Endoscopic management of patients with high-risk colorectal colitis–associated neoplasia: a Delphi study

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Background and Aims: Current guidelines recommend endoscopic resection of visible and endoscopically resectable colorectal colitis–associated neoplasia (CAN) in patients with inflammatory bowel disease (IBD). However, patients with high-risk CAN (HR-CAN) are often not amenable to conventional resection techniques, and a consensus approach for the endoscopic management of these lesions is presently lacking. This Delphi study aims to reach consensus among experts on the endoscopic management of these lesions.

Methods: A 3-round modified Delphi process was conducted to reach consensus among worldwide IBD and/or endoscopy experts (n = 18) from 3 continents. Consensus was considered if ≥75% agreed or disagreed. Quality of evidence was assessed by the criteria of the Cochrane Collaboration group.

Results: Consensus was reached on all statements (n = 14). Experts agreed on a definition for CAN and HR-CAN. Consensus was reached on the examination of the colon with enhanced endoscopic imaging before resection, the endoscopic resectability of an HR-CAN lesion, and endoscopic assessment and standard report of CAN lesions. In addition, experts agreed on type of resections of HR-CAN (< 20 mm, >20 mm, with or without good lifting), endoscopic success (technical success and outcomes), histologic assessment, and follow-up in HR-CAN.

Conclusions: This is the first step in developing international consensus–based recommendations for endoscopic management of CAN and HR-CAN. Although the quality of available evidence was considered low, consensus was reached on several aspects of the management of CAN and HR-CAN. The present work and proposed standardization might benefit future studies. (Gastrointest Endosc 2023;97:767-79.)

(footnotes appear on last page of article)

American and European guidelines recommend endoscopic resection for visible and endoscopically resectable colorectal dysplasia in patients with inflammatory bowel disease (IBD).[1-3] Two meta-analyses provide support for this strategy but emphasize the need for close endoscopic follow-up because of the risk of recurrence (2-5.3/1000 person-years of follow-up) and metachronous dysplasia.[4,5]

Endoscopic resection of colitis-associated neoplasia (CAN), especially of larger lesions, can be challenging because of ongoing inflammation, mucosal scarring, and submucosal fibrosis.[6] Both EMR and endoscopic submucosal dissection (ESD) are used for the resection of CAN. These techniques are reportedly effective, safe in cases of sporadic adenomas, and associated with low proctocolectomy rates for neoplasia.[7,8] However, the optimal use of these techniques and follow-up strategy in CAN are presently unclear.

Several studies have suggested that EMR and ESD are safe and feasible in the setting of CAN.[9-23] These relatively small, retrospective studies comprised 552 patients (589 lesions).[9-23] Most patients were diagnosed with ulcerative colitis (UC).[9-23] Ten studies exclusively reported on ESD procedures,[9,12,14-17,19-22] whereas 5 studies described both ESD and EMR procedures[10,11,13,18,23] or ESD-assisted EMR.[10,11,13,18,23] A recent analysis of pooled data suggested en-bloc and R0 resection rates of 86% and 70%, respectively,

for nonpolypoid lesions with a potential superiority for ESD.[24] After endoscopic resection, patients with nonpolypoid dysplasia seemed to have higher colorectal cancer (CRC) and metachronous neoplasia incidence rates, warranting closer endoscopic follow-up.[24] Of note, high-quality data from large prospective studies are lacking.

Current recommendations in guidelines are largely based on expert opinion, and important questions concerning the endoscopic management of CAN remain unanswered.[1-3] This study aimed to generate a consensus on standardized endoscopic management of CAN based on current evidence and expert opinion.

METHODS

Development of consensus statements and literature review

A modified Delphi approach was used to reach consensus on statements concerning the endoscopic management of CAN.[25] Members of the expert panel were invited by the senior authors (L.M.G.M. and B.O.) and had extensive IBD expertise (n = 9) and/or were EMR/ESD experts (n = 12). Before the first meeting in March 2021, a literature review was conducted by the study coordinator (M.T.J.B.) and 1 senior author (L.M.G.M.) in MEDLINE and EMBASE for relevant literature.

Population, intervention, comparison, and outcomes (PICO) frameworks were developed for several statements. Search strings of the population, intervention, comparison, and outcomes are presented in Appendix 1 (available online at www.giejournal.org). This literature search and the results were shared with all invited experts. In the first phase, the literature was shared among all experts, and statements were drafted (Fig. 1). Three online meetings were organized to discuss and reach consensus on the proposed statements. After the meetings, participants were asked to vote electronically and provide feedback on the statements. For adjusted or new statements, the systematic review was updated. Feedback was incorporated into the second and third rounds of voting.

Electronic voting rounds

Experts were asked to vote on statements on a 5-point Likert scale in 3 rounds of electronic voting ranging from "strongly disagree" to "strongly agree." In the second and third rounds of voting, experts were given the overall results of each question of the prior voting round and their own voting. Only the study coordinator (M.T.J.B.) had access to the voting results. The senior authors were blinded to the feedback of the individual participants.

Acceptance of statements and quality of evidence

Consensus was defined as ≥75% agreement ("agree" and "strongly agree" or "disagree" and "strongly disagree") on an individual statement. Participants were asked individually to assess the quality of evidence of the provided literature. Quality of evidence was assessed with the criteria of the Cochrane Collaboration Review Group.[26] The final recommendation for the quality of evidence was based on the majority of votes.

RESULTS

Participants

Eighteen experts from 10 countries and 3 continents were invited to participate. Response rates in the first, second, and third rounds of voting were 94.4% (n = 17), 66.7% (n = 12), and 94.4% (n = 17), respectively. Quality of evidence was assessed by 83.3% (n = 15) of the respondents.

Consensus statements

Results of the statements that reached consensus in the third and final round of voting are shown in Table 1. Consensus was reached on all statements (n = 14). Based on the statements, a flowchart was developed (Fig. 2). Details on the third and final round of voting are presented in Appendix 2 (available online at www.giejournal.org).

Nomenclature of high-risk CAN

Statement 1: We suggest adoption of the term colitis-associated neoplasia (CAN) for all neoplastic lesions detected in a section of previously or presently inflamed colon.

(Agreement, 100%; quality of evidence, no evidence)

Patients with IBD have an increased risk of developing CRC.[27] Although most mechanisms underlying tumorigenesis in CAN are similar to those involved in sporadic CRC, timing and frequency of driver events differ.[28] Also, endoscopic features and clinical behavior of CAN diverge from sporadic adenomas or CRC. To date, no clear definition of CAN is provided in the current literature and guidelines.[1-3] CAN develops in areas with chronic inflammation and may present as endoscopically visible or invisible lesions (the latter referring to lesions, identified by random biopsy sampling). Visible lesions can be classified morphologically into polypoid and nonpolypoid types.[29] Both colitis-associated adenomas and colitis-associated serrated lesions have been found to carry an increased risk of metachronous and synchronous multifocal visible dysplasia.[30]

Neoplastic lesions that are encountered in (previously) noninflamed areas of the colon are considered to be sporadic adenomas and unrelated to colitis.[31] Results from previous studies do not indicate an increased risk of CRC development after endoscopic removal of these lesions,[32-36] even when the resected polyps contain high-grade dysplasia (HGD).[37]

