Geometry of cold snare polypectomy and risk of incomplete resection

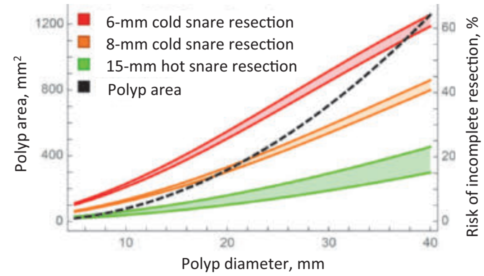
GRAPHICAL ABSTRACT

Geometry of cold snare polypectomy and risk of incomplete resection

Mathematical modeling study

$$RIR = 1 - (1 - RER)^n$$

RIR, risk of incomplete resection; RER, resection error risk; n, number of snare resections.



Polyp area increases quadratically with increasing polyp radius.

Resection error risk (RER) is assumed constant for given snare type and size.

Risk of incomplete resection (RIR) increases with the number of snare resections.

Endoscopy

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ABSTRACT

Background Cold snare polypectomy (CSP) is safer than and equally efficacious as hot snare polypectomy (HSP) for the removal of small (<10 mm) colorectal polyps. The maximum polyp size that can be effectively managed by piecemeal CSP (p-CSP) without an excessive burden of recurrence is unknown.

Methods Resection error risks (RERs), defined as the estimated likelihood of incomplete removal of adenomatous tissue for a single snare resection pass, for CSP and HSP were calculated, based on an incomplete resection rate. Polyp area, snare size, estimated number of resections, and optimal resection defect area were modeled. Overall

risk of incomplete resection (RIR) was defined as RIR = 1 – $(1-p)^n$, where p is the RER and n the number of resections.
Results A 40-mm polyp has a four times greater area than a 20-mm polyp (314.16mm^2 vs. 1256.64mm^2), and requires three times more resections (11 vs. 33, respectively, assuming 8-mm piecemeal resection pieces for p-CSP). RIRs for a 40-mm polyp by HSP and p-CSP were 15.1%–23% and 40.74%–60.60% respectively.

Conclusion RER is more important with p-CSP than with HSP. The number of resections, n, and consequently RIR increases with increasing polyp size. Given the overwhelming safety of CSP, specific techniques to minimize the RER should be studied and developed.

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide [1]. The majority of tumors arise from colorectal polyps and colonoscopy exerts its beneficial effect by polypectomy [2]. Ideally polypectomy should be safe, efficient, cost-effective and curative. Recurrence occurs due to incomplete resection which compromises clinical outcomes and increases cost.

The overwhelming majority of colonic polyps are less than 10 mm and are safely and effectively managed with en bloc or oligo-piecemeal cold snare polypectomy. The absence of electrocautery all but eliminates the risks of perforation and post-polypectomy bleeding [3]. This safety and simplicity holds appeal for resection of larger lesions. While these have traditionally been removed by hot snare endoscopic mucosal resection (EMR), the use of diathermy carries with it a small but significant risk of perforation and delayed bleeding [4, 5].

The upper limit of lesion size where piecemeal cold snare polypectomy (p-CSP) remains clinically effective, without excessive and burdensome recurrence rates, is currently unknown. We undertook a modelling study to address this important question.

Methods

Incomplete resection rates for hot snare polypectomy (HSP) and CSP were determined after a review of relevant literature. A formal systematic review with a comprehensive electronic search strategy was not employed. Rather, targeted literature searches were conducted for publications available up to 1st June 2022. The PubMed database was searched using the following terms: "cold snare" AND polypectomy AND incomplete (n = 36); "cold snare" AND polypectomy AND residual (n = 37)."

There were no restrictions on the type of publication and no restriction on study size. Language was limited to English. Data extracted included: author, journal, year of publication, polyp size, injectate used, study size, and rate of incomplete resection (**Table 1s**, available online-only in Supplementary material).

