



Comparing disease activity indices in ulcerative colitis

A.J. Walsh^a, A. Ghosh^b, A.O. Brain^g, O. Buchel^c, D. Burger^d, S. Thomas^e, L. White^g, G.S. Collins^f, S. Keshav^g, S.P.L. Travis^{g,*}

^a Currently at Department of Gastroenterology, St Vincent's Hospital, Sydney, Australia

^b Medical Sciences Division, University of Oxford, Oxford, UK

^c Currently at Department of Surgery, Universitas Hospital, University of the Free State, Bloemfontein, South Africa

^d Currently at Department of Gastroenterology, Princess Alexandra Hospital, Brisbane, Australia

^e Currently at Department of Biomedical Sciences, University of Sheffield, Sheffield, UK

^f Centre for Statistics in Medicine, University of Oxford, Oxford, UK

^g Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford, UK

Received 1 August 2013; received in revised form 28 August 2013; accepted 9 September 2013

KEYWORDS

Ulcerative colitis;
Activity index;
Endoscopy;
Mayo Clinic index;
Clinical trial design

Abstract

Background: Comparisons between disease activity indices for ulcerative colitis (UC) are few. This study evaluates three indices, to determine the potential impact of inter-observer variation on clinical trial recruitment or outcome as well as their clinical relevance.

Methods: One hundred patients with UC were prospectively evaluated, each by four specialists, followed by videosigmoidoscopy, which was later scored by each specialist. The Simple Clinical Colitis Activity (SCCAI), Mayo Clinic and Seo indices were compared by assigning a disease activity category from published thresholds for remission, mild, moderate and severe activity. Inter-observer variation was evaluated using Kappa statistics and its effect for each patient on recruitment and outcome measures for representative clinical trials calculated. Clinical relevance was assessed by comparing an independently assigned clinical category, taking all information into account as if in clinic, with the disease activity assigned by the indices.

Results: Inter-observer agreement for SCCAI ($\kappa = 0.75$, 95% CI 0.70–0.81), Mayo Clinic ($\kappa = 0.72$, 95% CI 0.67–0.78) and Seo ($\kappa = 0.89$, 95% CI 0.83–0.95) indices was good or very good as was the agreement for rectal bleeding ($\kappa = 0.77$) and stool frequency ($\kappa = 0.90$). Endoscopy in the Mayo Clinic index had the greatest variation ($\kappa = 0.38$). Inter-observer variation alone would have excluded up to 1 in 5 patients from recruitment or remission criteria in representative trials. Categorisation by the SCCAI, Mayo Clinic and Seo indices agreed with the independently assigned clinical category in 61%, 67% and 47% of cases respectively.

* Corresponding author at: Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford OX3 9DU, UK. Tel.: +44 1865 228753; fax: +44 1865 228763.

E-mail address: simon.travis@ndm.ox.ac.uk (S.P.L. Travis).

Conclusions: Trial recruitment and outcome measures are affected by inter-observer variation in UC activity indices, and endoscopic scoring was the component most susceptible to variation. Crown Copyright © 2013 Published by Elsevier B.V. on behalf of European Crohn's and Colitis Organisation. All rights reserved.

1. Introduction

Instruments for assessing disease activity in ulcerative colitis (UC) are needed to define inclusion criteria and outcomes of clinical trials with precision, although they are less often used in routine clinical practice. This is despite, or even because of, a multiplicity of disease activity indices for UC, with almost a dozen developed for use in clinical trials.¹ The Pediatric Ulcerative Colitis index (PUCAI), for use in children, is the only clinical index that has been validated for symptom severity.² None in inter-observer variation has been examined and there has been only one systematic study evaluating the activity indices in UC,¹ which made no empirical comparisons between different indices. Inter-observer variation is known to be substantial in endoscopic assessment.³ The effect of variation in clinical assessment on trial recruitment or reported outcomes has not been studied.

