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## Endoscopic resection of non-ampullary duodenal adenomas: Is cold snaring the promised land?

Ludovico Alfarone, Marco Spadaccini, Gianluca Franchellucci, Kareem Khalaf, Davide Massimi, Alessandro De Marco, Silvia Ferretti, Valeria Poletti, Antonio Facciorusso, Roberta Maselli, Alessandro Fugazza, Matteo Colombo, Antonio Capogreco, Silvia Carrara, Cesare Hassan, Alessandro Repici

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### Abstract

Due to the high risk of morbidity and mortality associated with surgical resection in this tract, endoscopic resection (ER) has taken the place of surgical resection as the first line treatment for non-ampullary duodenal adenomas. However, due to the anatomical characteristics of this area, which enhance the risk of post-ER problems, ER in the duodenum is particularly difficult. Due to a lack of data, no ER technique for superficial non-ampullary duodenal epithelial tumours (SNADETs) has yet been backed by strong, high-quality evidence; yet, traditional hot snare-based techniques are still regarded as the standard treatment. Despite having a favourable efficiency profile, adverse events during duodenal hot snare polypectomy (HSP) and hot endoscopic mucosal resection, such as delayed bleeding and perforation, have been reported to be frequent. These events are primarily caused by electrocautery-induced damage. Thus, ER techniques with a better safety profile are needed to overcome these shortcomings. Cold snare polypectomy, which has already been shown as a safer, equally effective procedure compared to HSP for treatment of small colorectal polyps, is being increasingly evaluated as a potential therapeutic option for non-ampullary

duodenal adenomas. The aim of this review is to report and discuss the early outcomes of the first experiences with cold snaring for SNADETs.

**Key Words:** Non-ampullary duodenal adenomas; Endoscopic resection; Cold snare polypectomy; Hot snare polypectomy; Safety; Efficacy

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**Core Tip:** A high risk of adverse events has been associated with endoscopic resection of non-ampullary duodenal adenomas. As cold snare polypectomy demonstrated a better safety profile and a similar efficacy comparing with conventional hot polypectomy in the colon, it has been increasingly considered also in the duodenum over the very last few years. Goal of this review is to summarize efficiency and safety outcomes of cold resection as a treatment for non-ampullary duodenal adenomas.

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## INTRODUCTION

With a relatively low incidence, non-ampullary duodenal adenomas make up a small portion of gastrointestinal (GI) tumors[1-3]. In about 40% of instances, they could be spontaneous or related to familial hereditary diseases such Familial Adenomatous Polyposis (FAP)[4,5]. Incidence of superficial non-ampullary duodenal epithelial tumours (SNADETs) has increased[6] recently due to an increase in endoscopies conducted on the general population and a considerable improvement in endoscopic equipment that have facilitated the identification and characterization of such lesions[7,8]. As duodenal adenoma represents the precursor of duodenal carcinoma similarly to the colorectal adenoma-carcinoma sequence, an effective treatment is required[9,10]. However, since surgical options are too invasive and significantly associated with high rates of morbidity and mortality[11-13], endoscopic resection (ER) has become the preferred approach for SNADETs[14]. However, due to the lack of evidence and the unique properties of the duodenum, which is more susceptible to complications than other parts of the GI tract, the optimum resection approach has been controversial at best[15].

Nowadays, hot snare polypectomy (HSP) and conventional endoscopic mucosal resection (EMR) have been shown highly effective and are considered the standard choices for non-ampullary duodenal adenomas[16]. However, a considerable amount of electrocautery-related complications has been reported with major adverse events mainly secondary to thermal injury[15]. Thus, cold snaring, which has been shown equally effective and safer than hot snaring for removal of colorectal lesions[17-20], has been increasingly considered for SNADETs over the last few years. In this review we summarize efficacy and safety outcomes of cold approach for non-ampullary duodenal adenomas.

## CURRENT STATUS AND ISSUES OF ER FOR SNADETS

ER is currently regarded as the gold standard treatment of SNADETs as it is a more conservative approach than surgery, preserving patients' anatomy and quality of life[14]. Although a well-established first-line ER technique for SNADETs has not been established by robust high-quality evidence, hot snare techniques are conventionally regarded as the standard of care for these lesions[16].