There is a paucity of data for incomplete resection rates, particularly for piecemeal p-CSP. The data does include a recent large multicenter trial (n = 1393) which reported an incomplete resection rate of 1.5% for polyps ≤10 mm [6]. However, there is little data reporting the incomplete resection rate using p-CSP for polyps >20 mm. Given the scarcity of relevant studies, a reasonable surrogate measure was taken from the CARE study [7]; this reported an incomplete resection rate of 17.3% for polyps 10–20 mm (n = 110). This may underestimate the actual incomplete resection rate for p-CSP given that this study used HSP [7].

Snare size and shape

A 10-mm snare was assumed for CSP modelling. Resection pieces vary between 6 and 8 mm in diameter [8]. A 15-mm snare was assumed for HSP, with a resection diameter of 15 mm. The snare shape has been assumed to be circular, as a surrogate for the true slightly elliptical shape of a snare.

Resection error risk

Resection error risk (RER) is defined as the likelihood of incomplete removal of adenomatous tissue per snare resection. This constant risk applies to each individual snare resection during piecemeal EMR and thus the overall risk accumulates with each sequential resection. Based on a 20-mm polyp area with a 3-mm margin of normal tissue (530.93^{mm2}), the number of p-CSP resections assuming 8-mm resection pieces (area 50.26^{mm2}) is 10.56. This is supported by the "disc covering problem" which estimates the smallest number of smaller discs required to cover a larger disc [9]. Clinically, this equates to 10 or 11 sequential snare resections. Dividing 17.3%, the incomplete resection rate from the literature, by the number of sequential snares (10 or 11) the p-CSP RER is estimated at 1.57%–1.73%.

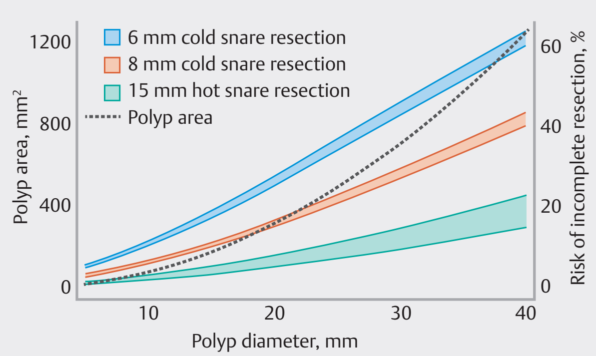
HSP has evolved with advances such as thermal ablation of the defect margin which have greatly reduced recurrence rates [10, 11]. The incomplete resection rate with HSP is also likely to be lower due to the tissue destruction from the thermal penumbra of the hot snare. However, conservatively, based on the study by Pohl et al., it is reasonable to assume an incomplete resection rate of 17.3% for 20-mm polyps [7]. A 20-mm polyp resected with a 15-mm hot snare, with 15-mm resection pieces would require 10 resections. RER for HSP is estimated at 1.73%.

Incomplete resection risk equation

The overall risk of incomplete resection (RIR) = $1 - (1 - \text{RER})^n$, where n is the total number of resections required. This dynamic equation estimates the cumulative risk of missed adenoma with each piecemeal snare resection.

Data analyses

Polyp area, snare area, and defect area were estimated using area = πr^2, where *r* was the radius. A 3-mm edge of normal tissue was added to the resection size, irrespective of polyp size.



▶ **Fig. 1** Risk of incomplete resection (RIR). A mathematical model demonstrating the RIR with cold snare polypectomy and hot snare polypectomy for increasing polyp size.

RER has been assumed as constant with each resection. Data were computed and graphically illustrated using Mathematica 12.3.1 (Wolfram Research) by a mathematician with expertise in mathematical modeling.

Results

Polyp area

Polyp area increases quadratically with increasing polyp radius (▶ **Fig. 1**). For example, the areas of a 5-mm, 10-mm, and 20-mm polyp are 19.6mm^2, 78.5mm^2, and 314.2mm^2, respectively (▶ **Table 1, Fig. 2**, ▶ **Fig. 3**). This difference is further emphasized when comparing a 30-mm and 40-mm polyp which have areas of 706.9mm^2 and 1256.6mm^2 respectively. With the addition of a 3-mm margin of normal tissue, the area difference between a 10-mm and 20-mm polyp is 329.9mm^2 (2.6 times larger).