There are many problems with current disease activity indices for UC, not least the absence of formal evaluation. Most are modifications of pre-existing indices, which therefore use similar terms, few of which are consistently defined, but omit symptoms of importance to patients, such as urgency or faecal continence. Since thresholds for remission, active disease and response to treatment vary,^{1,4} it is difficult to compare therapeutic trials and this is another reason that indices for UC are rarely used in clinical practice.

In clinical practice, disease activity in UC is assessed to a greater or lesser degree by clinical symptoms, endoscopic appearance, histopathology, biomarkers and quality of life. Consequently composite indices have been developed, such as the Mayo Clinic index, that include clinical symptoms, endoscopy, aspects of quality of life and the physician's global assessment (PGA).⁵ In an attempt to bring objectivity to the assessment of disease activity, the Seo index⁶ combines biomarkers with clinical symptoms. On the other hand, it may be better to separate symptoms from endoscopy,³ histopathology,⁷ biomarkers and quality of life.⁸ The Simple Clinical Colitis Activity Index⁹ is based on clinical symptoms alone. It is easier to validate separate indices^{3,7,8} so composite thresholds might then be set for recruitment or outcomes in clinical trials.

Recruitment to clinical trials requires that minimum and maximum disease activities are specified in the inclusion and exclusion criteria. Furthermore, the outcomes of treatment are typically defined as the number of patients with a defined change in disease activity index, or meeting a threshold criterion, typically for remission. Clearly therefore, inter-observer variation in determining clinical index scores would affect recruitment and outcomes. The implications of such variation have already been demonstrated in a trial of mesalazine for UC, where the outcome was contingent on inter-observer variation in endoscopy alone.¹⁰

The aim of this study was to evaluate the inter-observer variation in a subset of UC indices in the same set of patients.

A clinical index (Simple Clinical Colitis index⁹), a composite clinical and endoscopy index (Mayo Clinic index⁵) and a composite clinical and biomarker index (Seo index⁶) were selected. This allowed an assessment of the impact that inter-observer variation in the assessment of activity might have on recruitment or remission outcomes defined in representative clinical trials. It additionally helped determine which items of which index have the most variability and assessed the potential clinical relevance of the three indices.

2. Methods

2.1. Patients

Patients with UC of varying disease activities and extent of disease who requested a review appointment at the Inflammatory Bowel Disease clinic at the John Radcliffe Hospital, Oxford, were invited to participate. UC had previously been diagnosed by conventional criteria.¹¹ Patients with Crohn's disease or colitis yet to be classified were excluded.

2.2. Clinic logistics and endoscopy

One hundred patients were prospectively evaluated in 16 consecutive, specially designed clinics between August 2007 and April 2008. Each patient consented (Oxford LREC 536407Q1605/58ORH) to be seen and examined by the same four specialists in inflammatory bowel disease (AB, AW, SK, ST), to have a blood test, and to undergo videosigmoidoscopy on the same day. Each patient completed a record of symptoms (Supplementary file A) before being seen and examined by each specialist in random order. Each specialist recorded the clinical symptoms on a standard form that captured the terms for each index, blinded to other results (Supplementary file B). The last specialist to see the patient was responsible for the treatment decisions. The patient then proceeded to videosigmoidoscopy on the same day, performed by a fifth specialist (OB), according to a standard protocol.¹² Videos were anonymised and then scored at a later date (Baron,¹³ Modified Baron,¹³ Mayo Score Flexible Proctosigmoidoscopy Assessment,⁵ Sutherland Mucosal Appearance Assessment¹⁴) (Supplementary file C), in random order, by the first four specialists who were asked to score the worst affected area, blinded to all clinical details. Videosigmoidoscopy was unavailable for 4 patients (pregnancy 1, patient left prior to sigmoidoscopy 2, recording equipment failure 1).

2.3. Indices

Three indices were selected for comparison. Six other indices were recorded (Truelove and Witts' index,¹⁵ Powell-Tuck/St Mark's index,¹⁶ Sutherland index/Ulcerative Colitis Disease

Download English Version:

<https://daneshyari.com/en/article/3312597>

Download Persian Version:

<https://daneshyari.com/article/3312597>

[Daneshyari.com](https://daneshyari.com)