Nevertheless, more recent retrospective studies reported a delayed bleeding rate of about 4%-17%, while perforations occurred in about 2%-7% of cases[1,15,21-25], being these risk increased with the size of the lesion. Notably, recently Probst *et al*[26] carried out the largest prospective trial on hot EMR for SNADETs enrolling 110 patients and 118 duodenal lesions (mean size 15 mm, range 4-70 mm). Authors reported an excellent complete resection rate (94.1%)[26]. However, complications and major complications had an incidence of 22.9% and 15.3%, respectively, with a procedure-related death rate of 1.7%; off note, the most common adverse events were delayed bleeding (18.6%) and perforation (4.2%)[26].

These consequences are typical of HSP and conventional EMR and are linked to the damage brought on by electrocautery. Additionally, ER in the duodenum is more difficult and potentially risky than in

the other GI tracts due to physical factors. The duodenum is heavily vascularized, and the scope's inadequate capacity to manoeuvre in this tight space hinders a proper approach to the lesion and, consequently, the viability of resection. In addition, the duodenal wall is extremely thin and can be easily perforated. Furthermore, bile acid and pancreatic juice have an impact on the post-ER defect. Compared to hot EMR of lesions in the other GI tracts, duodenal hot EMR is more likely to have post-procedural bleeding and perforation due to these characteristics[27].

Preventive measures to minimize these complications after duodenal EMR have been evaluated. Prophylactic argon plasma coagulation (APC) of the resection bed has been shown to reduce the risk of delayed bleeding in a prospective study enrolling 61 duodenal lesions, although statistical significance was not achieved due to the small sample size ( $P = 0.31$ ); moreover, as one of the six patients treated with APC suffered from delayed perforation, the safety of this approach is questionable[28]. A retrospective study, including 37 duodenal adenomas treated by hot EMR, reported delayed bleeding rate was significantly lower in patients treated by prophylactic clipping than in the no prophylaxis group (0% *vs* 21.7%,  $P < 0.05$ )[29]. Additionally, post-EMR prophylactic clipping was associated with a significant decrease in delayed bleeding rate (from 32% to 7%,  $P < 0.004$ ) in another retrospective study encompassing 121 duodenal adenomas[14]. Furthermore, in a prospective study the systematic preventive application of hemostatic clips after underwater EMR of 31 duodenal lesions resulted in the absence of major complications[30]. However, despite these encouraging results, evidence is still very limited and controversial. In the retrospective study by Tomizawa and Ginsberg[15] no decrease in delayed bleeding rate after prophylactic clip placement was observed[15]. Similarly, in the large prospective study by Probst *et al*[26], delayed bleeding rate was not reduced by endoscopic prophylaxis [26]. Moreover, the unneglectable perforation risk due to clips application, the costs, the inefficacy of a partial closure and the unfeasibility of a complete closure for mucosal defects larger than 20 mm remarkably hinder the wide implementation of this option in clinical practice.

Thus, to overcome these drawbacks, in the last few years alternative resectional techniques with a better safety and cost-effectiveness profile have been increasingly proposed for ER of duodenal lesions.

## COLD SNARE POLYPECTOMY

Tappero *et al*[31] first described cold snare polypectomy (CSP) for excision of colorectal tumors[31]. CSP is an easy and safe endoscopic procedure in which a lesion is captured and resected using only a snare without electrical current. Instead, if a submucosal injection is used to better visualize and capture the polyp, in case of large flat lesions or in presence of unclear margins, the resection technique is named cold EMR.

CSP has proved to be a valuable ER method for colorectal lesions. A prospective multicenter trial by Repici *et al*[17] enrolling 1015 subcentimetric polyps in 823 patients, showed CSP had a very low rate of post-polypectomy bleeding (2.2%), which was easily managed with endoscopic hemostasis in all cases [17]. A multicenter randomized controlled study compared the outcomes of CSP with HSP for removal of 796 sessile adenomatous colorectal polyps that were 4-9 mm in size. CSP and HSP achieved a similar complete resection rate (98.2% and 97.4%, respectively)[18]. Moreover, a systematic review and meta-analysis including 32 trials, reported that the pooled incomplete resection rate of CSP and HSP for colorectal polyps 1 to 10 mm was 17.3% [95% confidence intervals (CI): 14.3–20.3%] and 14.2% (95% CI: 14.3–20.3%), respectively, with no significant difference[32]. Furthermore, Sidhu *et al*[33] carried out a multicenter randomized trial enrolling 660 patients who underwent CSP for small (5-9 mm) colorectal polyps. An excellent incomplete resection rate was revealed (1.5%)[33].

