Thieme

Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline

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Bibliography

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Appendix e1, e2
Online content viewable at: https://www.thieme-connect.com/DOI/DOI?10.1055/s-0043-102569

MAIN RECOMMENDATIONS

1 ESGE recommends cold snare polypectomy (CSP) as the preferred technique for removal of diminutive polyps (size ≤ 5 mm). This technique has high rates of complete resection, adequate tissue sampling for histology, and low complication rates. (High quality evidence, strong recommendation.)

2 ESGE suggests CSP for sessile polyps 6 – 9 mm in size because of its superior safety profile, although evidence comparing efficacy with hot snare polypectomy (HSP) is lacking. (Moderate quality evidence, weak recommendation.)

3 ESGE suggests HSP (with or without submucosal injection) for removal of sessile polyps 10 – 19 mm in size. In most cases deep thermal injury is a potential risk and thus submucosal injection prior to HSP should be considered. (Low quality evidence, strong recommendation.)

4 ESGE recommends HSP for pedunculated polyps. To prevent bleeding in pedunculated colorectal polyps with head ≥ 20 mm or a stalk ≥ 10 mm in diameter, ESGE recommends pretreatment of the stalk with injection of dilute adrenaline and/or mechanical hemostasis. (Moderate quality evidence, strong recommendation.)

5 ESGE recommends that the goals of endoscopic mucosal resection (EMR) are to achieve a completely snare-resected lesion in the safest minimum number of pieces, with adequate margins and without need for adjunctive ablative techniques. (Low quality evidence; strong recommendation.)

6 ESGE recommends careful lesion assessment prior to EMR to identify features suggestive of poor outcome. Features associated with incomplete resection or recurrence include lesion size > 40 mm, ileocecal valve location, prior failed attempts at resection, and size, morphology, site, and access (SMSA) level 4. (Moderate quality evidence; strong recommendation.)

7 For intraprocedural bleeding, ESGE recommends endoscopic coagulation (snare-tip soft coagulation or coagulating forceps) or mechanical therapy, with or without the combined use of dilute adrenaline injection. (Low quality evidence, strong recommendation.)

An algorithm of polypectomy recommendations according to shape and size of polyps is given (▶ **Fig. 1**).

This Guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE). The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was adopted to define the strength of recommendations and the quality of evidence.

Introduction

The endoscopic removal of colorectal polyps reduces the incidence and mortality of colorectal cancer (CRC) and is considered an essential skill for all endoscopists who perform colonoscopy [1 – 3]. Various polypectomy techniques and devices are available, their use often varying based on local preferences and availability [4 – 6]. This evidence-based Guideline was commissioned by the European Society of Gastrointestinal Endoscopy (ESGE). It addresses all major issues concerning the practical use of polypectomy and endoscopic mucosal resection (EMR), to inform and underpin this fundamental technique in colonoscopy and in CRC prevention.

This Guideline does not address management of anticoagulants and other medications in the periprocedural setting, nor post-polypectomy surveillance or quality measurements, as these are addressed in separate Guidelines [7 – 9].

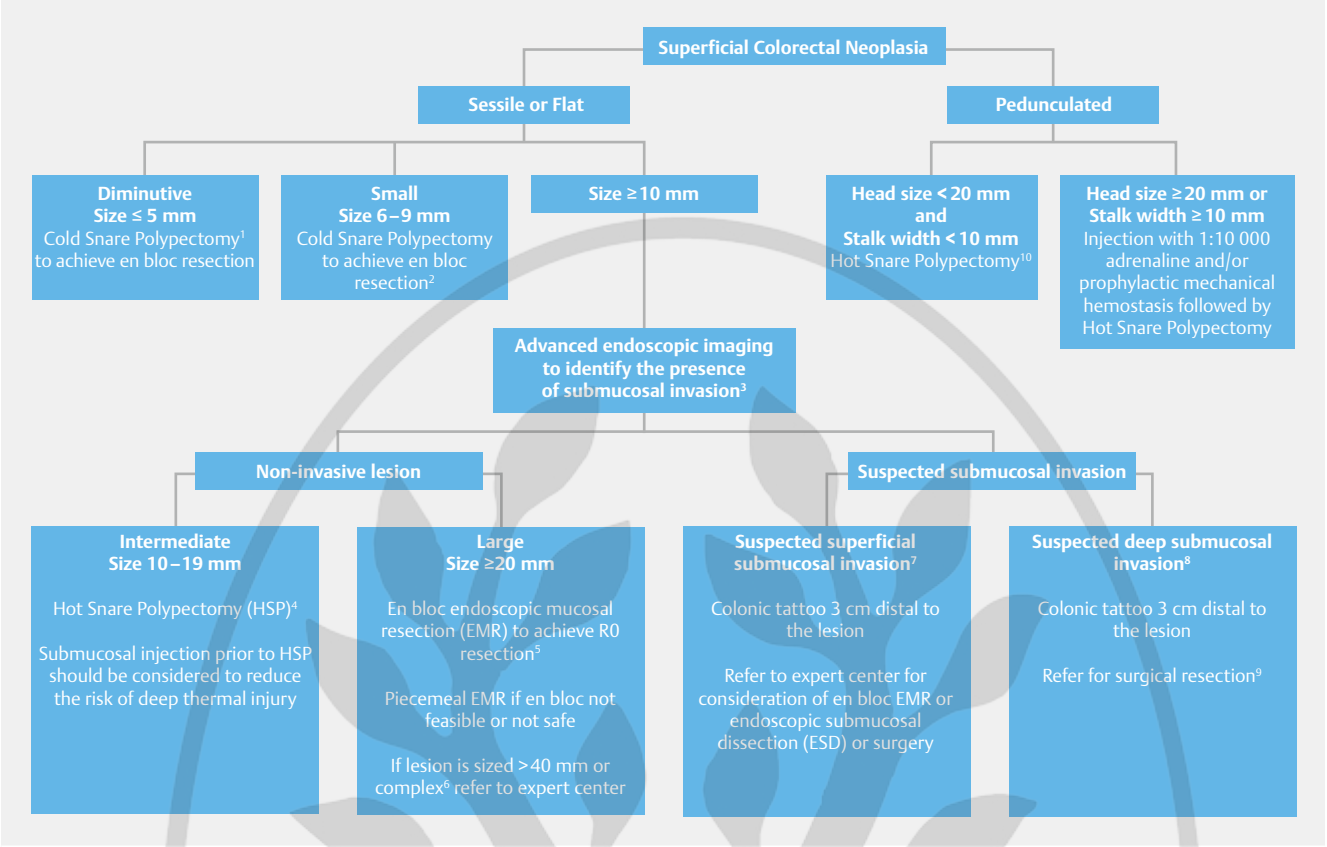
Methods

The European Society of Gastrointestinal Endoscopy (ESGE) commissioned this Guideline and appointed a Guideline leader (M. F.) who invited the listed authors to participate in the project development. The key questions were prepared by the coordinating team (M. F, A. M., M. J. B., C. H.) and then approved by the other members. The coordinating team formed task force subgroups, each with its own leader, and divided the key topics (polyp classification, polypectomy for polyps sized < 20 mm, EMR for polyps ≥ 20 mm, technical considerations, adverse events, histopathology) among these task forces (see **Appendix 1,** available online in Supplementary material).

Each task force performed a systematic literature search to prepare evidence-based and well-balanced statements on their assigned key questions. Searches were performed in Medline. Articles were first selected by title; their relevance was then confirmed by review of the corresponding manuscripts, and articles with content that was considered irrelevant were excluded. Evidence tables were generated for each key question, summarizing the evidence of the available studies (see **Appendix 2,** available online in Supplementary material). For important outcomes, articles were individually assessed by the level of evidence and strength of recommendation according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system [10, 11].

ABBREVIATIONS

ASGE	American Society for Gastrointestinal Endoscopy
CBF	cold biopsy forceps
CI	confidence interval
CRC	colorectal cancer
CSP	cold snare polypectomy
EMR	endoscopic mucosal resection
ESD	endoscopic submucosal dissection
ESGE	European Society of Gastrointestinal Endoscopy
FICE	flexible spectral imaging color enhancement (also Fuji Intelligent Chromo Endoscopy)
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBF	hot biopsy forceps
HD-WLE	high definition white light endoscopy
HSP	hot snare polypectomy
IPB	intraprocedural bleeding
I-SCAN	i-SCAN digital contrast (Pentax; image processing providing digital image-enhanced endoscopy [IEE])
LSL	laterally spreading lesion
LST	laterally spreading tumor
MP	muscularis propria
NBI	narrow-band imaging
NICE	NBI International Colorectal Endoscopic Classification
NPV	negative predictive value
PEC	prophylactic endoscopic coagulation
PPB	post polypectomy bleeding
PPV	positive predictive value
RCT	randomized controlled trial
RR	relative risk
SMI	submucosal invasion
SMSA	size, morphology, site, and access
STSC	snare-tip soft coagulation
TEMS	transanal endoscopic microsurgery
WHO	World Health Organization
WLE	white light endoscopy



▶ **Fig. 1** Recommended resection techniques for colorectal polyps according to shape and size. [1] Cold biopsy forceps could be considered as a second-line option, but should only be used for polyps of size ≤ 3 mm where cold snare polypectomy (CSP) is technically difficult. [2] When en bloc resection is not achieved, oligo-piecemeal excision is acceptable; however complete retrieval of specimens for histology is necessary. [3] Standard chromoendoscopy if advanced endoscopic imaging is not available. [4] Piecemeal cold snare resection may be considered in cases where risk of deep thermal injury is high or unable to be tolerated, but further evidence of efficacy is required. [5] This may be feasible for lesions of size ≤ 25 mm and especially those in the left colon or rectum. [6] Difficult location or poor access (e. g. ileocecal valve, periappendiceal, or anorectal junction); prior failed attempts at resection; non-lifting with submucosal injection; size, morphology, site, and access (SMSA) level 4. [7] Kudo Vi, Sano IIIa. [8] Kudo Vn, Sano IIIb, narrow-band imaging (NBI) International Colorectal Endoscopic (NICE) classification 3, polyp morphology including ulceration, excavation, deep demarcated depression. [9] Surgical resection is required because both the lesion and the local draining lymph nodes require excision. [10] When bleeding risk is high because of antiplatelet or anticoagulant medication or coagulopathy, an individualized approach is justified and prophylactic mechanical hemostasis should be considered.

Each task force proposed statements on their assigned key questions which were discussed and voted on during a guideline meeting in Barcelona in October 2015. In July 2016, a draft prepared by the leaders and coordinating team was sent to all group members. The manuscript was also reviewed by two members of the ESGE Governing Board and sent for further comments to the National Societies and Individual Members. After agreement on a final version, the manuscript was submitted to the journal *Endoscopy* for publication. All authors agreed on the final revised manuscript.

This Guideline was issued in 2017 and will be considered for review and update in 2022 or sooner if new and relevant evidence becomes available. Any updates to the Guideline in the interim will be noted on the ESGE website: http://www.esge.com/esge-guidelines.html.

1. Definition, classification, removal, and retrieval of polyps

RECOMMENDATION

ESGE recommends that gross morphology of polyps should be described using the Paris classification system and sized in millimeters. (Moderate quality evidence; strong recommendation.)

RECOMMENDATION

ESGE recommends that for flat and sessile (Paris II and Is) polyps ≥ 10 mm, termed laterally spreading lesions (LSLs) or laterally spreading tumors (LSTs), surface morphology should be also described as granular or nongranular. (Moderate quality evidence; strong recommendation.)

The Paris classification of superficial neoplastic lesions (▶ **Table 1**) [12] updated in 2005 [13], has been adapted from the Kudo classification of early colorectal cancers published in 1993 [14], The Paris classification allows prediction of advanced histology and invasive cancer (type IIc lesions) [15 – 17] and it is associated with completeness of endoscopic resection [18]. However, its validity has been questioned as, in a recent study, the interobserver agreement between 7 Western expert endoscopists was only moderate (kappa 0.42) and pairwise agreement, before and after training, was also low at 60 % [19].

LSTs, described in the original Kudo classification, were not included in the Paris classification. LSTs have been further subdivided into granular (homogeneous or nodular-mixed) and nongranular (elevated or pseudodepressed) types because of substantial differences in the risk of invasive cancer [13, 20, 21].

The size of both polypoid and nonpolypoid lesions has been shown to be an additional predictive factor for the risk of invasive cancer, allowing a more accurate stratification of the risk according to morphology and size [12, 15 – 17].

RECOMMENDATION

ESGE recommends that all polyps be resected except for diminutive (≤ 5 mm) rectal and rectosigmoid polyps that are predicted with high confidence to be hyperplastic. (High quality evidence; strong recommendation.)

RECOMMENDATION

ESGE recommends retrieval of all resected polyps for histopathological examination. In expert centers, where optical diagnosis may be made with a high degree of confidence, a "resect and discard" strategy may be considered for diminutive polyps. (Moderate quality evidence; strong recommendation.)

Diminutive colonic polyps present a very low risk of cancer (0 – 0.6 %) that justifies a "resect and discard" strategy. For hyperplastic polyps located in the rectosigmoid, a "diagnose and leave behind" strategy is appropriate because these harbor an even lower risk of cancer [22]. To guide decisions for diminutive colonic polyps, their histopathology should be assessed during endoscopy in real time with a high accuracy, and the American Society for Gastrointestinal Endoscopy (ASGE) has proposed that, in order to:

1. "Diagnose and leave behind" rectosigmoid diminutive hyperplastic polyps, the technology used should provide a negative predictive value (NPV) ≥ 90 % for adenomatous histopathology;
2. "Resect and discard" diminutive polyps, the technology, when used with high confidence and in combination with the histopathological assessment of polyps > 5 mm, should provide a ≥ 90 % agreement in assignment of post-polypectomy surveillance intervals compared to decisions based on histopathological assessment of all polyps [23].

▶ **Table 1** The original Paris classification of superficial neoplastic lesions [12 – 14].

Pedunculated	Ip
Semipedunculated	Isp
Sessile, higher than height of closed forceps (2.5 mm)	Is
Slightly elevated, below height of closed forceps (2.5 mm)	IIa
Completely flat lesion, does not protrude above mucosal surface	IIb
Slightly depressed, lower than mucosa but depth less than 1.2 mm	IIc
Excavated/ulcerated, deep ulcer below mucosa below 1.2 mm	III

A meta-analysis showed that the NPVs of narrow band imaging (NBI), flexible spectral imaging color enhancement (FICE; also Fuji Intelligent Chromo Endoscopy) and i-SCAN digital contrast (I-SCAN) for adenomatous polyp histology of small and diminutive colorectal polyps were, for all endoscopists, 91 %, 84 %, and 80 %, respectively; in expert and novice hands, respectively, the NPVs were 93 % and 87 % (NBI), 96 % and 72 % (FICE), and 80 % and 80 % (I-SCAN) [24 – 26]. Therefore, NBI complies with the abovementioned requirements for both strategies. The important caveats with regard to real-time optical diagnosis concern the endoscopist's expertise in optical biopsy and degree of confidence.

2. Resection of polyps < 20 mm in size

2.1 Resection of diminutive polyps (≤ 5 mm)

RECOMMENDATION

ESGE recommends cold snare polypectomy (CSP) as the preferred technique for removal of diminutive polyps (size ≤ 5 mm). This technique has high rates of complete resection, adequate tissue sampling for histology, and low complication rates. (High quality evidence; strong recommendation.)

Studies show that cold snare polypectomy (CSP) is superior to cold biopsy forceps (CBF) for completeness of diminutive polyp resection. In a randomized controlled trial (RCT) that included 117 diminutive polyps sized < 5 mm in 52 consecutive patients, the rate of histologic eradication was significantly higher in the

CSP group than in the CBF group (93 % vs. 76 %, $P = 0.009$). Furthermore, the time taken for polypectomy was significantly shorter in the CSP group (14 s vs. 22 s, $P < 0.001$) [27]. In another RCT that included 145 polyps sized < 7 mm, the complete resection rate for adenomatous polyps was significantly higher in the CSP group compared with the CBF group (96.6 % vs. 82.6 %; $P = 0.01$) [28]. CSP also avoids the adverse events associated with thermal electrocautery in hot biopsy forceps (HBF) and hot snare techniques.

RECOMMENDATION

ESGE recommends against the use of cold biopsy forceps (CBF) excision because of high rates of incomplete resection. In the case of a polyp sized 1 – 3 mm where cold snare polypectomy is technically difficult or not possible, cold biopsy forceps may be used. (Moderate quality evidence; strong recommendation.)

In a prospective study of 52 patients with diminutive polyps that were removed by CBF until no residual polyp tissue was visible, the polypectomy sites were then excised by EMR. The EMR histology showed that only 39 % of the polyps were completely resected using CBF [29]. However, higher complete resection rates have been demonstrated in another study where CBF excision of 86 diminutive polyps was performed with chromoendoscopy until no visible polyp was observed. Each polyp base was then resected using EMR. The complete resection rate was 92 % for all diminutive adenomas (95 % confidence interval [95 %CI] 85.8 – 98.8 %) and 100 % for 1 – 3-mm adenomas (95 %CI 81.5 – 100 %) [30]. Furthermore, in a retrospective study that evaluated the results from 102 jumbo biopsy forceps polypectomy and 161 standard biopsy forceps polypectomy, one-bite CBF polypectomy using either standard or jumbo forceps achieved complete resection for diminutive polyps < 3 mm, though more bites were required with standard forceps for polyps sized 4 – 5 mm [31].

RECOMMENDATION

ESGE recommends against the use of hot biopsy forceps (HBF) because of high rates of incomplete resection, inadequate tissue sampling for histopathological examination, and unacceptably high risks of adverse events in comparison with snare excision (deep thermal injury and delayed bleeding). (High quality evidence; strong recommendation.)

In a prospective study involving 62 diminutive rectosigmoid polyps removed via HBF, 17 % had persisting viable polyp remnants as shown during follow-up flexible sigmoidoscopy 1 – 2 weeks later [32]. Another prospective study involving patients with diminutive rectal adenomas found that the rate of remnant adenoma tissue after HBF polypectomy was 10.8 % [33]. The overall diagnostic quality of specimens removed by HBF was shown to be inferior to those removed by jumbo CBF in a prospective study (80 % vs. 96 %; $P < 0.001$); furthermore, 92 % of HBF specimens in this study demonstrated cautery damage or crush artifact [34]. In a retrospective study of 1964 diminutive polyps in 753 consecutive colonoscopies, 1525 were removed by HBF, 436 were removed by CBF, and 3 were removed by snare. The risk of significant hemorrhage with HBF was 0.4 % overall, with the risk highest in the right colon (1.3 % in cecum and 1.0 % in the ascending colon) [35]. High rates (32 % – 44 %) of transmural colonic injury with HBF were demonstrated in animal studies [36, 37].

2.2 Resection of small polyps (6 – 9 mm)

RECOMMENDATION

ESGE recommends snare polypectomy for sessile polyps 6 – 9 mm in size. ESGE recommends against the use of biopsy forceps for resection of such polyps because of high rates of incomplete resection. (High quality evidence; strong recommendation.)

In an RCT of CSP versus CBF, the rate of residual neoplastic tissue found after polypectomy for polyps sized 5 – 7 mm was significantly lower in the CSP group compared with the CBF polypectomy group (6.2 % vs 29.7 %; $P = 0.13$) [28]. A similarly low rate of residual neoplastic tissue (6.8 %) was found in a prospective study that evaluated hot snare polypectomy (HSP) for polyps sized 5 – 9 mm [38].

RECOMMENDATION

ESGE suggests CSP for sessile polyps 6 – 9 mm in size because of its superior safety profile, although evidence comparing efficacy with HSP is lacking. (Moderate quality evidence; weak recommendation.)

An RCT of HSP vs. CSP for polyps up to 10 mm in size in 70 patients receiving anticoagulation treatment found that there were significantly higher rates of intraprocedural bleeding (23 % vs. 5.7 %, $P = 0.042$) and post-procedural bleeding requiring hemostasis (14 % vs. 0 %; $P = 0.027$) in the HSP group compared to the CSP group. Complete polyp retrieval rates were equivalent (94 % vs. 93 %) [39]. Another RCT found higher rates of intraprocedural bleeding for CSP vs. HSP (9.1 % vs. 1.0 %; $P < 0.001$) for 3 – 8-mm polyps, although bleeding resolved spontaneously in all cases and therefore was of little clinical significance [40]. In another RCT involving 80 patients with polyps sized ≤ 8 mm, no bleeding requiring hemostasis occurred in the HSP or in the CSP group. However, post-procedure abdominal symptoms were more common in the HSP group (20.0 % vs. 2.5 %; $P = 0.029$), and procedure time was significantly shorter with CSP [41]. The advantages of CSP over HSP therefore include lower rates of delayed bleeding, lower frequency of post-polypectomy syndrome, and shorter procedure duration.