Resection number

Resection number is influenced by polyp area and sequential resection area (▶ **Table 1**). A 20-mm polyp (with a 3-mm margin of normal tissue) removed by p-CSP, would requires 18.8 or 10.6 resections, using piecemeal resection sizes of 6-mm or 8-mm diameter, respectively.

Risk of incomplete resection (RIR)

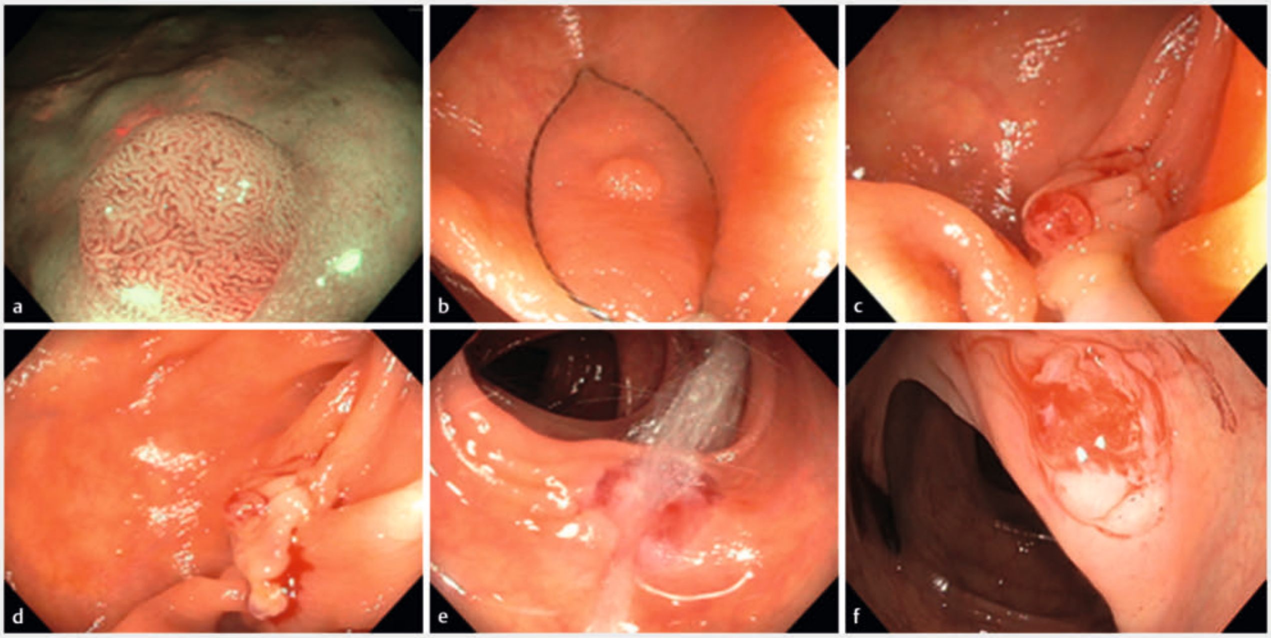
RIR is directly proportional to the number of resections, influenced by polyp size and snare area. The predicted RIRs for a 20-mm versus 40-mm polyp removed by p-CSP with a 6-mm resection piece size are 25.7% and 60.6% respectively. The predicted risks of incomplete resection for a 20-mm versus 40-mm polyp removed by p-CSP with an 8-mm resection piece size are 15.4% and 40.7%, respectively (▶ **Table 1, Fig. 1**).

