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Investigating the effects of resolving intestinal narrowing in Crohn's disease – a study of gut bacteria, movement and products

Submission date 26/12/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 20/02/2019	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 18/07/2023	**Condition category** Digestive System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Crohn's disease (CD) is a chronic gastrointestinal condition with serious health implications. CD is characterised by the presence of small and large bowel inflammation. CD patients frequently experience abdominal pain, nausea, and diarrhoea. These symptoms may result from 'narrowings' within the bowel known as 'strictures'. Crohn's patients who have intestinal surgery experience 'stricturing' (the formation of strictures) more often.

The 'CS3M Crohn's Stricture Study' will give new insights into 'strictures' in this context. There are many unanswered questions. It is unclear how strictures affect bowel contraction, bacteria within the gut and bacterial by-products. It is also not clear how to best treat patients with strictures.

This study will investigate four separate aspects of intestinal strictures in Crohn's disease:
1. How stenting of strictures affects the movement of the bowel (a.k.a. motility).
2. How stenting of strictures affects the bacterial content of the gut (a.k.a. microbiome).
3. How stenting of the strictures affects bacterial by-products from the gut (a.k.a. metabolomics).
4. The clinical impact of CD stricture stenting.

The results from this pilot study may inform future large scale trials involving stenting in CD. This research will generate novel data about stenting impact in CD and will consist of the first global report such findings.

Who can participate?
Only Crohn's disease patients with identified 'intestinal strictures' will be asked to participate. Several different treatment options exist. Intestinal 'stenting' is one of the available therapies. It involves the endoscopic placement of an opening device, known as a 'stent', into the affected area.

Should a patient choose to undergo stent therapy, they will then be asked to take part in the study. Only adult patients (ages 18-80), who can give consent and are not enrolled in other research studies will be eligible. No healthy controls will be enrolled in the study.

What does the study involve?
Each patient will undergo a Magnetic Resonance (MR) scan before and after stent treatment. Stool samples will be collected prior to and following 'stenting'. These stool samples will be analysed for bacterial content and by-products. The techniques used for stool analysis will include bacterial genetic analysis and gas-chromatography analysis of bacterial metabolites. Each patient's clinical progress will be reviewed and assessed with validated Inflammatory Bowel Disease (IBD) scoring tools.

What are the possible benefits and risks of participating?
The risks to each study participant (from stool collection, and MRI scanning) has been deemed to be low. The novel insights into strictures in CD will be delivered by data produced by stool analysis and MRI scans of the intestine. Clinical data will further our understanding of stent treatment in Crohn's disease. Personal research findings will be relayed to study participants.

Where is the study run from?
All study activities will be conducted at a single research centre - Royal Derby Hospital – UK. The study is being sponsored by the University of Nottingham.

When is the study starting and how long is it expected to run for?
Beginning from January 2019, the study will run for a total of 18 months.

Who is funding the study?
All study activities are being funded by an internal Royal Derby Hospital - Gastroenterology research fund and a further Royal Derby Hospital charity source.

Who is the main contact?
Dr Ronit Das, ronitkdas@gmail.com

Study website
http://www.cs3m.online/

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number
252808

ClinicalTrials.gov number

Secondary identifying numbers
DHRD/2018/078, IRAS 252808

Study information

Scientific Title
Characterising the effects of relieving stricture obstruction by ileocolonic stenting - a pilot study into motility, microbiomics and metabolomics in Crohn’s disease

Acronym
CS3M

Study objectives
The relief of ileocolonic, Crohn’s stricture-related mechanical obstruction has a quantifiable impact on bowel motility, the intestinal bacterial population and associated metabolomic profiles.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Health and Social Care Research Ethics Committee B (HSC REC B), 24/12/2018, ref. 18/NI/0241

Study design
Pilot observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
http://www.cs3m.online/

Health condition(s) or problem(s) studied
Crohn's Disease.

Interventions
Patients with Crohn’s disease and abnormal intestinal ‘narrowings’ (known as ‘strictures’) will be asked to take part in the study. Each patient will have routine clinical treatment of their ‘stricture’ with a removable expanding device. Before and after treatment, specific studies will be performed. Each patient with undergo two intestinal MRI scans examining gut movements. Stool samples will be collected before and following therapy. Each stool sample will be analysed for bacterial content and separate chemical by-products. Patient progress will be monitored throughout the study. The total time of involvement for each patient will be between 8 to 10 months.

Intervention Type
Other

Primary outcome measure
1. The bowel microbiome will be measured using stool bascterial 16sRNA analysis pre-therapy, during therapy and post-therapy.
2. Intestinal motility will be measured using magnetic resonance-assessed small bowel motility at baseline and after 6 weeks of therapy.
3. The stool metabolic profile will be measured using gas-chromatography stool metabolomic analysis pre-therapy and post-therapy.
4. Clinical impact on Crohn’s ileocolonic strictures will be measured using paired assessment with validated IBD scoring tools (CDAI, HBI, IBD-Q) at baseline and at 6-8 weeks.

Secondary outcome measures
1. Progression onto Surgery
2. Recruitment Rate
3. Complications / Adverse Events

Overall study start date
01/05/2018

Completion date
01/01/2021

Eligibility

Key inclusion criteria
1. Crohn’s Disease as an established diagnosis (established diagnosis based on histology and supportive imaging)
2. Previous right hemicolectomy or partial resection and subsequent large and small bowel re-anastomosis

3. Identified anastomotic or de novo stricture accessible by colonoscopy – endoscopic or imaging identification (MR or CT or endoscopy)
4. Aged 16-80 years
5. Symptoms attributable to a focal ileocolonic stricture
6. Ability to give informed consent
Inclusion into the study will only be following Inflammatory Bowel Disease Multidisciplinary Team referral and strict adherence to the given inclusion criteria.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
14

Key exclusion criteria
1. Malignancy
2. Significant cardiovascular or respiratory disease
3. Uncontrolled thyroid disease
4. Neurological or cognitive impairment
5. Significant physical disability
6. Hepatic disease or renal failure
7. Abnormal blood results other than those explained by CD in CD participants
8. Co-enrolment in other CD study
9. Pregnancy or ongoing breastfeeding
10. Any condition that precludes MRI scanning (e.g. pacemaker)
11. Routine usage of any medication that affects gastric emptying or small bowel motility (i.e. hyoscine butylbromide, mebeverine, domperidone, ondansetron, metoclopramide)
12. Inability to endoscopically access stricture or place stent

Date of first enrolment
10/04/2019

Date of final enrolment
01/03/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

Royal Derby Hospital
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Sponsor information

Organisation
University of Nottingham

Sponsor details
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Sponsor type
University/education

Website
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ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Gastroenterology Departmental Research Fund - Royal Derby Hospital

Funder Name
Charitable Fund - Royal Derby Hospital

Results and Publications

Publication and dissemination plan
Publication of results is expected in peer-reviewed journals within 12 months of trial end.

Intention to publish date
01/12/2022

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No