2.3 Polypectomy of sessile polyps (10 – 19 mm)

RECOMMENDATION

ESGE suggests hot snare polypectomy (HSP) (with or without submucosal injection) for removal of sessile polyps 10 – 19 mm in size. In most cases deep thermal injury is a potential risk and thus submucosal injection prior to HSP should be considered. (Low quality evidence; strong recommendation.)

HSP is the predominant technique for removal of polyps of size 10 – 19 mm, though the data comparing HSP to other techniques in this setting are limited. In a retrospective study of 941 polyps, of the 248 polyps sized > 5 mm that were removed endoscopically, 191 (77 %) were resected using HSP [42]. For polyps sized 10 – 19 mm, CSP usually cannot achieve "en bloc" resection and the use of biopsy forceps is ineffective for achieving complete resection as well as time-consuming.

In contrast, en bloc resection via HSP is possible, particularly if submucosal injection is used. Submucosal injection can also enhance the safety of HSP for polyps of this size, by reducing the risk of deep thermal injury. The choice of the substance used for submucosal injection used may influence outcomes of HSP for polyps of this size. For example, 196 patients with polyps sized < 20 mm were randomized to undergo EMR following submucosal injection with either 0.13 % hyaluronic acid or normal saline. Complete resection was achieved in 79.5 % of polyps in the 0.13 % hyaluronic acid group and in 65.6 % of polyps in the normal saline group ($P < 0.05$).

The Complete Adenoma Resection ("CARE") study showed that the rates of incomplete resection with HSP are significantly higher for polyps sized 10 – 20 mm compared to smaller polyps (17.3 % vs. 6.8 %; $P = 0.003$) [38]. Therefore, colonoscopists must take time to ensure completeness of resection.

RECOMMENDATION

In certain situations, there may be a role for piecemeal cold snare polypectomy to reduce the risk of deep mural injury, but further studies are needed. (Low quality evidence; weak recommendation.)

In a retrospective study that evaluated piecemeal CSP outcomes in sessile polyps of size > 10 mm, 30 sessile polyps > 10 mm in size were analyzed, of which 15 were between 10 and 19 mm. All polyps were completely retrieved without any adverse events such as delayed bleeding, post-polypectomy syndrome, or perforation [43]. Of 27 patients who underwent follow-up colonoscopy within 6 months, 80 % did not have residual polypoid tissue at the resection site.

A prospective Argentinian cohort study involving 124 patients, evaluated the safety of CSP where a piecemeal technique was used as required. Of 171 sessile polyps, 43 were sized between 10 and 19 mm. Although there were no subgroup analyses of 10 – 19-mm lesions, no immediate or delayed adverse events such as bleeding or perforation were observed in the overall cohort [44].

Piecemeal CSP has therefore been shown to be safe; however subsequent histological assessment may be less accurate and further prospective studies are required to determine the clinical relevance of this technique and its efficacy for completeness of resection for sessile polyps sized 10 – 19 mm.

2.4 Polypectomy of pedunculated lesions

RECOMMENDATION

ESGE recommends HSP for pedunculated polyps. To prevent bleeding, in pedunculated colorectal polyps with head ≥ 20 mm or a stalk ≥ 10 mm in diameter, ESGE recommends pretreatment of the stalk with injection of dilute adrenaline and/or mechanical hemostasis. (Moderate quality evidence; strong recommendation.)

Most pedunculated lesions are usually easily removed completely by HSP. The main adverse event is post-polypectomy bleeding (PPB). Large pedunculated polyps have an increased risk of PPB because of the presence of a large blood vessel within the stalk [45]. Studies have shown that polyp-related risk factors for PPB include polyp size > 10 mm, stalk diameter > 5 mm, location in the right colon, and the presence of malignancy [45 – 48].

Mechanical hemostasis with endoloops or clips and pharmacological intervention with injection of dilute adrenaline are effective in reducing PPB in pedunculated polyps of size > 10 mm, with the greatest benefit observed in polyps > 20 mm [49, 50]. RCTs showed that pretreatment by infiltration of the polyp stalk with 1:10 000 adrenaline significantly reduces PPB compared with no intervention ($P < 0.05$) [49, 51]. However, in another RCT of adrenaline vs. normal saline injection before polypectomy of polyps > 10 mm in size, the lower rates of bleeding found with adrenaline did not reach statistical significance [52]. Mechanical prophylaxis such as the use of endoloops or endoclips may be superior to adrenaline injections in achieving hemostasis. Two RCTs involving polyps > 20 mm in size, showed that the use of mechanical devices for pretreatment of the stalk, alone or in combination with adrenaline injection, significantly decreased PPB compared with adrenaline injection alone [53, 54].

2.5 Which polyps should be removed by an expert endoscopist in a referral or tertiary center?

RECOMMENDATION

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. (Moderate quality evidence, strong recommendation.)

Large laterally spreading and sessile colorectal lesions ≥ 20 mm in size (Paris classification 0-IIa, 0-Is, 0-Isp), or lesions located in difficult sites such as the ileocecal valve, appendiceal orifice, and anorectal junction, or located behind haustral folds, should be referred to an expert endoscopist in a tertiary center for removal [4, 55 – 57]. In the largest cohort of advanced lesions involving the ileocecal valve (53 patients, median lesion size 35 mm), among 47 patients who underwent EMR, complete adenoma clearance was achieved endoscopically in 94 % and ultimately surgery was avoided in 81 % [56]. Although surgery was previously the preferred technique for these "defiant" lesions, endoscopic resection techniques such as EMR offer a safe and effective alternative [58 – 61]. Recent large EMR cohort studies have demonstrated technical success rates of > 90 % for large laterally spreading and sessile colorectal lesions [55, 57, 60].

There are few studies that compare differences in outcomes between expert and non-expert colonoscopists. In a retrospective cohort study that compared the outcomes of endoscopic resections of 130 large sessile polyps by 2 specialist and 2 non-specialist colonoscopists, specialist colonoscopists had a higher success rate (75 % vs. 40 %, $P = 0.01$) [62]. However, a clear definition of an expert endoscopist is not evident in the literature. Similarly, there is no clear definition of what constitutes an appropriately resourced endoscopy center. However, since EMR for large or complex polyps carries substantially greater risk than standard diagnostic colonoscopy, to ensure that patient safety is optimized, the health facility should have the capability to address the range of possible adverse events such as perforation or bleeding. These would include radiology with computed tomography scanning, surgical support, and capability for blood product administration.

2.6 Polyps requiring other (non-snare) techniques, e. g. endoscopic submucosal dissection (ESD) or surgery

RECOMMENDATION

The majority of colonic and rectal lesions can be effectively removed in a curative way by standard polypectomy and/or by EMR. (Moderate quality evidence; strong recommendation.)

Many studies have shown that snare polypectomy or EMR using submucosal injection followed by en bloc or piecemeal snare resection are suitable for removing the majority of nonmalignant colonic polyps [4, 61, 63, 64]. Piecemeal EMR for large polyps is associated with moderate rates of recurrent adenoma (16 % in a large prospective study); however, these recurrent lesions are usually diminutive in size and can mostly be easily removed at surveillance colonoscopy, with an ultimately high success rate of 93 % [4, 60]. The EMR approach is safe, efficient, and cost-effective compared to surgical or other more complex endoscopic alternatives [57, 65 – 69].

RECOMMENDATION

En bloc resection techniques such as en bloc EMR, ESD, or surgery should be the techniques of choice in cases of suspected superficial invasive carcinoma. (Moderate quality evidence; strong recommendation.)

In cases of suspected superficial invasive carcinoma, endoscopic treatment may be considered curative where the histology shows complete en bloc R0 resection, well-differentiated adenocarcinoma, and sm1 type (< 1 mm submucosal invasion) with no lymphovascular invasion [70]. En bloc resection allows optimal histologic assessment of these factors (see below for additional high risk factors). En bloc EMR is generally limited to lesions 20 mm in size, with larger lesions usually requiring ESD or surgery for achievement of en bloc resection [71].

RECOMMENDATION

ESD can be considered for removal of colonic and rectal lesions with high suspicion of superficial submucosal invasion and which otherwise cannot be removed en bloc by standard polypectomy or EMR. (Moderate quality evidence; strong recommendation).

Where the risk of submucosal invasive carcinoma within a lesion is considered high, and en bloc EMR or polypectomy is not achievable, ESD or surgery is recommended.

Surgery is currently the gold standard of treatment with no study showing that ESD has better outcomes than surgery [70]. Surgery has the additional benefit of removing the local lymph nodes in most cases. The main exception may be in the rectum where the complexity of the traditional surgical approach with a higher risk of poor functional outcomes and the risk of abdominoperineal amputation might prompt ESD instead of surgery. A surgical transanal approach may be considered; however this also has limitations including the possibilities of difficult access, suboptimal visualization risking incomplete excision, and postoperative complications [70].

Good outcomes from ESD have been demonstrated in Japanese studies, with disease-specific survival rates of 100 % at the 3-year and 5-year marks, in a cohort with a median follow-up of 38.7 months (range 12.8 – 104.2 months) [72]. A systematic re-

view of ESD reported complete resection rates for large colonic polyps of 96 % (95 %CI 91 % – 98 %) and a per-lesion summary estimate for R0 resection rate of 88 % (95 %CI 82 % – 92 %) [73]. However, ESD of large colonic lesions is technically difficult, time-consuming, mandates multiday hospital stay, and, in Western countries, limited numbers of endoscopists have sufficient experience and expertise to achieve the results described in the East Asian literature.

According to the ESGE ESD Guideline, colorectal ESD may be considered for lesions with high suspicion of limited submucosal invasion based on depressed morphology or irregular surface pattern, or for lesions that otherwise cannot be optimally and radically removed by snare-based techniques [70]. However, further studies comparing ESD to surgery in a Western setting are required to establish the optimal technique. Local expertise will play a major role in determining which approach is used.

RECOMMENDATION

ESGE recommends that successful EMR be defined endoscopically by the absence of neoplastic tissue at the completion of the procedure after careful inspection of the post-EMR mucosal defect and margin. (Low quality evidence, strong recommendation.)

RECOMMENDATION

ESGE recommends that endoscopic cure for lesions resected by EMR should be confirmed at surveillance colonoscopy by advanced endoscopic imaging and systematic biopsy. (Low quality evidence; strong recommendation.)

RECOMMENDATION

ESGE recommends that suspected residual or recurrent adenoma identified at surveillance colonoscopy is snare-resected within the same procedure. Where snare resection is not possible, ablation should be performed. (Moderate quality evidence; strong recommendation.)

The goal of EMR is to resect the entire lesion, avoiding recurrence or residual tissue. Ideally the lesion should be resected en bloc, with histologically assessed clear margins (R0 resection). Piecemeal resection prevents the histological assessment of complete excision as the snare excision margins divide the polyp and cannot be distinguished from the in vivo polyp margins.

Complete endoscopic resection refers to complete removal of endoscopically visible polyp either piecemeal [74 – 76] or en bloc [77]. Inspection of the margins by magnifying endoscopy at the completion of resection has been shown to result in lower rates of recurrence, in a retrospective case – control analysis [78]. There is however no prospective evidence that use of magnification or high definition endoscopy reduces recurrence. It has been suggested that extending excision margins may reduce recurrence after EMR [74, 79, 80]; however a prospective observational cohort study of > 800 patients failed to show any reduction in recurrence at scheduled surveillance at 4 – 6 months [81].

Snare resection should be prioritized at the initial resection to remove all polyp, or as much polyp as possible [82]. The detection of residual or recurrent polyp at surveillance colonoscopy is of high importance. Recurrence occurs in 15 % – 20 % of EMRs [83]. There are few studies that have examined the accuracy of endoscopic imaging for the prediction of histological recurrence. Recently a large prospective study using a simple standardized imaging protocol with high definition white light endoscopy followed by NBI showed an NPV for recurrence of 98.6 % (95 %CI 95.1 % – 99.8 %). The use of NBI in addition to high definition white light endoscopy improved sensitivity for recurrence from 67 % to 93 %, the difference mainly due to detection of flat recurrence [84].

Residual or recurrent polyp tissue detected at endoscopic surveillance can be effectively treated [60]. Snare resection provides superior outcomes to other modalities [60]. For areas not amenable to snare resection, multiple endoscopic modalities have been described in the past to destroy residual polyp, although none have been demonstrated in a systematic way to reduce recurrence in conjunction with contemporary EMR techniques [85]. Hot avulsion is a technique that can be applied to small areas of non-lifting polyp and was effective in a small prospective study [86, 87]. Alternative strategies for non-lifting polyp including cold avulsion in conjunction with thermal ablation are being investigated. Recurrent lesions with substantial fibrosis may be suitable for ESD resection. The en bloc resection rate in Japanese studies is lower for salvage ESD than for naive lesions [88]. Underwater EMR has been examined in a small study as an alternative salvage therapy, with en bloc resection rates in this setting of 47.2 % vs. 15.9 % for standard EMR [75].

RECOMMENDATION

ESGE recommends the use of advanced endoscopic imaging to identify the potential presence of superficial submucosal invasion. (Moderate quality evidence; strong recommendation.)

Advanced imaging techniques such as narrow band imaging (NBI) and magnifying chromoendoscopy (MCE) have been shown to improve the identification of morphological features suggestive of submucosal invasion, such as irregular or absent surface vascular patterns [89 – 91]. NBI studies showed that the Sano capillary pattern IIIB, Hiroshima C3, and NBI International Colorectal Endoscopic Classification (NICE) 3 are highly indicative of deep invasion [92 – 95]. MCE studies demonstrated that Kudo pit pattern Vn is associated with a high likelihood of deep submucosal invasion [96, 97]. Sano IIIA, and Kudo pit pattern Vi are predictive of superficial submucosal invasive carcinoma, and can therefore identify patients who will benefit from en bloc resection.

RECOMMENDATION
ESGE suggests that when advanced imaging is not available, standard chromoendoscopy may be beneficial. (Moderate quality evidence; strong recommendation.)

Polyp morphology such as ulceration, excavation, deep demarcated depression, Paris classification II-c and IIa + c, nongranularity, mucosal friability, fold convergence and Kudo pit pattern V are associated with submucosal invasive carcinoma [4, 98 – 101]. Many of these features may be visible with standard or high definition white light inspection. Even when magnification technology is not available, standard chromoendoscopy may be useful in further enhancing the identification of these features.

RECOMMENDATION
ESGE recommends that polyps with advanced endoscopic imaging characteristics of deep submucosal invasion should not be considered for endoscopic treatment and should be referred for surgery. (Moderate quality evidence; strong recommendation.)

Polyps demonstrating endoscopic signs of deep submucosal invasion are at high risk of lymphovascular invasion and lymph node metastasis [102 – 104]. In a meta-analysis of 23 cohort studies involving 4510 patients, a significantly higher risk of lymph node metastasis was associated with a depth of submucosal invasion > 1 mm compared with superficial invasion (odds ratio [OR 3.87], 95 %CI 1.50 – 10.00; $P = 0.005$). Lymphovascular invasion (OR 4.81, 95 %CI 3.14 – 7.37; $P < 0.001$), poorly differentiated tumors (OR 5.60, 95 %CI 2.90 – 10.82; $P < 0.001$), and tumor budding (OR 7.74, 95 % CI 4.47 – 13.39; $P < 0.001$) were significantly associated with lymph node metastasis [104]. Therefore, in addition to excision of the lesion, the local draining lymph nodes must also be removed when deep submucosal invasion is suspected or proven, which can only be achieved by surgery.

RECOMMENDATION
ESGE recommends that polyps without characteristics of deep submucosal invasion should not be referred for surgery without consultation with an expert endoscopy center for evaluation for polypectomy/EMR. (Low quality evidence, strong recommendation.)

Polyps without characteristics of deep submucosal invasion, have a high likelihood of being successfully removed endoscopically at expert centers, and these patients should be offered a consultation to discuss endoscopic management before proceeding to surgery [105]. In a recent EMR study, 36 patients with 38 large or complex polyps without biopsy-proven cancer were redirected to consultation with an EMR expert by a colorectal surgeon who received the original referrals: 79 % of lesions could be successfully treated endoscopically and surgery was avoided in 71 % of the patients [106].

2.7 Colonic tattooing: which lesions should be tattooed, and what is the best technique and location for tattoo placement?

RECOMMENDATION
ESGE recommends that lesions that may need to be located at future endoscopic or surgical procedures should be tattooed during colonoscopy. (Low quality evidence, strong recommendation.)

Colonoscopic tattooing is performed to enable future identification, at colonoscopy or surgery, of malignant lesions (proven or suspected), polypectomy, EMR, or ESD sites, difficult-to-detect polyps, or dysplastic areas. All such lesions, other than those definitely located in the cecum, adjacent to the ileocecal valve, or in the low rectum, should be tattooed.

RECOMMENDATION
ESGE recommends sterile carbon particle suspension as the preferred tattoo agent. (Low quality evidence, strong recommendation.)

A variety of substances were previously used for endoscopic tattooing, including india ink, methylene blue, indigo carmine, and indocyanine green [107]. These were limited by difficulties including lack of permanence, infection resulting from impurities, or complex preparation. A sterile and biocompatible prepackaged suspension containing highly purified and very fine carbon particles (Spot; GI Supply, Camp Hill, Pennsylvania, USA) has been developed for endoscopic tattooing and this has enhanced the accessibility, ease of use, and safety of the procedure [108].

RECOMMENDATION
ESGE recommends the formation of a saline bleb in the submucosal layer of the colon prior to tattoo injection. (Low quality evidence; strong recommendation.)

Sterile carbon particle suspension is not biologically inert and has been associated with clinically significant complications [109]. These include reported cases of peritonitis resulting from transmural injection [107, 109, 110] and submucosal fibrosis that makes EMR or ESD difficult and hazardous and has contributed to endoscopic perforation [109, 111]. Furthermore, poor injection technique has resulted in failure to identify the tattoo at surgery [110]. These risks can be reduced by choosing an appropriate location for tattooing [109, 112, 113],

and by the use of the saline bleb injection method [110, 114]. The saline bleb injection method involves performing a normal saline injection initially to find the submucosal plane and ensure that a submucosal bleb is safely created. Once the submucosal bleb has been formed, the normal saline syringe is replaced with the tattoo syringe, and injection is recommenced. This ensures tattoo injection into the submucosal plane, avoiding transmural injection that may cause localized peritonitis, and is also associated with more accurate surgical location compared with standard tattooing [110, 114].

RECOMMENDATION

ESGE recommends that tattoos be placed ≥ 3 cm anatomically distal (anal side) to the lesion, with 2 or 3 separate injections being made at this level on opposite sides of the lumen, to increase the likelihood of detection. Endoscopic and surgical team members should agree on a standardized location of tattoo injection at their institution. The details of tattoo injection should be clearly text- and photo-documented in the endoscopy report, using unambiguous terminology. (Low quality evidence; strong recommendation.)

The recommended tattoo location of 2 – 3 cm distal (on the anal side) to the lesion [109, 112, 113] is at an adequate distance to limit the likelihood of inadvertent spread beneath the lesion and also avoid inadvertent injection through the lesion that may cause needle-track seeding [109, 112, 115, 116]. The carbon particles can spread a significant and often unexpected distance within the submucosal plane as the submucosal bleb flattens and expands laterally, potentially spreading underneath the lesion and inducing submucosal fibrosis, which can limit subsequent endoscopic therapy.

It is also recommended that 2 or 3 separate injections should be performed at this level of 2 – 3 cm distal (anal side) to the lesion. One injection should be in line with the lesion, and one should be on the opposite aspect of the lumen. This may increase the likelihood that the tattoo will be seen at future endoscopy or surgery. A tattoo volume of at least 1.0 – 1.5 mL at each injection site has been recommended [109, 110]. A volume of 3 mL of sterile carbon particle suspension has also been suggested if one is confident that the needle-tip is located within the submucosal plane [110].

3. Endoscopic mucosal resection (EMR) for sessile laterally spreading lesions ≥ 20 mm in size

EMR involves injection of a solution into the submucosal space to separate a mucosal lesion from the underlying muscularis propria. The lesion can then be resected by snare electrosurgery. The submucosal cushion theoretically reduces the risk of thermal or mechanical injury to the underlying muscularis propria.

