Chromoendoscopy in Lynch syndrome patients

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The aim of this study is to determine whether chromoendoscopy, including polypectomy of all detected lesions, reduces the development of colorectal neoplasia in Lynch syndrome patients at follow-up endoscopy.

Ethical review	Approved WMO
Status	Pending
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON32242

Source
ToetsingOnline

Brief title
ChromoLynch

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
HNPCC, Lynch syndrome

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Chromoendoscopy, HNPCC, Lynch syndroom

Outcome measures

Primary outcome

The primary endpoints of the study are the number of adenomas, advanced adenomas, carcinomas at baseline and the number of the number of adenomas, advanced adenomas, carcinomas and the number of patients requiring colectomy at 2-year follow-up.

Secondary outcome

The secundary endpoints of the study are the number of complications from colonoscopy at baseline and at 2-year follow-up.

Study description

Background summary

Lynch syndrome (LS), or hereditary nonpolyposis colorectal cancer (HNPCC), is an autosomally dominantly inherited disorder that accounts for 1-2 % of colorectal cancer cases [1-4]. LS is caused by germline genomic alterations in one of the mismatch repair (MMR) genes hMLH1, hMSH2, hMSH6 and hPMS2 [1]. Genetic alterations in the hMLH1 and hMSH2 genes account for the large majority of LS cases. The lifetime incidence of colorectal cancer is 20-75 % in these mutation carriers [5, 6]. Individuals with LS-associated colorectal cancer differ from those with sporadic disease in several ways: the tumours are diagnosed at an earlier age; the majority of tumours is located in the proximal colon; there is an increased risk of developing synchronous or metachronous colorectal cancers and the prognosis relatively favourable compared to sporadic cases [1]. It is generally accepted that LS associated colorectal cancers develop along the adenoma-carcinoma sequence as in sporadic cases [1]. There is evidence suggesting that the adenoma-carcinoma sequence is accelerated in LS patients as compared to the general population [1].
Colonoscopic screening and subsequent removal of polyps at a 3-year interval in asymptomatic at-risk members of LS families has shown to reduce the incidence of colorectal cancer and improve overall survival [7]. However, within such an

interval in surveillance programs, interval cancers have been observed [8, 9]. It is therefore currently recommended that MMR gene mutation carriers should be kept under surveillance by regular colonoscopy every 1-2 years beginning at the age of 20-25 or 5-10 years younger than the earliest affected family member [10, 11].

LS adenomas are predominantly located in the proximal colon [12] and frequently carry villous architecture and high-grade dysplasia, markers that are associated with an increased risk of developing colorectal cancer [13-16]. Even in LS adenomas smaller than 5-7 mm in size, high-grade dysplasia can be encountered [12, 16]. Therefore, the identification of high-risk precursor lesions in LS is considered of paramount importance.

It is known that conventional colonoscopy has a certain miss rate for colorectal neoplasms, especially small adenomas [17]. A few years ago, the technique of chromoendoscopy was introduced. Chromoendoscopy, in which one of various dyes are sprayed onto the colonic mucosa via a spray catheter passed through the working channel of the endoscope, offers detailed evaluation of the mucosal surface [18]. Indigo carmine is a contrast stain that is not absorbed and does not react with the surface mucosa. In 2 large randomised controlled trials chromoendoscopy significantly increased the detection of small adenomas in the proximal colon as compared to conventional colonoscopy [19, 20]. Recently, 2 trials in LS patients revealed that chromoscopic endoscopy improved the detection of adenomas, particularly flat lesions, compared to conventional colonoscopy [21, 22]. Together, these data suggest that chromoendoscopy may improve detection rates of significant neoplastic colonic lesions in LS patients. However, the true value of chromoendoscopy in the management of LS patients remains to be demonstrated.

The aim of this study is to determine whether chromoendoscopy, including polypectomy of all detected lesions, reduces the development of colorectal neoplasia and the need for colectomy in LS patients at follow-up endoscopy. The results of the study will indicate the value of chromoendoscopy in the management of LS patients and whether the technique should be implemented in current surveillance procedures.

References

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Study objective

The aim of this study is to determine whether chromoendoscopy, including polypectomy of all detected lesions, reduces the development of colorectal neoplasia in Lynch syndrome patients at follow-up endoscopy.

Study design

This is a national multi-center randomised trial.

Intervention

Patients will be randomised between conventional colonoscopy and chromoendoscopy at baseline, followed by chromoendoscopy in all patients at two year follow-up.

Study burden and risks

Participation will result in minimal burden for this patient group. Chromoendoscopy requires slightly longer endoscopy procedure times (minutes). All neoplastic lesions encountered will be removed if technically possible, associated with known low risks of complications. Otherwise, the study will not be associated with additional endoscopic procedures, visits, additional blood sampling, additional physical examinations or other tests.

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

- Proven or obligate (carrier state based on the position in the pedigree) mutation carriers, with a known mutation in the hMLH1, hMSH2 or hMSH6 gene,
- who have their entire proximal colon in situ and
- are aged between 20 and 70 years and
- if written informed consent is provided.

Exclusion criteria

Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2008
Enrollment:	300
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL20612.042.07