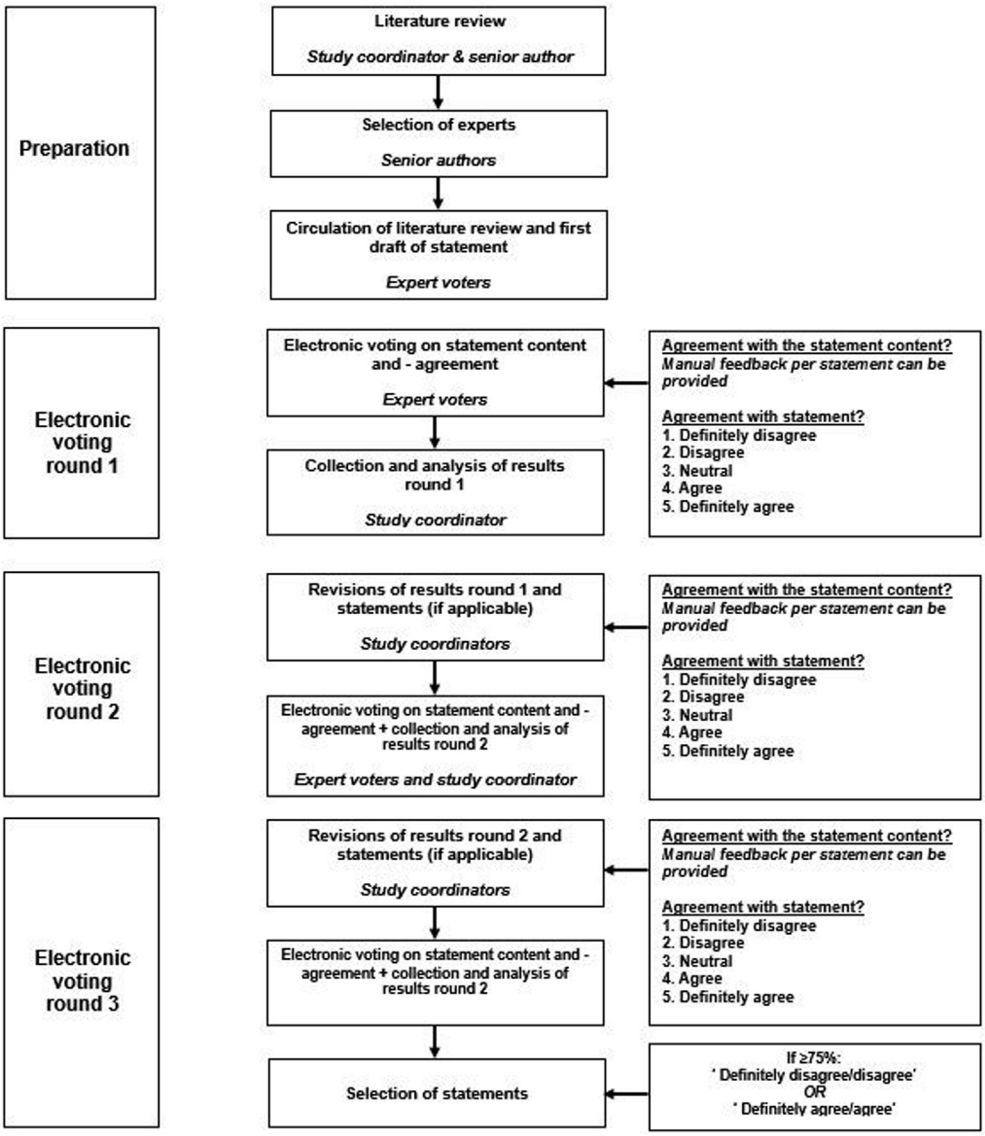

Figure 1. Flowchart of consensus development.

Statement 2: Extent of previous or present inflammation should have been or should be confirmed by endoscopy and/or histology.

(Agreement, 100%; quality of evidence, no evidence)

Confirmation of inflammation is warranted because CAN arises characteristically in previously or presently inflamed mucosa. Biopsy specimens can be used to discriminate between quiescent disease and different grades of disease activity.[29,38] According to the current European guidelines, biopsy specimens should be accompanied by clinical information such as endoscopic findings.[29,38] An adequate number of biopsy samples should be obtained from inflamed and noninflamed mucosa because mild or even severe inflammation can be detected in endoscopically normal-appearing mucosa.[29] Histologic disease activity in UC can be assessed with the use of validated histologic score indices (ie, Geboes score, Nancy Index, and Robarts Histopathology Index).[39]

To date, there is no validated histologic scoring index for evaluation of Crohn's disease (CD) activity.[40] Several endoscopic scores have been established and used in clinical practice to monitor endoscopic activity for UC and CD. The most obvious candidates for UC are the formally validated UC endoscopic index of severity and UC colonoscopic index of severity, whereas in CD the CD endoscopic index of severity or the simple endoscopic score for CD can be used.[41-44] The latter scores were shown to be highly reproducible with demonstration of excellent interobserver agreement and have been prospectively validated.[3]

TABLE 1. Overview of consensus statements

Statement	Agreement grade	Quality of evidence
1. We suggest adopting the term colitis-associated neoplasia (CAN) for all neoplastic lesions detected in a section of previously or presently inflamed colon.	100%	No evidence
2. Extent of previous or present inflammation should have been or should be confirmed by endoscopy and/or histology.	100%	No evidence
3. Nonpolypoid lesions and large (>20 mm) nonpedunculated colon polyps should be considered high-risk CAN.	88.2%	Limited evidence
4. Careful examination of the colon (preferably using enhanced endoscopic imaging) should precede local excision of HR-CAN.	100%	Moderate evidence
5. An HR-CAN lesion is considered endoscopically resectable if 1. The lesion has distinct margins 2. The lesion can (preferably) be removed en bloc with clear deep and lateral resection margins *and* there is *no* evidence of 3. Synchronous *invisible* dysplasia 4. Moderate-to-severe inflammation of mucosa surrounding the area with HR-CAN interfering with delineation of the lesion 5. Signs of deep submucosal invasion.	76.5%	Limited evidence
6. Surgical resection is indicated when HR-CAN is nonresectable.	100%	Moderate evidence
7. All suspected HR-CANs should be assessed according to a standardized approach and recorded in the endoscopy report. The description should include at least the following features: 1. Size, delineation, and location 2. Description of gross morphology a. Granular/nongranular b. Paris classification 3. Assessment of the pit and vascular pattern using enhanced endoscopic imaging 4. Assessment of endoscopic activity of the colitis in the segment, harboring the dysplastic lesion (eg, using the Mayo subset index, UC endoscopic index of severity, or simple endoscopic score for CD).	94.1%	Limited evidence
8. HR-CAN should preferably be removed en bloc to lower the risk of recurrence and optimize the histologic assessment.	94.1%	Limited evidence
9. HR-CAN <20 mm with good lifting (Kato I and II) can be removed using en-bloc (including underwater) EMR.	94.1%	Moderate evidence
10. HR-CAN <20 mm without good lifting (Kato III and IV) or HR-CAN >20 mm without signs of deep submucosal invasion should be removed with techniques that preferably allow en-bloc resection.	82.4%	No evidence
11. Endoscopic local excision of HR-CAN should be performed by endoscopists with sufficient skills in both EMR and ESD techniques.	88.2%	No evidence
12. Endoscopic resection should be captured by recording: 1. Technical success a. En-bloc resection b. R0 resection c. Adverse events (intra- or postprocedural bleeding, perforation, postcoagulation syndrome, need of emergency surgery, other) 2. Outcomes a. Local recurrence at 6 months and 3 years b. Surgery for recurrence after 1, 3, and 5 years.	82.4%	No evidence
13. The histologic report should at least include the following items: 1. Size (mm) 2. Grade of dysplasia according the World Health Organization classification 3. Lateral resection margin (in mm, free if >.1 mm) 4. Deep resection margin (in mm, free if >.1 mm) In case of submucosal invasion: 1. Maximum depth of submucosal (Sm) invasion in μm (taken from the deepest margin of the muscularis mucosae) 2. Lymphatic and/or venous invasion confirmed with D2-40 immunohistochemistry 3. Tumor budding (Bd1-3) according to the International Tumor Budding Consensus Conference 4. Grade of differentiation according to World Health Organization classification.	94.1%	No evidence
14. After complete endoscopic resection of HR-CAN, assessment of local recurrence should be performed within 3 to 6 months and annually thereafter if no residual disease is found.	88.2%	Limited evidence

ESD, Endoscopic submucosal dissection; *HR-CAN*, high-risk colitis-associated neoplasia; *CD*, Crohn's disease; *UC*, ulcerative colitis.