Sessile and flat colorectal laterally spreading lesions (LSLs) (or laterally spreading tumors [LSTs]) ≥ 20 mm in size require advanced techniques for resection. Large prospective studies have demonstrated that EMR is safe and efficacious [4, 63, 117]. There is now a growing evidence base for several key technical aspects of the procedure, aimed at improving complete resection rates, reducing recurrence, and lowering rates of complications including perforation, bleeding, and post-procedural pain. Advanced endoscopic resection requires a patient- and lesion-centered approach, where the endoscopist must carefully appraise the risks of submucosal invasive cancer, the risks and benefits of resection techniques, and the co-morbidities of the patient. Although EMR is effective and safe for the vast majority of sessile flat colorectal LSLs without imaging features suggestive of invasive disease, surgical resection or endoscopic submucosal dissection (ESD) may be appropriate alternatives for higher risk lesions.

RECOMMENDATION

ESGE recommends careful lesion assessment prior to EMR to identify features suggestive of poor outcome. Features associated with incomplete resection or recurrence include lesion size > 40 mm, ileocecal valve location, prior failed attempts at resection, and size, morphology, site, and access (SMSA) level 4. (Moderate quality evidence; strong recommendation.)

Large polyp size as a predictor of recurrence or failed endoscopic therapy has been demonstrated in several studies [4, 55, 61, 118]. Prior attempts at resection have been shown to be associated with failed subsequent endoscopic resection. Non-lifting due to previous intervention was associated with failed resection in the large prospective Australian Colonic EMR (ACE) study (OR 3.75) [60] and a US study identified prior resection attempts as a risk factor for failure of complete resection (OR 0.081; $P < 0.001$), or recurrence (OR 18.8; $P < 0.001$) [119]. Lesion location may be associated with incomplete resection. Lesions at the ileocecal valve were associated with failed resection in the ACE study (OR 2.61) and, although good endoscopic outcomes can be achieved in this location, involvement of the ileum or both the superior and inferior lips of the valve was associated with recurrence [120]. Other locations that may prove challenging include the appendiceal orifice and anorectal junction [121]. Methods to overcome these challenges have been described and prospectively studied [120, 121]. Difficult access was associated with failed endoscopic resection in the ACE study [4] (OR 2.17), and locations behind folds, in a constrained sigmoid colon, or in peridiverticular locations may also reduce complete resection rates.

Post-EMR bleeding occurs in 5 % – 7 % following resection of lesions ≥ 20 mm [122, 123]. Identified risk factors for bleeding include proximal colon location [48, 122, 124] and increasing lesion size, especially ≥ 40 mm [77, 125]. The combined effects of size and location in the English Bowel Cancer Screening Programmme identified a predicted risk of bleeding of 1 in 8 [125]. Perforation is an uncommon event, and meta-analyses show pooled estimates of 1.4 % – 1.5 % [123, 126]. Few studies have identified independent risk factors for perforation as analyses

are prone to error when there are few outcomes. In large series examining standard polypectomy, "adverse event" outcomes (combining bleeding and perforation) have identified endoscopist inexperience and increasing lesion size as risk factors [127 – 130].

A simple method for stratifying lesion complexity, based on the size, morphology, site, and access (SMSA), has been developed by a working group of UK experts [131]. This stratifies polyps into four levels of difficulty with level 1 being the easiest and level 4 being very difficult to resect. Validation of this system in 220 lesions ≥ 20 mm in size demonstrated higher complication rates (8.6 % vs. 0 %, $P = 0.007$) and lower clearance rates (87.5 % vs. 97.5 %, $P = 0.009$) for SMSA level 4 polyps as compared to SMSA level 2 and 3 [55]. The classification is user-friendly, takes account of most described risk predictors and may be valuable for the assessment of large and complex polyps.

Lesions that have high risk features suggesting poor outcomes may be more safely and effectively handled at a high volume tertiary referral centre. The endoscopist must be confident that the resources available to them (staff, equipment, time, and endoscopic skill) are sufficient to remove the entire lesion safely and manage potential adverse events. If not, referral to a tertiary care center should be strongly considered [57, 61].

RECOMMENDATION

ESGE recommends that the goals of EMR are to achieve a completely snare-resected lesion in the safest minimum number of pieces, with adequate margins, and without need for adjunctive ablative techniques. (Low quality evidence; strong recommendation.)

Effective resection technique relies on multiple interdependent factors, but is difficult to study objectively as it requires the intersection of a number of endoscopic skills, including optical diagnosis, endoscope shaft and tip control, injection technique, snare selection and manipulation, visual and haptic feedback, and judgment. Several sources including technical reviews and expert opinion are available to guide technique [78, 82,132,133].

Complete and safe excision often requires an adaptable approach to the lesion and the techniques employed may vary slightly between operators. Factors associated with the lowest recurrence risk are complete snare resection, en bloc or oligopiecemeal excision, and the absence of adjunctive thermal ablative techniques.

RECOMMENDATION

ESGE suggests the use of submucosal injectates for EMR that are more viscous than normal saline and whose safety has been proven, including succinylated gelatin, hydroxyethyl starch, or glycerol, since their use is associated with superior technical outcomes and reduced procedural time. (High quality evidence; weak recommendation.)

RECOMMENDATION

ESGE recommends that a biologically inert blue dye such as indigo carmine should be incorporated into the submucosal injection solution to facilitate identification of fluid cushion extent, lesion margins, and deep mural injury. (Moderate quality evidence; strong recommendation.)

The ideal submucosal injectate should provide a sustained lift, facilitate en bloc or oligo-piecemeal resection, be inexpensive, widely available, and have few adverse effects [134]. The traditional EMR submucosal injectate is normal saline; however several other solutions have been investigated [135, 136].

Succinylated gelatin (Gelofusine; B. Braun, Crissier, Switzerland), has been compared to normal saline in an Australian double-blind RCT of EMR for lesions ≥ 20 mm (n = 80 patients). Succinylated gelatin results in fewer snare resections per lesion (3.0 vs. 5.5, $P = 0.028$) and shorter procedure duration (12.0 min vs. 24.5 min, $P = 0.006$) [137]. Succinylated gelatin is not universally available and there is a theoretical risk of an allergic reaction to bovine protein; however it has been used in a large multicenter cohort of over 1000 patients without complications [60].

Hydroxyethyl starch (Voluven; Fresenius Kabi Ltd, Runcorn, UK) has been shown to improve mucosal lift time, reducing the need for additional injections in a randomized controlled study [138]. Hyaluronic acid has also been demonstrated to improve complete resection and prolong mucosal elevation in several animal and human studies [139 – 142]. It is commonly used in ESD procedures [143]; however it is expensive [144] and not widely available, which has limited its uptake. In addition, murine models have suggested a potential for the stimulation of growth of residual adenoma [145].

Glycerol is a hypertonic solution consisting of 10 % glycerin and 5 % fructose in normal saline. In a retrospective case – control study, en bloc resection rates were improved with use of glycerol compared with normal saline [146]. Glycerol is widely available and inexpensive in Japan, but is not used extensively elsewhere [144].

Other hypertonic crystalloid solutions have been investigated in human and animal studies. Hydroxypropyl methyl cellulose sustains mucosal lift in animal studies [147] and is non-inferior to normal saline in humans [148 – 150]. Dextrose solutions produce a sustained mucosal lift [151 – 153]; however tissue damage has been reported in animal studies, particularly with concentrations over 20 % [154]. In a double-blind, randomized human EMR study, post-polypectomy syndrome was significantly more likely in patients treated with submucosal injection of 50 % dextrose with adrenaline compared with normal saline with adrenaline [151]. Similar effects have been noted with hypertonic saline [154].

Fibrinogen and blood injectates have also been used for EMR in animal models; however there are concerns regarding pathogen contamination and practicality [155, 156].

Incorporation of a biologically inert dye into the submucosal injectate facilitates identification of fluid cushion extent, lesion margins, and deep mural injury [5, 135]. Topical application of injectate with a chromic agent to resection defects may assist in the delineation of deep injury [157].

RECOMMENDATION

ESGE suggests that en bloc EMR should be limited to lesions ≤ 20 mm in the colon and ≤ 25 mm in the rectum. (Low quality evidence, weak recommendation.)

En bloc resection by EMR for lesions ≥ 20 mm is reported in 16 % – 48 % of lesions [60, 61, 79, 158]. It is associated with lower recurrence rates than piecemeal resection in both EMR and ESD studies [60, 143]. No studies have defined a cutoff point for size where en bloc resection is unsafe, so it remains a decision that is based on lesion morphology and location. The factors that limit en bloc resection by EMR are polyp size, location, EMR technique, and the experience of the endoscopist [159]. Finally however the primary driver must be consideration of safety. For flat and sessile colonic lesions the maximum size that can be reliably excised en bloc by EMR is 15 – 20 mm proximal to the splenic flexure where the risk of perforation is higher, and 20 – 25 mm in the sigmoid and rectum [160]. If en bloc resection is not possible, the lesion should be removed in as few pieces as possible [160].

Circumferential incision of lesions using ESD techniques (c-EMR, CSI-EMR, or EMR-precut) may allow extension of the size limits while mitigating perforation risk [79, 80, 161]. Use of special devices such as dual-loop snares may also increase the rate of en bloc resection for lesions ≥ 20 mm to 64 % [162]. Underwater EMR has demonstrated en bloc resection rates of 55 % for colorectal lesions of 20 – 40 mm [163].

RECOMMENDATION

ESGE recommends complete snare resection during EMR, because adjunctive thermal ablative techniques (e. g. argon plasma coagulation [APC]) are not as effective and are associated with higher adenoma recurrence. (Moderate quality evidence; strong recommendation.)

RECOMMENDATION

ESGE suggests that where complete snare excision cannot be achieved, the optimal method for adjunctive removal of residual adenoma requires further study. (Low quality evidence; weak recommendation.)

RECOMMENDATION

ESGE suggests that where complete snare excision EMR has been achieved, the role of adjuvant thermal ablation of the EMR resection margins to prevent recurrence requires further study. (Low quality evidence; weak recommendation.)

Ablation at the margins of the EMR defect may have two roles: as an “adjunct” treatment, where residual tissue not amenable to snare resection is ablated, or as an “adjuvant” treatment, where ablation is applied to clean defect margins in an effort to reduce recurrence.

Two small RCTs have demonstrated conflicting results for adjuvant APC, with one showing a significantly reduced rate of recurrence with APC application [164, 165] and the other showing no effect [141]. There are no contemporary high quality studies examining adjuvant thermal ablation techniques.

Small low quality prospective cohort studies have examined adjunctive thermal ablation with APC; however results have been inconclusive [85, 166].

The prospective ACE study (n = 479 patients, 514 lesions, mean size 35.6 mm) aimed for a treatment goal of complete snare resection. Where this was not achieved, remnant tissue was ablated by APC or snare-tip soft coagulation. Independent predictors of lesion recurrence included lesion size > 40 mm (OR 4.37) and use of APC (OR 3.51) [4]. The role of adjuvant thermal ablation of the post-EMR margin, where no endoscopically visible adenoma remains despite meticulous inspection, requires further rigorous evaluation.

RECOMMENDATION

ESGE recommends that when a lesion appears suitable for EMR, but does not lift with submucosal injection, referral should be made to an expert endoscopist in a tertiary center. (Moderate quality evidence, strong recommendation.)

Obliteration of the submucosal space that precludes lesion elevation with submucosal injection may be caused by early colorectal cancer, and with the associated desmoplastic response the mucosal layer can be tethered to the underlying muscularis propria. Fibrosis related to polyp prolapse, prior resection attempts [119, 167], or as a reaction to submucosal injection of tattoo particles [109] may also cause this. Non-lifting is evident when submucosal injection fails to elevate the lesion, but lifts the surrounding mucosa creating a canyoning effect. Infiltration into the submucosal space may not be possible, resulting in a jet of fluid exiting the lesion under pressure.

Non-lifting was first described in 1994 in a prospective series [168] and was strongly associated with submucosal invasion (SMI). It was subsequently shown that superficial SMI (SM1, involvement of the submucosa < 1000 µm; SM2, involvement of the submucosa < 2000 µm) was not as strongly associated with

non-lifting as deep SMI (SM3, > 2000 µm involved), as the underlying preserved submucosa may still expand [169]. Other studies have re-demonstrated this association of non-lifting with SM3 disease [170, 171]. Kobayashi et al. showed that endoscopic assessment with chromoendoscopy was superior to non-lifting for predicting submucosal invasion [171], so careful endoscopic assessment of surface pattern and morphology is considered to be the optimal method of determining invasion, preferably using magnification endoscopy and digital or topical chromoendoscopy [172].

Endoscopic resection by a typical inject and resect method may be ineffective or incomplete, requiring the use of adjunctive thermal ablation [173] or avulsion techniques (hot or cold) [86, 87] to remove all visible polyp. All visible adenoma should be excised before ablation is considered. Good outcomes have been reported at high volume tertiary referral centers [4, 61, 119] and in series using ESD techniques [88].

RECOMMENDATION

ESGE recommends that all EMR specimens be retrieved for histological evaluation. (Moderate quality evidence; strong recommendation.)

Although the Roth retrieval net device is usually used to retrieve polyp fragments after large or piecemeal polypectomy without compromising pathologic evaluation [174], systematic literature search yields no evidence-based data on this point regarding LSLs.

4. Equipment considerations for polypectomy and EMR

4.1 Type of current

RECOMMENDATION

ESGE suggests the use of a microprocessor-controlled electrocautery generator for polypectomy. (Low quality evidence; weak recommendation.)

Electrosurgical units convert energy from high frequency currents (between 300 kHz and 1 MHz) into heat. When high frequency electrosurgical current flows from a snare wire through tissue, the high density current at the point of contact results in a sharp rise in tissue temperature.

Cutting currents are produced at temperatures greater than 100 °C, which leads to boiling of cellular water and subsequent cellular rupture.

Coagulation currents are produced at temperatures of 70 – 100 °C. This leads to dehydration and contracting of cells, without rupture.

With use of blended currents, the ratio of cells cut to those coagulated can be varied.

For polypectomy, it is recommended that automated microprocessor technologies are used that enable controlled tissue cutting by providing an appropriate blend of cutting and coagulation currents. This provides enough coagulation current to maximize the hemostatic effect and minimize the risk of perforation [175, 176].

RECOMMENDATION

ESGE recommends against using low power coagulation current for EMR because of the increased risk of post-procedural bleeding. (Low quality evidence; strong recommendation.)

Use of diathermy current for polypectomy varies according to individual practitioner. A North American survey [177] of polypectomy practice of nearly 200 endoscopists demonstrated that 46 % favour a blended current, 46 % a pure coagulation current, 3 % a pure cutting current, and 4 % used a variety. More recently an Israeli survey [178] showed similar results, with 42 % favouring pure coagulation and 38 % blended current with a higher use of pure cutting current at 20 %. Pure cutting current is best avoided because of the risk of immediate post-polypectomy bleeding [47].

Pure coagulation current is popular amongst endoscopists because of its efficient hemostatic properties; however, it is well recognised that prolonged use of coagulation results in deep thermal tissue injury [179], increasing the risk of perforation, particularly in the right colon. A large study of nearly 1500 polypectomies [180] retrospectively compared blended versus pure coagulation current. Overall complication rates were the same between the two groups. However, there was a statistically significant difference in the timing of bleeding: for blended current within 12 hours, and for pure coagulation current within 2 – 8 days. Pure coagulation current when applied for EMR of flat lesions especially in the right colon is likely to increase the risk of perforation and is best avoided.

Use of an electrosurgical current not controlled by a microprocessor was associated with clinically significant post-endoscopic bleeding (OR 2.03; $P = 0.038$) [122].

RECOMMENDATION

ESGE recommends against using pure cutting current for pedunculated polypectomy because of an increased risk of intraprocedural bleeding. (Low quality evidence; strong recommendation.)

Pure cutting current is not recommended for polypectomy because of the increased associated risk of intraprocedural bleeding. A large, multicenter Korean study [47], with a total of 9336 polypectomies, found that cutting current and inadvertent cold polypectomy had the highest ORs for immediate post-polypectomy bleeding, at 6.95 (95 %CI 4.42 – 10.94) and 7.15, (95 %CI 3.13 – 16.36), respectively. A large retrospective study

[180] also found that immediate post-polypectomy bleeding was observed more with blended current and delayed post-polypectomy bleeding occurred more frequently with coagulation current.

A retrospective review encompassing 4735 polypectomies performed using pure cutting current found that bleeding occurred in 3.1% of the patients. In this study, hemoclips were prophylactically placed at the endoscopist's discretion and a significant proportion of patients (12%) received them [181].

Resection of pedunculated polyp is achieved by cutting the pedicle. This minimizes the risk of perforation as the pedicle is away from the colon wall, but the pedicle could contain a thick vessel. Inadequate coagulation of this vessel can result in catastrophic bleeds. Therefore, it may be logical to use pure coagulation current for resection of pedunculated polyps. However, there are no high level data comparing pure coagulation current to microprocessor controlled current for pedunculated polyps.

4.2 Carbon dioxide (CO_2) insufflation

RECOMMENDATION

ESGE suggests the use of carbon dioxide (CO_2) insufflation during colonoscopy and polypectomy. (Low quality evidence, strong recommendation.)

Carbon dioxide (CO_2) is absorbed > 100 times more quickly than air and can reduce patient discomfort during and after the procedure. A meta-analysis of 9 RCTs involving 1577 patients showed fewer patients with intraprocedural abdominal pain in the CO_2 group (relative risk [RR] 0.77, 95%CI 0.62 – 0.96). Use of CO_2 also reduced immediate post-procedural pain at 1 hour (RR 0.26, 95%CI 0.16 – 0.43) and 6 hours (RR 0.36, 0.20 – 0.64), and post-procedure discomfort at 24 hours (RR 0.53, 0.31 – 0.91) though there was no significant difference in cecal intubation rate [182].

An RCT assessing the impact of CO_2 insufflation on toilet use after screening colonoscopy showed that at 2 hours post-procedure, 30% in the CO_2 group had used the toilet at least once, compared to 83% in the air insufflation group (P<0.001). The average duration of each toilet visit was also significantly shorter in the CO_2 group [183].

RECOMMENDATION

ESGE recommends the use of CO_2 insufflation for EMR. (Moderate quality evidence; strong recommendation.)

EMR is associated with a higher risk of perforation than standard colonoscopy.

Performing EMR also lengthens the procedure time and the duration of gas insufflation. A prospective cohort study of patients undergoing EMR of large colonic lesions demonstrated a 62% reduction in the number of post-procedure admissions when CO_2 insufflation was used compared to air (8.9% vs. 3.4%, P=0.01) [184]. CO_2 insufflation is advisable in case EMR leads to perforation, as use of CO_2 will allow clinicians more time to manage the perforation as compared to use of air which can lead to rapid abdominal distension, tension pneumoperitoneum, gas tracking, pain, and hemodynamic compromise.

4.3 Type of snare

Limited data exist that compare the roles of different types of snares. We recommend that clinicians use snares with which they are familiar and whose performance characteristics are known. Snare size should be appropriately selected depending on the size and morphology of the polyp. Snares come in different shapes (circular, oval, hexagonal, etc.) but no clear benefit of one shape over the other has been demonstrated. Structurally, snares are either monofilament or polyfilament. The potential advantage of monofilament snares is that the snare wire is thin (<0.4 mm), so current density is greater, tissue transection swifter, and unintentional diathermic injury to the colonic wall less likely. The potential advantage of polyfilament snares are that the wire is thicker (0.4 mm – 0.5 mm) and thus they may better grip the mucosal surface (depending on what other performance enhancements have been included in the wire design) enabling more effective capture of flat polyps. However, these differences in performance have not been proven and ESGE strongly recommends further research in this field.

4.4 Fluid pump

RECOMMENDATION

ESGE suggests the use of a fluid jet pump to enable efficient irrigation of the colonic mucosa and polypectomy sites and management of bleeding. (Low quality evidence; weak recommendation.)

Use of a fluid jet can be very effective in locating the exact point of bleeding during polypectomy or EMR. This fluid may be water or normal saline. If the fluid jet is delivered via a separate dedicated channel in the endoscope (as in most modern endoscopes) then the working channel of the endoscope is available for the endoscopist to employ hemostatic devices whilst the fluid jet is delineating the precise bleeding point.

5. Polypectomy-associated adverse events: definitions and management

5.1 Bleeding

Consensus on the definition of post-polypectomy bleeding is lacking. Definitions vary throughout the literature. For the purposes of these guidelines, two terms were used: intraprocedural bleeding and post-procedural bleeding. These were defined as follows:

- Intraprocedural bleeding (IPB) is bleeding occurring during the procedure that persists for more than 60 seconds or requires endoscopic intervention.

- Post-procedural bleeding (PPB) is bleeding occurring after the procedure, up to 30 days post-polypectomy, that results in an unplanned medical presentation such as emergency department visit, hospitalization, or re-intervention (repeat endoscopy, angiography, or surgery).

