Protocol

Assessing the safety of routine snare tip soft coagulation (STSC) in patients undergoing endoscopic mucosal resection for large polyps during colonoscopy

Protocol Version 2.0

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1. INTRODUCTION

Colorectal cancer (CRC) is a major cause of cancer-related morbidity and mortality. In Australia, CRC was the 3rd most common cancer diagnosed in 2018 and the 2nd most common cause of cancer-related death[1]. Colonoscopy and polypectomy has been shown to reduce CRC mortality by interrupting the natural history of polyp progression from pre-malignant lesions to cancer.

Larger polyps (> 10mm) are associated with a higher risk of malignancy and non-pedunculated polyps are usually resected using endoscopic mucosal resection (EMR). EMR is widely considered to be safe and associated with lower rates of mortality and cost compared to surgery. One of the limitations to EMR is the rate of recurrent or residual adenoma at subsequent surveillance colonoscopies, with rates in literature up to 15-30%.

A prospective study published in 2019 by Klein et al showed a four-fold reduction in rates of adenoma recurrence at first surveillance colonoscopy from 23% to 4.7% when snare tip soft coagulation (STSC) was applied to the margin of the mucosal defect following removal of a large polyp using a hot snare (ie. With electrocautery). No adverse events were related to the addition of STSC in the cohort of patients involved in this study (192 patients total). The benefit of routine STSC following cold snare polypectomy to reduce adenoma recurrence rates is unclear.

Cold EMR (cEMR) is a modification of the standard technique where no electrocautery is used for snare transection of tissue. Whilst cEMR has several safety advantages over conventional (or hot) EMR, such as a significantly reduced rate of post-procedural bleeding, and is the preferred removal modality for the majority of adenomatous polyps in the unit, it remains limited by significant rates of residual. The safety and efficacy of STSC in reducing residual after cEMR is unknown. The current standard of care is that polyps removed with cEMR do not warrant further endoscopic therapy.

2. AIMS

Key Research Question

Is STSC of the cEMR defect margin of large non-pedunculated polyps safe and effective in reducing residual polyp rates? .

Objectives

To assess the rates of adverse events associated with routine STSC of defect margins following cold snare resections of polyps ≥ 15mm in diameter.

Outcomes include:

- Adenoma recurrence rates (determined at first follow up colonoscopy) in patients who undergo STSC compared to a control group who undergo cold snare resection only
- Adverse event rate in patients who undergo STSC compared to the control group, who will receive no further endoscopic therapy after removal of the polyp as per current standard practice

3. HYPOTHESIS

Routine STSC of the defect margin following cold snare polypectomy is safe and does not have a significantly increased risk of adverse events compared to current standard of care.

4. STUDY SETTING

Prospective study performed in an endoscopy unit which serves as a secondary and tertiary referral centre of large colonic polyps by endoscopists experienced an trained in advanced endoscopic resection.

5. STUDY POPULATION

Patients over 18 years of age who present for an elective colonoscopy and subsequently have a non-pedunculated polyp removed which is ≥ 15mm in diameter.

6. ELIGIBILITY CRITERIA

Inclusion criteria

All patients over 18 years of age who present for an elective colonoscopy at the QEII Jubilee Hospital will be invited to participate in this study. Subsequently, patients in which an eligible polyp is found and removed will be included in the data collection.

- An eligible polyp is an adenomatous appearing polyp ≥15mm in size with a flat or sessile morphology (Paris 0-Is or 0-IIa) and NICE 2 surface where cold EMR is performed for removal.

A consent form will be provided (attached). Patients are able to withdraw consent at any time during the study.

Exclusion criteria

Patients with active inflammatory bowel disease

Patients with implanted permanent pacemakers, implanted cardiac defibrillators or spinal cord stimulators

7. STUDY DESIGN

Prospective randomised study. Patients presenting for an elective colonoscopy who have a polyp ≥ 15mm resected will be randomised to one of two treatments following complete resection of the polyp: no further treatment as per current standard of care (ie. The control group), or STSC of the resection margins. Patients will be monitored in endoscopy recovery as per standard post-procedure nursing care.

Clinical observations (such as temperature, blood pressure, heart rate and oxygen saturation) will be monitored and patients will be assessed by nursing staff in recovery for signs of adverse events including pain and bleeding. Clinically significant pain will be defined as pain requiring analgesia.

