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Cold EMR for Large Colon Polyps

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ENDOSCOPY

This summary reviews Pohl H, Rex DK, Barber J, *et al.* Cold snare endoscopic resection for large colon polyps: A randomised trial. *Gut* Published Online First: 19 May 2025. doi: 10.1136/gutjnl-2025-335075.

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STRUCTURED ABSTRACT

Question: Is cold snare endoscopic mucosal resection (EMR) safer and more effective than hot EMR for removing large (≥ 20 mm) non-pedunculated colorectal polyps ?

Design: Multicenter, randomized controlled 2×2 factorial trial comparing cold vs hot EMR.

Setting: Fifteen centers across the US and Canada.

Patients: Adults aged 18 years or older who presented for resection of large (≥20 mm) non-pedunculated colon polyp. 660 patients undergoing EMR for large non-pedunculated colorectal polyps. Patients were excluded if they had inflammatory bowel disease, severe comorbidities (American Society of Anesthesiologists score >3), or a coagulopathy (international normalized ratio (INR)

>1.5 or platelets <50). Pedunculated polyps (Paris classification IP), ulcerated polyps (Paris classification III) or those with suspected deep submucosal invasive cancer based on morphological assessment were also excluded.

Exposure/Intervention: Patients were randomized to either cold snare EMR (without the use of electrocautery) or hot snare EMR (with the use of electrocautery), and to 1 of 2 submucosal injection solutions, either viscous solution or normal saline. Cold EMR permitted crossover if complete resection wasn't feasible. Hot EMR required margin ablation and defect closure in the proximal colon. Type of resection (cold vs hot EMR) was the primary intervention and type of submucosal injectate was the secondary and exploratory intervention. Participants were assigned to one of four study groups (hot EMR + viscous solution, hot EMR + saline, cold EMR + viscous solution, cold EMR + saline).

Outcomes: The primary outcomes was rate of severe adverse events (SAEs), and the secondary outcome was recurrence at first surveillance colonoscopy (SC1). Recurrence was defined as a resection site that harbored any visible or biopsy-proven neoplastic polyp tissue at SC1 following prior complete polyp resection. SAEs were also assessed by polyp location (proximal vs distal) and by use of antithrombotic medications. Other factors assessed included whether recurrence was affected by polyp size (20–29 mm vs >30 mm), polyp histology (serrated vs adenomatous), polyp morphology (flat or Paris 2a vs sessile or any Paris 1s), and polyp height.

Data Analysis: Intention-to-treat (ITT), per-protocol, and complier average causal effect (CACE) analyses were conducted. Multivariable models were also adjusted for baseline differences and clustering.

Funding: Steris and Cosmo Pharmaceuticals supported the study but had no role in design, data collection, or analysis.

Results: Overall, 660 patients were randomized and analyzed, including 336 patients with 371 polyps in the cold EMR group and 324 patients with 343 polyps in the hot EMR group. ITT analysis showed SAEs in 2.1% of patients in the cold EMR group vs. 4.3% in the hot EMR ($P = 0.10$) group. No perforations occurred in the cold EMR group compared with 1.6% in the hot EMR group ($P = 0.028$). Recurrence was significantly higher in the cold EMR group (28% vs 14%, $P<0.001$). Recurrence was not significantly different for 20–29 mm polyps (18.6%

vs 13.4%, $P = 0.24$) and for sessile serrated lesions (14.1% vs 8.5%, $P = 0.33$). In the cold EMR group, 14.6% of polyps were removed by hot EMR, and in the hot EMR group, 14.0% were removed by cold EMR (**Table 1**). There was no significant difference in SAEs by type of submucosal injection agent.

Outcome	Cold EMR	Hot EMR	*P*-value
Intention-to-Treat Analysis			
Severe Adverse Events	2.1%	4.3%	0.10
Perforations	0%	1.6%	0.028
Recurrence (all polyps)	28%	14%	<0.001
Recurrence (20–29 mm polyps)	18.6%	13.4%	0.24
Recurrence (sessile serrated lesions)	14.1%	8.5%	0.33
Per-Protocol Analysis			
Severe Adverse Events	1.4%	5.0%	0.017

Table 1. Cold EMR vs hot EMR outcomes.