RECOMMENDATION

For intraprocedural bleeding, ESGE recommends endoscopic coagulation (snare-tip soft coagulation or coagulating forceps) or mechanical therapy, with or without the combined use of dilute adrenaline injection. (Low quality evidence; strong recommendation.)

IPB occurs in 2.8 % of patients undergoing standard polypectomy [49] and in 11.3 % of patients with lesions ≥ 20 mm treated with endoscopic mucosal resection (EMR) [122] and it is rarely serious. Management of IPB can be achieved with endoclips, coagulation forceps, and snare-tip soft coagulation. Snare-tip soft coagulation has been shown to be an effective method of IPB control [185]. Coagulating forceps are reserved for more severe cases [82, 132]. Vigorous irrigation, preferably by using a water pump, improves visualization and may aid cessation of bleeding originating from small vessels [82, 132]. Adrenaline injection (1:10 000 or 1:20 000 dilution with saline) may be used to gain initial control of active bleeding but should always be used in combination with a second mechanical or thermal hemostatic method.

IPB that occurs after removal of a pedunculated polyp, can be managed by placing a clip or an endoloop. In cases of immediate massive IPB, the snare may be used to resnare the remaining stalk with temporary control of bleeding providing time for subsequent clip or endoloop application. Where a significant volume of blood is pooling and overlying the bleeding point, this can make it difficult to identify and treat the precise bleeding point. In such a case, rolling the patient so that the bleeding point is away from the gravity-dependent position will enable the bleeding point to be clearly visualized and treated. The over-the-scope clip (OTSC; Ovesco Endoscopy, Tuebingen, Germany) has also been shown to be effective for control of IPB that is refractory to other endoscopic modalities [186]. The advantage of using this device is that it can grasp a much wider area and larger volume of tissue than the through-the-scope endoclips; however withdrawal of the endoscope to load the device is necessary, further delaying hemostasis.

RECOMMENDATION

ESGE does not recommend routine endoscopic clip closure or other methods of prophylaxis to prevent delayed bleeding for sessile polyps. (Moderate quality evidence; weak recommendation.)

An RCT, has reported that prophylactic clip application does not decrease PPB after EMR [187]. However, in an uncontrolled retrospective study of 524 unselected polyps ≥ 20 mm in size, prophylactic clipping of resection sites was found to reduce the risk of PPB [188]. More RCTs on this subject are required. Moreover, in another RCT, prophylactic endoscopic coagulation of nonbleeding visible vessels within the mucosal defect after wide-field EMR, using coagulation forceps at fixed low power, did not reduce the incidence of PPB [189].

RECOMMENDATION

ESGE suggests that there may be a role for mechanical prophylaxis (e. g. clip closure of the mucosal defect) in certain high risk cases after polypectomy or EMR. This decision must be individualized based on the patient's risk factors. (Low quality evidence; weak recommendation.)

Factors associated with the incidence of post-procedural bleeding (PPB) are either related to polyp characteristics such as size, morphology, and location of the polyp, or to the patient's health status such as age > 65 years, the presence of hypertension, renal disease, and use of anticoagulant. PPB complicates 6 % – 7 % of wide-field EMRs [122]. Data from EMR of sessile colorectal polyps ≥ 20 mm in size showed, that PPB was associated with proximal location, use of an electrosurgical current not controlled by a microprocessor, occurrence of IPB, and aspirin use [122, 124]. In the Munich Polypectomy Study, polyp size and the proximal location of the polyp were risk factors for adverse events such as PPB [128]. A meta-analysis has shown that the risk of PPB was significantly increased for patients using clopidogrel [190]. A cost-efficacy decision analysis of prophylactic clip placement after endoscopic removal of large polyps has shown that this strategy appears to be cost-effective for patients who receive antiplatelet or anticoagulation therapy [191]. Prophylactic endoscopic clipping may thus be considered for preventing delayed bleeding in patients receiving antiplatelet or anticoagulant medications [192].

The use of mechanical prophylaxis in certain high risk cases after standard polypectomy or EMR should be individualized on the basis of patient or polyp risk factors. A clinical risk score derived from a prospective multicenter dataset of more than 2000 colonic EMRs has recently been described. Importantly, it is simple to use and independently confirms the key risk factors identified in previous studies [193], including lesion size > 30 mm, proximal colon location, and presence of major co-morbidity. Further research regarding prophylactic therapies in this high risk group is required.

RECOMMENDATION

Patients admitted to hospital with delayed bleeding who are hemodynamically stable, without ongoing bleeding, may be initially managed conservatively. If intervention is required, ESGE recommends colonoscopy as the first-line investigation. (Moderate quality evidence, strong recommendation.)

PPB is one of the most common causes of lower gastrointestinal bleeding amenable to endotherapy [194]. Not all patients presenting with PPB need urgent colonoscopy; however a clear means of identifying those that do has not been defined. No relevant study has been conducted and only expert opinion exists. Patients responding to resuscitation should initially be observed [195]. If bleeding persists, patients should be given an adequate bowel preparation and repeat colonoscopy performed [196, 197]. Using a decision model it was calculated that a tandem colonoscopy for identification and treatment of PPB is beneficial in about 22 % of patients [198]. In a multicenter, prospective study of colonic lesions ≥ 20 mm treated by EMR, 55 % of patients avoided repeat colonoscopy because bleeding spontaneously stopped. When colonoscopy was performed, endoscopic therapy was only necessary in 21 of 27 cases (70 %). On the basis of these data, a risk-based algorithm for the management of PPB has been proposed [199].

RECOMMENDATION

When the polypectomy site is identified during colonoscopy for post-polypectomy bleeding, and active bleeding or other high risk stigmata are identified, ESGE recommends forceps coagulation or mechanical therapy, with or without the combined use of dilute adrenaline injection. (Moderate quality evidence; strong recommendation.)

The optimal technique for achieving endoscopic hemostasis in cases of active PPB or other high risk stigmata has not been determined. Technique selection is based on location and characteristics of the lesion, endoscopist preference and experience, and device availability. The most commonly used methods are clipping, or forceps coagulation with or without the combined use of adrenaline injection [124, 195, 200, 201]. Clipping, with or without adrenaline injection, may be superior to forceps coagulation therapy since it limits further tissue injury. Caution is necessary during the application of hemostatic techniques, as transmural injury from thermocoagulation and perforation during clipping have been reported among other complications [124]. Endoscopic band ligation has also been used to manage PPB in cases of pedunculated or semipedunculated polyps [202, 203].

5.2 Prevention of perforation

RECOMMENDATION

ESGE recommends careful inspection of the post-resection mucosal defect to identify features of or risk factors for impending perforation. Where these risk factors are identified, clip closure should be performed. (Moderate quality evidence; strong recommendation.)

Careful analysis of the post-resection mucosal defect is a critical part of polypectomy, particularly in wide-field EMR. Injury to the muscularis propria layer should be identified before it becomes a frank perforation where surgical treatment is mandatory. Full-thickness perforation needs immediate closure endoscopically or surgically [204]. Thorough inspection of the post-EMR specimen and resection defect may reveal the “target sign,” a marker of either partial- or full-thickness muscularis propria resection and imminent perforation. In these cases, immediate endoscopic clipping is indicated [5, 205]. Incorporation of a blue chromic dye into the submucosal injectate facilitates inspection of the submucosal defect which should appear as a relatively homogeneous blue mat of intersecting obliquely oriented submucosal fibres. Topical submucosal chromoendoscopy is a simple and effective technique that rapidly confirms the level of resection and may improve detection of intraprocedural perforation [157]. Endoscopic signs such as exposure of the muscularis propria layer, submucosal fibrosis, or submucosal fat should be noted and further evaluated by topical submucosal chromoendoscopy. Areas that stain poorly because of submucosal fibrosis should be treated by clip closure, since they do not allow endoscopic exclusion of muscularis propria injury and carry a risk of delayed perforation [82, 206].

Risk factors for deep mural injury include attempted en bloc snare excision for lesions ≥ 25 mm, high grade dysplasia/early cancer, and transverse colon location.

5.3 Audit of adverse events

RECOMMENDATION

ESGE recommends audit of adverse events. (Moderate quality evidence; strong recommendation.)

Methods of collecting data on adverse events following endoscopic procedures, including colorectal polypectomy, are not uniform and vary from nonsystematic self-reporting to complete registry reporting including linkage to databases other than endoscopic ones. One study revealed that the different methods of collecting data may result in up to 3.1-fold differences in reported frequency of adverse events [206]. A uniform methodology for auditing immediate and delayed (up to 30 days) adverse events is required and studies on completeness of data are needed. One such methodology of auditing polypectomy complications was described in a study from Munich

[128]. Other proposals include the creation of obligatory national databases of adverse events, as proposed in the Netherlands, together with systematic quality assurance programs. Additionally, ESGE guidelines concerning definitions and reporting of adverse events should be followed and usage should be audited [205].

However, currently no systematic audits concerning polypectomy complications are functioning outside of research studies. Optimally an audit should contain: (a) immediate self-reporting by the endoscopic service; (b) 30-day structured telephone interview or patient questionnaire followed by telephone contact, in the case of no face-to-face contact; and (c) linkage to a national hospitalizations database.

6. How is the histology specimen best managed and reported upon? Processing, analysis, and reporting (minimum reporting standards)

RECOMMENDATION

ESGE recommends that polypectomy specimens be placed in separate containers, one for each lesion. Local factors may play a role in whether this is feasible. Fixation should be by buffered 10% formalin. The pathologist should measure the size of each specimen in millimeters. (Moderate quality evidence; strong recommendation.)

RECOMMENDATION

ESGE suggests that large (≥20 mm) sessile lesions removed en bloc, or lesions suspicious for submucosal invasion removed piecemeal, should be pinned to cork to optimize histological assessment. (Low quality evidence; weak recommendation.)

RECOMMENDATION

ESGE recommends that specimens be sliced and totally embedded, allowing the identification of the deep and lateral margins. (Moderate quality evidence; strong recommendation.)

The pathological work-up of the resection specimens plays a central role in the management of patients undergoing colorectal polypectomy. The quality and accuracy of the histopathological diagnosis directly affect clinical management and decision-making, ranging from surveillance to further local and/or major resection. Multidisciplinary evidence-based guidelines for quality assurance in colorectal cancer screening have recently been developed by a group of experts in a project coordinated by the International Agency for Research on Cancer (IARC) and co-funded by the Public Health Programme of the European Union [207]. The guidelines' pathology content has been published in four papers in both pathological [208, 209] and clinical [210, 211] journals. These publications define the current standard of care in the pathological work-up of polypectomy specimens, in Europe and beyond. The following subsection is a brief summary.

6.1 Technical considerations

Specimen handling is an important issue, as poor handling and dissection procedures can impair diagnostic accuracy. Specimen handling starts with the endoscopic removal and ends with the histopathological diagnosis and report [208, 210]. It is recommended that specimens be placed in separate containers, one for each lesion. This helps to avoid confusion about the exact location of the lesion(s), and also increases the accuracy of histopathological diagnosis by avoiding false-positive diagnoses of mixed lesions, e.g. sessile serrated adenomas with dysplasia. Biopsies from the same lesion can be placed in the same container. Fixation should be by buffered 10% formalin. Specimens can shrink due to formalin fixation, therefore measurements taken after fixation can differ from those prior to fixation [208, 210].

Size is an important objective measurement, best performed by the pathologist. Pathology measurements are auditable, accurate, and simple to perform [210]. Lesion size should be given in millimeters. If possible, the maximum size should be measured from the histological slide, and only measured from the formalin-fixed gross specimen if the lesion is disrupted or too large [211].

Polypoid lesions must be sliced and totally embedded. While smaller lesions may be bisected through the stalk, larger lesions should be trimmed to generate a central section containing the intact stalk for further analysis. As the pathology report should verify the complete removal of a neoplastic lesion, special attention needs to be paid to the evaluation of the resection margin, which should be identified and described (broad, stalked, etc.) and either dissected tangentially into an extra cassette or sliced in a way that allows complete assessment [208, 210].

It is recommended that the resections of sessile or flat lesions be pinned out (mucosal surface upwards), e.g. on a piece of cork or other suitable material, by inserting pins through the periphery of the specimens. Needles should not be placed directly through a lesion. After fixation, the specimens are described and sectioned transversely into 3-mm slices (submitted for histological evaluation in sequentially labelled cassettes), thereby allowing the identification of involvement of the deep and lateral margins. Particular attention should be paid to any areas of ulceration or induration for signs of invasion [208, 210].

Piecemeal resection precludes a reliable assessment of completeness of resection. Whenever possible, the entire lesion should be embedded to allow exclusion of invasive malignancy.

Inking of margins is recommended. The distance to the excisional margin should be reported in millimeters. The European guidelines recommend that clearance of 1 mm or less indicates margin involvement [208, 210]. Cases of incomplete removal should be highlighted, which is most important for advanced adenomas and early cancer. Three or more levels should be cut through each block and stained with hematoxylin and eosin [208, 210].

6.2 Adenoma grading, and reporting of cytological dysplasia

RECOMMENDATION

ESGE recommends the grading of adenomas/neoplasia as low grade or high grade according to the World Health Organization (WHO) classification. (High quality evidence; strong recommendation.)

RECOMMENDATION

ESGE recommends that sessile serrated adenomas/polyps should be reported as containing cytological dysplasia when it is present. (Moderate quality evidence; strong recommendation.)

7. Diagnosis of lesions in the adenoma–carcinoma sequence

7.1 Lesion types

Colorectal adenoma is defined as a lesion in the colon or rectum containing unequivocal (intra)epithelial neoplasia (dysplasia) [212]. Classification of adenomas should include grading of neoplasia according to the revised Vienna classification to apply a two-tiered categorization of low grade and high grade neoplasia. This system aims to minimize intraobserver and interobserver variation and to facilitate the management of endoscopically detected lesions by improving correlation between the histopathology of biopsy and resection specimens.

Most adenomas measure less than 10 mm in size and have tubular architecture. Villous architecture is defined as leaflike or fingerlike projections of epithelium overlying a small amount of lamina propria. Tubulovillous adenomas are defined by a mixture of tubular and villous structures, with arbitrary percentages in different studies, typically with between 25 % and 75 % villous component. Grading of neoplasia is performed by assessing the degree of architectural complexity, the extent of nuclear stratification, and the severity of abnormal nuclear morphology [213].

Approximately one third of colorectal cancers develop from serrated lesions, a heterogeneous group of lesions characterized morphologically by a serrated (sawtoothed or stellate) architecture of the epithelial compartment. Hyperplastic polyps, sessile serrated adenomas/polyps, and traditional serrated adenomas are the lesions included in this group [213].

Hyperplastic polyps are very common, accounting for 70 % to 95 % of all serrated lesions, or 25 % – 30 % of resected polyps [214, 215]. They occur as usually small (< 5 mm) nondysplastic polyps in the left colon, particularly the sigmoid colon and rectum, and only rarely in the right colon [213 – 215].

Sessile serrated adenomas/polyps are more likely to be located in the right colon (75 %), accounting for approximately 5 % – 25 % of all serrated lesions [213, 216]. Their size is larger than that of hyperplastic polyps: More than half of the lesions measure > 5 mm and 15 % – 20 % of the lesions > 10 mm, respectively. They may develop de novo or from pre-existing hyperplastic polyps. Upon histological examination, sessile serrated adenomas/polyps show distorted crypt architecture, with hyperserration, often at the base of the crypts, and with dilated, mucus-filled, L-shaped (“boot”) and T-shaped (“anchor”) crypts [214 – 219]. Uncomplicated sessile serrated adenomas/polyps are nondysplastic, but they may acquire overt dysplasia during tumor progression, often in conjunction with methylation of the *hMLH1* gene promoter [213 – 215, 217].

Traditional serrated adenomas are rare, accounting for only about 1 % of colorectal polyps. They prevail in the left colon. They are often polypoid or pedunculated, but sessile lesions do also occur, predominantly in the right colon [220, 221].

Early colorectal cancer is defined as invasive adenocarcinoma invading into but not beyond the submucosa [212]. The term ‘malignant polyp’ refers to an adenoma that appears benign endoscopically, but which shows invasion through the muscularis mucosa into the submucosa upon histological assessment. A malignant polyp is therefore an early carcinoma. Malignant polyps account for 0.75 % to 5.6 % of large-bowel polyps removed in general diagnostic colonoscopy practice [102].

Patient management following endoscopic removal of a malignant polyp is difficult because of the potential risk of residual cancer tissue within the bowel wall and/or metastatic cancer spread to regional lymph nodes. The depth of invasion into the submucosal layer, assessed according to the Haggitt classification [17, 102] (for pedunculated lesions), the Kikuchi classification [222] (for nonpolypoid lesions), or by direct measurement (in microns from the bottom line of the muscularis mucosae), has been associated with regional lymph node spread. Angioinvasion, in particular lymphatic invasion, poor tumor differentiation or grade, and resection margin status have been identified as additional risk factors [223, 224]. The combined assessment of these features increases the accuracy of risk prediction [102, 225, 226] and allows the stratification of patients into low risk and high risk groups [102, 227, 228].

7.2 Histological findings that require further action

RECOMMENDATION

ESGE recommends that where submucosal invasion is present, the depth of invasion should be measured and reported, in addition to other risk factors, such as poor differentiation, lymphovascular invasion and tumor budding. The distance to the deep/vertical and to the lateral/horizontal resection margin should be measured and reported. (Moderate quality evidence; strong recommendation.)

RECOMMENDATION

The opinion of a second histopathologist may be warranted when reviewing high risk features. (Low quality evidence; weak recommendation)

Endoscopic resection is an effective cure for colorectal lesions confined to the mucosa. Invasion across the muscularis mucosa into the submucosa constitutes T1 disease. Complete resection of a T1 lesion is often readily achievable; however even if completely resected, T1 tumors are associated with a risk of lymph node metastasis (LNM) which, if present, has a significant impact on survival and cure. The 5-year survival for a T1 lesion without LNM (stage 1) is >95%, whereas T1 disease with any LNM (stage III) reduces overall 5 year survival to 68.4%–87.6% [229]. Surgery and lymph node dissection is essential in those with suspected LNM to completely stage the disease and improve outcomes.

LNM is present with a minority of T1 cancers (6.3%–17.6%) (see Table 14, **Appendix 2**; available online in Supplementary material); thus the majority of patients may be cured by endoscopic resection alone. Although definitive, surgery for colorectal cancer is costly, invasive, and can be associated with significant morbidity and mortality [66, 230]. Risk stratification of T1 lesions is therefore important to identify patients at low risk of LNM who may safely avoid surgery.

There are a large number of studies that aim to address risk factors for LNM; however the majority are small and retrospective. Many studies are restricted to surgically resected tumors, potentially producing a bias towards larger and higher grade lesions. The most commonly identified risk factors for LNM are deep vertical penetration (submucosal invasion >1000 µm for flat or sessile lesions and Haggitt level 4 for pedunculated lesions), lymphovascular invasion, poor tumor differentiation, tumor budding, and a positive resection margin. There are no identified clinical or patient features which are reliably associated with LNM, aside from rectal location [224].

7.3 Submucosal invasion depth

Methods for classifying the extent of submucosal invasion vary depending on the morphology of the polyp, and are prone to interobserver variation. The most established classification methods are Haggitt levels [102] for pedunculated lesions and Kikuchi levels [222] for flat or sessile lesions.

The Haggitt classification divides the polyp into five zones. Level 0 is noninvasive disease which does not cross the muscularis mucosa. Levels 1–4 describe progressive involvement of head, stalk, and submucosa below the stalk. In a small series (n=129), Haggitt et al. showed that the deepest level of invasion (level 4) was associated with LNM or death from colorectal cancer [102]. The system is widely adopted, and endoscopically resected level 1–3 disease has been shown to be associated with a low risk of LNM [103, 231]. Despite this, studies have described LNM with 6.2%–8.0% of polyps with level 3 invasion [232]. Pathological assessment of Haggitt levels may be hampered by endoscopic trauma and cautery artefact during removal, by shrinkage after fixation, and by suboptimal tissue orientation due to the plane of sectioning.