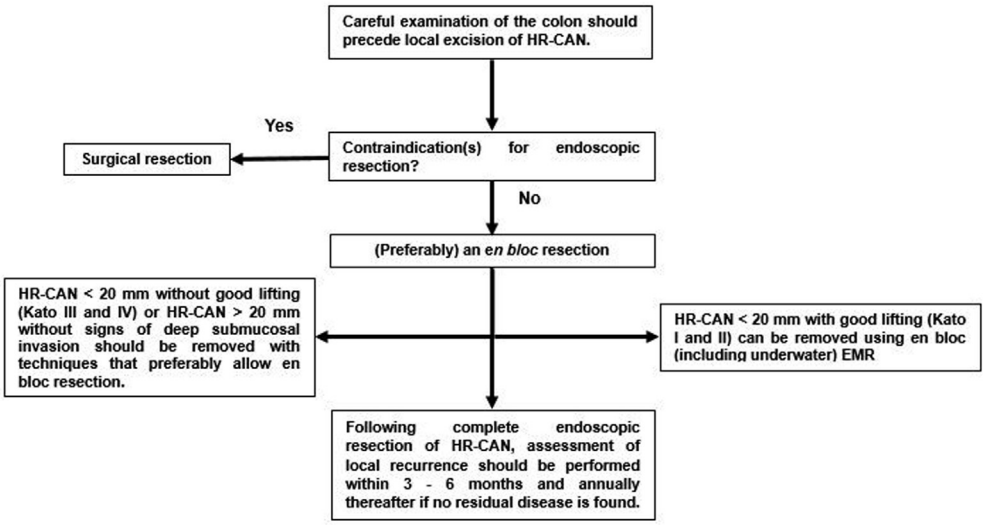

Figure 2. Flowchart after detection of HR-CAN. Note: Details can be found in the statements in the text. *HR-CAN*, High-risk colitis-associated neoplasia.

Statement 3: Nonpolypoid lesions and large (>20 mm) nonpedunculated colon polyps should be considered high-risk CAN.

(Agreement, 88.2%; quality of evidence, limited evidence)

Given its potentially worse outcome, an agreed definition of high-risk CAN (HR-CAN) is desirable because it constitutes the first step toward a coherent therapeutic strategy. Two studies identified nonpolypoid lesions as an independent risk factor for (advanced) colorectal neoplasia (aCRN) development in patients with IBD.[45,46] In addition, pooled data reported higher CRC and metachronous neoplasia incidence rates after endoscopic resection of nonpolypoid lesions as compared with polypoid lesions.[5] In contrast, several studies have shown that polypoid lesions with low-grade dysplasia (LGD) or HGD in IBD patients have a low risk of future CRC.[35-37,46,47] Moreover, studies have shown that the risk of CRC was similar between polypoid lesions in diseased segments and sporadic adenomas in disease-free segments.[35,47] Therefore, the risks of CRC in individuals with polypoid lesions, with and without IBD, can probably be considered comparable.

Large nonpedunculated colorectal polyps (LNPCPs) are defined as sessile and flat lesions with a size ≥20 mm. LNPCPs are believed to be especially at risk of progression to submucosal invasive cancer.[48] Endoscopic resection of these lesions is technically more demanding because of their large size and lack of intraluminal protrusion. This translates into a higher risk of postresection adverse events and recurrence rates up to 30%.[48,49] En-bloc resection might overcome the drawbacks associated with standard polypectomy in these cases.[50] To date, the literature concerning these lesions in the IBD population is virtually absent. Only 1 retrospective study reported a significant association of large polyps (defined as ≥1 cm) with the progression to aCRN (defined as HGD or CRC).[46] Nevertheless, LNPCPs can be considered a high-risk factor in patients with IBD because of the risk of progression to submucosal invasion and the high risk of recurrence in the non-IBD population.

Preresection assessment of HR-CAN

Statement 4: Careful examination of the colon (preferably using enhanced endoscopic imaging) should precede local excision of HR-CAN.

(Agreement, 100%; quality of evidence, moderate evidence)

Pooled data showed that incidental synchronous CRC has been found in 2.7% and 13.7% of colectomy specimens of IBD patients with preoperative visible lesions containing LGD or HGD.[51] Another study reported a pooled prevalence synchronous CRC rate of 17% in patients with UC after a preoperative diagnosis of LGD.[52] Therefore, careful examination of the entire colon is warranted before a local excision.

The use of high-definition white-light endoscopy or (dye or virtual) chromoendoscopy instead of standard white-light endoscopy is recommended.[53,54] Add-on devices, such as distal attachment devices, to improve the adenoma detection rate in the non-IBD setting have been studied in 2 meta-network analyses. Both studies reported a significant increase of the adenoma detection rate for add-on devices as compared with standard colonoscopy.[55,56] Although no data are available in the IBD population, add-on devices may have an additional value for the detection of HR-CAN as well. We suggest using the term *enhanced endoscopic imaging* for these technologies (ie, high-definition white-light endoscopy or dye or virtual chromoendoscopy). In addition, add-on devices can be considered for the detection of HR-CAN.

The recommendation to obtain random biopsy samples in the setting of (surveillance) endoscopies in the IBD

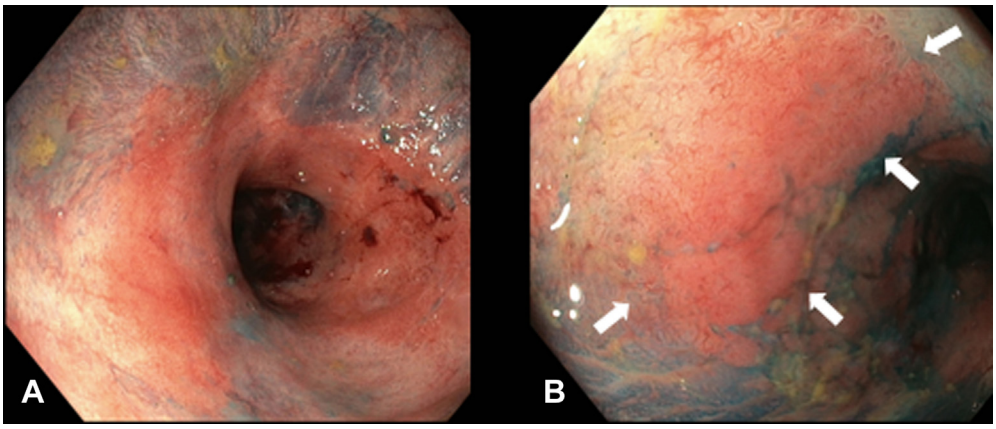

Figure 3. In a tubular, scarred sigmoid (**A**) of a patient with ulcerative colitis, a 2.5 × 1.5-cm dysplastic field was identified (**B**). The lesion could not completely be delineated. Biopsy specimens from the surrounding normal-appearing mucosa revealed high-grade dysplasia. The patient was referred for proctocolectomy.

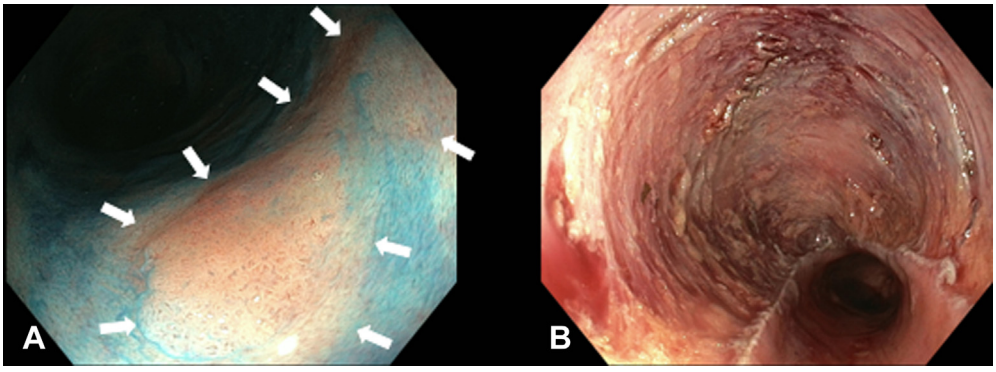

Figure 4. A, A 75-year-old man with longstanding ulcerative colitis was referred for endoscopic resection of a 1.2 × 2.5-cm well-demarcated lesion in the rectum identified with chromoendoscopy. **B,** The lesion was successfully resected using endoscopic submucosal dissection. Histology revealed high-grade dysplasia.

population varies in the current guidelines.[1-3] Although the dysplasia yield of random biopsy sampling during surveillance in IBD is relatively low, 12% to 20% of the dysplastic specimens were obtained by random biopsy sampling in 2 studies.[57,58] A large cohort study reported a greater proportion of patients with neoplasia after targeted biopsy sampling (19.1%) as compared with random biopsy sampling (8.2%).[59] Random biopsy sampling has a significant yield in IBD patients with a personal history of neoplasia, concomitant primary sclerosing cholangitis, or a tubular colon during colonoscopy.[58] Therefore, random biopsy sampling is recommended in this subset of patients before endoscopic resection of HR-CAN.

