Recurrences after standard EMR vs plus thermal ablation EMR of advanced sessile and lateral spreading colorectal adenoma: a multicenter, randomized controlled trial

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Does STSC decreases the recurrence rate after EMR in patients with large lateral spreading or sessile polyps?

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Benign neoplasms gastrointestinal
Study type	Interventional

Summary

ID

NL-OMON54419

Source
ToetsingOnline

Brief title
RESPECT

Condition

- Benign neoplasms gastrointestinal
- Gastrointestinal therapeutic procedures

Synonym
Benign polyps, benign tumors

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: INTERREG (Europese Unie)

Intervention

Keyword: Coagulation, EMR, Intervention, Recurrence

Outcome measures

Primary outcome

The primary objective of this trial is to investigate whether thermal ablation EMR with soft tip snare coagulation (STSC) reduces the recurrence rate of lateral spreading or sessile polyps >=20mm compared to standard EMR. The primary endpoint therefore is polyp recurrence after 6 months follow up. Recurrence is evaluated histologically with biopsies taken during follow up colonoscopy.

Secondary outcome

Secondary objectives are to evaluate the efficiency and safety of STSC EMR and to identify predictors for higher recurrence rates. We will also compare macroscopic with histologic recurrence evaluation. Therefore the following secondary objectives are formulated:

Data on perforation, post procedural bleeding, post polypectomy syndrome and death are collected in order to further evaluate the safety EMR.

EMR procedure time

The procedure time of all EMR procedures will be recorded in order to compare duration between standard EMR and EMR with STSC.

Localization

The localization of each polyp will be described in the colonoscopy report: cecum, ascending colon, descending colon, transverse colon, and rectosigmoid colon. Localization will be assessed as a possible risk factor for recurrence.

Polyp size

All polyps will be measured during colonoscopy as size is reported to be an independent risk factor for polyp recurrence [1, 2].

Polyp histology

All polyps will be classified according to the Kudo*s pit pattern classification [3], Paris classification [4] and Hiroshima classification [5] and NICE classification [6].

Macroscopic recurrence

Recurrence is both macroscopically and microscopically assessed in clinical practice, depending on local protocols and preferences. In this study, we will compare both assessments.

Intraprocedural bleeding

Polyp or resection site bleeding during the EMR is also described to enhance the risk for recurrence [1, 7].

Health-related quality of life

Data on quality of life will be collected at baseline and during follow up.

Medical and non-medical costs.

Study description

Background summary

Colorectal cancer (CRC) is the third most common cancer in men and the second in women worldwide [1]. In Western societies, approximately 40% of all CRC patients die within the first five years of the disease [2]. CRC predominately develops from premalignant polypoid lesions of the colon. Colonoscopy with polypectomy is able to detect and subsequently remove these (pre)malignant lesions and thus reducing the incidence and mortality of CRC [3]. In order to achieve this in an early stage before the polyps become invasive, a national colorectal cancer screening program is implemented in various countries [4]. Whereas endoscopic removal of small polyps is a straightforward routine procedure, the resection of large lateral spreading lesions (LSL) and sessile polyps require advanced techniques. Historically, these difficult lesions were treated with surgery [5]. Nowadays the standard treatment is endoscopically with endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) [6, 7]. Colonic EMR is an effective and save minimally invasive outpatient therapy for large sessile polyps, the greatest drawback is the high adenoma recurrence rate of approximately 20% with even greater rates in piecemeal resections [8, 9].

Although these recurrences are small and often easily treated endoscopically, they require an intensive surveillance program. Interventions studied to decrease EMR recurrences are argon plasma coagulation (APC) [10-13], thermal ablation EMR [10, 14, 15] and extended EMR (X-EMR) [16]. Whilst the APC studies are relatively small in size and findings being conflicting, a prospective multicenter randomized trial in Australia with 390 patients by Klein et al. [14] on thermal ablation, showed promising results. They conducted a study in which patients were randomly assigned to thermal ablation of the entire post-EMR mucosal defect margin or no additional intervention. Thermal ablation was achieved using snare tip soft coagulation (STSC) originally used for control of intraprocedural bleeding during polypectomy [17]. Their study concluded that STSC is a fast, safe and effective method in significantly decreasing the recurrence rate in EMR compared to a conservative approach, respectively: 5.2 % versus 21.0 % ($p<0.001$). These results were corroborated by a retrospective single center case-control study in 2019 (12% vs. 30%,

p=0.01) [15].