All patient followed up will follow current clinical care pathways at the facility. Post procedure 30 day questionnaire will be employed to assess for adverse events. Surveillance colonoscopy will be completed at 6 months (as per current NHMRC guidelines) to assess the piecemeal polypectomy site for residual or recurrent adenoma. The scar will also be biopsied for histological analysis.

8. PATIENT RECRUITMENT

Patients who meet the inclusion criteria will be invited to participate in the study at the time of the colonoscopy preparation visit. This will be obtained by a research team member. Patient information and consent forms will be given to the patient. Consent will be completed on the day of the procedure. Those who have eligible polyps resected with be randomised to either “no further treatment” or “STSC” once the polyp has been adequately resected. Randomisation will occur during the procedure as not all patients who are consented will have eligible polyps identified during their colonoscopy. Patients in whom an eligible polyp is not identified will not have their clinical information collected as they will not be assigned to either treatment arms.

9. STATISTICAL ANALYSIS

Clinical information collected will include patient demographics, procedure details (duration), polyp characteristics (polyp size, location, histology), rates and types of adverse

events, and the rates of residual adenoma on subsequent colonoscopies. This information will be collected from patient medical records available on ieMR during the course of the study up from the time of the index colonoscopy up until their next colonoscopy, which is planned to occur 6 months after their initial procedure.

Analyses will be performed comparing the control group to the STSC group to assess whether there were statistically significant differences with regards to different adverse events and adenoma recurrence rates. Subgroup analyses may also be performed to determine whether specific groups of patients were at increased risk of adverse events.

Based on a presumed adenoma recurrence rate of 15% in the control group and a predicted reduction rate to 5% in the STSC group, the sample size required to detect a difference in adenoma recurrence with 80% power and an alpha of 0.05 is 144 patients per group (288 patients total).

10. OUTCOME

This study will provide further information regarding whether STSC is safe to perform routinely following resection of large polyps. This is clinically relevant given it has been shown to reduce adenoma recurrence rates and may therefore impact on surveillance intervals for patients long term, resulting in a reduced healthcare burden.

Safety considerations / Patient safety

There are no expected additional risks to patient safety (outside of the standard risks of colonoscopy that they are usually consented for) in the proposed study however they will be monitored closely for adverse events post-procedurally as per department guidelines.

Source documents

Researchers will maintain adequate and accurate records to enable the conduct of the study to be fully documented and the study data to be subsequently verified.

Ethical consideration

This protocol will be reviewed and approved by a relevant HREC committee.

Ethical conduct

This study will be conducted in accordance with the protocol, ICH guidelines and guidelines governing clinical study conduct and ethical principles that have their origin in the Declaration of Helsinki.

Risk

There are no expected risks from this study.

Confidentiality and Use of information

Source notes containing medical information are identifiable. These will be stored in a locked office area in the QEII Jubilee Hospital. A unique patient number will be assigned to each patient at the time of randomisation to a treatment arm and will serve as the patient's identifier for the study. Patient data will be stored and collected under this number. Identifying information will not be shared with any other institutions. Data protection and privacy regulations will be observed in capturing, forwarding, processing and storing of patient data. Investigators and research staff will assure that patient anonymity is strictly maintained and that patient identifiers are protected from unauthorised parties. Information entered into the results database will be de-identified. Patient names will be replaced with an identification number. This database will contain the patients' age at the time of procedure and demographic information. It will be saved in the QEII computer system and password protected. Research documents which include identifiable patient information will be held for a maximum of 5 years and will be disposed in a secure fashion at the relevant time.

Completion of study

The researcher will provide a final report to the HREC following conclusion of the study

11. References

1. Bowel cancer (Colorectal cancer) in Australia statistics | Cancer Australia [Internet]. Canceraustralia.gov.au. 2021 [cited 8 April 2021]. Available from: https://www.canceraustralia.gov.au/affected-cancer/cancer-types/bowel-cancer/bowel-cancer-colorectal-cancer-australia-statistics

2. Klein A, Tate D, Jayasekeran V, Hourigan L, Singh R, Brown G et al. Thermal Ablation of Mucosal Defect Margins Reduces Adenoma Recurrence After Colonic Endoscopic Mucosal Resection. Gastroenterology. 2019;156(3):604-613.e3.