Statement 5: An HR-CAN lesion is considered endoscopically resectable if:

1. The lesion has distinct margins
2. The lesion can (preferably) be removed en bloc with clear deep and lateral resection margins

***and* there is *no* evidence of**

3. Synchronous *invisible* dysplasia
4. Moderate-to-severe inflammation of mucosa surrounding the area with HR-CAN interfering with delineation of the lesion
5. Signs of deep submucosal invasion.

(Agreement, 76.5%; quality of evidence, limited evidence)

Although current guidelines recommend the endoscopic resection of visible CAN, it may be impossible to (completely) remove HR-CAN lesions when the above criteria are not met (Fig. 3).[1-3] Criteria for successful endoscopic resection are macroscopically identifiable, distinct margins and the absence of deep submucosal invasion (DSI) (Fig. 4). Proper delineation of dysplasia enables a complete, preferably en-bloc, resection, thereby improving the quality and reliability of histopathologic findings.[60] Despite the use of enhanced endoscopic imaging, invisible dysplasia should be considered a contraindication for endoscopic resection and warrants consideration of surgical resection.[61] The experts agreed that signs of DSI, such as excavation and demarcated depressed areas, are a contraindication to endoscopic

resection.[62] Recently pooled data reported an overall rate of lymph node metastasis of 11.2% in the presence of DSI in sporadic lesions (non-IBD patients).[63] Although this meta-analysis concluded that DSI is not a strong independent predictor for lymph node metastasis, an R0 resection was only achieved in 62% to 65% of the polyps with DSI after ESD.[63] Data on the correlation between DSI and en-bloc or R0 resection rates in HR-CAN are presently lacking, but in general signs of DSI are considered a contraindication for endoscopic resection in this setting. All cases of HR-CAN should be discussed at multidisciplinary team meetings before the endoscopic procedure to ensure the delivery of patient-specific management.

Statement 6: Surgical resection is indicated when HR-CAN is nonresectable.

(Agreement, 100%; quality of evidence, moderate evidence)

Nonpolypoid lesions and LNPCPs (ie, HR-CAN) are associated with a high risk of aCRN development.[45,46,48] Thus, removal of these lesion types is warranted. Current international guidelines recommend surgery for endoscopically nonresectable lesions in the IBD population.[1,3,84] Close endoscopic surveillance or segmental resection is proposed for LGD or patients who are at high risk for dismal postoperative outcomes.[84] A proctocolectomy is advised for aCRN because of the high rates of metachronous recurrence after segmental resection, based on a limited number of studies.[84] A recent multicenter, retrospective study reported similar long-term survival outcomes of segmental colectomy compared with proctocolectomy.[85] Because of the risk of progression to aCRN, the type of surgical resection should be discussed with a multidisciplinary team in which other prognostic risk factors for aCRN should be taken into account.[86] If segmental resection is undertaken, continued close surveillance of the residual colon is imperative.

Statement 7: All suspected HR-CANs should be assessed according to a standardized approach and recorded in the endoscopy report. The description should include at least the following features:

1. Size, delineation, and location
2. Description of gross morphology
   a. Granular/nongranular
   b. Paris classification
3. Assessment of the pit and vascular pattern using enhanced endoscopic imaging
4. Assessment of endoscopic activity of the colitis in the segment harboring the dysplastic lesion (eg, using the Mayo subset index, UC endoscopic index of severity, or simple endoscopic score for CD disease).

(Agreement, 94.1%; quality of evidence, limited evidence)

To date, minimum standardized endoscopy reporting elements for CAN lesions have not been established.[60,64,65] Standardized endoscopy reports are crucial for clinical management decision-making to facilitate longitudinal monitoring and enable the establishment of a potential relationship between morphology and histopathology.

In line with recommendations for non-IBD–related dysplastic lesions, common endoscopic descriptors such as size, location, and description of gross morphology should be included in endoscopy reports.[60,64,65] The delineation of the lesion should be recorded in the standardized report to identify the lateral resection margins and enable en-bloc resection. Furthermore, the experts agreed to include an assessment of the granularity of the lesion because nongranular-type lesions have been associated with submucosal invasion, especially in the rectosigmoid.[66-68] The assessment of the Kudo pit pattern classification has shown high specificity and sensitivity (both 93%) in differentiating neoplastic lesions from nonneoplastic lesions in IBD patients.[69] In addition, a prospective study and a randomized controlled trial reported that pit pattern types III to V were predictive of CAN.[68,70] Conversely, pit pattern types I and II were found to have a high negative predictive value for CAN.[70,71] In addition, irregular vascular patterns were identified as predictors for dysplasia in IBD patients.[72]

As noted previously, the presence of moderate-to-severe inflammation interferes with the detection of dysplasia and is therefore considered a contraindication for endoscopic resection of HR-CAN. Thus, a careful assessment of the endoscopic severity of the disease using a validated endoscopic score (eg, Mayo subset index score, UC endoscopic index of severity, and simple endoscopic score for CD) should be included in the endoscopy report.[1-3]

Endoscopic resection of HR-CAN

Statement 8: HR-CAN preferably should be removed en bloc to lower the risk of recurrence and optimize the histologic assessment.

(Agreement, 94.1%; quality of evidence, limited evidence)

Because of the higher CRC and metachronous neoplasia incidence rates after resection of nonpolypoid lesions and the potential risk of DSI of LNPCPs, en-bloc resection is preferred to lower the risk of recurrence.[1,5,49] Furthermore, en-bloc resection enables a more accurate histopathologic evaluation of the resection margins and achievement of R0 resection.[73] Both EMR and ESD are commonly used endoscopic resection techniques allowing an en-bloc resection. In addition, endoscopic full-thickness resection and endoscopic intermuscular dissection, for rectal lesions with signs of DSI, are relatively new techniques for an en-bloc resection of colorectal lesions. Both techniques have recently been found to have high overall technical success and R0 resection rates in sporadic lesions, and further experience is required to determine the role of these techniques for managing HR-CAN.[74,75] Whether endoscopic full-thickness resection or

endoscopic intermuscular dissection can be successfully and safely used in HR-CAN is presently not clear because data for HR-CAN are not available.

A recent meta-analysis reported pooled en-bloc and R0 resection rates of 86% and 70%, respectively, after a hybrid endoscopic resection technique (ie, a combination of EMR and ESD) or ESD of nonpolypoid lesions with a pooled recurrence rate of 8%.[24] En-bloc resection rates were significantly higher after ESD (93%) as compared with the hybrid technique (65%, $P < .001$).[24] In line with these findings, pooled R0 resection rates were higher using ESD (75%) versus the hybrid technique (60%) but did not reach significance ($P = .454$).[24] We recognized that long-term outcomes of these different techniques have not been published.

Piecemeal resection does not always allow complete retrieval of the lesion, which renders complete histologic assessment sometimes difficult.[65] The data on piecemeal resection outcomes are conflicting. Piecemeal EMR has been shown to achieve excellent early- and long-term outcomes for >20-mm sporadic adenomas.[60] But piecemeal resections of sporadic nonpolypoid lesions have also been associated with a pooled recurrence rate of 20% versus 3% after en-bloc resection.[76] The recurrence rate even exceeds 30% in larger polyps (>20 mm).[50] However, with the recent introduction of improved EMR techniques and the use of adjuvant thermal ablation (snare-tip soft coagulation or argon plasma coagulation) of the resected lesion margin, the risk of recurrence after a piecemeal resection has been significantly reduced.[50,77] Because studies in IBD patients are virtually absent, it is not clear if these results can be extrapolated to the setting of HR-CAN.

In conclusion, HR-CAN should preferably be removed en bloc to lower the risk of recurrence and optimize the histologic assessment. Advanced endoscopic resection techniques should be considered for the endoscopic resection of an HR-CAN lesion. According to the current evidence, ESD has higher en-bloc and R0 resection rates, which may be a reason to prefer ESD over EMR.

