Delayed Surveillance Colonoscopy following Piecemeal EMR – a Randomized Study

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Abstract

Background

Colorectal cancer (CRC) is a major cause of cancer-related morbidity and mortality. Piecemeal endoscopic mucosal resection (pEMR) is an effective treatment for large non-pedunculated colorectal polyps (LNPCPs), which are high-risk precursors of CRC. Previous data have shown that residual and recurrent adenoma (RRA) may occur in 15–30% of cases following pEMR. Accordingly, current guidelines recommend intensive follow-up, which can cause patient morbidity and lack of compliance and financial healthcare burdens. Recent advances in EMR techniques, particularly margin ablation, have significantly reduced RRA rates to approximately 5%. In a recent retrospective analysis, we found that delayed surveillance (12 months post-EMR) was not associated with higher recurrence rates compared to early surveillance (3–6 months). This prospective randomized trial aims to confirm and validate these findings.

Objectives and Hypotheses

To evaluate whether a relaxed surveillance strategy involving fewer colonoscopies (12 and 48 months) is non-inferior to the standard intensive strategy (6, 18, and 48 months) in management of residual or recurrent disease.

Hypothesis: A relaxed surveillance protocol does not increase the rate of residual or recurrent adenoma detected at long-term follow-up, in patients undergoing pEMR of LNPCPCs with margin ablation.

Methods

This multicenter prospective randomized controlled trial will enroll approximately 760 patients undergoing pEMR for LNPCPs at Rambam Health Care Campus, Tel Aviv Sourasky Medical Center (Ichilov Hospital), Nazareth Holy Family Hospital and HaEmek Medical Center (Afula). Detailed clinical, endoscopic, and histologic data will be collected on lesion morphology, size, histopathology, and procedural techniques.

Patients will be randomized into two surveillance groups: **the Standard Surveillance Group**: Colonoscopies at 6, 18, and 48 months after the index procedure and **the Relaxed Surveillance Group**: Colonoscopies at 12 and 48 months after the index procedure (similar to surveillance protocols following en-bloc excision by ESD)

Significance and Relevance to Cancer Care

This study directly addresses a major clinical question in post-polypectomy surveillance: whether all patients require early intensive follow-up after piecemeal EMR. If the relaxed surveillance approach proves non-inferior, it may support a revision of current guidelines. This would result in fewer colonoscopies, reduced burden on patients and health systems, improved adherence, and lower costs—without compromising oncologic safety. The findings of this trial may contribute to the development of more efficient and personalized follow-up strategies in colorectal cancer prevention, with the potential to influence future clinical practice guidelines and national health policy.

Background and Aim

Colorectal cancer (CRC) is among the most common cancers globally, with significant morbidity and mortality [1]. Numerous studies have demonstrated that removing colorectal polyps reduces the incidence and mortality of CRC [2]. Large non-pedunculated colorectal polyps (LNPCPs) are considered high-risk precursors of colorectal cancer. Piecemeal endoscopic mucosal resection (pEMR) is the recommended treatment for most non-invasive LNPCPs according to societal guidelines, due to its excellent safety and efficacy profile [3,4,5,6].

One major drawback of colonic pEMR is the potential for residual and recurrent adenoma (RRA). Studies have shown that RRA occurs in 15-30% of cases, with risk factors including high-grade dysplasia, lesion size, lesion location, intra-procedural bleeding, and previous attempts at removal [7,8,9]. Recurrence at the first surveillance colonoscopy (SC1) can be identified endoscopically with high accuracy [10], and endoscopic treatment during SC1, which includes re-excision of the RRA with or without ablation, results in a very low residual RRA rate (2%-4%) at the second surveillance colonoscopy (SC2) [7].

Recent data suggests that RRA can be significantly reduced by systematically applying ablative measures to the post-EMR resection margin. Multiple studies show that in expert hands, the risk of RRA at SC1 can be reduced to 3-5% [6,7,8,12,13]. Currently, an intensive follow-up schedule is recommended following pEMR, with SC1 performed 3-6 months after the initial procedure and SC2 one year after SC1. However, this intensive follow-up places additional burdens on both patients and the healthcare system and may hinder patient compliance [9]. Given that with the advent of margin ablation, RRA rates at SC1 are extremely low, the impact of early surveillance on long-term recurrence rates may be minimal.