For nonpolypoid lesions, depth of submucosal invasion can be classified using the Kikuchi level system. Kikuchi et al. adapted an existing schema whereby sm1, sm2, and sm3 denote the upper, middle, and lower thirds of the submucosa respectively [14]. Reported risks of LNM are 0–3% for sm1 invasion, 8%–10% for sm2, and 23%–25% for sm3 [222, 233]. The classification cannot be applied when lesions have been resected endoscopically, as the muscularis propria is not included. As a result, some authors have proposed using a measurement of the distance of invasion from the muscularis mucosa. Ueno et al. described an elevated risk of LNM when invasion extends deeper than 2000 µm beyond the muscularis mucosa (2.5% vs. 18.2%) or when the invasion width is >4000 µm (3.9% vs. 17.1%) [225]. In a retrospective UK study, invasion width (>11.5 mm) and area were also found to be risk factors for LNM after multivariable adjustment for other significant risk factors (grade of differentiation, lymphatic and vascular invasion) [234]. Four meta-analyses have shown that invasion >1000 µm is a risk factor for LNM, although all four studies comment on the small sizes, heterogeneity, and retrospective nature of the included papers [104, 224, 235, 236].

7.4 Lymphovascular invasion

The majority of studies examining histological risk factors for LNM report on lymphatic or vascular invasion. Five meta-analyses have all demonstrated that lymphatic or lymphovascular invasion is one of the stronger risks for LNM [104, 224, 235–237]. In patients undergoing surgery for T1 lesions, lymphatic invasion is reported in 27%–31% and approximately 27% of these patients have LNM. Vascular invasion, when separately reported, is seen in 19% with LNM in 21%–24% [224, 235].

It may be difficult to detect lymphatic invasion by standard light microscopy because of retraction artifact, which can result in an artificial space surrounding tumor nests that mimics a lymphatic channel. The use of immunohistochemistry with an antihuman podoplanin antibody such as D2–40 may improve the ability to detect and characterize lymphoid invasion [238]. A meta-analysis of histopathological predictive factors showed that the strongest predictive factors for LNM were lymphatic vessel invasion identified by an antihuman podoplanin antibody (OR 5.19, 95%CI 3.31–8.15; $P=0.01$) or tumor budding (OR 7.45, 95%CI 4.27–13.02; $P=0.0077$) [237]. Immunohistochemical markers such as D2–40 are not in widespread use.

7.5 Tumor differentiation

Grading of colorectal carcinomas should be performed according to the WHO classification, and tumors are graded as well-differentiated (>95% gland formation), moderately differentiated (50%–95% gland formation), or poorly differentiated (<50% gland formation). Carcinomas may be heterogeneous, so the tumor should be graded according to the least differentiated component. The interobserver agreement between pathologists when grading colorectal adenocarcinoma specimen is fair at best, and it has been suggested that use of the high grade and low grade categories should be standardized [239].

High grade, or poorly differentiated tumors are associated with LNM and residual disease following endoscopic resection. In a pooled analysis of retrospective studies, Hassan et al. reported poor differentiation in 116/1612 polyps (7.2%) [227]. In patients with poor differentiation LNM was apparent in 23%

compared to 7 % with low grade changes. Poor differentiation was also associated with hematogenous metastases and mortality. A meta-analysis of sessile early colorectal cancer showed an RR of 8.19 (95 % CI 4.65 – 14.43) for LNM in poorly compared to well-differentiated tumors and of 3.48 (95 %CI 2.08 – 5.81) for poor compared to moderate differentiation [236]. Two other meta-analyses of more heterogeneous studies also confirmed this association of LNM with poor differentiation with RRs of 5.60 (95 %CI 2.90 – 10.82; $P < 0.001$) [104] and 4.8 (95 % CI 3.3 – 6.9; $P < 0.001$) [224].

7.6 Tumor budding

Budding refers to the presence of single cells or small groups of tumor cells scattered within the stroma at the leading edge of invasion. Several studies have identified this feature as a risk factor for LNM [240, 241], and it is associated with venous and lymphatic invasion [242] as well as with poorer outcome in colorectal cancer [243]. In early colorectal cancer, tumor budding has been reported primarily in Japanese studies. Its assessment suffers from a lack of standardized international criteria. Usually, budding is either described as present or absent, or it is graded. Despite this lack of conformity (high grade) budding has been associated reliably with LNM and has hence been identified as a strong and independent predictor of LNM in five meta-analyses [104, 224, 235 – 237]. Prospective studies, and a consensus definition for the reporting of tumor budding are required for the inclusion of this characteristic in standard histopathological reporting of T1 cancer.

7.7 Resection margin

Involvement of the deep resection margin is associated with residual tumor, hematogenous metastasis, and mortality [225, 227, 244]. Margin involvement should be reported routinely by the pathologist and clearance from the resection margin should be described and measured in millimeters.

There is no generally accepted consensus definition, and a positive margin has been defined variably as cancer within the diathermy margin, within one high power field of the margin [225, 245, 246], 0.1 mm or less from the margin [247], 1 mm or less from the margin [248, 249], or 2 mm or less from the margin [250, 251]. Residual tumor or recurrence is < 2 % where the margin of resection is > 1 mm and in the absence of other unfavorable histological features [223, 247, 252, 253]. Cunningham et al. reported that in the absence of unfavorable factors, 16.6 % of polyps with a margin clearance ≤ 1 mm had residual disease at surgery [254]. Cooper et al. showed in a retrospective single-center study that in patients without risk factors but where margin clearance was ≤ 1 mm, an adverse outcome (endoscopic recurrence, tumor in the surgical specimen, or LNM) was present in 19.4 %. By contrast, there were no adverse outcomes in low risk patients with margins > 1 mm [249]. Resection margins of > 2 mm are associated with very low rates of recurrence [251]. However the inclusion of a < 2 mm margin as an unfavorable risk factor may result in overtreatment of lesions without other risk factors [255]. Unequivocal deep margin involvement is certainly an unfavorable risk factor and further resection is required, with the modality (surgical resection or transanal endoscopic microsurgery [TEMS]) based on tumor location and patient co-morbidities. Clearance of ≤ 1 mm is associated with similar outcomes to definite margin involvement, and clearance > 1 mm appears to be helpful in defining low risk patients. Other European guidelines currently recommend a level of ≤ 1 mm as equivalent to margin involvement [256, 257].

7.8 Combined risk assessment

Several risk factors have been established as high risk features for the prediction of LNM or residual disease in endoscopically resected lesions containing a malignant focus. These factors include deep submucosal invasion (> 1000 µm for flat or sessile lesions and Haggitt level 4 for pedunculated lesions), lymphovascular invasion, poor tumor differentiation, tumor budding, and a positive resection margin. Consequently, all these factors should be addressed in the pathology report in order to provide clinicians with a risk estimate for discussing further management in a multidisciplinary setting and with the patient [256]. The combination of risk factors is important, as an absence of defined high risk features has been shown to identify a “low risk group” of patients. Patients in this low risk group may still have a small risk of LNM and they should be followed as such.

8. Conclusion

This ESGE Guideline comprehensively addresses critical areas in the assessment and management of colorectal polyps. Polypectomy is among the most important colonoscopy skills. The ability to perform complete and safe polypectomy enables us to significantly benefit our patients. Mastery of basic polypectomy, and an understanding of the issues involved in advanced polypectomy, should be goals of all colonoscopists.

The diverse topics covered in this polypectomy and EMR Guideline include the classification of colorectal polyps, the optimal evidence-based approaches to polypectomy for polyps of all sizes and morphologies, colonic tattooing, a guide to effective and safe EMR for large sessile polyps, the role of advanced imaging in polypectomy, and which lesions require the involvement of expert centers or more complex interventions such as ESD or surgery. Technical aspects such as equipment and auxiliary devices to optimize polypectomy are also discussed. The Guideline defines the key adverse events during and following polypectomy, the recommended management of adverse events, and the need for audit of outcomes to monitor quality and safety of polypectomy and EMR. Finally, guidelines for the histological evaluation of resected polypectomy specimens and practice recommendations for high risk histological features are discussed. Throughout this Guideline, areas where further research is required to answer critical questions are highlighted, providing direction for researchers to design further studies. We look forward to the opportunity to incorporate the results of such studies into updates of this Guideline in the years to come.

ESGE guidelines represent a consensus of best practice based on the available evidence at the time of preparation. They may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may be needed to clarify aspects of the statements, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations. ESGE guidelines are intended to be an educational device to provide information that may assist endoscopists in providing care to patients. They are not a set of rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

Competing interests

P. Bhandari has served on Advisory Boards for Fujifilm, Pentax, and Boston Scientific (1 Nov 2015 – 31 Dec 2016, for all); he has participated in preparation of similar guidelines for the British Society of Gastroenterology (BSG). P. Fockens provides ongoing consultancy to Cook, Olympus, Medtronic, and Fujifilm. L. Moons' department has received a grant from Boston Scientific (1 Jan 2016 – 1 January 2017. J. Pohl provides consultancy to Karl Storz (Jan 2016 –). T. Ponchon has provided consultancy to Olympus, Boston Scientific, and Cook Medical (2007 – 2016, for all); his department has received financial support for clinical research from Boston Scientific. M. Rutter's department received an unrestricted grant for a trial (non-polypectomy) from Olympus (2013 – 2016); he is a member of the BSG (2000 –). The following authors have no competing interests: M. Bronzwaer, M. Bourke, N. Burgess, J.-M. Dumonceau, M. Ferlitsch, I. Gralnek, M. Gschwantler, C. Hassan, R. Hazzan, D. Heresbach, P. Jeschek, R. Jover, C. Langner, A. Lemmers, A. Moss, K. Nalankilli, K. Paraskeva, G. Paspatis, D. Penz, J. Regula, A. Repici, E. Waldmann.

References

[1] Zauber AG, Winawer SJ, O'Brien MJ et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012; 366: 687 – 696

[2] Bretthauer M, Kaminski MF, Loberg M et al. Population-based colonoscopy screening for colorectal cancer: a randomized clinical trial. JAMA Intern Med 2016; 176: 894 – 902

[3] Brenner H, Stock C, Hoffmeister M. Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies. BMJ 2014; 348: g2467

[4] Moss A, Bourke MJ, Williams SJ et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology 2011; 140: 1909 – 1918

[5] Swan MP, Bourke MJ, Moss A et al. The target sign: an endoscopic marker for the resection of the muscularis propria and potential perforation during colonic endoscopic mucosal resection. Gastrointest Endosc 2011; 73: 79 – 85

[6] Britto-Arias M, Waldmann E, Jeschek P et al. Forceps versus snare polypectomies in colorectal cancer screening: are we adhering to the guidelines? Endoscopy 2015; 47: 898 – 902

[7] Veitch AM, Vanbiervliet G, Gershlick AH et al. Endoscopy in patients on antiplatelet or anticoagulant therapy, including direct oral anticoagulants: British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guidelines. Endoscopy 2016; 48: 385 – 402

[8] Hassan C, Quintero E, Dumonceau JM et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2013; 45: 842 – 851

[9] Rembacken B, Hassan C, Riemann JF et al. Quality in screening colonoscopy: position statement of the European Society of Gastrointestinal Endoscopy (ESGE). Endoscopy 2012; 44: 957 – 968

[10] Atkins D, Best D, Briss PA et al. Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490

[11] Dumonceau JM, Hassan C, Riphaus A et al. European Society of Gastrointestinal Endoscopy (ESGE) Guideline Development Policy. Endoscopy 2012; 44: 626 – 629

[12] [Anonymous] The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003; 58: S3 – 43

[13] Endoscopic Classification Review Group. Update on the Paris classification of superficial neoplastic lesions in the digestive tract. Endoscopy 2005; 37: 570 – 578

[14] Kudo S. Endoscopic mucosal resection of flat and depressed types of early colorectal cancer. Endoscopy 1993; 25: 455 – 461

[15] Bianco MA, Cipolletta L, Rotondano G et al. Prevalence of nonpolypoid colorectal neoplasia: an Italian multicenter observational study. Endoscopy 2010; 42: 279 – 285

[16] Saitoh Y, Obara T, Watari J et al. Invasion depth diagnosis of depressed type early colorectal cancers by combined use of videoendoscopy and chromoendoscopy. Gastrointest Endosc 1998; 48: 362 – 370

[17] Uraoka T, Saito Y, Matsuda T et al. Endoscopic indications for endoscopic mucosal resection of laterally spreading tumours in the colorectum. Gut 2006; 55: 1592 – 1597

[18] Pohl H, Srivastava A, Bensen SP et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013; 144: 74 – 80.e71

[19] van Doorn SC, Hazewinkel Y, East JE et al. Polyp morphology: an interobserver evaluation for the Paris classification among international experts. Am J Gastroenterol 2015; 110: 180 – 187

[20] Kudo Se, Lambert R, Allen JI et al. Nonpolypoid neoplastic lesions of the colorectal mucosa. Gastrointest Endosc 2008; 68: S3 – 47

[21] Lambert R, Kudo S, Vieth M et al. Pragmatic classification of superficial neoplastic colorectal lesions. Gastrointest Endosc 2009; 70: 1182 – 1199

[22] Kamiński MF, Hassan C, Bisschops R et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2014; 46: DOI: 10.1055/s-0034–1365348

[23] Rex DK, Kahi C, O'Brien M et al. The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on real-time endoscopic assessment of the histology of diminutive colorectal polyps. Gastrointest Endosc 2011; 73: 419 – 422

[24] Abu Dayyeh BK, Thosani N, Konda V. ASGE Technology Committee. et al. ASGE Technology Committee systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting real-time endoscopic assessment of the histology of diminutive colorectal polyps. Gastrointest Endosc 2015; 81: 502.e501 – 502.e516

[25] Basford P, Longcroft-Wheaton G, Bhandari P. ASGE Technology Committee reviews on real-time endoscopic assessment of the histology of diminutive colorectal polyps, and high-definition and high-magnification endoscopes. Gastrointest Endosc 2015; 82: 1139 – 1140

[26] Dayyeh BA, Banerjee S. Response. Gastrointest Endosc 2015; 82: 1140 – 1141

[27] Lee CK, Shim JJ, Jang JY. Cold snare polypectomy vs. cold forceps polypectomy using double-biopsy technique for removal of diminutive colorectal polyps: a prospective randomized study. Am J Gastroenterol 2013; 108: 1593 – 1600

[28] Kim JS, Lee BI, Choi H et al. Cold snare polypectomy versus cold forceps polypectomy for diminutive and small colorectal polyps: a randomized controlled trial. Gastrointest Endosc 2015; 81: 741 – 747

[29] Efthymiou M, Taylor AC, Desmond PV et al. Biopsy forceps is inadequate for the resection of diminutive polyps. Endoscopy 2011; 43: 312 – 316

[30] Jung YS, Park JH, Kim HJ et al. Complete biopsy resection of diminutive polyps. Endoscopy 2013; 45: 1024 – 1029

[31] Aslan F, Cekic C, Camci M et al. What is the most accurate method for the treatment of diminutive colonic polyps? Standard versus jumbo forceps polypectomy Medicine (Baltimore) 2015; 94: e621

[32] Peluso F, Goldner F. Follow-up of hot biopsy forceps treatment of diminutive colonic polyps. Gastrointest Endosc 1991; 37: 604 – 606

[33] Paspatis GA, Vardas E, Charoniti I et al. Bipolar electrocoagulation vs conventional monopolar hot biopsy forceps in the endoscopic treatment of diminutive rectal adenomas. Colorectal Dis 2005; 7: 138 – 142

[34] Yasar B, Kayadibi H, Abut E et al. The histological quality and adequacy of diminutive colorectal polyps resected using jumbo versus hot biopsy forceps. Dig Dis Sci 2015; 60: 217 – 225

[35] Weston AP, Campbell DR. Diminutive colonic polyps: histopathology, spatial distribution, concomitant significant lesions, and treatment complications. Am J Gastroenterol 1995; 90: 24 – 28

[36] Savides TJ, See JA, Jensen DM et al. Randomized controlled study of injury in the canine right colon from simultaneous biopsy and coagulation with different hot biopsy forceps. Gastrointest Endosc 1995; 42: 573 – 578

[37] Metz AJ, Moss A, McLeod D et al. A blinded comparison of the safety and efficacy of hot biopsy forceps electrocauterization and conventional snare polypectomy for diminutive colonic polypectomy in a porcine model. Gastrointest Endosc 2013; 77: 484 – 490

[38] Pohl H, Srivastava A, Bensen SP et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013; 144: 74 – 80 e71

[39] Horiuchi A, Nakayama Y, Kajiyama M et al. Removal of small colorectal polyps in anticoagulated patients: a prospective randomized comparison of cold snare and conventional polypectomy. Gastrointest Endosc 2014; 79: 417 – 423

[40] Paspatis GA, Tribonias G, Konstantinidis K et al. A prospective randomized comparison of cold vs hot snare polypectomy in the occurrence of postpolypectomy bleeding in small colonic polyps. Colorectal Dis 2011; 13: e345 – 348

[41] Ichise Y, Horiuchi A, Nakayama Y et al. Prospective randomized comparison of cold snare polypectomy and conventional polypectomy for small colorectal polyps. Digestion 2011; 84: 78 – 81

[42] Voiosu TA, Margarit C, Rimbas M et al. Polypectomy practices in a real life setting. Do we do enough for our patients? A review of 1061 colonoscopies Rom J Intern Med 2011; 49: 257 – 265

[43] Muniraj T, Sahakian A, Ciarleglio MM et al. Cold snare polypectomy for large sessile colonic polyps: a single-center experience. Gastroenterol Res Pract 2015; 2015: 175959

[44] Augusto Barros R, Monteverde MJ, Federico Barros R et al. [Safety and efficacy of cold snare resection of non-polypoid colorectal lesions (0-IIa and 0-IIb)]. Acta Gastroenterol Latinoam 2014; 44: 27 – 32

[45] Dobrowolski S, Dobosz M, Babicki A et al. Blood supply of colorectal polyps correlates with risk of bleeding after colonoscopic polypectomy. Gastrointest Endosc 2006; 63: 1004 – 1009

[46] Watabe H, Yamaji Y, Okamoto M et al. Risk assessment for delayed hemorrhagic complication of colonic polypectomy: polyp-related factors and patient-related factors. Gastrointest Endosc 2006; 64: 73 – 78

[47] Kim HS, Kim TI, Kim WH et al. Risk factors for immediate postpolypectomy bleeding of the colon: a multicenter study. Am J Gastroenterol 2006; 101: 1333 – 1341

[48] Buddingh KT, Herngreen T, Haringsma J et al. Location in the right hemi-colon is an independent risk factor for delayed post-polypectomy hemorrhage: a multi-center case-control study. Am J Gastroenterol 2011; 106: 1119 – 1124

[49] Di Giorgio P, De Luca L, Calcagno G et al. Detachable snare versus epinephrine injection in the prevention of postpolypectomy bleeding: a randomized and controlled study. Endoscopy 2004; 36: 860 – 863

[50] Iishi H, Tatsuta M, Narahara H et al. Endoscopic resection of large pedunculated colorectal polyps using a detachable snare. Gastrointest Endosc 1996; 44: 594 – 597

[51] Dobrowolski S, Dobosz M, Babicki A et al. Prophylactic submucosal saline-adrenaline injection in colonoscopic polypectomy: prospective randomized study. Surg Endosc 2004; 18: 990 – 993

[52] Lee SH, Chung IK, Kim SJ et al. Comparison of postpolypectomy bleeding between epinephrine and saline submucosal injection for large colon polyps by conventional polypectomy: a prospective randomized, multicenter study. World J Gastroenterol 2007; 13: 2973 – 2977

[53] Paspatis GA, Paraskeva K, Theodoropoulou A et al. A prospective, randomized comparison of adrenaline injection in combination with detachable snare versus adrenaline injection alone in the prevention of postpolypectomy bleeding in large colonic polyps. Am J Gastroenterol 2006; 101: 2805; quiz 2913

[54] Kouklakis G, Mpoumponaris A, Gatopoulou A et al. Endoscopic resection of large pedunculated colonic polyps and risk of postpolypectomy bleeding with adrenaline injection versus endoloop and hemoclip: a prospective, randomized study. Surg Endosc 2009; 23: 2732 – 2737

[55] Longcroft-Wheaton G, Duku M, Mead R et al. Risk stratification system for evaluation of complex polyps can predict outcomes of endoscopic mucosal resection. Dis Colon Rectum 2013; 56: 960 – 966

[56] Nanda KS, Tutticci N, Burgess NG et al. Endoscopic mucosal resection of laterally spreading lesions involving the ileocecal valve: technique, risk factors for failure, and outcomes. Endoscopy 2015; 47: 710 – 718

[57] Swan MP, Bourke MJ, Alexander S et al. Large refractory colonic polyps: is it time to change our practice? A prospective study of the clinical and economic impact of a tertiary referral colonic mucosal resection and polypectomy service (with videos) Gastrointest Endosc 2009; 70: 1128 – 1136

[58] Kao KT, Giap AQ, Abbas MA. Endoscopic excision of large colorectal polyps as a viable alternative to surgical resection. Arch Surg 2011; 146: 690 – 696