Statement 9: HR-CAN <20 mm with good lifting (Kato I and II) can be removed using en-bloc (including underwater) EMR.

(Agreement, 94.1%; quality of evidence, moderate evidence)

No statements concerning HR-CAN and the use of particular endoscopic resection techniques are made in the current international guideline.[60,64,65] Moreover, no clear cutoff point for lesion size where an en-bloc resection can be considered safe and feasible has been defined. The decision for an en-bloc resection is mostly based on the morphology and size of the lesion.[65]

To date, 4 relatively small retrospective studies have reported outcomes on EMR in patients with CAN.[10,11,13,18] The outcomes of studies with a focus on resection technique (based on lesion size) were described in 3 studies.[10,11,13] Nishio et al[10] described the results of endoscopic resection of superficial tumors in patients with UC. EMR was used for most polyps (62.0%) that were predominantly <20 mm (98%) and polypoid (68%). The overall en-bloc resection rate after EMR was 94%. The en-bloc resection rate after EMR as compared with ESD did not significantly differ in polyps <20 mm. The en-bloc resection rate in nonpolypoid lesions was significantly higher in ESD (100%) compared with EMR (85%, $P = .044$). Of note, documentation of the presence of submucosal fibrosis was not reported.[10] Yadav et al[11] reported on the endoscopic treatment of polyps >10 mm in IBD patients, with 54.8% of polyps <20 mm. Most polyps (95.2%) were resected using EMR, yielding an en-bloc resection rate of 70.9%. A multicenter, retrospective study on the use of EMR or ESD in colitis-associated polyps (<20 mm in 90.8%) reported an overall en-bloc rate of 63% after EMR and 65.9% after ESD.[13] All lesions with submucosal fibrosis were resected with ESD or a "knife-assisted" resection.[13]

Based on these results, the experts agreed that HR-CAN <20 mm with good lifting (Kato I and II) can be removed using en-bloc EMR. In sporadic adenomas, recent pooled data reported higher en-bloc rates and lower recurrence rates in favor of underwater EMR compared with conventional EMR.[78] The role of underwater EMR has not been studied in HR-CAN, but underwater EMR might be useful in the setting of these cases as well.

Statement 10: HR-CAN <20 mm without good lifting (Kato III and IV) or HR-CAN >20 mm without signs of DSI should be removed with techniques that preferably allow en-bloc resection.

(Agreement, 82.4%; quality of evidence, no evidence)

Chronic inflammation (or submucosal invasion)-related submucosal fibrosis might lead to inadequate lifting and to incomplete resection of lesions if EMR is used.[6,65] ESD may overcome the limitations of EMR and should therefore be considered as a first choice to resect lesions when good lifting is not achieved.[65] The presence of concomitant submucosal fibrosis in CAN lesions is reported in most studies with a range from 28.6% to 100% of the cases.[9,12,13,15-20,22,23] In studies that reported relative high frequencies of submucosal fibrosis (>60%), en-bloc rates ranging from 78% to 100% after ESD were achieved.[12,14-17,19,20,23] Of note, most of these lesions were nonpolypoid (76%-100%).[12,14-17,19,20,23] Although the use of endoscopic full-thickness resection and endoscopic intermuscular dissection has not been assessed in patients with IBD, these new techniques may prove useful in the treatment of HR-CAN lesions with (severe) fibrosis.[79,80]

EMR and ESD are generally considered the preferable options for endoscopic removal of polyps >20 mm because of the limited size of the snare, difficulty in positioning the endoscope, and extension of the polyp over 1 or multiple folds.[81] Pooled data suggest that ESD results in higher en-bloc and R0 resection rates as compared with EMR (93% vs 65% and 75% vs 60%, respectively) in the resection of

large HR-CAN lesions (mean size, 31.4 mm).[24] No data on recurrence rates specific to the endoscopic resection techniques used were reported. A recent meta-analysis reported significantly lower recurrence rates after ESD as compared with EMR in large (>20 mm) sporadic colorectal nonpolypoid lesions.[82] Thus, ESD could be considered as the first choice of technique in the endoscopic resection of HR-CAN >20 mm without signs of submucosal invasion because of the higher technical successes and probable lower recurrence rates.

Statement 11: Endoscopic local excision of HR-CAN should be performed by endoscopists with sufficient skills in both EMR and ESD techniques.

(Agreement, 88.2%; quality of evidence, no evidence)

To date, no studies are available comparing the outcomes of endoscopic resection of HR-CAN by expert versus nonexpert endoscopists. One older retrospective study by Brooker et al[83] reported that expert endoscopists had a significantly higher success rate as compared with nonexperts for the resection of sporadic sessile colonic polyps. The guideline of the European Society of Gastrointestinal Endoscopy recommends referring patients with nonlifting polyps without characteristics of DSI or lesions with high-risk features to an expert endoscopy center for evaluation before surgery is considered.[60,65] Furthermore, the guideline also states that large (>20 mm) sessile and laterally spreading or complex polyps should be removed by an appropriately trained and experienced endoscopist in an appropriately resourced endoscopy center. Finally, the guideline stipulates that ESD should be restricted to tertiary referral centers. The American Society for Gastrointestinal Endoscopy guideline states that referral to an expert or tertiary referral center is indicated for patients with lesions in a difficult location (eg, appendiceal valve) or if the endoscopist is not confident about removing the lesion.[64]

Both EMR and ESD can achieve an en-bloc resection of HR-CAN lesions. However, a recent meta-analysis suggested a superiority of ESD over EMR because of higher en-bloc and R0 resection rates in large nonpolypoid lesions.[24] In addition, ESD should be considered the first choice in cases of submucosal fibrosis. Because of the potential complexity of these procedures in patients with large nonpolypoid lesions or with submucosal fibrosis, we recommend referring patients with these kinds of lesions to centers experienced in EMR and ESD techniques.

Outcomes and follow-up of endoscopic resection of HR-CAN

Statement 12: Endoscopic resection should be captured by recording.

1. Technical success
   a. En-bloc resection
   b. R0 resection
   c. Adverse events (intra- or postprocedural bleeding, perforation, postcoagulation syndrome, need of emergency surgery, other)
2. Outcomes
   a. Local recurrence at 6 months and 3 years
   b. Surgery for recurrence after 1, 3, and 5 years.

(Agreement, 82.4%; quality of evidence, no evidence)

Endoscopy reporting elements capturing the different aspects of technical success and outcomes of endoscopic resection of HR-CAN lesions are currently not defined. Technical success in non-IBD lesions is often defined as the rates of en-bloc and R0 resection and adverse events. The most common adverse events for both EMR and ESD comprise bleeding and perforation.[60] Although these adverse events can be predominantly managed conservatively, adverse event–related (emergency) surgery was reported in 1%.[60] In addition, postcoagulation syndrome was considered an adverse event after endoscopic resection because the incidence varies from 1% (EMR) to 9% (ESD).[87] Because of the incidence of these adverse events in combination with potential dismal outcomes, documentation of these adverse events is warranted. Local recurrence (at 6 months and 3 years) and surgery for recurrence (after 1, 3, and 5 years) were proposed as outcome measures for endoscopic resection of HR-CAN.

Statement 13: The histologic report should at least include the following items:

1. Size (in mm)
2. Grade of dysplasia according the World Health Organization classification
3. Lateral resection margin (in mm, free if >.1 mm)
4. Deep resection margin (in mm, free if >.1 mm)

In case of submucosal invasion:

1. Maximum depth of submucosal (Sm) invasion in μm (taken from the deepest margin of the muscularis mucosae)
2. Lymphatic and/or venous invasion confirmed with D2-40 immunohistochemistry
3. Tumor budding (Bd1-3) according to the International Tumor Budding Consensus Conference
4. Grade of differentiation according to World Health Organization classification.