We recently completed a retrospective study to evaluate this hypothesis. The study showed no significant difference in recurrence rates between the standard group, which underwent surveillance after 3-6 months, and a group of patients who had delayed surveillance (mean follow-up of 11 months).

The aim of this study is to confirm and validate these findings, in a prospective randomized study. This will solidify the results we observed in our previous retrospective study and potentially lead to a less intensive surveillance strategy.

Methods

Study Design:

We will conduct a multicenter, prospective, non-inferiority randomized study in four academic centers in Israel: Rambam Health Care Campus, Tel Aviv Sourasky Medical Center (Ichilov Hospital), Nazareth Holy Family Hospital and HaEmek Medical Center. Following complete pEMR of a LNPCP, participants will be randomly assigned to either the standard surveillance protocol or the relaxed surveillance protocol. Patients will be consented prior to the EMR procedure.

Randomization – computer-generated dynamic block randomization with a 1:1 allocation ratio will be performed to achieve balance of multiple baseline covariates including: demographic data, procedural data, and lesion characteristics.

Patients:

We will include adult patients who undergo pEMR for LNPCPs (≥20 mm) and provide informed consent. Inclusion criteria include

- Adults aged 18 years and older.
- Undergoing pEMR of LNPCPs.
- Able to provide informed consent and comply with follow-up requirements.

Exclusion criteria include:

- Patients with invasive cancer identified during the index procedure.
- en bloc resection.
- Patients unable to attend follow-up colonoscopies due to comorbid conditions.

- Patients who require additional surgery for polyp removal or other complications.

Informed Consent:

Before enrollment, each patient will receive a detailed explanation about the study. They will be given the opportunity to ask questions and discuss any concerns. Written informed consent will be obtained from all participants prior to any study-related procedures.

Procedures:

All pEMR procedures and surveillance colonoscopies will be performed by experienced endoscopists trained in pEMR techniques. Specifically, A.K. was lead author on the randomized trial on margin ablation [13] and practiced this technique routinely since early 2016. Procedures will be conducted using high-definition endoscopes (Olympus 190 series Q190 PCF/CF or Fuji 760 series), following a standardized protocol:

1. Inspection and photo documentation of LNPCPs with high-definition white light (HDWL) and optical chromoendoscopy before resection to exclude features suggestive of deep submucosal invasion.
2. Standard pEMR technique with the objective of complete snare excision, using sub-mucosal injections of Succinilated Gelatine (Gelofusin) or Normal Saline and braided snares of various sizes.
3. Thermal ablation of the mucosal defect margin using snare soft tip coagulation (STSC) to create a 2- to 3-mm rim of ablated tissue.

Groups and Follow-Up:

- Standard Surveillance Group: Patients will undergo surveillance colonoscopy at 6 and 18 months after the index procedure. The standard surveillance group will have an additional colonoscopy at 48 months in order to converge the timeline with the delayed group.
- Relaxed Surveillance Group: Patients will undergo surveillance colonoscopy at 12 and 48 months after the index procedure.

Data Collection:

We will collect demographic data, lesion characteristics, procedural details, and surveillance outcomes. All recurrences will be identified using endoscopic evaluation. Routine biopsies will be taken only when recurrence is suspected endoscopically, based on a validated approach that has shown a negative predictive value (NPV) of 99% for identifying normal scars without recurrence [14].

Data Management, Storage and Security:

All data will be collected on data collection forms. These will be stored in a locked cabinet at the Gastroenterology department. This data will be entered into electronic data sheets (Excel and Redcap). The electronic files will be password protected and stored on a password-protected computer in the Gastroenterology department. Access to the data will be given to the study investigators and the study research assistant.

Primary Endpoint

The primary endpoint is the rate of residual or recurrent adenoma at the second surveillance colonoscopy (SC2), comparing the relaxed and standard surveillance groups.

Secondary Endpoints

Secondary endpoints include: recurrence rates at SC1; risk factors associated with recurrence; subgroup analysis of high risk lesions (e.g., high-grade dysplasia, sessile serrated morphology); rates of new or missed polyps at SC2; adverse events related to EMR or surveillance procedures; and comparative cost effectiveness of both surveillance strategies.

Timetable

We anticipate 4-5 years are required to complete the study: 1-2 years for recruitment and an additional 36 months for follow-up to SC2.

Funding and Competing Interests

There are no disclosures. No commercial funding is sought. We will apply for research grants to help with study funding, specifically research assistant salary and management of the electronic database.

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