CyTOF and microbiota analysis on Crohn*s disease-associated and idiopathic perianal fistulas

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To determine the differences in immune cell populations, microbiota and fibroblasts between fistulas from patients with and without Crohn*s disease.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anal and rectal conditions NEC
Study type	Observational invasive

Summary

ID

NL-OMON48904

Source
ToetsingOnline

Brief title
CyTOF and microbiome analysis fistulas

Condition

- Anal and rectal conditions NEC

Synonym
fistulas, Perianal fistulas

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Crohn, CyTOF, fistulas, microbiome

Outcome measures

Primary outcome

Differences in immune cell populations analysis between fistula tracts from patients with and without Crohn*s disease.

Secondary outcome

Differences in immune cell population in rectum biopsies from patients with and without Crohn*s disease.

Correlation of immune cell populations in the fistula tracts with immune cells in peripheral blood and rectum biopsies.

Differences in microbiota between fistula tracts from patients with and without Crohn*s disease.

Differences in the microbiota of the gut and the fistula tract.

Differences in fibroblast expression patterns between fistula tracts from patients with and without Crohn's disease

Differences in the fibroblast expression patterns of fistula tract and the rectum biopsies

Study description

Background summary

Perianal fistulas are a common clinical problem in patients with Crohn*s disease. The cumulative incidence of perianal fistulas is estimated at 23-26% after 20 years of CD 1, 2. Even with the best available medical treatment for this condition, the chance of complete healing for an extended period of time

is less than 50% and the enduring remission rates of complex perianal fistulas remains low at 37.0%. Also patients without Crohn*s disease can develop fistulas without any known underlying cause. These patient groups are treated differently. Patients with Crohn*s disease will receive preferably anti-TNF therapy together with local surgery, while patients without Crohn*s disease will only receive local surgical treatment.
The current understanding of the pathophysiology of CD-associated perianal fistulas, though not complete, seems to involve at least two mechanisms. First the immune cells with the epithelial-to-mesenchymal transition (EMT) and matrix remodelling enzymes.In addition the matrix metalloproteinases (MMPs), which are enzymes that can degrade all components of the extracellular matrix (ECM). Furthermore, our unpublished data on cytokine profiles in perianal fistulas showed high amounts of several inflammatory cytokines inside the fistulas.The second aspect of the pathophysiology involves the microbiota. The innate immune system recognizes general microbe-associated molecular patterns. The adaptive immune system is also programmed by commensal microbiota and microbes have been shown to impact the differentiation of T cell populations. Commensal bacteria are also capable of modulating the host innate immune system to promote their own fitness in the intestinal niche. So it is not surprising that our immune system, and especially the mucosal immune system, has developed an intricate connection with our associated microbiota.
Fibroblasts, which are abdundantly present in fistulas, were recently reported to regulate Th1 cell activity in inflammatory bowel diseases (IBD) and specific fibroblasts subsets were identified and associated with IBD. However, studies about their role in the pathogenesis of CD-associated fistulas are lacking. In this study we would like to compare the immune subsets, microbiota and fibroblasts in perianal fistulas of patients with Crohn*s disease and without Crohn*s disease. CyTOF analysis will be used to compare the subsets of immune cells in great detail.

Study objective

To determine the differences in immune cell populations, microbiota and fibroblasts between fistulas from patients with and without Crohn*s disease.

Study design

Prospective cohort study. At day of surgery extra blood will be drawn and a feces sample will be collected from the patients. During surgery 4 biopsies from the rectum will be taken. The fistula scraping (waste material) and a swab of the fistula tract will also be collected.

Study burden and risks

Burden: in addition to regular care (which includes the fistula surgery);
- A feces sample will be collected before surgery.

- Venepuncture; if feasible blood will be drawn from the entrance that is already there.
- A swab of the fistula tract will be collected.Will be taken during surgery (under anesthesia) and will cause no extra burden.
- 4 biopsies of the rectum during surgery. Will be taken during surgery (under anesthesia) and will cause no extra burden. However there is a small risk on bleeding after biopsy (<0.1%).

Benefit: there will be no direct benefit for the individual patient. However patients with perianal fistulas suffer from a disease that is very hard to treat. This study will provide new information about the pathogenesis of perianal fistulas and can thereby help to develop new therapies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in the *Crohn-fistula group* of this study, a subject must meet all of the following criteria:
- Patients with perianal fistulas who will have surgery for their perianal fistula including scraping of the fistula.
- Patients with confirmed Crohn*s disease (clinical and endoscopic).
In order to be eligible to participate in the *non-Crohn-fistula group* of this study, a subject must meet all of the following criteria:
- Patients with perianal fistulas who will have surgery for their perianal fistula including scraping of the fistula.
- Patients with no clinical suspicion for IBD (based on the fecal calprotectin (FCP)) or no signs of inflammation on endoscopy.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- In the *non-CD-fistula group* perianal fistulas cannot be the result of pelvic malignancy or radiation therapy or another known medical condition in the pelvic region.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-01-2019
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	18-09-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	04-07-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	19-09-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	02-01-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL65019.058.18