In terms of safety profile, Yamashina *et al*[19] observed in a retrospective cohort of 538 patients with colorectal polyps of 2-11 mm in size a significantly higher delayed bleeding rate after HSP in comparison with CSP (0.02% *vs* 0%,  $P = 0.04$ )[19]. Further, a large multicenter randomized controlled trial, recruiting 4270 patients, found that HSP arm had a significantly higher delayed bleeding rate than CSP arm (1.5% *vs* 0.4%,  $P < 0.001$ )[34]. Moreover, a prospective randomized study comparing HSP and CSP for polyps up to 10 mm in 70 anticoagulated patients proved a significantly lower delayed bleeding rate in the CSP arm (0% *vs* 14%,  $P = 0.27$ )[35].

A systematic review and meta-analysis, encompassing 8 trials, confirmed a comparable complete resection rate between HSP (95%) and CSP (94%), but demonstrated HSP was associated with significantly longer colonoscopy and polypectomy time (mean difference: 7.1 min and 30.9 s, respectively). A higher delayed bleeding rate was reported in HSP group, although statistically significance was not achieved[36].

According to the established excellent efficacy and safety profile, CSP is currently regarded as the standard treatment for the resection of nonpedunculated colorectal polyps of size  $< 10$  mm[37-39]. Additionally, the potential expanded application of cold snare resection for nonpedunculated polyps larger than 10 mm has increasingly raised attention. A recent retrospective study compared outcomes of piecemeal CSP with piecemeal hot EMR for removal of large ( $\geq 20$  mm) sessile serrated lesions assessing 562 lesions in 474 patients[40]. Authors reported comparable technical success and recurrence rates for both techniques; while no adverse event was reported in the CSP group, deep mural injury and delayed

bleeding occurred in 3.4% and 5.1% of lesions treated by hot EMR, respectively[40]. Moreover, a systematic review and meta-analysis by Thoguluva Chandrasekar *et al*[41] evaluating outcomes of endoscopic removal of 1137 sessile serrated lesions that were > 10 mm in size, found cold EMR had similar rates of recurrence, but significantly lower rates of delayed bleeding than conventional hot EMR (0% *vs* 2.3%;  $P = 0.03$ )[41]. Another systematic review and meta-analysis by the same author evaluated outcomes of cold snare resection of polyps larger than 10 mm, including 8 trials. The overall adverse event rate was 1.1% with a delayed bleeding rate of 0.5%; no perforations were found. Authors reported a complete resection rate of 99.3%, with an overall recurrence rate of 4.1% at follow-up colonoscopy[42]. Furthermore, a very recent randomized multicenter controlled trial, including 286 colorectal polyps of 6-15 mm, reported cold approach was safer, less time-consuming and had lower incomplete resection rates than hot snare techniques[20].

Therefore, even though larger randomized controlled comparative trials are still required for validation, cold snare techniques are now widely acknowledged to be just as effective as hot snare techniques for larger colorectal polyps while carrying a significantly lower risk of delayed bleeding and perforation because electrocautery is not used.

## CSP IN DUODENUM

Given the remarkable achievements of cold snaring for colorectal lesions and the lower rate of complications compared with hot techniques, the cold approach may also be valuable for ER in duodenum, where the risk of perforation and delayed bleeding is considerable. Although current guidelines suggest CSP for small (< 6 mm) duodenal lesions[16], this recommendation is mostly derived from studies on diminutive colorectal polyps[37], as data on CSP for SNADETs were very limited. To address these drawbacks, over the very last few years, several studies have been carried out to assess efficacy and safety of cold resection as a novel therapeutic technique for SNADETs (Table 1).

In a case series of 15 patients, who underwent cold EMR for duodenal lesions ranging from 10 to 60 mm in size (mean size was 24 mm), no perforation and post-polypectomy syndrome were reported and only one case of delayed bleeding occurred in a patient who was on warfarin[43].