(Agreement, 94.1%; quality of evidence, no evidence)

Standardization of the histologic reporting of HR-CAN is virtually absent in the current guidelines. A detailed pathology report containing a number of standard data elements is essential for clinical decision-making and facilitates future research in this field. These standard data elements are size in millimeters, grade of dysplasia according to the World Health Organization, and both lateral and vertical/deep resection margin in millimeters.[60,64,65,88] A resection margin is considered free if it is >1-mm free margin, based on the fact that indeterminate margins or margins <1 mm are associated with high recurrence rates of 15% to 20%.[89]

For submucosal invasion, additional reporting on maximum depth of invasion (taken from the lowest fiber of the muscularis mucosae) and lymphatic and/or venous infiltration is recommended because it predicts lymph node metastasis.[90] Tumor cell budding appears to be a

promising marker for lymph node metastasis as well and has been found to have therapeutic consequences in sporadic lesions.[90] Although the role of tumor budding in the setting of IBD is presently unclear, a study reported the prognostic value of tumor budding of CD-associated small-bowel carcinomas.[91] Therefore, we suggest including tumor cell budding in the histology report after endoscopic resection of HR-CAN.

Statement 14: After complete endoscopic resection of HR-CAN, assessment of local recurrence should be performed within 3 to 6 months and annually thereafter if no residual disease is found.

(Agreement, 88.2%; quality of evidence, limited evidence)

To date, no studies have been conducted to assess the optimal follow-up strategy after endoscopic resection of CAN lesions. The American Society for Gastrointestinal Endoscopy– endorsed guideline recommends endoscopic surveillance between 3 and 6 months after a complete endoscopic resection in IBD patients.[1] The European Society of Gastrointestinal Endoscopy recommends performing endoscopic surveillance 3 to 6 months after the index treatment. If no recurrence is found, a follow-up total colonoscopy should be scheduled after 1 year.[60,65] After piecemeal resection or in cases of positive lateral margins without an indication for surgery, colonoscopy with biopsy sampling at 3 months is recommended.[60,64,65] A recent randomized controlled trial by Nakajima et al[92] studied the optimal interval for surveillance after piecemeal resection in non-IBD patients. All patients underwent postprocedural surveillance colonoscopy at 6, 12, and 24 months. The intervention group underwent an additional colonoscopy at 3 months. No significant differences in recurrence were observed between both groups.[92] Therefore, agreement was reached that endoscopic surveillance should be performed within 3 to 6 months and annually thereafter if no residual disease is found after complete endoscopic resection of HR-CAN.

DISCUSSION

The lack of high-quality evidence is the main limitation of this Delphi study. However, the methodologically rigorous and structured approach using a 3-step voting process allowed us to achieve consensus on the important and clinically relevant issues described here. The international expert panel from 12 different countries covered, in our view, the expertise relevant for the issues in question.

In conclusion, this is the first step in developing international consensus–based recommendations for endoscopic management of HR-CAN. Although the quality of available evidence was considered low, consensus was reached on several aspects of the management of HR-CAN. The present work and proposed standardization might be a useful foundation for future studies by offering greater standardization to the approach to colorectal CAN.

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Abbreviations: aCRN, advanced colorectal neoplasia; CAN, colitis-associated neoplasia; CD, Crohn's disease; CRC, colorectal cancer; DSI, deep submucosal invasion; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; HR-CAN, high-risk colitis-associated neoplasia; IBD, inflammatory bowel disease; LGD, low-grade dysplasia; LNPCP, large nonpedunculated colorectal polyp; UC, ulcerative colitis.

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APPENDIX 1

Search strings of the population, intervention, comparison, and outcomes

Statement 3: Nonpolypoid lesions and large (>20 mm) nonpedunculated colon polyps should be considered high-risk CAN.

Population, intervention, comparison, and outcomes

Question	Which polyps have the highest risk for progression to cancer in IBD?
P	IBD patients with nonpolypoid or large (>20 mm) polyps
I	All polyps
C	A specific risk profile based on descriptive features gross morphology and (virtual) chromoendoscopy
O	Percentage of risk of progression to cancer, risk of metachronous CAN

Search string: population, intervention, comparison, and outcomes

((Inflammatory Bowel Diseases [MeSH Terms]) OR (Inflammatory Bowel Disease*[Title/Abstract]) OR (inflammatory bowel disorder[Title/Abstract]) OR (IBD[Title/Abstract]) OR (colitis [MeSH Terms]) OR (colitis[Title/Abstract]) OR (ulcerative colitis[Title/Abstract]) OR (colitis ulcerosa[Title/Abstract]) OR (colitis, ulcerative[Title/Abstract]) OR (colitis gravis[Title/Abstract]) OR (proctocolitis[Title/Abstract]) OR (ulcerative proctocolitis[Title/Abstract]) OR (UC[Title/Abstract]) OR (Crohn Disease[Title/Abstract]) OR (Crohn's Disease[Title/Abstract]) OR (CD[Title/Abstract]) OR (inflammation AND colon[Title/Abstract]))

AND

((polyps [MeSH Terms] OR (polyp*[Title/Abstract]) OR (lesion[Title/Abstract])) AND ((non-polypoid [Title/Abstract] OR non-pedunculated [Title/Abstract] OR large [Title/Abstract] OR >20mm [Title/Abstract]) AND (Intestine, large [MeSH Terms]) OR (Large intestine [Title/Abstract]) OR (Cecum[Title/Abstract]) OR (Colon[Title/Abstract]) OR (Colon ascendens[Title/Abstract]) OR (Ascending colon [Title/Abstract]) OR (Colon descendens[Title/Abstract]) OR (Descending colon[Title/Abstract]) OR (Proximal colon[Title/Abstract]) OR (Distal colon[Title/Abstract]) OR (Sigmoid [Title/Abstract]) OR (Sigmoid colon[Title/Abstract]) OR (Rectum[Title/Abstract]) OR (Colorectal[Title/Abstract])))

AND

((Colorectal Neoplasms [MeSH Terms]) OR (colorectal neoplasm*[Title/Abstract]) OR (Intestinal Neoplasms [MeSH Terms]) OR (intestinal neoplasm*[Title/Abstract]) OR (neoplasms [MeSH Terms]) OR (neoplas*[Title/Abstract]) OR (precancerous conditions [MeSH Terms]) OR (precancerous condition*[Title/Abstract]) OR (cancer) OR (carcinoma*) OR (adenocarcinoma [MeSH Terms]) OR (adenocarcinoma*[Title/Abstract]) OR (malignancy[Title/Abstract]) OR (dysplasia[Title/Abstract]) OR (high-grade dysplasia[Title/Abstract]) OR (HGD[Title/Abstract]) OR (low-grade dysplasia[Title/Abstract]) OR (LGD[Title/Abstract]) OR (CRC[Title/Abstract]))

Hits: 2.747

Statement 8: HR-CAN should preferably be removed en bloc to lower the risk of recurrence and optimize the histologic assessment.

Population, intervention, comparison, and outcomes

Question	Is en bloc resection preferred over a piecemeal resection for endoscopic resection of colitis-associated dysplasia?
P	Patients with HR-CAN in IBD
I	En-bloc resection
C	Piecemeal resection
O	Progression to cancer, recurrence, need for surgery <12-24 months, histologic assessment

Search string: population, intervention, comparison, and outcomes

((Inflammatory Bowel Diseases [MeSH Terms]) OR (Inflammatory Bowel Disease*) OR (inflammatory bowel disorder) OR (IBD) OR (colitis [MeSH Terms]) OR (colitis) OR (ulcerative colitis) OR (colitis ulcerosa) OR (colitis, ulcerative) OR (colitis gravis) OR (proctocolitis) OR (ulcerative proctocolitis) OR (UC) OR (Crohn Disease) OR (Crohn's Disease) OR (CD) OR (inflammation AND colon))

AND

((Colorectal Neoplasms [MeSH Terms]) OR (colorectal neoplasm*) OR (Intestinal Neoplasms [MeSH Terms]) OR (intestinal neoplasm*) OR (neoplasms [MeSH Terms]) OR (neoplas*) OR (precancerous conditions [MeSH Terms]) OR (precancerous condition*) OR (cancer) OR (carcinoma*) OR (adenocarcinoma [MeSH Terms]) OR (adenocarcinoma*) OR (malignancy) OR (dysplasia) OR (high-grade dysplasia) OR (HGD) OR (low-grade dysplasia) OR (LGD) OR (CRC))

AND

((en bloc resection) AND ((endoscopic mucosal resection) OR (EMR) OR (endoscopic submucosal dissection) OR (ESD) OR (endoscopic full thickness resection) OR (eFTR))

AND

(((piecemeal) AND (endoscopic mucosal resection) OR (EMR) OR (endoscopic resection)) OR (pEMR) OR (snare) OR (polypectomy)))

Hits: 29

Statement 9: HR-CAN <20 mm with good lifting (Kato I and II) can be removed using en-bloc (including underwater) EMR.

