The identification of mutations associated with Serrated Polyposis Syndrome

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal tract disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON38510

Source
ToetsingOnline

Brief title
Genetic identification of SPS

Condition

- Gastrointestinal tract disorders congenital
- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
Hyperplastic polyposis syndrome, Serrated Polyposis Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Mozaiek beurs

Intervention

Keyword: Genetics, Mutations, Serrated Polyposis Syndrome, Serrated polyps

Outcome measures

Primary outcome

To identify the SPS causative gene using exome sequencing technique in well-characterized SPS patients and families.

Secondary outcome

• To give an overview of polyposis and SPS patients identified in a retrospective PALGA search in a tertiary medical centre over 27 years

• To distinguish different subtypes in phenotypes of patients with serrated and mixed polyposis

• To confirm the possible genes in additional SPS families, SPS singletons and exclude it in healthy controls.

• To study the effect of the mutation on protein level

• To elucidate the genetic mechanism underlying the serrated carcinoma pathway and molecular etiology in SPS

• To identify patients at increased risk for colorectal carcinoma and family members at increased risk for polyposis or CRC

Study description

Background summary

The serrated polyposis syndrome (SPS), formerly known as the hyperplastic polyposis syndrome, is a relatively rare condition, which has been first

recognized about 10 years ago. Hallmark of SPS is de occurrence of multiple serrated polyps in the large intestine. SPS is associated with an increased risk for both patients and their first degree relatives to develop a colorectal carcinoma. As such, there is evidence for a hereditary behavior of this syndrome. Unfortunately, to date the initial germline mutation remains unknown. With this study, we want to identify the genetic mutation associated with SPS. We want to expand a previous study in only one large SPS family with other families, singletons and healthy family members to broaden our search for the genetic background of SPS.

Study objective

Primary objective of this study is the identification of familial germline mutations in SPS. Secondary objectives are to get a better insight in the molecular pathway of SPS and associated colorectal carcinoma, to discriminate those family members at risk for SPS and colorectal cancer from those who are not at risk, and to diagnose patients in an early phase of the disease.

Study design

This study is a cross-sectional study in all SPS patients diagnosed at our Gastroenterology, Pathology and Human Genetics departments and their first degree relatives. All relevant clinical data will be collected in a digital database. There will be no additional treatment administered, introduced or recommended to subjects by the study itself. After obtaining written informed consent, from each individual 10 cc EDTA blood will be sampled for isolation of DNA. When colonoscopy is performed, healthy colonic tissue samples will be collected for isolation of DNA. In blood, colon tissue and polyp/tumor tissue we will search for mutations associated with SPS. To start, DNA will be analyzed by exome sequencing to identify possible pathogenic mutations. If the results of the first tests need stronger evidence, in a second run more family members with SPS will be recruited and included for exome sequencing. If one or more candidate genes are identified, all family members, both SPS and non-SPS, and SPS singletons will be analyzed for an association between SPS and the candidate genes.

Study burden and risks

The physical risks that are introduced to the participants by this study are considered to be minimal. It is limited to a bruise caused by a single venapunction for the withdrawal of 10 cc blood. This small amount has no influence on the health status of the subject. Next to this, there exists 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 polyps in these patients is far larger than simple biopsies. The mental burden for the included

subjects in general is predicted to be low.

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

Patients fulfilling the WHO criteria for SPS (5) or first degree family members (both SPS as non-SPS suspects), from identified patients with SPS
Age >= 18 years

Exclusion criteria

Age < 18 years

Incapacitated subjects
Patients with known germline mutations (e.g. mutations in APC or MUTYH)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-11-2013
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	01-10-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-12-2017
Application type:	Amendment
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	NL44839.091.13