The results of the Australian group are promising, but performed only in tertiary care centers. Furthermore, exclusion criteria of the RCT by Klein et al. led to a 9.8% exclusion rate because of endoscopic incomplete resection. Persistent polyp remnants can be removed with cold avulsion techniques or hot biopsy forceps. The high incomplete resection percentage is perhaps due to large polyps or to very conservative management of residual polyp removal techniques. An alternative method to reduce recurrence after EMR, the so called extended EMR method (X-EMR), failed to do so. In this technique, the resection plan of the margins of the polyp were extended by at least 1cm. Interestingly, X-EMR increased intraprocedural bleeding but did not significantly reduce the recurrence rate (10.1% vs 11.7%) of colonic flat polyps [16]. So why is STSC effective and X-EMR is not in reducing polyp recurrence after colonic EMR? Perhaps the STSC technique is not as effective as promised by only 1 RCT? Or did the X-EMR included polyps with center fibrosis? In the current proposal we aim to generalize the intervention by including non-academic hospitals and broaden the field of this intervention by including lesion with central non-lifting parts, which can be removed by newer techniques (cold avulsion or hot biopsy), which are nowadays common practice in our consortium. Lowering the recurrence rate will potentially lead to fewer colonoscopies resulting in less additional costs, less compliance burdens and less exposure to possible procedure-related risks.

Study objective

Does STSC decreases the recurrence rate after EMR in patients with large lateral spreading or sessile polyps?

Study design

This study entails a patient-blinded multicenter prospective randomized controlled trial conducted between October 2020 and October 2022 in 1 academic and 4 non-academic hospitals in The Netherlands and Germany and it will take place in the outpatient clinics of the participating centers.

After EMR, included patients will be randomly assigned in a 1:1 ratio to:

1. Intervention group - Soft tip snare coagulation (STSC) immediately after EMR

OR

2. Control group - No intervention after EMR

Patients will be randomly allocated by web-based randomization.

We anticipate to start our trial in the summer of 2020 with an inclusion period of 1,5 year. The end of the study is defined the date of the last surveillance colonoscopy ate six months after the final inclusion.

Intervention

The technique that will be assessed is called soft tip snare coagulation (STSC). It requires the same equipment used with standard EMR or snare polypectomy: polypectomy snare. In this technique, the snare tip is not complete extended from the sheath but the tip is positioned 1 to 2 mm beyond the end of the snare sheath. The snare tip is applied directly on the tissue compromising the entire border of the resection site creating a 2-3 mm coagulation rim after energy transfer. The energy is delivered by a microprocessor-controlled generator in accordance with standard polypectomy but a reduced voltage. The usage of polyp snare type and microprocessor-controlled generator depends on local expertise and availability.

Since these medical devices are already registered and widely used for coagulation, additional safety studies are not required.
As mentioned before, Bahin et al. described the STSC technique in 2013 for control of intraprocedural bleeding during EMR [1]. In this study, STSC was able to reduce intraprocedural bleeding without adverse advents and without a higher complication risk. Klein et al. and Kandel et al. adopted this technique for thermal ablation in accordance with our study protocol. They also demonstrated STSC to be a safe procedure with no adverse effect and without higher procedural complication risks compared to the standard procedure [2, 3].
To our knowledge, there are no potential risks described. The aim of our study is to compare the ability of STSC to reduce the recurrence rate after EMR. If the recurrence rate is reduced with STSC, surveillance protocols can be more flexible resulting in fewer colonoscopies with extended intervals.

We would like to emphasize that this intervention entails snares originally designed for polypectomies. With STSC, instead of the entire snare, only the tip is used for coagulation of mucosal tissue. This intervention is already common among andvances endoscopists for the treatment of recurrent polyps, visible residues and intraprocedural bleeding.

1. Fahrtash-Bahin, F., et al., Snare tip soft coagulation achieves effective and safe endoscopic hemostasis during wide-field endoscopic resection of large colonic lesions (with videos). Gastrointest Endosc, 2013. 78(1): p. 158-163 e1.
2. Klein, A., et al., Thermal Ablation of Mucosal Defect Margins Reduces Adenoma Recurrence After Colonic Endoscopic Mucosal Resection. Gastroenterology, 2019. 156(3): p. 604-613.e3.
3. Kandel, P., et al., Prophylactic Snare Tip Soft Coagulation and Its Impact

on Adenoma Recurrence After Colonic Endoscopic Mucosal Resection. Dig Dis Sci, 2019. 64(11): p. 3300-3306.

Study burden and risks

N.A.

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

All patients aged >= 18 years with proven colorectal sessile of lateral spreading polyps (Paris classification 0-IIa/b/c, Is) with a diameter of >= 20mm requiring piecemeal resection with EMR are eligible for inclusion.

Exclusion criteria

Previously attempted intervention
Endoscopic appearance of invasive malignancy
Histologically confirmed malignancy
Presence or suspicion of inflammatory bowel disease
En bloc resection
Incomplete resection

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-03-2022
Enrollment:	300
Type:	Actual

Medical products/devices used

Generic name:	Soft tip snare coagulation
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	22-04-2021
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-01-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-04-2023
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	NL74632.091.20