A retrospective single center pilot feasibility study by Hamada *et al*[44] evaluated CSP for small multiple duodenal adenomas in 4 patients with FAP. 126 lesions ranging from 2 to 16 mm were removed with CSP without any complications[44]. Further, the same group carried out a single center prospective study to investigate the safety of CSP in an analogue cohort. 10 patients with FAP underwent CSP with removal of 332 duodenal adenomas; most of these lesions were ≤ 10 mm[45]. No adverse event was reported; one case of intra-procedural bleeding occurred and was easily controlled with hemoclips[45].

However, these above mentioned studies lacked efficacy outcomes and follow-up endoscopy data, such as adenoma recurrence rates.

Maruoka *et al*[46] performed a single center prospective study to assess the safety and efficacy of CSP for sporadic SNADETs. In 22 patients, 25 duodenal adenomas that had a median size of 4.3 mm (range was 2-6 mm), were resected using CSP[46]. No adverse event was reported. The *en bloc* and R0 resection rates were 96% and 68.0%, respectively, with no evidence of recurrence at 3 mo follow-up endoscopy [46].

A study with similar design and goals was later carried out by Takizawa *et al*[47] enrolling 21 patients. CSP was attempted on 21 sporadic SNADETs ranging from 3 to 10 mm (median size 8 mm) [47]. CSP was completed in 18 lesions (86%), while three SNADETs could not entirely be removed with CSP and, thus, were resected using conventional HSP. Among the group with complete CSP, the *en bloc* resection rate was 94%. Only 1 recurrent adenoma was detected at follow-up endoscopy 3 mo after CSP. Neither intra-procedural nor delayed complications were observed[47].

On the basis of the increasing evidence of good cold snaring outcomes for large colorectal polyps, Dang *et al*[48] conducted a single center retrospective study for assessing efficacy and safety of cold EMR for small bowel adenomas ≥ 10 mm; 39 adenomatous lesions (37 duodenal, 2 jejunal) that had a mean size of 26.5 mm (range 10-70 mm) were removed with piecemeal cold EMR[48]. Follow-up endoscopy showed an adenoma recurrence rate of 46% (18/39), which was significantly associated with polyp size. Regarding safety, 12% of patients suffered from cold EMR-related adverse events; the only case of delayed bleeding (2.6%) occurred 11 days after the procedure in a patient who was in warfarin and had an international normalized ratio of 4.6 and it was easily managed with hemoclips. 3 post-treatment strictures (7.7%) were reported. All these patients had lesions ≥ 30 mm involving more than half of the small-bowel circumference; when symptomatic, the strictures were treated successfully with endoscopic dilation[48].

Furthermore, a multicenter retrospective comparative study by Repici *et al*[49] assessed efficacy and safety outcomes of cold EMR in comparison with conventional hot EMR for removal of large (≥ 20 mm) sporadic duodenal adenomas. Data from 33 consecutive patients, who were treated with cold EMR, were analyzed and compared with an historical cohort of 101 patients who underwent hot EMR[49]; mean lesion size for cold and hot EMR groups was 31.5 mm and 37.7 mm, respectively. The *en bloc*

Table 1 Cold snaring for superficial non-ampullary duodenal epithelial tumours; study outcomes

Ref.	Center	Design	Group	Patients (n)	Age (mean)	Gender (M)	Polyposis (n)	Lesions (n)	Size (mean, mm)	En-bloc (n)	Recurrence (n)	Follow up (mean, months)	Adverse events (n)	Delayed bleeding (n)	Perforation (n)	Strictures (n)
Choksi <i>et al</i> [43], 2015	Single	Retrospective	Cold	15	64	9	NA	15	24	NA	NA	0.5	1	1	0	0
Hamada <i>et al</i> [44], 2016	Single	Retrospective	Cold	4	45	2	4	126	NA	NA	NA	2.75	0	0	0	0
Maruoka <i>et al</i> [46], 2017	Single	Prospective	Cold	22	64.7	16	0	25	4.3	24	0	3	0	0	0	0
Hamada <i>et al</i> [45], 2018	Single	Prospective	Cold	10	39.3	6	10	332	NA	328	NA	NA	0	0	0	0
Repici <i>et al</i> [49], 2022	Multi	Retrospective	Cold	33	63	18	0	33	31.5	0	4	3.8	0	0	0	0
			Hot	101	66.4	42	0	101	37.7	9	21	13	26	17	6	2
Trivedi <i>et al</i> [50], 2022	Multi	Retrospective	Cold	41	72	28	0	46	12	22	7	5.8	0	0	0	0
			Hot	69	68	34	0	74	15	35	7	5.8	7	6	1	0
Takizawa <i>et al</i> [47], 2022	Single	Prospective	Cold	21	NA	16	0	21	NA	17	1	3	0	0	0	0
Dang <i>et al</i> [48], 2022	Single	Retrospective	Cold	39	66.8	12	NA	39	26.5	0	18	5.09	5	1	0	3
Okimoto <i>et al</i> [51], 2022	Single	Retrospective	Cold	29	66.6	24	0	37	4.4	36	1	39.2	0	0	0	0

