present with typical symptoms plus either extraintestinal manifestations,