Discussion

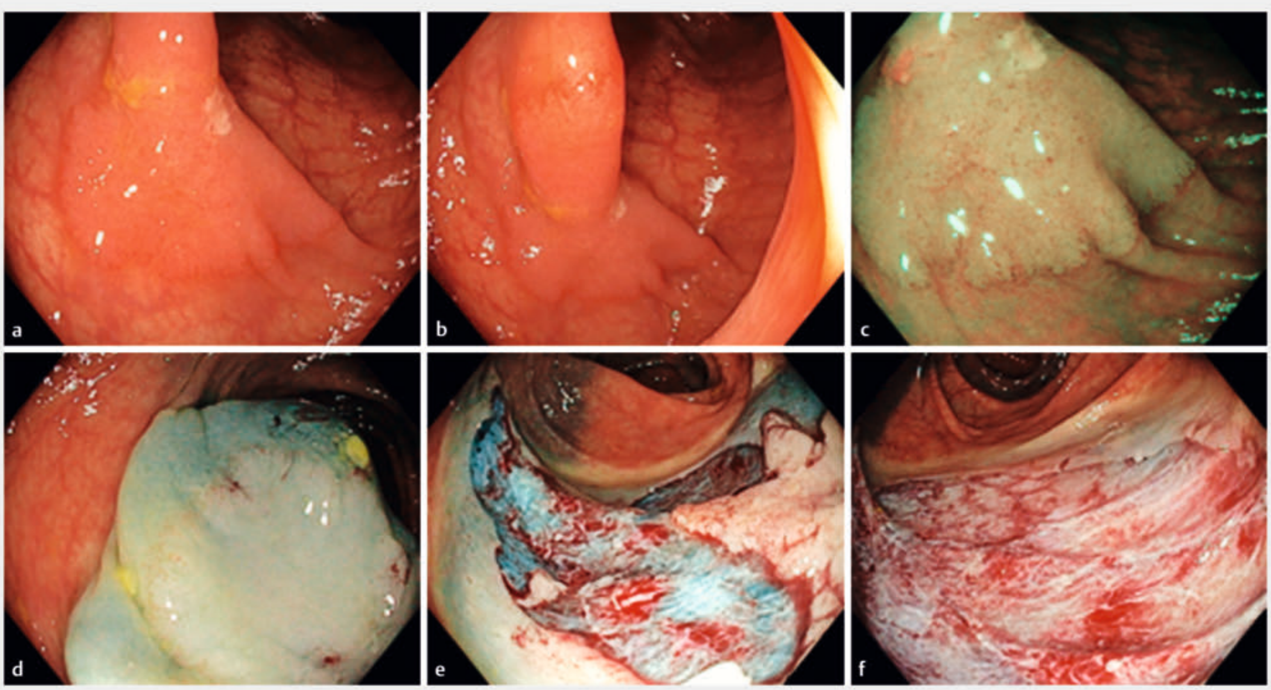
It has been shown that p-CSP is safer than HSP. However, anecdotally for adenomas recurrence seems to be excessive. We undertook a mathematical modeling study to better understand the size at which recurrence from p-CSP might become particularly burdensome. Data are scarce for the rates of incomplete resection for piecemeal CSP and HSP. After extensive review of the literature, we used contemporary data from the highest quality publications to inform our model. The RIR using p-CSP for polyps >20 mm in size and 6-mm resection pieces was 25.7%. The corresponding value with 8-mm resection pieces

▶ **Table 1** Mathematical modelling of risk of incomplete resection (RIR) for hot and cold and hot snare polypectomy. Polyp area, based on polyp and defect area, resection error risk (RER), and number and size of resections.

	Polyp diameter,mm							
	5	**10**	**15**	**20**	**25**	**30**	**35**	**40**
Polyp area,mm^2	19.63	78.54	176.71	314.16	490.87	706.86	962.11	1256.64
Defect area,mm^2	95.03	201.06	346.36	530.93	754.77	1017.88	1320.25	1661.90
6-mm resections								
Number of resections	3.36	7.11	12.25	18.78	26.70	36.00	46.70	58.79
Risk of incomplete resection (RER 1.57%)	5.20%	10.60%	17.60%	25.70%	34.50%	43.40%	52.20%	60.60%
8-mm resections								
Number of resections	1.89	4.00	6.89	10.56	15.01	20.25	26.26	33.06
Risk of incomplete resection (RER 1.73%)	2.95%	6.13%	10.33%	15.39%	21.14%	27.42%	34.00%	40.74%
Hot snare resections (15-mm)								
Number of resections	0.54	1.14	1.96	3.00	4.27	5.76	7.47	9.40
Risk of incomplete resection (RER 1.73%)	0.94%	1.97%	3.36%	5.10%	7.18%	9.56%	12.22%	15.13%