[59] Church JM. Experience in the endoscopic management of large colonic polyps. ANZ J Surg 2003; 73: 988 – 995

[60] Moss A, Williams SJ, Hourigan LF et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and

risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut 2015; 64: 57 – 65

[61] Buchner AM, Guarner-Argente C, Ginsberg GG. Outcomes of EMR of defiant colorectal lesions directed to an endoscopy referral center. Gastrointest Endosc 2012; 76: 255 – 263

[62] Brooker JC, Saunders BP, Shah SG et al. Endoscopic resection of large sessile colonic polyps by specialist and non-specialist endoscopists. Br J Surg 2002; 89: 1020 – 1024

[63] Conio M, Repici A, Demarquay JF et al. EMR of large sessile colorectal polyps. Gastrointest Endosc 2004; 60: 234 – 241

[64] Binmoeller KF, Weilert F, Shah J et al. "Underwater" EMR without submucosal injection for large sessile colorectal polyps (with video). Gastrointest Endosc 2012; 75: 1086 – 1091

[65] Jayanna M, Burgess NG, Singh R et al. Cost analysis of endoscopic mucosal resection vs surgery for large laterally spreading colorectal lesions. Clin Gastroenterol Hepatol 2016; 14: 271 – 278.e271–272

[66] Ahlenstiel G, Hourigan LF, Brown G et al. Actual endoscopic versus predicted surgical mortality for treatment of advanced mucosal neoplasia of the colon. Gastrointest Endosc 2014; 80: 668 – 676

[67] Keswani RN, Law R, Ciolino JD et al. Adverse events after surgery for benign colon polyps are common and associated with increased length of stay and costs. Gastrointest Endosc 2016; 84: 296 – 303.e1

[68] Moss A, Nalankilli K. Completing the circle of informed consent for EMR versus surgery for nonmalignant large or complex colorectal polyps. Gastrointest Endosc 2016; 84: 304 – 306

[69] Lee EY, Bourke MJ. Endoscopic mucosal resection should be the first-line treatment for large laterally spreading colorectal lesions. Gastrointest Endosc 2016; 64: 326 – 328

[70] Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015; 47: 829 – 854

[71] Repici A, Pellicano R, Strangio G et al. Endoscopic mucosal resection for early colorectal neoplasia: pathologic basis, procedures, and outcomes. Dis Colon Rectum 2009; 52: 1502 – 1515

[72] Niimi K, Fujishiro M, Kodashima S et al. Long-term outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. Endoscopy 2010; 42: 723 – 729

[73] Repici A, Hassan C, De Paula Pessoa D et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. Endoscopy 2012; 44: 137 – 150

[74] Hong YM, Kim HW, Park SB et al. Endoscopic mucosal resection with circumferential incision for the treatment of large sessile polyps and laterally spreading tumors of the colorectum. Clin Endosc 2015; 48: 52 – 58

[75] Kim HG, Thosani N, Banerjee S et al. Underwater endoscopic mucosal resection for recurrences after previous piecemeal resection of colorectal polyps (with video). Gastrointest Endosc 2014; 80: 1094 – 1102

[76] Masci E, Viale E, Notaristefano C et al. Endoscopic mucosal resection in high- and low-volume centers: a prospective multicentric study. Surg Endosc 2013; 27: 3799 – 3805

[77] Kim HH, Kim JH, Park SJ et al. Risk factors for incomplete resection and complications in endoscopic mucosal resection for lateral spreading tumors. Dig Endosc 2012; 24: 259 – 266

[78] Tanaka S, Oka S, Chayama K et al. Knack and practical technique of colonoscopic treatment focused on endoscopic mucosal resection using snare. Dig Endosc 2009; 21: (Suppl. 01): S38 – 42

[79] Lee EJ, Lee JB, Lee SH et al. Endoscopic treatment of large colorectal tumors: comparison of endoscopic mucosal resection, endoscopic mucosal resection-precutting, and endoscopic submucosal dissection. Surg Endosc 2012; 26: 2220 – 2230

[80] Sakamoto T, Matsuda T, Nakajima T et al. Efficacy of endoscopic mucosal resection with circumferential incision for patients with large colorectal tumors. Clin Gastroenterol Hepatol 2012; 10: 22 – 26

[81] Bahin FF, Pellise M, Williams SJ et al. Extended endoscopic mucosal resection does not reduce recurrence compared with standard endoscopic mucosal resection of large laterally spreading colorectal lesions. Gastrointest Endosc 2016: DOI: 10.1016/j.gie.2016.05.015

[82] Klein A, Bourke MJ. Advanced polypectomy and resection techniques. Gastrointest Endosc Clin N Am 2015; 25: 303 – 333

[83] Belderbos TD, Leenders M, Moons LM et al. Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: systematic review and meta-analysis. Endoscopy 2014; 46: 388 – 402

[84] Desomer L, Tutticci N, Tate DJ et al. A standardized imaging protocol is accurate in detecting recurrence after endoscopic mucosal resection. Gastrointest Endosc 2016: Jun 22. pii: S0016-5107(16)30277-2. DOI: 10.1016/j.gie.2016.06.031 [Epub ahead of print]

[85] Regula J, Wronska E, Polkowski M et al. Argon plasma coagulation after piecemeal polypectomy of sessile colorectal adenomas: long-term follow-up study. Endoscopy 2003; 35: 212 – 218

[86] Andrawes S, Haber G. Avulsion: a novel technique to achieve complete resection of difficult colon polyps. Gastrointest Endosc 2014; 80: 167 – 168

[87] Veerappan SG, Ormonde D, Yusoff IF et al. Hot avulsion: a modification of an existing technique for management of nonlifting areas of a polyp (with video). Gastrointest Endosc 2014; 80: 884 – 888

[88] Sakamoto T, Saito Y, Matsuda T et al. Treatment strategy for recurrent or residual colorectal tumors after endoscopic resection. Surg Endosc 2011; 25: 255 – 260

[89] Wada Y, Kudo SE, Kashida H et al. Diagnosis of colorectal lesions with the magnifying narrow-band imaging system. Gastrointest Endosc 2009; 70: 522 – 531

[90] Oba S, Tanaka S, Oka S et al. Characterization of colorectal tumors using narrow-band imaging magnification: combined diagnosis with both pit pattern and microvessel features. Scand J Gastroenterol 2010; 45: 1084 – 1092

[91] Shimura T, Ebi M, Yamada T et al. Magnifying chromoendoscopy and endoscopic ultrasonography measure invasion depth of early stage colorectal cancer with equal accuracy on the basis of a prospective trial. Clin Gastroenterol Hepatol 2014; 12: 662 – 668 e661–662

[92] Yoshida N, Naito Y, Kugai M et al. Efficacy of magnifying endoscopy with flexible spectral imaging color enhancement in the diagnosis of colorectal tumors. J Gastroenterol 2011; 46: 65 – 72

[93] Jang HW, Park SJ, Cheon JH et al. Does magnifying narrow-band imaging or magnifying chromoendoscopy help experienced endoscopists assess invasion depth of large sessile and flat polyps? Dig Dis Sci 2014; 59: 1520 – 1528

[94] Ikematsu H, Matsuda T, Emura F et al. Efficacy of capillary pattern type IIIA/IIIB by magnifying narrow band imaging for estimating depth of invasion of early colorectal neoplasms. BMC Gastroenterol 2010; 10: 33

[95] Hayashi N, Tanaka S, Hewett DG et al. Endoscopic prediction of deep submucosal invasive carcinoma: validation of the narrow-band imaging international colorectal endoscopic (NICE) classification. Gastrointest Endosc 2013; 78: 625 – 632

[96] Hurlstone DP, Cross SS, Adam I et al. Endoscopic morphological anticipation of submucosal invasion in flat and depressed colorectal lesions: clinical implications and subtype analysis of the kudo type V pit pattern using high-magnification-chromoscopic colonoscopy. Colorectal Dis 2004; 6: 369 – 375

[97] Tobaru T, Mitsuyama K, Tsuruta O et al. Sub-classification of type VI pit patterns in colorectal tumors: relation to the depth of tumor invasion. Int J Oncol 2008; 33: 503 – 508

[98] Horie H, Togashi K, Kawamura YJ et al. Colonoscopic stigmata of 1 mm or deeper submucosal invasion in colorectal cancer. Dis Colon Rectum 2008; 51: 1529 – 1534

[99] Saito Y, Fujii T, Kondo H et al. Endoscopic treatment for laterally spreading tumors in the colon. Endoscopy 2001; 33: 682 – 686

[100] Uraoka T, Saito Y, Matsuda T et al. Endoscopic indications for endoscopic mucosal resection of laterally spreading tumours in the colorectum. Gut 2006; 55: 1592 – 1597

[101] Kudo S, Tamura S, Nakajima T et al. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 1996; 44: 8 – 14

[102] Haggitt RC, Glotzbach RE, Soffer EE et al. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. Gastroenterology 1985; 89: 328 – 336

[103] Nivatvongs S, Rojanasakul A, Reiman HM et al. The risk of lymph node metastasis in colorectal polyps with invasive adenocarcinoma. Dis Colon Rectum 1991; 34: 323 – 328

[104] Beaton C, Twine CP, Williams GL et al. Systematic review and meta-analysis of histopathological factors influencing the risk of lymph node metastasis in early colorectal cancer. Colorectal Dis 2013; 15: 788 – 797

[105] Moss A. From gastroenterologist to surgeon to gastroenterologist for management of large sessile colonic polyps: something new under the sun? Gastrointest Endosc 2014; 79: 108 – 110

[106] Friedland S, Banerjee S, Kochar R et al. Outcomes of repeat colonoscopy in patients with polyps referred for surgery without biopsy-proven cancer. Gastrointest Endosc 2014; 79: 101 – 107

[107] Kethu SR, Banerjee S, Desilets D et al. Endoscopic tattooing. Gastrointest Endosc 2010; 72: 681 – 685

[108] Askin MP, Waye JD, Fiedler L et al. Tattoo of colonic neoplasms in 113 patients with a new sterile carbon compound. Gastrointest Endosc 2002; 56: 339 – 342

[109] Moss A, Bourke MJ, Pathmanathan N. Safety of colonic tattoo with sterile carbon particle suspension: a proposed guideline with illustrative cases. Gastrointest Endosc 2011; 74: 214 – 218

[110] Park JW, Sohn DK, Hong CW et al. The usefulness of preoperative colonoscopic tattooing using a saline test injection method with prepackaged sterile India ink for localization in laparoscopic colorectal surgery. Surg Endosc 2008; 22: 501 – 505

[111] Ono S, Fujishiro M, Goto O et al. Endoscopic submucosal dissection for colonic laterally spreading tumors is difficult after target tattooing. Gastrointest Endosc 2009; 69: 763 – 766

[112] Elarini T, Wexner SD, Isenberg GA. The need for standardization of colonoscopic tattooing of colonic lesions. Dis Colon Rectum 2015; 58: 264 – 267

[113] Moss A. Colonic tattooing: the revival of a black art? Gastrointest Endosc 2012; 76: 801 – 803

[114] Fu KI, Fujii T, Kato S et al. A new endoscopic tattooing technique for identifying the location of colonic lesions during laparoscopic surgery: a comparison with the conventional technique. Endoscopy 2001; 33: 687 – 691

[115] Kang HJ, Lee BI, Kim BW et al. Potential cancer cell inoculation of tattoo site through use of a contaminated needle. Gastrointest Endosc 2006; 63: 884 – 886

[116] Yeung JM, Maxwell-Armstrong C, Acheson AG. Colonic tattooing in laparoscopic surgery - making the mark? Colorectal Dis 2009; 11: 527 – 530

[117] Ferrara F, Luigiano C, Ghersi S et al. Efficacy, safety and outcomes of "inject and cut" endoscopic mucosal resection for large sessile and flat colorectal polyps. Digestion 2010; 82: 213 – 220

[118] Lee TJ, Rees CJ, Nickerson C et al. Management of complex colonic polyps in the English Bowel Cancer Screening Programme. Br J Surg 2013; 100: 1633 – 1639

[119] Kim HG, Thosani N, Banerjee S et al. Effect of prior biopsy sampling, tattoo placement, and snare sampling on endoscopic resection of large nonpedunculated colorectal lesions. Gastrointest Endosc 2015; 81: 204 – 213

[120] Nanda KS, Tutticci N, Burgess NG et al. Endoscopic mucosal resection of laterally spreading lesions involving the ileocecal valve: technique, risk factors for failure, and outcomes. Endoscopy 2015; 47: 710 – 718

[121] Holt BA, Bassan MS, Sexton A et al. Advanced mucosal neoplasia of the anorectal junction: endoscopic resection technique and outcomes (with videos). Gastrointest Endosc 2014; 79: 119 – 126

[122] Burgess NG, Metz AJ, Williams SJ et al. Risk factors for intraprocedural and clinically significant delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol 2014; 12: 651 – 661

[123] Hassan C, Repici A, Sharma P et al. Efficacy and safety of endoscopic resection of large colorectal polyps: a systematic review and meta-analysis. Gut 2016; 65: 806 – 820

[124] Metz AJ, Bourke MJ, Moss A et al. Factors that predict bleeding following endoscopic mucosal resection of large colonic lesions. Endoscopy 2011; 43: 506 – 511

[125] Rutter MD, Nickerson C, Rees CJ et al. Risk factors for adverse events related to polypectomy in the English Bowel Cancer Screening Programme. Endoscopy 2014; 46: 90 – 97

[126] Fujiya M, Tanaka K, Dokoshi T et al. Efficacy and adverse events of EMR and endoscopic submucosal dissection for the treatment of colon neoplasms: a meta-analysis of studies comparing EMR and endoscopic submucosal dissection. Gastrointest Endosc 2015; 81: 583 – 595

[127] Chukmaitov A, Bradley CJ, Dahman B et al. Association of polypectomy techniques, endoscopist volume, and facility type with colonoscopy complications. Gastrointest Endosc 2013; 77: 436 – 446

[128] Heldwein W, Dollhopf M, Rosch T et al. The Munich Polypectomy Study (MUPS): prospective analysis of complications and risk factors in 4000 colonic snare polypectomies. Endoscopy 2005; 37: 1116 – 1122

[129] Rabeneck L, Paszat LF, Hilsden RJ et al. Bleeding and perforation after outpatient colonoscopy and their risk factors in usual clinical practice. Gastroenterology 2008; 135: 1899 – 1906 , 1906 e1891

[130] Singh H, Penfold RB, DeCoster C et al. Colonoscopy and its complications across a Canadian regional health authority. Gastrointest Endosc 2009; 69: 665 – 671

[131] Gupta S, Miskovic D, Bhandari PS et al. A novel method for determining the difficulty of colonoscopic polypectomy. Frontline Gastroenterol 2013; 4: 244 – 248

[132] Burgess NG, Bahin FF, Bourke MJ. Colonic polypectomy (with videos). Gastrointest Endosc 2015; 81: 813 – 835

[133] Holt BA, Bourke MJ. Wide field endoscopic resection for advanced colonic mucosal neoplasia: current status and future directions. Clin Gastroenterol Hepatol 2012; 10: 969 – 979

[134] Hwang JH, Konda V, Abu Dayyeh BK et al. Endoscopic mucosal resection. Gastrointest Endosc 2015; 82: 215 – 226

[135] Ferreira AO, Moleiro J, Torres J et al. Solutions for submucosal injection in endoscopic resection: a systematic review and meta-analysis. Endosc Int Open 2016; 4: E1 – E16

[136] Huai ZY, Feng Xian W, Chang Jiang L et al. Submucosal injection solution for endoscopic resection in gastrointestinal tract: a traditional and network meta-analysis. Gastroenterol Res Pract 2015; 2015: 702768

[137] Moss A, Bourke MJ, Metz AJ. A randomized, double-blind trial of succinylated gelatin submucosal injection for endoscopic resection of large sessile polyps of the colon. Am J Gastroenterol 2010; 105: 2375 – 2382

[138] Fasoulas K, Lazaraki G, Chatzimavroudis G et al. Endoscopic mucosal resection of giant laterally spreading tumors with submucosal injection of hydroxyethyl starch: comparative study with normal saline solution. Surg Laparosc Endosc Percutan Tech 2012; 22: 272 – 278

[139] Friedland S, Kothari S, Chen A et al. Endoscopic mucosal resection with an over-the-counter hyaluronate preparation. Gastrointest Endosc 2012; 75: 1040 – 1044

[140] Yamamoto H, Yahagi N, Oyama T et al. Usefulness and safety of 0.4% sodium hyaluronate solution as a submucosal fluid "cushion" in endoscopic resection for gastric neoplasms: a prospective multicenter trial. Gastrointest Endosc 2008; 67: 830 – 839

[141] Yoshida N, Naito Y, Inada Y et al. Endoscopic mucosal resection with 0.13% hyaluronic acid solution for colorectal polyps less than 20 mm: a randomized controlled trial. J Gastroenterol Hepatol 2012; 27: 1377 – 1383

[142] Kishihara T, Chino A, Uragami N et al. Usefulness of sodium hyaluronate solution in colorectal endoscopic mucosal resection. Dig Endosc 2012; 24: 348 – 352

[143] Oka S, Tanaka S, Saito Y et al. Local recurrence after endoscopic resection for large colorectal neoplasia: a multicenter prospective study in Japan. Am J Gastroenterol 2015; 110: 697 – 707

[144] Uraoka T, Saito Y, Yamamoto K et al. Submucosal injection solution for gastrointestinal tract endoscopic mucosal resection and endoscopic submucosal dissection. Drug Des Devel Ther 2009; 2: 131 – 138

[145] Matsui Y, Inomata M, Izumi K et al. Hyaluronic acid stimulates tumor-cell proliferation at wound sites. Gastrointest Endosc 2004; 60: 539 – 543

[146] Uraoka T, Fujii T, Saito Y et al. Effectiveness of glycerol as a submucosal injection for EMR. Gastrointest Endosc 2005; 61: 736 – 740

[147] Feitoza AB, Gostout CJ, Burgart LJ et al. Hydroxypropyl methylcellulose: A better submucosal fluid cushion for endoscopic mucosal resection. Gastrointest Endosc 2003; 57: 41 – 47

[148] Arezzo A, Pagano N, Romeo F et al. Hydroxy-propyl-methyl-cellulose is a safe and effective lifting agent for endoscopic mucosal resection of large colorectal polyps. Surg Endosc 2009; 23: 1065 – 1069

[149] Bacani CJ, Woodward TA, Raimondo M et al. The safety and efficacy in humans of endoscopic mucosal resection with hydroxypropyl methylcellulose as compared with normal saline. Surg Endosc 2008; 22: 2401 – 2406

[150] Woodward T, Crook JE, Raimondo M et al. Improving complete EMR of colorectal neoplasia: a randomized trial comparing snares and injectate in the resection of large sessile colon polyps. Gastrointest Endosc 2015; 81: 673 – 681

[151] Katsinelos P, Kountouras J, Paroutoglou G et al. A comparative study of 50% dextrose and normal saline solution on their ability to create submucosal fluid cushions for endoscopic resection of sessile rectosigmoid polyps. Gastrointest Endosc 2008; 68: 692 – 698

[152] Varadarajulu S, Tamhane A, Slaughter RL. Evaluation of dextrose 50% as a medium for injection-assisted polypectomy. Endoscopy 2006; 38: 907 – 912

[153] Hurlstone DP, Fu KI, Brown SR et al. EMR using dextrose solution versus sodium hyaluronate for colorectal Paris type I and 0-II lesions: a randomized endoscopist-blinded study. Endoscopy 2008; 40: 110 – 114

[154] Fujishiro M, Yahagi N, Kashimura K et al. Tissue damage of different submucosal injection solutions for EMR. Gastrointest Endosc 2005; 62: 933 – 942

[155] Jung YS, Park DI. Submucosal injection solutions for endoscopic mucosal resection and endoscopic submucosal dissection of gastrointestinal neoplasms. Gastrointestinal Intervention 2013; 2: 73 – 77

[156] Al-Taie OH, Bauer Y, Dietrich CG et al. Efficacy of submucosal injection of different solutions inclusive blood components on mucosa elevation for endoscopic resection. Clin Exp Gastroenterol 2012; 5: 43 – 48

[157] Holt BA, Jayasekeran V, Sonson R et al. Topical submucosal chromoendoscopy defines the level of resection in colonic EMR and may improve procedural safety (with video). Gastrointest Endosc 2013; 77: 949 – 953

[158] Tajika M, Niwa Y, Bhatia V et al. Comparison of endoscopic submucosal dissection and endoscopic mucosal resection for large colorectal tumors. Eur J Gastroenterol Hepatol 2011; 23: 1042 – 1049

