An exploration of intestinal bacterial biofilms in Lynch syndrome patients as disease markers for colorectal cancer

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON43143

Source
ToetsingOnline

Brief title
Bacterial biofilms in colorectal cancer

Condition

- Other condition
- Benign neoplasms gastrointestinal
- Gastrointestinal neoplasms malignant and unspecified

Synonym
Colorectal cancer in Lynch syndrome patients

Health condition

Lynch syndroom

Research involving

Human

Sponsors and support

Primary sponsor: Pathologie
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: biofilm, cancer, colon, microbiota

Outcome measures

Primary outcome

Revealing an assocation between the presence of biofilms and the development of

colorectal cancer in Lynch patients.

Secondary outcome

- Determining the effects of biofilms on the mucosal tissue of the colon

- Determining the effects of biofilms on oncogenesis markers in epithelial cells

- Studying which bacteria are present in the biofilm and determining which

bacteria could be potentially pathogenic

Study description

Background summary

Colorectal cancer (CRC) affects 1.2 million people worldwide, of which 15% is due to inherited genetic mutations. Lynch syndrome, caused by germ line defects in one of the mismatch repair genes MLH1, MSH2, PMS2 or MSH6, frequently leads to CRC (25-70%), endometrial cancer (25-70%) and, to a lesser extent, cancers of the small bowel, stomach, ovary, ureter, bladder and hepatobiliary tract. Lynch patients often develop recurrent colorectal tumors, making them an ideal study group to prospectively analyze the development of adenomas. Interestingly, some Lynch patients have a very high risk on developing recurrent colorectal tumors, whilst some Lynch patients seem to be at a very low risk. For surveillance of the development of colorectal tumors in Lynch patients it is important to differentiate between the low and the high risk

patients.

Study objective

Lynch-related tumors mostly develop in the ascending right side of the colon (70-85%). Strikingly, it was recently discovered that dense bacterial biofilms and invasive bacteria occur in the colonic mucosa of 87% of right-sided colorectal cancer (CRC) patients, versus only 11% of left-sided CRC patients and 13% of healthy controls. These biofilms could be identified both on tumors and on the adjacent normal tissue. This is particularly relevant since recent evidence showed that the intestinal microbiota is critically involved in CRC pathogenesis. We hypothesize that biofilms host pathogenic bacteria and can thereby contribute to CRC development. We think that biofilms may help to differentiate between Lynch patients who are at high risk of developing CRC and which ones are at low risk. In this study, we aim to determine whether biofilms are present before CRC development and whether they can predict CRC development in an early stage.

Study design

Extra biopties from colon mucosa will be collected from both Lynch syndrome patients or control patients that are already scheduled for a colonoscopy. These biopties will be studied for the presence of biofilms with modern microscopy techniques. Subsequently, we will use these results to determine whether patients with biofilms develop tumors more frequently. Additionally, will also study the effect of biofilms on the mucosal barrier and oncogenesis markers. Lastly, we aim to identify which bacteria are present within the biofilms and study the functions and/or pathogenicity of these bacteria.

Study burden and risks

There is a minimal risk for bleeding associated with taking biopsies during colonoscopy. The perforation risk after taking biopsies is negligible. The risk for bleeding (about 2%) or perforation (about 0.01 to 0.1 %) after removing neoplastic lesions is far larger than taking simple superficial biopsies as is the case in this study. Biopsies are only taken from the mucosa and will not reach the deeper layers of the colon as is for example the case when removing polyps with diathermy. Furthermore, also colonoscopies without taking biopsies or neoplastic lesion removal give a risk of perforation that is comparable to colonoscopies with taking biopsies (0.6 per 1000 procedures). In this procedure colonoscopy is part of regular patient care and only taking the biopsies is part of the study. Therefore the additional risk of taking biopsies for this study is estimated to be very small.

Contacts

Public
Selecteer

Geert Grooteplein Zuid 10
Nijmegen 6500HB
NL
Scientific
Selecteer

Geert Grooteplein Zuid 10
Nijmegen 6500HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Lynch patients who are scheduled for multiple colonoscopies.
Other patients who are scheduled for multiple colonoscopies. (control)

Exclusion criteria

- antibiotics in the past 3 months.
- a history with inflammatory diseases of the intestine.
- vaccination to prevent colorectal cancer.
- coagulation disorders or patients taking anti-coagulation medicine.
- a (sub)total colectomie

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	14-03-2017
Enrollment:	140
Type:	Actual

Ethics review

Approved WMO

Date:	05-01-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL57875.091.16