NA: Not available.

resection rate was 8.9% for hot EMR, while all lesions in the cold EMR group were removed piecemeal. Both groups achieved similar technical success rates (94% and 89.1% for cold and hot EMR, respectively,  $P = 0.42$ ). At the first follow-up endoscopy (mean follow-up time was 3.8 mo), adenoma recurrence rates were comparable (12.1% vs 20.8% for cold and hot EMR, respectively,  $P = 0.27$ ) [49]. Instead, procedural mean time was significantly lower for cold EMR (48 min vs 96.9 min,  $P < 0.01$ ). Of note, no intra-procedural or delayed adverse events were reported in the cold EMR group. Whereas, in the hot EMR cohort 17 intra-procedural major complications (16.8%), including 4 perforations and 13 cases of severe bleeding, were reported. Moreover, 26 post-procedural major complications (25.7%) occurred, encompassing 17 cases of delayed bleeding and 6 perforations with 1 procedure-related death [49].

Another multicenter retrospective comparative study, carried out by Trivedi *et al* [50], compared efficacy and safety of CSP with HSP for treatment of sporadic SNADETs; of the 120 adenomatous lesions included, 74 were treated by HSP and 46 by CSP [50]. All polyps were  $\geq 5$  mm with a similar



mean size (12 and 15 mm for the cold and the hot group, respectively,  $P = 0.27$ ). The *en bloc* resection rate was comparable (47.8% *vs* 47.3% for CSP and HSP, respectively). Of the 110 patients enrolled, a follow-up endoscopy 174 days after polypectomy was available only for 54 patients (49.1%); 19 in the CSP group (35.2%) and 35 in the HSP group (64.8%). The two techniques did not differ significantly in recurrent adenoma rates (20% and 36.8% in HSP and CSP group, respectively,  $P = 0.18$ ), which were statistically correlated with polyp size[50]. While intra-procedural bleeding was similar between the two groups, 7 delayed major complications were reported after HSP (10.1%) and none after CSP. These adverse events included 6 cases of delayed bleeding and 1 perforation[50].

While no long-term follow-up data were available for these above reported studies, Okimoto *et al*[51] performed a single center retrospective study to evaluate long-term outcomes of CSP for SNADETs. 29 patients underwent CSP for 37 sporadic duodenal adenomatous lesions; mean size was 4.4 mm[51]. The *en bloc* and R0 resection rates were 97.3% and 70.3%, respectively. The mean follow-up time was 39.2 mo (range 3-64 mo). The observation period was  $\geq 12$  mo after CSP for almost all lesions (94.6%). During this follow-up period, only one adenoma recurrence (2.7%) was detected 12 mo after CSP; this recurrent adenoma was successfully resected with CSP. The relapse free survival rate per lesion after 12 mo was 97.1%. Neither delayed bleeding nor perforation was reported and no procedure-related death occurred [51].