COMMENTARY

Why Is This Important?

Endoscopic resection is central to colorectal cancer prevention. Larger colon polyps have higher risk of harboring advanced dysplasia. Cold EMR is hypothesized to reduce adverse events, especially bleeding and perforation, but limited high-quality comparative data exist for large polyps ≥ 20 mm.

Key Study Findings

This randomized trial comparing cold and hot EMR for resection of large (≥20 mm) colorectal polyps showed that the overall rate of severe adverse events was not significantly different between the 2 groups (2.1% vs. 4.3%). However, cold EMR was associated with a 2-fold higher recurrence rate (28% vs. 14%). Recurrence was not significantly different for 20–29 mm polyps (18.6% vs 13.4%, $P = 0.24$) and for sessile serrated lesions (14.1% vs 8.5%, $P = 0.33$). These findings suggest that cold EMR should not be universally applied to all ≥ 20 mm polyps but may be suitable for sessile serrated lesions, adenomatous lesions measuring 20-29 mm and carefully selected lesions, particularly in scenarios where minimizing procedural risk is a clinical priority.

Caution

The trial had by a high crossover rate of 14% in both directions, which may have

influenced the ITT analysis. Despite efforts to achieve wide resection margins, cold EMR was associated with high recurrence rates across all study sites. Furthermore, the wide variability in recurrence rates among participating centers raises concerns about inconsistencies in technique and highlights the need for standardized training and procedural protocols for cold EMR.

My Practice

My practice for managing large (≥ 20 mm) non-pedunculated colorectal polyps is individualized to the lesion. This includes evaluating the polyp morphology and histology.[1] The Paris classification is typically used to evaluate the polyp morphology. The Paris classification characterizes lesions in the gastrointestinal tract into three main categories based on their morphologic features, while for evaluating polyp histology, the Narrow Band Imaging Colorectal Endoscopic (NICE) classification is used. The NICE classification can be used to predict polyp histology based on surface features into sessile serrated lesions (SSLs) or hyperplastic polyps, adenomatous polyps or polyps concerning for deep submucosal invasion. For polyps with optical diagnosis suggestive of SSL histology, I prefer cold EMR given its favorable safety profile and similar recurrence rate for SSLs in comparison to hot EMR.[2-5] For large polyps, where optical diagnosis is suggestive of adenomatous histology, I prefer hot EMR or underwater EMR.[6] This approach is based on lower rate of recurrence for adenomatous polyps with hot EMR as seen in this trial and other recent randomized trials.[3-5]

In cases, where there are features suggestive of advanced histology such as high grade dysplasia or submucosal invasive cancer (non-granular laterally spreading tumors with ulceration, depression or nodular component, NICE type 3 lesions, Kudo pit pattern V_N, JNET2b or Paris classification 0-IIc), I prefer en-bloc resection with hot EMR if possible or use endoscopic submucosal dissection (ESD) or endoscopic full-thickness resection (EFTR). Lastly, I also use cold snare EMR in patients who are at high risk of adverse events such as those on systemic anti-coagulation, advanced liver or kidney disease and those in which perforation maybe challenging to manage (difficult or unstable position in the colon).

For Future Research

Future research is needed to compare different EMR modalities for various types of polyps based on size and histology. In addition, the role of margin and base ablation with cold EMR needs to be studied. Lastly, standardization of cold EMR technique is need to minimize recurrence associated with cold EMR.

Conflict of Interest

Dr. Bilal is a consultant for Boston Scientific, Steris Endoscopy, Aspero Medical and Cook Medical.

Abbreviations

EMR, endoscopic mucosal resection; INR, international normalized ratio; ITT, intention-to-treat; SAE, severe adverse events; SSL, sessile serrated lesions.

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