the YODA PROJECT | Forging a unified scientific community

Principal Investigator

First Name: Neeraj
Last Name: Narula
Degree: MD, MPH, FRCPC
Primary Affiliation: McMaster University
E-mail: wonge12@mcmaster.ca
Phone number: 9055259140 x73884
Address: 1280 Main Street West
1280 Main Street West
City: Hamilton
State or Province: Ontario
Zip or Postal Code: L8S4L8
Country: Canada

General Information

Key Personnel (in addition to PI):
  First Name: Emily
Last name: Wong
Degree: BHSc
Primary Affiliation: McMaster University

  First Name: Neeraj
Last name: Narula
Degree: MD, MPH, FRCPC
Primary Affiliation: McMaster University

Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.
How did you learn about the YODA Project?: Colleague

Conflict of Interest

https://yoda.yale.edu/system/files/yoda_coi_-_narula_1.pdf
https://yoda.yale.edu/system/files/yoda_coi_-_wong_1.pdf

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT01190839 - REMICADECRD3001 - Prospective, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial Comparing REMICADE (Infliximab) and Placebo in the Prevention of Recurrence in Crohn's Disease Patients Undergoing Surgical Resection Who Are at Increased Risk of Recurrence

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

.misc-fixes { display: none; } #admin-region { z-index: 9999999; } #admin-menu { z-index: 99999999; }

Research Proposal

Project Title

Comparison of the Rutgeert's score with the SES-CD for prediction of post-operative clinical recurrence in Crohn's disease

Narrative Summary:

The Rutgeert's score is used to evaluate the recurrence of Crohn's disease after patients undergo surgical removal of their ileum/colon. The Simplified Endoscopic Score for Crohn's disease (SES-CD) is a simplified score that assesses the severity of endoscopic disease in patients with Crohn's disease. It is usually used in clinical trials as one measure of disease severity for patients with Crohn's disease. However, it is not used in practice to evaluate recurrence on patients who have undergone surgical removal of their colon. The aim of this study is to determine if the SES-CD ileum sub-score better predicts clinical recurrence of Crohn's disease than the Rutgeert's score.

Scientific Abstract:

Background
The Rutgeert's score is presently used as the gold standard for the evaluation of recurrence of Crohn's disease at the level of the ileocolonic anastomosis after patients undergo ileocolonic resection. The Simplified Endoscopic Score for Crohn's disease (SES-CD) is a simplified score that assesses four endoscopic parameters in patients with Crohn's disease, and is intended for use in the five ileocolonic segments.

Objective
The aim of this study is to determine if the SES-CD ileum sub-score better predicts clinical recurrence of Crohn's disease than the Rutgeert's score after ileocolonic resection for CD.

Study design
This will be a post-hoc analysis of NCT01190839, which was a multicentre, randomized, placebo-controlled trial. This post-hoc analysis aims to compare the performance of the Rutgeert's score and SES-CD score to predict clinical recurrence.

Participants
To be included in this study, patients must have a complete Rutgeert's score and SES-CD score at week 76 or end of study.

Main outcomes measures
The primary outcome of this study will be clinical recurrence, defined as Crohn's disease activity score (CDAI) > 200 with ?70 rise from baseline, at both week 76 and 104.

Statistical analysis
Week 76 colonoscopy scores will be used to evaluate how well each score predicts clinical recurrence at week 76 and 104. Area under the receiver operating characteristic curves will be compared for the SES-CD and Rutgeert's score. Multivariate regression analyses will be conducted to evaluate endoscopic score severity and clinical recurrence.

Brief Project Background and Statement of Project Significance:

The Rutgeert's score is presently used as the gold standard, although lacking formal validation, for the evaluation of recurrence of Crohn's disease at the level of the ileocolonic anastomosis after patients undergo ileocolonic resection. The Rutgeert's score includes components such as size and number of ulcers, degree of inflammation, and any narrowing/stenosis seen on endoscopy. Up to 70% of patients who undergo resection due to CD develop post-operative endoscopic recurrence at or proximal to the anastomotic site within 1 year. The severity of endoscopic recurrence has been demonstrated to predict likelihood of future resection (Rutgeerts et al., 1990). Hence, there may be benefit in assessing for and titrating treatment according to endoscopic appearance. There

are some limitations to use of the Rutgeert's score however. For instance, patients with a score of i2a (recurrence at the anastomosis site) are not thought to have the same likelihood of recurrence as patients with i2b (more than 5 apthous ulcers), but these are often lumped together for the purposes of endoscopic scoring and treatment decisions. Another criticism is the arbitrariness of scoring i1 vs. i2, which is based on number of apthous ulcers seen. A patient with four apthous ulcers and another with six apthous ulcers of the neo-terminal ileum likely have similar prognoses but the Rutgeert's method assigns them a different score.