## CURRENT STATE OF ART

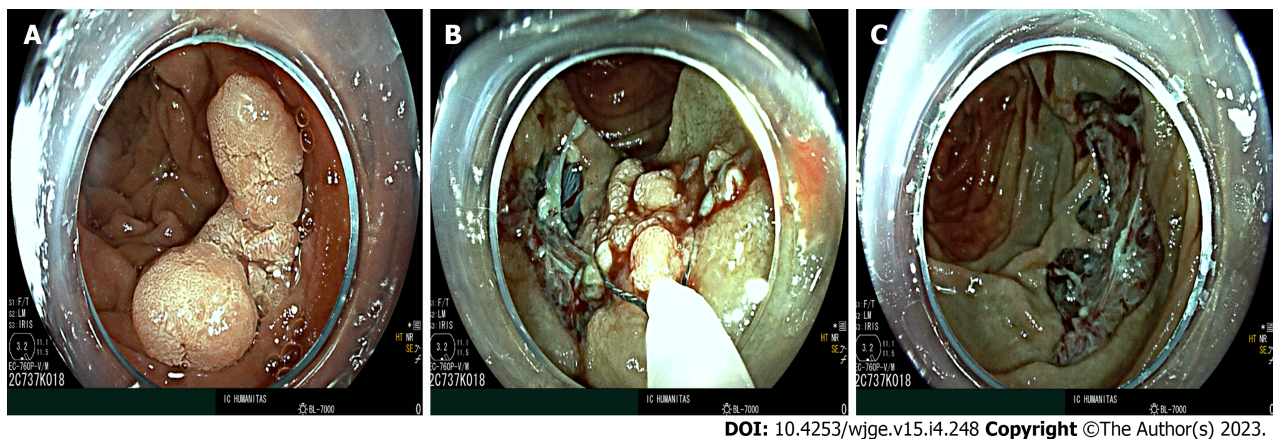
The use of electrocautery-based snare techniques is widely regarded as the standard of care for resection of duodenal polyps  $\geq 6$  mm[16]. This assumption is based on the rationale that HSP provides transection through thick tissue and prevents immediate bleeding through instant vascular coagulation of small arterial and venous branches. Moreover, as electrocautery also allows for the *en bloc* resection of larger polyps and ablates residual dysplastic tissue, it is believed to reduce the risk of recurrent adenoma. However, the use of electrosurgical current also induces submucosal and deeper thermal injury to the bowel wall and, thus, can result in adverse events such as perforation, postpolypectomy syndrome, and delayed bleeding due to coagulum sloughing off exposing an incompletely coagulated submucosal artery[15]. Furthermore, delayed bleeding and perforation after HSP occur more frequently in duodenum in comparison to other bowel tracts according to available data in literature[27]. Indeed, the duodenum has a thin, highly vascularized wall and a high concentration of digestive secretions such as pancreatic enzymes and bile. Particularly, in a recent prospective study delayed bleeding and perforation occurred in 18.6% and 4.2%, respectively, of cases after duodenal hot EMR[26].

CSP does not require use of electrosurgical current and has been demonstrated safer than conventional HSP, avoiding deep thermal injury. Due to a similar efficacy and a better safety profile than HSP [18,19], CSP has become the gold standard treatment for nonpedunculated colorectal polyps  $< 10$  mm [37-39]. Furthermore, CSP and cold EMR are being recently extended to larger nonpedunculated colonic polyps, showing comparable efficacy outcomes with cautery-based techniques but with a significant safety advantage[20,40,41].

Nevertheless, some concerns have been raised for this approach. Cold snare techniques had been historically regarded as inferior to hot snare methods for curability. Indeed, HSP allows an *en bloc* resection for larger polyps than CSP and the absence of electrosurgical current does not provide eradication of neoplastic tissue around the snare. Moreover, it has been shown that CSP has a lower depth of resection and higher rates of incomplete resection than conventional polypectomy for colorectal polyps[52,53]. However, a recent prospective randomized controlled trial reported CSP has enough resection width and depth to enable complete polyp resection[54]. Furthermore, assessment of complete histologic resection, and thereby, curability is often challenging after CSP. In fact, specimen's margins can be damaged by suction through the operative channel or are not visible due to lack of thermal effect. Thus, even if the polyp was pathologically judged to be completely resected, an adenomatous component may remain and vice versa. Since assessment of complete histologic resection is tough for pathologists, it is believed that the most reliable efficiency outcome after CSP is the adenoma recurrence rate at follow-up endoscopy[55].

In the light of his safety superiority over conventional hot techniques for resection of colorectal polyps, in the very last few years cold snaring approach has been increasingly regarded as a potential optimal endoscopic treatment for duodenal adenomas (Figure 1).

