A randomized trial comparing the effectiveness of polyp resection treatments (hot snare vs cold snare vs hot EMR vs cold EMR)

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A randomized trial comparing the efficacy of polyp resection techniques for polyps sized 6-15mm (Hot snare vs. cold snare vs. hot EMR vs. cold EMR)

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Introduction:

The optimal method for removal of polyps 6-9 and 10-15 mm in size is not established. In recent years, the use of cold resection techniques (resection without the use of electrocautery) has been demonstrated to be effective and safer than techniques utilizing electrocautery (hot techniques) for diminutive polyps that are 1-5 mm in size. However, the effectiveness of cold techniques for 6-15 mm polyps has been questioned. Recent studies have shown that cold snare endoscopic mucosal resection (*EMR*) is non-inferior to hot EMR for 6-9 mm polyps [1-3]. Another trial showed that hot EMR was superior to cold snaring [4]. Cold EMR, or EMR in general, are both more time consuming than non-EMR techniques. EMR refers to a submucosal injection that takes place prior to the removal of a polyp with a snare. In this study, we propose to evaluate four different treatments for polyps (sized 6mm-15mm). The four treatments are cold snaring

without injection, hot snaring without injection, cold EMR, and hot EMR. Previous published failure rates for 6-9 mm polyps are shown in the attached table.

RCTs of hot vs cold snaring – efficacy data

Author, date	Polyp sizes	Number of polyps	Cold snaring eradication rate	Hot snaring eradication rate	P value
Aslan, 2013 (abstract)	5-10 mm	118	94.87%	94.37%	NS
Papastergiou, 2017	6-10 mm	164	92.8% * EMR	96.3% * EMR	3.5% difference non-inferior
Kawamura, 2017	4-9 mm	796	98.4%	97.2%	NS
Zhang, 2017	6-9	525 (79% adenomas)	91.5%	98.5%* * EMR	0.01 (for adenomas)

Methods:

A member of the research team will approach a potential subject to discuss participation in the study, including background of the proposed study, inclusion and exclusion criteria, benefits and risks of the procedures and follow-up. If this is of interest to the subject, the informed consent form will be discussed and presented. The subject must sign the consent form prior to enrollment.

All of the colonoscopies will be performed by Dr. Douglas Rex or one of the Sub-Investigators listed above. During the procedure, once a polyp has been identified and its size fits within the range of the target groups (Group 1: 6-9mm or Group 2: 10-15mm), each subject will be randomized to one of the four resection techniques in a 1:1:1:1 ratio using a computer generated randomization sequence. This treatment will be applied to additional polyps found within either of the target groups (correct size ranges) at the discretion of the physician in that patient. The PI has no preference and actively uses all four of the treatments and is expert in all four of the proposed treatments.

Data will be collected by research team members authorized to be on the study. Data that will be assessed from each polyp include its size, a photograph, location of the polyp in the colon, shape (Paris classification), removal time (in seconds) of each polyp resection, prediction of complete resection, prediction of pathology, actual pathology, and efficacy of resection. Efficacy of resection will be assessed by biopsies in four quadrants of the perimeter of the defect and one biopsy from the center of the defect.

Subjects will receive a follow-up phone call 30 ± 7 days after their colonoscopy.

Objectives:

The primary endpoint of the study will be the efficacy of resection. The hypothesis centers on hot EMR as the gold standard, with an estimated effective resection rate of 97% (Table 1). The trial will be powered for non-inferiority, that is, each of the other arms will be non-inferior compared to hot EMR within a > 7% margin[2]. Complications will be recorded, but the study will not be powered for complications.

The study will help to establish the optimal resection technique for 6-9 and 10-15 mm polyps. Although previous studies have compared two of the potential resection methods[1-4], no previous study has evaluated all four of the resection methods.

Criteria:

Inclusion Criteria:

- Aged 40 years or older
- Ability to provide informed consent

Exclusion Criteria:

- Subjects with a history of inflammatory bowel disease
- Lesions less than 6mm or greater than 15mm in largest dimension

Randomization:

Once a polyp has been identified and its size fits within the range of the target groups (Group 1: 6-9mm or Group 2: 10-15mm), each subject will be randomized in a 1:1:1:1 ratio using a computer generated randomization sequence. Randomization outcomes include: cold snaring without injection, hot snaring without injection, cold EMR, and hot EMR. The randomized treatment will be applied to additional polyps found within either of the target groups (correct size ranges) at the discretion of the physician in that patient.

The randomization list will include 324 treatments. These randomized treatments will be printed and placed into sealed envelopes pertaining to the randomization number and will be opened following confirmation that the patient is eligible. Randomization will occur on a per procedure basis. Not all 324 randomization numbers generated will be used in the study. Instead, enrollment will be competitive and each site will continue to enroll until a total of 264 patients have been randomized study-wide.

Statistical Analysis & Sample Size:

A sample size of 66 polyps per treatment (264 total subjects) will have 80% power to detect a non-inferiority margin difference of 7% for the cold EMR, hot snare, and cold snare treatments compared to the hot EMR treatment with an alpha of 0.05.

Data Integrity and Safety

All paper charts pertaining to the patient will be kept under lock and key in

coordinators office away from the endoscopy area. Each VA site will securely transfer their data to the main site electronically in a manner that is approved by their local IRBs (ie REDCap, Azure AMS System, faxed over a secure line to research office). Only de-identified data from external sites will be added to the database (no HIPAA identifiers will be collected from external sites besides procedure dates). Virtual data will be stored on an internal network drive with encryption and password security. Only approved personnel by the IRB will have access to the file storage. This file will also not have any identifiable patient information. A study log with the identifiable information will be kept in a separate folder to enable the investigators to assist in any research audit. No procedural data except the date of examination will be entered into this log. There will be regular back-ups of the data.

The Data Safety Monitoring Board will consist of Dr Michael Gleeson and Dr. Charles Kahi. Dr. Gleeson will chair the DSMB which will meet every six months to review study related data. Additionally, Dr. Rex's research team will provide him up to date information regarding the status of patients and any reportable events. All SAEs and Unanticipated or Unexpected problems will be reported to the DSMB.

Any subject who wishes to withdraw from this investigation on his/her own accord and for whatever reason is entitled to do so without obligation and prejudice to further treatment. In addition, the Investigator may decide for reasons of medical prudence, to withdraw a subject. In either event, the Investigator will clearly document the date and reason(s) for the subject's withdrawal from this investigation in the CRF and should indicate whether or not he considers it was related to the study interventions.

1. Aslan, F., et al. Cold SNARE polypectomy versus standard SNARE polypectomy in endoscopic treatment of small polyps. GIE May 2013; 77(5s): AB561.
2. Papastergiou, V., et al. Cold versus hot endoscopic mucosal resection for nonpedunculated colorectal polyp sized 6-10 mm: a randomized trial. Endoscopy 2017; doi: 10.1055/s-0043-118594.
3. Kawamura, T,. Comparison of the resection rate for cold and hot snare polpectomy from 4-9 mm colorectal polyps: a multicenter randomized controlled trial (CRESCENT study). GUT 2017; 0:1-8; doi: 10.1136/gutjnl-2017-314215.
4. Zhang, Q., et al. Polypectomy for complete endoscopic resection of small colorectal polyps. GIE 2017; doi: 10.1016/j.gie.2017.06.010.