The Simplified Endoscopic Score for Crohn's disease (SES-CD) is a simplified score that assesses size and extent of ulceration, inflamed surface area involved, and areas of stenosis to assess the severity of endoscopic disease in patients with Crohn's disease. It is usually used in clinical trials as one measure of disease severity for patients with Crohn's disease, and is intended for use in the ileum, right colon, transverse colon, left colon, and rectum. Individual subscores from each segment are added up to compile a total score. However, this score has not been validated, nor is it clinically used in the population that is post-resection for evaluation of recurrence.

The PREVENT trial was conducted to see if infliximab compared to placebo reduces clinical recurrence in those with ileocolonic resection for Crohn's disease (Regueiro et al., 2016). Although the trial did not demonstrate a significant reduction in clinical recurrence in infliximab-treated patients compared to placebo, it did show that Infliximab reduces endoscopic recurrence (major secondary end point) as compared to placebo, when defined only by a Rutgeert's score >= i2 (22.4% and 51.3% respectively, ARR with infliximab 28.9%).

The authors and the researchers with the PREVENT group also completed simultaneous assessment with the Rutgeert's score and the SES-CD score. This presents a unique opportunity to compare how well the SES-CD endoscopic score predicts clinical recurrence as compared to the Rutgeert's score.

Specific Aims of the Project:

The aim of this study is to determine if the SES-CD ileum sub-score better predicts clinical recurrence of Crohn's disease than the Rutgeert's score after ileocolonic resection for CD. Should the SES-CD score be found to better predict clinical recurrence, this could argue for its future use in post-operative Crohn's disease clinical trials.

What is the purpose of the analysis being proposed? Please select all that apply.
Research on clinical prediction or risk prediction

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

Data from NCT01190839 is being requested for this study. To be included in this study, patients must have a complete Rutgeert's score and SES-CD score at week 76 or end of study (in the case of early termination).

Main Outcome Measure and how it will be categorized/defined for your study:

The main outcome measure of this study is clinical recurrence, defined as Crohn's disease activity score (CDAI) > 200 with >=70 point rise from baseline, at both week 76 and week 104.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

The main predictor of this study is endoscopic disease severity, based on the Rutgeert's score and SES-CD at week 76.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

Infliximab trough level and antibody status will be evaluated at several timepoints, including week 104. Other demographic variables at baseline, such as concomitant immunomodulator use, corticosteroid use, disease duration, smoking status, age, gender, prior biologic exposure, Crohn's disease Montreal classification/phenotype and presence of perianal disease, will be used for the purposes of multivariate regression analyses.

Statistical Analysis Plan:

Week 76 colonoscopy scores (or end of study scores for those patients who did not make it to week 76) will be used to evaluate how well each score predicts clinical recurrence (defined in PREVENT as CDAI score >200, with >=70 point rise from baseline) at both week 76 and week 104. Receiver operating characteristic curves will be generated for each of the SES-CD and Rutgeert's score and area under the curves will be compared between the two to determine if one performs more favourably with prediction of clinical recurrence.

Multivariate regression analyses is also planned to evaluate the relationship between endoscopic score severity and clinical recurrence. Variables requested for this analysis include treatment allocation (infliximab or placebo), concomitant immunomodulator use, concomitant corticosteroid use, disease duration, and infliximab serum trough levels at week 76. Other demographics will also be considered for inclusion in the model, such as smoking status, age, gender, and prior biologic exposure. Univariate analyses will be conducted to identify any association with the outcome of interest. Any variables with a p-value < 0.10 will be considered for inclusion in the model.
Software Used:
STATA
Project Timeline:

Date to Start Project: November - December 2020.
Date to Complete Analysis: December 2020 – January 2021.
Date to Draft Manuscript: January – February 2021.
Date to Submit Manuscript: February – March 2021.

Dissemination Plan:

Analyses from this study may be shared to target audiences through presentations and abstracts. These may be submitted to conferences such as Canadian Digestive Diseases Week, Digestive Disease Week, and European Crohn's and Colitis Organisation. A manuscript may also be submitted for publication. The YODA Project will be acknowledged in all study products, which will be shared at the time of submission.

Bibliography:

Regueiro, M., Feagan, B. G., Zou, B., Johanns, J., Blank, M. A., Chevrier, M., … Younes, Z. (2016). Infliximab Reduces Endoscopic, but Not Clinical, Recurrence of Crohn's Disease after Ileocolonic Resection. Gastroenterology, 150, 1568–1578. https://doi.org/10.1053/j.gastro.2016.02.072

Rutgeerts, P., Geboes, K., Vantrappen, G., Beyls, J., Kerremans, R., & Hiele, M. (1990). Predictability of the postoperative course of Crohn's disease. Gastroenterology, 99(4), 956–963. https://doi.org/10.1016/0016-5085(90)90613-6