The above-mentioned in-depth research on the use of cold snaring techniques for SNADETs substantially support the approach's high level of safety by demonstrating a very low occurrence of negative outcomes. Dang *et al*[48], indicated a noteworthy rate of complications (12%) following cold EMR. The sole patient to experience delayed bleeding while taking warfarin had an INR of 4.6; in contrast, three post-treatment strictures formed following the removal of polyps that were bigger than 30 mm in diameter and covered more than half of the wall circumference. Notably, both comparative trials reported a significant higher adverse event rates after hot snaring comparing with cold snaring techniques; most frequent complications were delayed bleeding and perforation, as expected. Indeed, immediate bleeding is common after CSP as the result of small capillary bleeding and venous oozing,



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**Figure 1 Cold snare piecemeal resection of a large non-ampullary duodenal adenoma.** A: Assessment of the lesion; B: Piecemeal cold snare polypectomy; C: Post-polypectomy scar evaluation.

but resolves spontaneously in almost all patients and it is not considered a real adverse event. Whereas, the effect of cautery and coagulation used during HSP reduces immediate bleeding providing a false feeling of security, but increases the risk of more dangerous delayed bleeding from sloughing coagulated eschar.

As far as the efficiency outcomes are concerned, findings of these studies on cold approach for SNADETs are very amazing. In fact, adenoma recurrence rates were mostly low. Additionally, cold snaring and hot snaring techniques did not significantly differ in recurrence rates in both comparative trials. Furthermore, the only study reporting long-term follow-up data showed a very low incidence of recurrence. Notably, recurrence rates were not statistically associated with resection technique, but with polyp size. These promising results could increase the use of cold approach, which has been historically judged as less curative than hot snare techniques. However, these preliminary data together with the remarkable recurrence rate observed in the largest retrospective study on duodenal hot EMR[15] may even challenge the superiority of hot snare techniques over cold resection in terms of efficacy.

Since delayed bleeding and perforation are linked to hospital stays, blood transfusions, and more invasive operations, CSP can result in economic savings in addition to reducing adverse events and morbidity. Furthermore, due to low rate of delayed bleeding and perforation, the use of cold snare does not necessitate prophylactic clipping of the mucosal defect, which is a costly and time-consuming measure. As a result, a recent study found that treating big sessile colorectal polyps with cold EMR instead of hot EMR resulted in a \$955 per case cost savings[56].

Nevertheless, despite the fact that these results point to a safety benefit of CSP *vs* HSP with comparable adenoma eradication success, these studies were influenced by a number of limitations that make it difficult to draw firm conclusions.

First off, the majority were retrospective studies with a single center and a limited patient population. Furthermore, while follow-up data was available, it was almost typically only for a few months. The likelihood of underreporting problems rises in the absence of long-term follow-up results; particularly, the lack of trials with longer follow-up periods may significantly affect those recurrence rates reported. Additionally, the nature of retrospective studies might distort efficacy findings, which can be impacted by the initial patient selection for CSP. Additionally, cold snare resections were mainly performed by expert endoscopists in polyp resection at tertiary centers. Whether these findings can be extended to less experienced endoscopists in various environments have to be shown.

Thus, waiting for further randomized studies comparing cold snare technique with hot snare methods, endoscopists may strongly consider CSP for treatment of SNADETs, especially for subjects at increased risk of delayed bleeding or frail patients, in whom surgery would be hardly tolerated in case of perforation.

## CONCLUSION

Overall, despite preliminary, the efficacy and safety outcomes reported by these studies were highly promising and show that cold snaring can lead to significant safety and financial advantages over hot snare-based techniques for treatment of SNADETs, without an impairment in terms of curability. However, as cold resection can be considered a real paradigm shift from the standard of care for duodenal adenomas, larger multicenter prospective randomized comparative trials with long-term follow up are required to better assess safety and efficacy outcomes of this approach and compare to conventional hot snare options.

The cold snare technique is likely to overtake other methods as the preferred method for SNADETs in the near future as we are currently in standpoint revolution where the safety and effectiveness of CSP and cold EMR are being increasingly demonstrated for both colonic and duodenal polyps.

## FOOTNOTES

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