▶ **Fig. 2** Cold snare polypectomy for Paris 0-IIa polyp <10 mm. **a** 3-mm Paris 0-IIa colorectal adenoma. **b** En bloc R0 excision with thin-wire cold snare. Note wide margin of normal mucosa with snare placement. **c** The halo effect with blanching of the surrounding mucosa and hyperemia of the adenoma. **d** Post-excision halo effect. **e** Water expansion of the defect. **f** Careful inspection of margin.



▶ **Fig. 3** Piecemeal cold snare polypectomy for Paris 0-IIa lesion >20 mm. **a–c** Laterally spreading lesion, >20 mm, examined with high definition white-light and narrow-band imaging. **d** Lesion after submucosal injection. **e** Piecemeal cold snare excision. **f** Careful inspection of the post-resection defect margin.

was 15.4% and comparable to the pre-thermal ablation recurrence rates prior to thermal ablation of the margin. However, as size increased RIR for p-CSP became excessive at >40% for lesions ≥40 mm.

The risk profile of CSP is clearly advantageous. Delayed bleeding and perforation are extremely rare events. The mitigation of bleeding risk is also very appealing in an era where anticoagulant and antiplatelet agents are common. The safety profile of CSP has been demonstrated in a large retrospective study (n = 562) that compared conventional EMR to p-CSP for resection of large ≥20-mm sessile serrated lesions [12]. There were no adverse events reported in the p-CSP group compared to delayed bleeding and significant deep mural injury (Sydney classification type 3–5) [4] in the EMR group of 5.1% (n = 18) and 3.4% (n = 12) respectively. In both groups technical success was 100% and recurrence at 18 months was similarly low at <2% [12].

Paradoxically, despite the excellent safety profile of p-CSP, there is a hesitancy to resect wide margins of normal tissue and this potentially leads to higher recurrence rates. Without meticulous attention to ensure overlapping of sequential snares, there is a risk of incomplete resection with each snare resection. Each pass with the snare wire carries a small but cumulative error risk. The risk becomes unacceptably high when removing ever-larger lesions. In this study, the RIR for a 40-mm polyp was >40% with an 8-mm resection piece size and >60% with a 6-mm resection size.

Using modeling we have demonstrated that as lesion size increases, the risk of incomplete resection disproportionately increases and becomes potentially unacceptably high at >40% for lesions 40 mm. This indicates that current techniques or devices are inadequate to manage larger lesions in this way.

There is a lack of literature that assesses the natural history of incompletely resected adenomas. Approximately one-third of post-colonoscopy CRCs are found within the same colorectal segment where the adenoma was resected suggesting that these could be a result of incomplete resection [13]. Pohl et al.'s 2021 study (n = 233) demonstrated a greater risk for neoplastic polyps in colon segments after incomplete polyp resection compared to segments with a prior complete resection (odds ratio 3.0, 95%CI 1.12–8.17) [14]. There is also no guarantee that these patients will comply with a surveillance program or that the polypectomy site will be found during surveillance procedures. Moreover the financial burden of surveillance is significant.

In contrast to HSP, p-CSP relies purely on a wide resection margin and sequential snare resection overlap to prevent recurrence. Key factors in reducing recurrence rates include resecting a 2–3-mm margin of normal tissue and meticulous post-resection examination of the p-CSP defect [12, 15]. Although thin-wire snares (0.30 mm) have been developed for CSP, in an international multicenter randomized controlled trial (n = 1393) the rate of incomplete polyp resection was similar to that with use of a thick-wire snare (0.47 mm). There was only a single case of post-endoscopy bleeding; this was seen in the thin-wire snare group [6]. Although high quality technique is critical for optimizing outcomes, further reductions in RER are likely to be driven by advances in device design. Intraprocedural bleeding has also been identified as an independent risk factor for recurrence [16, 17]. In comparison to HSP, intraprocedural bleeding is more frequent when using CSP. Therefore we suggest the use of dilute adrenaline 1:100 000 added to the injectate to minimize bleeding when performing p-CSP for lesions >20 mm.