[159] Puli SR, Kakugawa Y, Gotoda T et al. Meta-analysis and systematic review of colorectal endoscopic mucosal resection. World J Gastroenterol 2009; 15: 4273 – 4277

[160] Bourke M. Current status of colonic endoscopic mucosal resection in the west and the interface with endoscopic submucosal dissection. Dig Endosc 2009; 21: (Suppl. 01): S22 – 27

[161] Moss A, Bourke MJ, Tran K et al. Lesion isolation by circumferential submucosal incision prior to endoscopic mucosal resection (CSI-EMR) substantially improves en bloc resection rates for 40-mm colonic lesions. Endoscopy 2010; 42: 400 – 404

[162] Yoshida N, Saito Y, Hirose R et al. Endoscopic mucosal resection for middle and large colorectal polyps with a double-loop snare. Digestion 2014; 90: 232 – 239

[163] Binmoeller KF, Weilert F, Shah J et al. "Underwater" EMR without submucosal injection for large sessile colorectal polyps (with video). Gastrointest Endosc 2012; 75: 1086 – 1091

[164] Brooker JC, Saunders BP, Shah SG et al. Treatment with argon plasma coagulation reduces recurrence after piecemeal resection of large sessile colonic polyps: a randomized trial and recommendations. Gastrointest Endosc 2002; 55: 371 – 375

[165] Albuquerque W, Arantes VN, Coelho LG et al. Complementation by argon plasma coagulation after endoscopic piecemeal resection of large colorectal adenomas. Rev Col Bras Cir 2013; 40: 404 – 408

[166] Neneman B, Gasiorowska A, Malecka-Panas E. The efficacy and safety of argon plasma coagulation (APC) in the management of polyp remnants in stomach and colon. Adv Med Sci 2006; 51: 88 – 93

[167] Han KS, Sohn DK, Choi DH et al. Prolongation of the period between biopsy and EMR can influence the nonlifting sign in endoscopically resectable colorectal cancers. Gastrointest Endosc 2008; 67: 97 – 102

[168] Uno Y, Munakata A. The non-lifting sign of invasive colon cancer. Gastrointest Endosc 1994; 40: 485 – 489

[169] Ishiguro A, Uno Y, Ishiguro Y et al. Correlation of lifting versus non-lifting and microscopic depth of invasion in early colorectal cancer. Gastrointest Endosc 1999; 50: 329 – 333

[170] Kato H, Haga S, Endo S et al. Lifting of lesions during endoscopic mucosal resection (EMR) of early colorectal cancer: implications for the assessment of resectability. Endoscopy 2001; 33: 568 – 573

[171] Kobayashi N, Saito Y, Sano Y et al. Determining the treatment strategy for colorectal neoplastic lesions: endoscopic assessment or the non-lifting sign for diagnosing invasion depth? Endoscopy 2007; 39: 701 – 705

[172] Tanaka S, Kashida H, Saito Y et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc 2015; 27: 417 – 434

[173] Oxenberg J, Hochwald SN, Nurkin S. Ablative therapies for colorectal polyps and malignancy. Biomed Res Int 2014; 2014: 986352

[174] Miller K, Waye JD. Polyp retrieval after colonoscopic polypectomy: use of the Roth Retrieval Net. Gastrointest Endosc 2001; 54: 505 – 507

[175] Rey JF, Beilenhoff U, Neumann CS et al. European Society of Gastrointestinal Endoscopy (ESGE) guideline: the use of electrosurgical units. Endoscopy 2010; 42: 764 – 772

[176] Tokar JL, Barth BA, Banerjee S et al. Electrosurgical generators. Gastrointest Endosc 2013; 78: 197 – 208

[177] Singh N, Harrison M, Rex DK. A survey of colonoscopic polypectomy practices among clinical gastroenterologists. Gastrointest Endosc 2004; 60: 414 – 418

[178] Carter D, Beer-Gabel M, Zbar A et al. A survey of colonoscopic polypectomy practice amongst Israeli gastroenterologists. Ann Gastroenterol 2013; 26: 135 – 140

[179] Chino A, Karasawa T, Uragami N et al. A comparison of depth of tissue injury caused by different modes of electrosurgical current in a pig colon model. Gastrointest Endosc 2004; 59: 374 – 379

[180] Van Gossum A, Cozzoli A, Adler M et al. Colonoscopic snare polypectomy: analysis of 1485 resections comparing two types of current. Gastrointest Endosc 1992; 38: 472 – 475

[181] Parra-Blanco A, Kaminaga N, Kojima T et al. Colonoscopic polypectomy with cutting current: is it safe? Gastrointest Endosc 2000; 51: 676 – 681

[182] Wu J, Hu B. The role of carbon dioxide insufflation in colonoscopy: a systematic review and meta-analysis. Endoscopy 2012; 44: 128 – 136

[183] Hsu WF, Hu WH, Chen YN et al. Carbon dioxide insufflation can significantly reduce toilet use after colonoscopy: a double-blind randomized controlled trial. Endoscopy 2014; 46: 190 – 195

[184] Bassan MS, Holt B, Moss A et al. Carbon dioxide insufflation reduces number of postprocedure admissions after endoscopic resection of large colonic lesions: a prospective cohort study. Gastrointest Endosc 2013; 77: 90 – 95

[185] Fahrtash-Bahin F, Holt BA, Jayasekeran V et al. Snare tip soft coagulation achieves effective and safe endoscopic hemostasis during wide-field endoscopic resection of large colonic lesions (with videos). Gastrointest Endosc 2013; 78: 158 – 163. e1

[186] Baron TH, Song LM, Ross A et al. Use of an over-the-scope clipping device: multicenter retrospective results of the first U.S. experience (with videos). Gastrointest Endosc 2012; 76: 202 – 208

[187] Shioji K, Suzuki Y, Kobayashi M et al. Prophylactic clip application does not decrease delayed bleeding after colonoscopic polypectomy. Gastrointest Endosc 2003; 57: 691 – 694

[188] Liaquat H, Rohn E, Rex DK. Prophylactic clip closure reduced the risk of delayed postpolypectomy hemorrhage: experience in 277 clipped large sessile or flat colorectal lesions and 247 control lesions. Gastrointest Endosc 2013; 77: 401 – 407

[189] Bahin FF, Naidoo M, Williams SJ et al. Prophylactic endoscopic coagulation to prevent bleeding after wide-field endoscopic mucosal resection of large sessile colon polyps. Clin Gastroenterol Hepatol 2015; 13: 724 – 730

[190] Gandhi S, Narula N, Mosleh W et al. Meta-analysis: colonoscopic post-polypectomy bleeding in patients on continued clopidogrel therapy. Aliment Pharmacol Ther 2013; 37: 947 – 952

[191] Parikh ND, Zanocco K, Keswani RN et al. A cost-efficacy decision analysis of prophylactic clip placement after endoscopic removal of large polyps. Clin Gastroenterol Hepatol 2013; 11: 1319 – 1324

[192] Friedland S, Soetikno R. Colonoscopy with polypectomy in anticoagulated patients. Gastrointest Endosc 2006; 64: 98 – 100

[193] Bahin FF, Rasouli KN, Byth K et al. Prediction of clinically significant bleeding following wide-field endoscopic resection of large sessile and laterally spreading colorectal lesions: a clinical risk score. Am J Gastroenterol 2016; 111: 1115 – 1122

[194] Ron-Tal Fisher O, Gralnek IM, Eisen GM et al. Endoscopic hemostasis is rarely used for hematochezia: a population-based study from the Clinical Outcomes Research Initiative National Endoscopic Database. Gastrointest Endosc 2014; 79: 317 – 325

[195] Church J. Complications of colonoscopy. Gastroenterol Clin North Am 2013; 42: 639 – 657

[196] Strate LL, Gralnek IM. ACG Clinical Guideline: Management of patients with acute lower gastrointestinal bleeding. Am J Gastroenterol 2016; 111: 459 – 474

[197] Jensen DM, Machicado GA, Jutabha R et al. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med 2000; 342: 78 – 82

[198] Sonnenberg A. Management of delayed postpolypectomy bleeding: a decision analysis. Am J Gastroenterol 2012; 107: 339 – 342

[199] Burgess NG, Williams SJ, Hourigan LF et al. A management algorithm based on delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol 2014; 12: 1525 – 1533

[200] Parra-Blanco A, Kaminaga N, Kojima T et al. Hemoclipping for postpolypectomy and postbiopsy colonic bleeding. Gastrointest Endosc 2000; 51: 37 – 41

[201] Paspatis GA, Vardas E, Theodoropoulou A et al. Complications of colonoscopy in a large public county hospital in Greece. A 10-year study. Dig Liver Dis 2008; 40: 951 – 957

[202] Slivka A, Parsons WG, Carr-Locke DL. Endoscopic band ligation for treatment of post-polypectomy hemorrhage. Gastrointest Endosc 1994; 40: 230 – 232

[203] Smith RE, Doull J. Treatment of colonic post-polypectomy bleeding site by endoscopic band ligation. Gastrointest Endosc 1994; 40: 499 – 500

[204] Paspatis GA, Dumonceau JM, Barthet M et al. Diagnosis and management of iatrogenic endoscopic perforations: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy 2014; 46: 693 – 711

[205] Adler A, Lieberman D, Aminalai A et al. Data quality of the German screening colonoscopy registry. Endoscopy 2013; 45: 813 – 818

[206] Burgess NG, Bassan MS, McLeod D et al. Deep mural injury and perforation after colonic endoscopic mucosal resection: a new classification and analysis of risk factors. Gut 2016: , Jul 27. pii: gutjnl-2015-309848. doi: DOI: 10.1136/gutjnl-2015-309848 Epub ahead of print

[207] von Karsa L, Patnick J, Segnan N et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis: overview and introduction to the full supplement publication. Endoscopy 2013; 45: 51 – 59

[208] Quirke P, Risio M, Lambert R et al. Quality assurance in pathology in colorectal cancer screening and diagnosis – European recommendations. Virchows Archiv 2011; 458: 1 – 19

[209] Vieth M, Quirke P, Lambert R et al. Annex to Quirke et al. Quality assurance in pathology in colorectal cancer screening and diagnosis: annotations of colorectal lesions. Virchows Archiv 2011; 458: 21 – 30

[210] Vieth M, Quirke P, Lambert R et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First edition – Annotations of colorectal lesions. Endoscopy 2012; 44: (Suppl. 03): SE131 – 139

[211] Hamilton SR, Bosman FT, Boffetta P et al. Carcinoma of the colon and rectum. In: Bosman FT, Carneiro F, Hruban RH, Theise ND, eds. WHO classification of tumours of the digestive system. 4th edn. Lyon: IARC; 2010: 134 – 146

[212] Langner C. Serrated and non-serrated precursor lesions of colorectal cancer. Dig Dis 2015; 33: 28 – 37

[213] Rex DK, Ahnen DJ, Baron JA et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. Am J Gastroenterol 2012; 107: 1315 – 1329 ; quiz 1314, 1330

[214] Bettington M, Walker N, Clouston A et al. The serrated pathway to colorectal carcinoma: current concepts and challenges. Histopathology 2013; 62: 367 – 386

[215] Hazewinkel Y, de Wijkerslooth TR, Stoop EM et al. Prevalence of serrated polyps and association with synchronous advanced neoplasia in screening colonoscopy. Endoscopy 2014; 46: 219 – 224

[216] Snover DC. Update on the serrated pathway to colorectal carcinoma. Hum Pathol 2011; 42: 1 – 10

[217] Ensari A, Bilezikci B, Carneiro F et al. Serrated polyps of the colon: how reproducible is their classification? Virchows Archiv 2012; 461: 495 – 504

[218] Rau TT, Agaimy A, Gehoff A et al. Defined morphological criteria allow reliable diagnosis of colorectal serrated polyps and predict polyp genetics. Virchows Archiv 2014; 464: 663 – 672

[219] Bettington ML, Walker NI, Rosty C et al. A clinicopathological and molecular analysis of 200 traditional serrated adenomas. Mod Pathol 2015; 28: 414 – 427

[220] Bettington ML, Chetty R. Traditional serrated adenoma: an update. Hum Pathol 2015; 46: 933 – 938

[221] Resch A, Langner C. Risk assessment in early colorectal cancer: histological and molecular markers. Dig Dis 2015; 33: 77 – 85

[222] Kikuchi R, Takano M, Takagi K et al. Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. Dis Colon Rectum 1995; 38: 1286 – 1295

[223] Williams JG, Pullan RD, Hill J et al. Management of the malignant colorectal polyp: ACPGBI position statement. Colorectal Dis 2013; 15: (Suppl. 02): 1 – 38

[224] Bosch SL, Teerenstra S, de Wilt JH et al. Predicting lymph node metastasis in pT1 colorectal cancer: a systematic review of risk factors providing rationale for therapy decisions. Endoscopy 2013; 45: 827 – 834

[225] Ueno H, Mochizuki H, Hashiguchi Y et al. Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology 2004; 127: 385 – 394

[226] Brown IS, Bettington ML, Bettington A et al. Adverse histological features in malignant colorectal polyps: a contemporary series of 239 cases. J Clin Pathol 2016; 69: 292 – 299

[227] Hassan C, Zullo A, Risio M et al. Histologic risk factors and clinical outcome in colorectal malignant polyp: a pooled-data analysis. Dis Colon Rectum 2005; 48: 1588 – 1596

[228] Resch A, Schneider NI, Langner C. Pathological evaluation of colorectal cancer specimens: advanced and early lesions. Cesk Patol 2015; 51: 12 – 22

[229] Gunderson LL, Jessup JM, Sargent DJ et al. Revised TN categorization for colon cancer based on national survival outcomes data. J Clin Oncol 2010; 28: 264 – 271

[230] Macias-Garcia F, Celeiro-Munoz C, Lesquereux-Martinez L et al. A clinical model for predicting lymph node metastasis in submucosal invasive (T1) colorectal cancer. Int J Colorectal Dis 2015; 30: 761 – 768

[231] Pollard CW, Nivatvongs S, Rojanasakul A et al. The fate of patients following polypectomy alone for polyps containing invasive carcinoma. Dis Colon Rectum 1992; 35: 933 – 937

[232] Matsuda T, Fukuzawa M, Uraoka T et al. Risk of lymph node metastasis in patients with pedunculated type early invasive colorectal cancer: a retrospective multicenter study. Cancer Sci 2011; 102: 1693 – 1697

[233] Nascimbeni R, Burgart LJ, Nivatvongs S et al. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum 2002; 45: 200 – 206

[234] Toh EW, Brown P, Morris E et al. Area of submucosal invasion and width of invasion predicts lymph node metastasis in pT1 colorectal cancers. Dis Colon Rectum 2015; 58: 393 – 400

[235] Choi JY, Jung SA, Shim KN et al. Meta-analysis of predictive clinicopathologic factors for lymph node metastasis in patients with early colorectal carcinoma. J Korean Med Sci 2015; 30: 398 – 406

[236] Mou S, Soetikno R, Shimoda T et al. Pathologic predictive factors for lymph node metastasis in submucosal invasive (T1) colorectal cancer: a systematic review and meta-analysis. Surg Endosc 2013; 27: 2692 – 2703

[237] Wada H, Shiozawa M, Katayama K et al. Systematic review and meta-analysis of histopathological predictive factors for lymph node metastasis in T1 colorectal cancer. J Gastroenterol 2015; 50: 727 – 734

[238] Kawaura K, Fujii S, Murata Y et al. The lymphatic infiltration identified by D2–40 monoclonal antibody predicts lymph node metastasis in submucosal invasive colorectal cancer. Pathobiology 2007; 74: 328 – 335

[239] Chandler I, Houlston RS. Interobserver agreement in grading of colorectal cancers-findings from a nationwide web-based survey of histopathologists. Histopathology 2008; 52: 494 – 499

[240] Choi DH, Sohn DK, Chang HJ et al. Indications for subsequent surgery after endoscopic resection of submucosally invasive colorectal carcinomas: a prospective cohort study. Dis Colon Rectum 2009; 52: 438 – 445

[241] Tateishi Y, Nakanishi Y, Taniguchi H et al. Pathological prognostic factors predicting lymph node metastasis in submucosal invasive (T1) colorectal carcinoma. Mod Pathol 2010; 23: 1068 – 1072

[242] Wang LM, Kevans D, Mulcahy H et al. Tumor budding is a strong and reproducible prognostic marker in T3N0 colorectal cancer. Am J Surg Pathol 2009; 33: 134 – 141

[243] Hase K, Shatney C, Johnson D et al. Prognostic value of tumor "budding" in patients with colorectal cancer. Dis Colon Rectum 1993; 36: 627 – 635

[244] Hackelsberger A, Fruhmorgen P, Weiler H et al. Endoscopic polypectomy and management of colorectal adenomas with invasive carcinoma. Endoscopy 1995; 27: 153 – 158

[245] Coverlizza S, Risio M, Ferrari A et al. Colorectal adenomas containing invasive carcinoma. Pathologic assessment of lymph node metastatic potential. Cancer 1989; 64: 1937 – 1947

[246] Morson BC, Whiteway JE, Jones EA et al. Histopathology and prognosis of malignant colorectal polyps treated by endoscopic polypectomy. Gut 1984; 25: 437 – 444

[247] Naqvi S, Burroughs S, Chave HS et al. Management of colorectal polyp cancers. Ann R Coll Surg Engl 2012; 94: 574 – 578

[248] Butte JM, Tang P, Gonen M et al. Rate of residual disease after complete endoscopic resection of malignant colonic polyp. Dis Colon Rectum 2012; 55: 122 – 127

[249] Cooper HS, Deppisch LM, Gourley WK et al. Endoscopically removed malignant colorectal polyps: clinicopathologic correlations. Gastroenterology 1995; 108: 1657 – 1665

[250] Netzer P, Binek J, Hammer B et al. Significance of histologic criteria for the management of patients with malignant colorectal polyps and polypectomy. Scand J Gastroenterol 1997; 32: 910 – 916

[251] Volk EE, Goldblum JR, Petras RE et al. Management and outcome of patients with invasive carcinoma arising in colorectal polyps. Gastroenterology 1995; 109: 1801 – 1807

[252] Kitajima K, Fujimori T, Fujii S et al. Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study. J Gastroenterol 2004; 39: 534 – 543

[253] Seitz U, Bohnacker S, Seewald S et al. Is endoscopic polypectomy an adequate therapy for malignant colorectal adenomas? Presentation

of 114 patients and review of the literature. Dis Colon Rectum 2004; 47: 1789 – 1796 ; discussion 1796–1787

[254] Cunningham KN, Mills LR, Schuman BM et al. Long-term prognosis of well-differentiated adenocarcinoma in endoscopically removed colorectal adenomas. Dig Dis Sci 1994; 39: 2034 – 2037

[255] Jass JR. Malignant colorectal polyps. Gastroenterology 1995; 109: 2034 – 2035

[256] Quirke P, Risio M, Lambert R et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First edition – Quality assurance in pathology in colorectal cancer screening and diagnosis. Endoscopy 2012; 44: (Suppl. 03): SE116 – 130

[257] National Institute for Health Care Excellence. Colorectal cancer: the diagnosis and management of colorectal cancer. National Institute for Health Care Excellence (NICE) Guideline. Available at: https://www.nice.org.uk/Guidance/cg131

Appendix 1. European Society of Gastrointestinal Endoscopy (ESGE) Guideline on colorectal polypectomy and endoscopic mucosal resection (EMR)

Key questions and task forces

General comments

Note that management of anticoagulation and other medications in the periprocedural setting is not covered here, as it is covered by other guidelines

This Guideline does not address post-polypectomy surveillance questions as these are covered in a separate guideline.