Population, intervention, comparison, and outcomes

Question	Can en-bloc (underwater) EMR be performed for HR-CAN <20 mm with good lifting (Kato I and II)?
P	Patients with HR-CAN <20 mm with good lifting (Kato I and II)
I	En-bloc (underwater) EMR
C	Other techniques of resection
O	Progression to cancer, recurrence, need for surgery <12-24 months, histologic assessment

Search string: population, intervention, comparison, and outcomes

((Inflammatory Bowel Diseases [MeSH Terms]) OR (Inflammatory Bowel Disease*) OR (inflammatory bowel disorder) OR (IBD) OR (colitis [MeSH Terms]) OR (colitis) OR (ulcerative colitis) OR (colitis ulcerosa) OR (colitis, ulcerative) OR (colitis gravis) OR (proctocolitis) OR (ulcerative proctocolitis) OR (UC) OR (Crohn Disease) OR (Crohn's Disease) OR (CD) OR (inflammation AND colon))

AND

((Colorectal Neoplasms [MeSH Terms]) OR (colorectal neoplasm*) OR (Intestinal Neoplasms [MeSH Terms]) OR (intestinal neoplasm*) OR (neoplasms [MeSH Terms]) OR (neoplas*) OR (precancerous conditions [MeSH Terms]) OR (precancerous condition*) OR (cancer) OR (carcinoma*) OR (adenocarcinoma [MeSH Terms]) OR (adenocarcinoma*) OR (malignancy) OR (dysplasia) OR (high-grade dysplasia) OR (HGD) OR (low-grade dysplasia) OR (LGD) OR (CRC))

AND

((en bloc resection) AND ((endoscopic mucosal resection) OR (EMR) OR (UEMR)))

AND

((good lifting) OR (Kato I) OR Kato (II) OR (lifting) OR submucosal fibrosis))

Hits: 9

Statement 10: HR-CAN <20 mm without good lifting (Kato III and IV) or HR-CAN >20 mm without signs of deep submucosal invasion should be removed with techniques that preferably allow en-bloc resection.

Population, intervention, comparison, and outcomes

Question	Can en bloc be performed for HR-CAN <20 mm without good lifting (Kato III and IV) or HR-CAN >20 mm without signs of deep submucosal invasion?
P	Patients with HR-CAN <20 mm without good lifting (Kato III and IV) or HR-CAN >20 mm without signs of deep submucosal invasion
I	Techniques allowing en-bloc resection
C	Other techniques of resection
O	Progression to cancer, recurrence, need for surgery <12-24 months, histologic assessment

Search string: population, intervention, comparison, and outcomes

((Inflammatory Bowel Diseases [MeSH Terms]) OR (Inflammatory Bowel Disease*) OR (inflammatory bowel disorder) OR (IBD) OR (colitis [MeSH Terms]) OR (colitis) OR (ulcerative colitis) OR (colitis ulcerosa) OR (colitis, ulcerative) OR (colitis gravis) OR (proctocolitis) OR (ulcerative proctocolitis) OR (UC) OR (Crohn Disease) OR (Crohn's Disease) OR (CD) OR (inflammation AND colon))

AND

((Colorectal Neoplasms [MeSH Terms]) OR (colorectal neoplasm*) OR (Intestinal Neoplasms [MeSH Terms]) OR (intestinal neoplasm*) OR (neoplasms [MeSH Terms]) OR (neoplas*) OR (precancerous conditions [MeSH Terms]) OR (precancerous condition*) OR (cancer) OR (carcinoma*) OR (adenocarcinoma [MeSH Terms]) OR (adenocarcinoma*) OR (malignancy) OR (dysplasia) OR (high-grade dysplasia) OR (HGD) OR (low-grade dysplasia) OR (LGD) OR (CRC))

AND

((en bloc resection) OR (endoscopic submucosal dissection) OR (ESD) OR (EMR))

AND

((non-lifting) OR (Kato III) OR Kato (IV) OR (lifting) OR submucosal fibrosis))

Hits: 17

Statement 11: Endoscopic local excision of HR-CAN should be performed by endoscopists with sufficient skills in both EMR and ESD techniques.

Population, intervention, comparison, and outcomes

Question	Should endoscopic resection of HR-CAN be formed by skilled/expert endoscopists?
P	Patients with HR-CAN suitable for endoscopic resection
I	Skilled/expert endoscopists
C	All endoscopists
O	Progression to cancer, recurrence, need for surgery <12-24 months, histologic assessment

Search string: population, intervention, comparison, and outcomes

((Inflammatory Bowel Diseases [MeSH Terms]) OR (Inflammatory Bowel Disease*[Title/Abstract]) OR (inflammatory bowel disorder[Title/Abstract]) OR (IBD[Title/Abstract]) OR (colitis [MeSH Terms]) OR (colitis[Title/Abstract]) OR (ulcerative colitis[Title/Abstract]) OR (colitis ulcerosa[Title/Abstract]) OR (colitis, ulcerative[Title/Abstract]) OR (colitis gravis[Title/Abstract]) OR (proctocolitis[Title/Abstract]) OR (ulcerative proctocolitis[Title/Abstract]) OR (UC [Title/Abstract]) OR (Crohn Disease[Title/Abstract]) OR (Crohn's Disease[Title/Abstract]) OR (CD[Title/Abstract]) OR (inflammation AND colon[Title/Abstract]))

AND

((Colorectal Neoplasms [MeSH Terms]) OR (colorectal neoplasm* [Title/Abstract]) OR (Intestinal Neoplasms [MeSH Terms]) OR (intestinal neoplasm*) OR (neoplasms [MeSH Terms]) OR (neoplas*) OR (precancerous conditions [MeSH Terms]) OR (precancerous condition*) OR (cancer) OR (carcinoma*) OR (adenocarcinoma [MeSH Terms]) OR (adenocarcinoma*) OR (malignancy) OR (dysplasia) OR (high-grade dysplasia) OR (HGD) OR (low-grade dysplasia) OR (LGD) OR (CRC))

AND

((skilled) OR (expert) OR (skilled endoscopist*) OR (expert endoscopist*) OR (tertiary referral center) OR (expert center))

AND

((en bloc resection) AND ((endoscopic mucosal resection) OR (EMR) OR (endoscopic submucosal dissection) OR (ESD) OR (endoscopic full thickness resection) OR (eFTR) OR (piecemeal) AND (endoscopic mucosal resection) OR (EMR) OR (endoscopic resection) OR (pEMR) OR (snare) OR (polypectomy))

Hits: 3

Population, intervention, comparison, and outcomes

Question	Can en-bloc resection be performed for HR-CAN >20 mm without signs of deep submucosal invasion?
P	Patients with HR-CAN >20 mm without signs of deep submucosal invasion
I	En-bloc resection
C	Other techniques of resection
O	Progression to cancer, recurrence, need for surgery <12-24 months, histologic assessment

Search string: population, intervention, comparison, and outcomes

((Inflammatory Bowel Diseases [MeSH Terms]) OR (Inflammatory Bowel Disease*) OR (inflammatory bowel disorder) OR (IBD) OR (colitis [MeSH Terms]) OR (colitis) OR (ulcerative colitis) OR (colitis ulcerosa) OR (colitis, ulcerative) OR (colitis gravis) OR (proctocolitis) OR (ulcerative proctocolitis) OR (UC) OR (Crohn Disease) OR (Crohn's Disease) OR (CD) OR (inflammation AND colon))

AND

((Colorectal Neoplasms [MeSH Terms]) OR (colorectal neoplasm*) OR (Intestinal Neoplasms [MeSH Terms]) OR (intestinal neoplasm*) OR (neoplasms [MeSH Terms]) OR (neoplas*) OR (precancerous conditions [MeSH Terms]) OR (precancerous condition*) OR (cancer) OR (carcinoma*) OR (adenocarcinoma [MeSH Terms]) OR (adenocarcinoma*) OR (malignancy) OR (dysplasia) OR (high-grade dysplasia) OR (HGD) OR (low-grade dysplasia) OR (LGD) OR (CRC))

AND

((en bloc resection) OR (endoscopic submucosal dissection) OR (ESD))

AND

((large polyp*) OR (> 20 millimetres) OR (>20 mm))

Hits: 46

HR-CAN, High-risk colitis-associated neoplasia; *IBD*, inflammatory bowel disease.