Preventing recurrence is important for several reasons. Due to the fibrosis typically encountered around a recurrent polyp, resection is more challenging [18]. This increases the risk of complications and resultant morbidity. Additional healthcare-related costs are attributed to an often prolonged procedure time to treat the recurrence, an increased risk of admission post-procedure and the need for additional procedures for ongoing surveillance. All of this assumes that the patient is adherent to the management plan and is not lost to follow-up. Hence, techniques to reduce recurrence risk are essential.

The results of this study have several important clinical implications. Piecemeal-CSP almost completely eliminates the risk of post-procedural bleeding and perforation; however recurrence is greatly increased in comparison to conventional EMR. Lesion location, morphology, and predicted histology, and patient frailty and comorbidities need to be factored into the process of selecting the appropriate resection technique; this ideally would minimize complications, achieve successful lesion excision, and avoid burdensome surveillance. For example, in the right colon, large nonpedunculated colonic polyps ≥20 mm have a 10%–12% risk of post-procedural bleeding in the absence of defect closure, but many of these lesions are very large and defy current closure techniques. However the risk of recurrence is also related to lesion size. These are some of the factors that need to be borne in mind. These considerations usher in a new approach to colonic tissue resection which may become more individualized and bespoke.

This study has several limitations. Firstly, a targeted review of the literature rather than a systematic review was employed to estimate RER for our equation. We acknowledge this method could have biased our model. However, our modelled RIRs are consistent with recurrence rates reported in a recent systematic review [19]. Abdallah et al. reported a recurrence rate of 12.3% (3.4%–35.7%) for polyps ≥20^{mm} resected by p-CSP), derived from 4 studies [12, 20, 21, 22]. Unfortunately, recurrence rates for adenomas and SSLs were not reported separately. SSLs are particularly suited to p-CSP due to their thin mucosal profile, and therefore have a lower recurrence rate, compared to adenomas. In particular, Van Hattem et al. included only SSLs (n = 562, 4.3%) [12]. The recurrence rate for adenomas ≥20 mm is therefore likely higher than concluded by Abdallah et al. and more in line with our model.

Secondly, this model assumes that each resection is an independent entity. In clinical practice however, each resection is related in varying degrees, to the previous resections. This model also does not account for snare overlap. Based on current literature, accounting for this is not feasible. Thirdly, it was assumed that polyp and snare shape are circular to make calculation of area and number of resections more practicable. This assumption probably underestimates the number of resections required to remove large noncircular lesions. Fourthly, technical challenges such as difficult access and intraprocedural bleeding have not been accounted for but are likely to increase the number of resections for a lesion of any given size. Fifthly, the analysis was based on a very low incomplete resection rate, in procedures conducted by experts who had received prior training, and it probably underestimates the true numerical value of RER. Other studies have reported a rate of incomplete resection of 8%–10%. Finally, during p-CSP re-excision of suspicious areas may serve to reduce the rate of incomplete resection; to what extent this occurs and its efficacy is currently unknown and not feasible to model.

Conclusions

It is important for any endoscopist undertaking p-CSP to have a deep understanding of the fundamentals which underpin endoscopic resection technique. These include sound optical evaluation skills and a willingness to resect a wide margin with meticulous defect inspection and sequential snare overlap. This study demonstrates that the benefits of p-CSP may begin to be outweighed by the risk of incomplete resection for polyps >30–40 mm. Further research is needed to develop better tools to minimize incomplete resection when using p-CSP, and to understand the upper limit for p-CSP where its safety advantages become outweighed by the burden of recurrence and its sequelae.

Conflict of Interest

Michael Bourke: Research Support: Olympus Medical, Cook Medical, Boston Scientific. Nauzer Forbes: Speaker and consultant for Boston Scientific and Pentax Medical; research support from Pentax Medical. There are no other potential conflicts of interest to report.

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