APPENDIX 2

Detailed overview of the third and final round of voting for consensus agreement (n = 17) and assessment of quality of evidence (n = 15)

Statement 1: We suggest to adopt the term colitis-associated neoplasia (CAN) for all neoplastic lesions detected in a section of previously or presently inflamed colon.

Strongly disagree	0%
Disagree	0%
Neutral	0%
Agree	52.9%
Strongly agree	47.1%
No evidence	40%
Conflicting evidence	6.7%
Limited evidence	33.3%
Moderate evidence	20%
Strong evidence	0%

Agreement: 100%

Quality of evidence: no evidence

Statement 2: Extent of previous or present inflammation should have been or should be confirmed by endoscopy and/or histology.

Strongly disagree	0%
Disagree	0%
Neutral	0%
Agree	76.5%
Strongly agree	23.5%
No evidence	33.3%
Conflicting evidence	13.3%
Limited evidence	26.7%
Moderate evidence	26.7%
Strong evidence	0%

Agreement: 100%

Quality of evidence: no evidence

Statement 3: Nonpolypoid lesions and large (>20 mm) nonpedunculated colon polyps should be considered high-risk CAN.

Strongly disagree	0%
Disagree	5.9%
Neutral	5.9%
Agree	58.8%
Strongly agree	29.4%
No evidence	20%
Conflicting evidence	20%
Limited evidence	40%
Moderate evidence	20%
Strong evidence	0%

Agreement: 88.2%

Quality of evidence: limited evidence

Statement 4: Careful examination of the colon (preferably using enhanced endoscopic imaging) should precede local excision of HR-CAN.

Strongly disagree	0%
Disagree	0%
Neutral	0%
Agree	17.6%
Strongly agree	82.4%
No evidence	6.7%
Conflicting evidence	6.7%
Limited evidence	13.3%
Moderate evidence	60%
Strong evidence	13.3%

Agreement: 100%

Quality of evidence: moderate evidence

Statement 5: An HR-CAN lesion is considered endoscopically resectable if

1. The lesion has distinct margins
2. The lesion can (preferably) be removed en bloc with clear deep and lateral resection margins
   and there is *no* evidence of
3. Synchronous *invisible* dysplasia
4. Moderate-to-severe inflammation of mucosa surrounding the area with HR-CAN interfering with delineation of the lesion
5. Signs of deep submucosal invasion.

Strongly disagree	0%
Disagree	23.5%
Neutral	0%
Agree	47.1%
Strongly agree	29.4%
No evidence	20%
Conflicting evidence	0%
Limited evidence	46.6%
Moderate evidence	26.7%
Strong evidence	6.7%

Agreement: 76.5%

Quality of evidence: limited evidence

Statement 6: Surgical resection is indicated when HR-CAN is nonresectable.

Strongly disagree	0%
Disagree	0%
Neutral	0%
Agree	47.1%
Strongly agree	52.9%
No evidence	26.7%
Conflicting evidence	0%
Limited evidence	20%
Moderate evidence	40%
Strong evidence	13.3%

Agreement: 100%

Quality of evidence: moderate evidence

Statement 7: All suspected HR-CANs should be assessed according to a standardized approach and recorded to the endoscopy report. The description should include at least the following features:

1. Size, delineation, and location
2. Description of gross morphology
   a. Granular/nongranular
   b. Paris classification
2. Assessment of the pit and vascular pattern using enhanced endoscopic imaging
3. Assessment of endoscopic activity of the colitis in the segment, harboring the dysplastic lesion (eg, using the Mayo subset index, UC endoscopic index of severity, or simple endoscopic score for CD).

Strongly disagree	0%
Disagree	0%
Neutral	5.9%
Agree	41.2%
Strongly agree	52.9%
No evidence	26.7%
Conflicting evidence	0%
Limited evidence	33.3%
Moderate evidence	33.3%
Strong evidence	6.7%

Agreement: 94.1%

Quality of evidence: limited evidence

Statement 8: HR-CAN should preferably be removed en bloc to lower the risk of recurrence and optimize the histologic assessment.

Strongly disagree	0%
Disagree	0%
Neutral	5.8%
Agree	47.1%
Strongly agree	47.1%
No evidence	26.7%
Conflicting evidence	6.6%
Limited evidence	40%
Moderate evidence	26.7%
Strong evidence	0%

Agreement: 94.1%

Quality of evidence: limited evidence

Statement 9: HR-CAN <20 mm with good lifting (Kato I and II) can be removed using en-bloc (including underwater) EMR.

Strongly disagree	0%
Disagree	0%
Neutral	5.9%
Agree	76.5%
Strongly agree	17.6%
No evidence	20%
Conflicting evidence	6.7%
Limited evidence	40%
Moderate evidence	33.3%
Strong evidence	0%

Agreement: 94.1%

Quality of evidence: moderate evidence

Statement 10: HR-CAN <20 mm without good lifting (Kato III and IV) or HR-CAN >20 mm without signs of deep submucosal invasion should be removed with techniques that preferably allow en-bloc resection.

Strongly disagree	5.9%
Disagree	0%
Neutral	11.8%
Agree	47.1%
Strongly agree	35.3%
No evidence	40%
Conflicting evidence	6.7%
Limited evidence	20%
Moderate evidence	33.3%
Strong evidence	0%

Agreement: 82.4%

Quality of evidence: no evidence

Statement 11: Endoscopic local excision of HR-CAN should be performed by endoscopists with sufficient skills in both EMR and ESD techniques.

Strongly disagree	5.9%
Disagree	0%
Neutral	5.9%
Agree	29.4%
Strongly agree	58.8%
No evidence	40%
Conflicting evidence	6.7%
Limited evidence	40%
Moderate evidence	13.3%
Strong evidence	0%

Agreement: 88.2%

Quality of evidence: no evidence

Statement 12: Endoscopic resection should be captured by recording

1. Technical success
   a. En-bloc resection
   b. R0 resection
   c. Adverse events (intra- or postprocedural bleeding, perforation, postcoagulation syndrome, need of emergency surgery, other)
2. Outcomes
   a. Local recurrence at 6 months and 3 years
   b. Surgery for recurrence after 1, 3, and 5 years.

Strongly disagree	0%
Disagree	11.8%
Neutral	5.9%
Agree	58.9%
Strongly agree	23.5%
No evidence	53.3%
Conflicting evidence	0%
Limited evidence	53.3%
Moderate evidence	6.6%
Strong evidence	0%

Agreement: 82.4%

Quality of evidence: no evidence

Statement 13: The histologic report should at least include the following items:

1. Size (in mm)
2. Grade of dysplasia according the World Health Organization classification
3. Lateral resection margin (in mm, free if >.1 mm)
4. Deep resection margin (in mm, free if >.1 mm)

In case of submucosal invasion:

1. Maximum depth of submucosal (Sm) invasion in μm (taken from the deepest margin of the muscularis mucosae)
2. Lymphatic and/or venous invasion confirmed with D2-40 immunohistochemistry
3. Tumor budding (Bd1-3) according to the International Tumor Budding Consensus Conference
4. Grade of differentiation according to World Health Organization classification.

Strongly disagree	0%
Disagree	5.9%
Neutral	0%
Agree	52.9%
Strongly agree	41.2%
No evidence	33.3%
Conflicting evidence	13.4%
Limited evidence	26.7%
Moderate evidence	13.3%
Strong evidence	13.3%

Agreement: 94.1%

Quality of evidence: no evidence

Statement 14: After complete endoscopic resection of HR-CAN, assessment of local recurrence should be performed within 3 to 6 months and annually thereafter if no residual disease is found.

Strongly disagree	0%
Disagree	0%
Neutral	11.8%
Agree	64.7%
Strongly agree	23.5%
No evidence	33.3%
Conflicting evidence	0%
Limited evidence	46.7%
Moderate evidence	20%
Strong evidence	0%

Agreement: 88.2%

Quality of evidence: limited evidence