Key questions	Task force (leader in bold)
1. Polyp definitions, definition of polypectomy, mucosectomy, polypectomy indications, and efficacy	**Dumonceau, J-M**
(a) What is the definition of a polyp? How should polyps be classified (Paris classification)?	Hassan, C
(b) Which polyps should be removed? Do all polyps require retrieval for histology (just mention, PIVI I, PIVI II)?	Bhandari, P
(c) Definition of polypectomy, mucosectomy.	Rutter, M
(d) What are the benefits of polypectomy? (mortality, colorectal cancer prevention, cost benefit)	Regula, J
2. What is the evidence-based approach to polypectomy of different polyp types and sizes?	**Moss, A**
What is the best approach to achieve safe and complete polypectomy for the following polyps?	
(a) Diminutive polyps ≤ 5 mm	Heresbach, D,
(b) Small polyps (6 – 9 mm)	Gschwantler, M
(c) Sessile polyps 10 – 19 mm	Gralnek, I
(d) Pedunculated lesions according to diameter of stalk and head size, does a specific cutoff exist: (stalk ≤ 5 mm, head ≤ 15 – 20 mm, pedunculated lesions: stalk > 5 mm, head > 15 – 20 mm)?	Paspatis, G
(e) Which polyps should be referred to experts (definition of an expert?) (better tertiary center???) for removal? Which polyps require greater level of support (e. g. hospital environment) for removal?	Fockens, P
(f) Which polyps require other (non-snare) techniques e. g. endoscopic submucosal dissection (ESD) or surgery. Pre-removal criteria (SMSA criteria: size, morphology, site, access)	Fockens, P
(g) Which lesions should be tattooed? What is the best technique and location for tattoo placement?	Moss, A
3. Endoscopic mucosal resection (EMR) for sessile laterally spreading polyps sized 20 mm or greater – evidence for:	**Bourke, M**
(a) Lesion specific assessment prior to EMR (SMSA): when not to proceed	Bhandari, P,
(b) Brief description of the EMR technique – injection technique, snare technique, approach to the lesion (en bloc/piecemeal, proximal/distal edge first) and snare selection (size and type)	Bourke, M
(c) Submucosal injection – which solution is best?	Paraskeva, K
(d) Limits of en bloc resection	Lemmers, A
(e) Adjunctive ablation, e. g. argon plasma coagulation (APC) or soft coagulation	Gralnek, I
(f) Management of the non-lifting polyp	Bourke, K,
(g) Definition of the successful EMR procedure and dealing with incomplete resection	Lemmers, A
(h) Specimen retrieval and dealing with the specimens for histology (belong in part to key question 6?)	Lemmers, A, Langner, C
4. Technical equipment	**Bhandari, P**
(a) What electrocautery generator for polypectomy is best?	Repici, A

(Continuation)

Key questions	Task force (leader in bold)
(b) Benefit of carbon dioxide (CO_2) use	Repici, A
(c) Indications for APC use	Bhandari, P
(d) Which types of snares should be used for different polyps	Bhandari, P
(e) Team working (snare, needle…)	De Pater, M
5. Completeness of polypectomy/prevention of polyp recurrence	**Jover, R**
(a) What is the rate of post-polypectomy and post-EMR recurrence?	Pohl, J
(b) What are the predictive factors for recurrence?	Pohl, J
(c) What are the endoscopic techniques to prevent/detect/treat recurrences?	Rutter, M
(d) How can we prove completeness of resection after forceps/snare polypectomy or EMR? When should we attempt to prove this, and using what technique?	Jover, R
(e) Interval cancer due to incomplete resection or missed lesions	Ferlitsch, M
6. Histological management of the histology specimen	**Langner, C**
(a) How is the histology specimen best managed and reported upon – processing, analysis and reporting. Are there requirements of a histologist managing polypectomy specimens (minimum reporting standards)?	Langner, C
(b) What histology findings should require further action e. g. referral for surgery. E.g. discussion about Haggitt level for pedunculated polyps, lymphovascular invasion, degree of differentiation, superficial submucosal invasion, and lymph node involvement risk	Bourke, M
7. Complications and their management	**Paspatis, G**
(a) What are the risks associated with polypectomy? How can those risks be mitigated/controlled (prevention of complications).	Gralnek, I
(b) Methods to ameliorate frequency and severity of post-polypectomy complications (bleeding and perforation): How to assess risk/stratify risk. Which techniques (e. g. prophylactic clip).	Gralnek, I
(c) Definition of bleeding (major, minor, go to upper GI ESGE guideline)	Gralnek, I
(d) Management of immediate, delayed and refractory bleeding	Gralnek, I
(e) Perforation – policy and protocols	Paspatis, G
(f) Management of complications: perforation: immediate and delayed, target sign, risk factors, peritoneal cavity management, diagnosis and endoscopic/surgical treatment	Paspatis, G
(g) Pain due to other causes (not perforation), post-polypectomy syndrome	Paspatis, G
(h) How to audit complication rate?	Regula, J
8: Other issues	**Ferlitsch, M**
(a) What are the quality indicators for polypectomy/mucosectomy?	Ferlitsch, M
(b) What is the training (minimal standards, volume of EMR)?	Bhandari, P
(c) Do we need tertiary centres? Role of the advanced tissue resection network for advanced colonic lesions.	Bhandari, P
(d) Research questions	Fockens, P

PIVI, Preservation and Incorporation of Valuable endoscopic Innovations

Appendix 2. Evidence tables: European Society of Gastrointestinal Endoscopy (ESGE) Guideline on colorectal polypectomy and endoscopic mucosal resection (EMR)

Table 1 Effect of polypectomy and colorectal cancer (CRC) screening programs on CRC incidence and CRC mortality.

First author, year [ref.]	Study design	Intervention and comparator	Participants	CRC incidence	CRC mortality	Level of evidence Remarks
Atkin, 1992 [1]	Cohort	Rectal and sigmoid cancer incidence among patients with adenomas removed from rectosigmoid compared with expected age- and sex-specific incidences in the UK general population	1618 patients enrolled between 1957 and 1980, following removal of at least one adenoma.	Standardized incidence ratio (after excluding 1st 2 years of observation): Rectal cancer: 1.2, 95%CI 0.7–2.1 Colon cancer: 2.1 95% CI 1.5–3.0		Low. Full colonoscopy was not performed. Majority of cancers were above sigmoid colon.
Citarda, 2001 [2]	Cohort	CRC incidence among patients with adenomas removed compared with expected age- and sex-specific incidences in the Italian general population	1693 patients enrolled between 1980 and 1987 following a total colon examination with removal of at least one adenoma larger than 5 mm in diameter Age 40–69 years,	Standardized incidence ratio: 0.34, 95%CI 0.23–0.63		Moderate
Cottett, 2012 [3]	Registry	CRC incidence among patients with adenomas removed compared with expected age- and	5779 patients enrolled between 1990 and 1999 following removal/biopsy(?)	Standardized incidence ratio (after excluding 1st year of		Low quality. It is not certain whether adenomas

		sex-specific incidences in the general population	of at least 1 adenoma	observation): 1.26; 95%CI 1,01–1,56 For initial advanced adenoma: 2.23, 95%CI 1.67–2.92 When surveillance present: 1.10, 95%CI 0.62–1.82, When no surveillance: 4.26, 95%CI 2.89–6.04		were really removed or biopsied. Not certain whether full colonoscopies were performed
Løberg, 2014 [4]	Registry	Between 1993 and 2007	40 826 patients 334 152 patient-years Median follow-up time, 7.7 years High risk adenoma group defined as: multiple adenomas (>2), villous component, HGD (size not included)		Standardized incidence-based mortality ratio (SMR) for high risk adenomas 1.16 95%CI 1.02–1.31 SMR for low risk adenomas: 0.75 95%CI 0.63–0.88)	Moderate quality.
Loeve, 2004 [5]	Registry	CRC incidence among patients with adenomas removed compared with expected age- and sex-specific incidences in the Dutch general population	78 473 patients enrolled between 1988 and 1998 following biopsy/ removal of at least 1 adenoma.	Standardized incidence ratio (SIR) (after excluding 1st year of observation): 1.5, 95%CI 1.4–1.6		Low quality. Not sure if full colonoscopy performed. Polyps were removed or only biopsied. The SIR was highest within first 2 years, which suggests low

						quality examination
Nishihara, 2013 [6]	Cohort	Hazard ratio of CRC among patients who underwent polypectomy as compared with patients who had no endoscopy	88 902 patients from two different cohorts between 1988 and 2008	Hazard ratio: 0.60, 95% CI 0.53–0.68		Moderate quality.
Winawer 1993, [7]	Cohort	CRC incidence among patients with adenomas removed compared with 3 reference populations (St Mark's cohort, the Mayo Clinic cohort, the SEER program cohort)	1418 patients with complete colonoscopy and 1 or more adenomas removed between November 1980 and February 1990 Mean age: 61 yrs (range 22–88)	Standardized incidence ratio: 1st ref. group: 0.12 95%CI 0.04–0.27 2nd ref group: 0.10 95%CI 0.03–0.24 3rd ref group: 0.24 95%CI 0.08–0.56		Moderate.
Zauber 2012, [8]	Cohort	Mortality from CRC among patients with adenomas removed, compared with the expected incidence-based mortality from CRC in the general population, and with the observed mortality from CRC among patients with nonadenomatous polyps (internal control	2602 patients who had adenomas removed during participation in the study (National Polyp Study initial colonoscopy between 1980 and 1990)		Standardized incidence-based mortality ratio: 0.47 95%CI 0.26–0.80, with colonoscopic polypectomy Mortality from CRC among patients with adenomas and those with nonadenomatous polyps during the first 10 years after	Moderate

		group)			polypectomy, RR, 1.2 95% CI 0.1–10.6	

CI, confidence interval; HGD, high grade dysplasia; SEER, Surveillance, Epidemiology, and End Results; RR, relative risk.

Table 2 Summary of studies on quality or completeness of polypectomy of diminutive polyps

First author, year [ref.]	**Study design,** **Study objective**	**Intervention***	**Participants**	**Outcomes**	**Results**	**Level of evidence,** **Conclusions**
Goldstein, 2001 [9]	Open study	HBF	119 diminutive polyps	Histological artifact impairing diagnosis	17%	Low quality
Yasar, 2015 [10]	Prospective study	HBF vs. JBF	237 diminutive polyps among 179 patients	Artefact and + diagnosis	30% vs. 10%* 80% vs. 96%*	Low quality
Vanagunas, 1989 [11]	Controlled study	HBF Fixed 2 seconds vs. until showing visible white necrosis	14 vs. 21 diminutive polyps	Polyps eradication	42% vs. 83%*	Moderate quality
Peluso, 1991 [12]	Open study	HBF	62 diminutive polyps	Remnant polyps	17%	Low quality
Woods, 1989 [13]	Randomized trial	BICAP vs. CBF	77 vs. 79 diminutive polyps	Remnant adenoma	21% vs. 27%	High quality
Paspatis, 2005 [14]	Randomized trial	BICAP vs. HBF	38 vs. 37 rectal diminutive polyps	Remnant polyps on systematic follow-up (2–4 months)	5.2% vs. 10.8%	High quality

Efthymiou, 2011 [15]	Prospective open study	CBF and EMR	54 diminutive polyps among 52 patients	Remnant polyps on systematic EMR post CBF	38%	Moderate quality
Jung, 2013 [16]	Prospective open study	CBF and indigo carmine chromoscopy	86 diminutive polyps among 65 patients	Remnant adenoma on systematic endoscopic indigo carmine chromoscopy post CBF	9%	Moderate quality
Lee, 2013 [17]	Randomized trial	CSP vs. CBF	117 diminutive polyps	Remnant polyps on systematic CBF post polypectomy	7% vs. 24%*	High quality
Kim, 2015 [18]	Randomized trial	CSP vs. CBF	59 diminutive polyps	Remnant polyps on systematic CBF post polypectomy	0 vs. 6%	Moderate quality
Gómez, 2015 [19]	Randomized trial	CBF vs. CSP vs. HSP	62 diminutive polyps	Remnant polyps on EMR of the polypectomy base or systematic 4 CBFs post polypectomy	12 vs. 11 vs. 6%	High quality
Weston, 1995 [20]	Retrospective study	HBF compared to CBF	1525 compared to 436 diminutive polyps	Significant hemorrhage	0.4% after HBF	Low quality
McAfee, 1994 [21]	Open study	CSP	183 diminutive polyps (<7 mm)	Clinical hemorrhage	0.52%	Low quality
Paspatis, 2011 [22]	Randomized trial	CSP compared to HSP	208 small polyps† (CSP) compared to 206 small polyps† (HSP)	Intraprocedural bleeding	8.2% vs. 0.5%	High quality

Aslan, 2014 [23]	Retrospective study	CSP compared to HSP	77 small polyps† (49 patients) compared to 71 small polyps† (48 patients)	Clinical hemorrhage	1.3% vs. 1.4%	Low quality

BICAP, biopsy with bipolar coagulation; EMR, endoscopic mucosal resection; CBF, cold biopsy forceps; CSP, cold snare polypectomy; HBF, hot biopsy forceps; HSP, hot snare polypectomy; JBF, jumbo biopsy forceps.

* Significant difference

† Small polyps <10 mm)

Table 3 Summary of studies on quality or completeness of polypectomy of small (6–9 mm) polyps

First author, year [ref.]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Pohl, 2013 [24]	2-center prospective study	Snare with blended coagulation, Forceps biopsies from resection margin	1427 patients with at least one 5–20 mm polyp	Incomplete resection rate	6.8% (for 5–9 mm)	Moderate quality
Kim, 2015 [25]	Single-center RCT	Cold snare vs. cold forceps	139 patients with at least one adenomatous polyp ≤7 mm	Complete resection rate	93.8% vs. 70.3% *P* = 0.013 (for 5–7 mm)	Moderate quality
Repici, 2012 [26]	Prospective multicenter trial	Cold snare (for 6–9 mm polyps)	832 patients with 1015 polyps <10 mm, including 193 polyps 6–9 mm	Immediate post-polypectomy bleeding	1.8% (successful endoscopic hemostasis in all cases)	Moderate quality
Paspatis, 2011 [22]	Prospective randomized study (unblinded, 3 endoscopists)	Hot snare vs. cold snare	414 patients with polyps (3–8 mm)	Intraprocedural bleeding; Early or late post-polypectomy bleeding	Intraprocedural bleeding: 1.0% vs. 9.1% (*P* < 0.001) but bleeding resolved spontaneously in all cases; No early or late post-polypectomy bleeding in both groups	Moderate quality
Ichise, 2011 [27]	RCT (3 endoscopists)	Hot snare vs. cold snare	80 patients with polyps ≤8 mm	Abdominal symptoms, bleeding, retrieval rate,	Symptoms 20.0% vs. 2.5% (*P* = 0.029);	Moderate quality

				procedure time	Bleeding 0% vs. 0%; Retrieval 96% vs. 96% Procedure time shorter with CSP (18 vs. 25 min, $P < 0.0001$)	
Horiuchi, 2014 [28]	Single center RCT	Hot snare vs. cold snare	70 **anticoagulated patients** with 159 polyps ≤10 mm	Immediate and delayed bleeding requiring hemostasis, complete polyp retrieval	23% vs. 5.7% ($P = 0.042$) for immediate bleeding; 14% vs. 0% ($P = 0.027$) for delayed bleeding; complete polyp retrieval (94% vs. 93%, n.s.)	Moderate quality

RCT, randomized controlled trial; n.s., not significant.

Table 4 Summary of studies on quality or completeness of polypectomy of polyps 10–19 mm

First author, year [ref.]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusion
Yoshida, 2012 [29]	Prospective randomized controlled trial	196 patients, colon polyps of <20 mm diameter, enrolled and randomized in a 1:1 ratio for EMR with 0.13% hyaluronic acid or normal saline	196 patients	Histopathologically confirmed complete resection	Compete resection: – 0.13% hyaluronic acid, 74 of 93 polyps (79.5%); – Normal saline, 63 of 96 polyps (65.6%) ($P < 0.05$) High mucosal elevation maintained: – 0.13% hyaluronic acid, 83.9% of procedures; – Normal saline, 54.1% ($P < 0.01$). Frequency of complete resection achieved by less experienced endoscopists: – Higher in the 0.13% hyaluronic acid group (79.3%) than in the normal saline group (62.1%); $P < 0.05$)	EMR using 0.13% hyaluronic acid for colon polyps of less than 20 mm diameter is more effective than normal saline for complete resection and maintenance of mucosal elevation High level
Muniraj, 2015 [30]	Retrospective	CSP outcomes in patients with sessile polyps ≥10 mm	30 sessile polyps ≥10 mm in a total of 30 patients 15 polyps 10–19 mm	Completeness of the polypectomy Secondary outcome measures: Immediate and delayed	Among 27 patients (90%) who had follow-up colonoscopy within 6 months, 80% had complete polyp resection and did not require any further intervention.	CSP was feasible in large sessile polyps with no adverse events (0/30) and with an acceptable rate of residual polyp on follow-up colonoscopy

				bleeding; Perforation; Post-polypectomy syndrome; Complication requiring admission.		Low level
Katsinelos, 2008 [31]	Prospective, double-blind, randomized	Polypectomy with D(50)+E or NS+E submucosal fluid cushions	Patients treated for sessile rectosigmoid polyps (>10 mm 1370 polypectomies in 2006	Duration of submucosal elevation, Volume of solution, Number of injections required to maintain elevation, Observations for complications	92 sessile rectosigmoid polyps removed Injected solution volumes: – Lower for D(50)+E than for NS+E (P = 0.033) Number of injections required: – Lower for D(50)+E than for NS+E (P = 0.028) Submucosal elevation duration : – Longer with D(50)+E (P = 0.043) This difference mainly included large (≥20 mm) and giant (>40 mm) polyps Post-polypectomy syndrome: – D(50)+E, 6 cases – NS+E, 1 case (P = 0.01).	D(50)+E is superior to NS+E for an EMR, particularly in large and giant sessile polyps, but the risk of thermal tissue injury should be considered High level
Augusto Barros, 2014 [32]	Prospective cohort study	NPCRLs of up to 20 mm were removed by means of a cold snare	171 NPCRLs removed from 124 patients Mean lesion size, was 9.22 +/– 4.7 mm	To assess safety of cold snare resection of NPCRLs up to 20 mm	No immediate or delayed complications were recorded	Cold snare resection could be used to remove NPCRL (0-IIa and 0-IIb) measuring up to 20 mm, without immediate or delayed complications.

						Moderate level

CSP, cold snare polypectomy; D(50)+E, 50% dextrose plus epinephrine; NS+E, normal saline plus epinephrine; EMR, endoscopic mucosal resection; NPCRL, nonpolypoid colorectal lesion

Table 5 Pharmacological and or mechanical hemostasis in pendunculated colorectal polyps.

First author, year [ref.]	Study design	Size of polyps	Type of treatment	Patients, n	Clinical efficacy
Dobrowolski, 2004 [33]	RCT	Head >1 cm	Epinephrine injection vs. nothing	69	2% vs. 16%
Lee, 2007 [34]	RCT	Head >1 cm	Epinephrine injection vs. normal saline	486 (128 with pedunculated polyps)	4.9% vs. 10.3%
Iishi, 1996 [35]	RCT	Head >1 cm	Detachable snare vs. nothing	89	0 vs. 12%
Di Giorgio , 2004 [36]	RCT	Head >1 cm	Detachable snare vs. epinephrine injection vs. nothing	488	2.7% vs. 2.9% vs. 15.1%, respectively, for polyps≥2 cm
Paspatis, 2006 [37]	RCT	Head >2cm	Detachable snare plus epinephrine vs. epinephrine injection	159	2.3% vs. 10.6%
Kouklakis, 2009 [38]	RCT	Head >2 cm	Detachable snare plus endoclip vs. epinephrine injection	64	3.12% vs. 12.5%
Ji, 2014 [39]	RCT	Heads ≥10 mm, stalks ≥5 mm in diameter, and stalk lengths ≥10 mm.	Detachable snare vs. endoclip	195	5.7% vs. 5.1%
Feagins, 2014 [40]	Retrospective	–	Endoclip vs. nothing	368 (206 with pedunculated polyps)	1.6% vs. 0.5 %

RCT, randomized controlled trial.

Table 6 Summary of evidence regarding removal of polyps by an expert endoscopist in a tertiary center or a referral center.

First author, year [ref.]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Nanda , 2015 [41]	Prospective observational cohort To evaluate the applicability, safety and effectiveness of endoscopic mucosal resection (EMR) for laterally spreading lesions (LSLs) involving the ileocecal valve (ICV) in a tertiary referral setting	EMR with a pediatric colonoscope with attached transparent plastic cap	All patients with an LSL involving the ICV, enrolled in prospective, observational study of consecutive patients referred to a single, tertiary-care referral center for EMR of LSLs ≥20 mm, from September 2008 to January 2014	Procedural success and adverse event frequency. Adverse events of interest included bleeding requiring therapy, perforations, pain or late stricture formation.	1079 lesions in 969 patients referred for EMR during the study period. Among these, 53 patients had LSLs involving the ICV. Median lesion size was 35.0 mm (range 20–100 mm). Majority of ICV LSLs were granular lesions with Paris 0-IIa or 0-IIa+Is morphology. EMR achieved complete adenoma clearance in 44 out of 47 attempted (93.6%). Surgery ultimately avoided in 43/53 (81.1%). Complications included bleeding in 6.4%. Early adenoma recurrence detected in 7/40 patients (17.5%), and 1/22 (4.5%) had late recurrence. All were successfully managed endoscopically. Factors associated with failure of ICV EMR were ileal infiltration and involvement of both ICV lips. Comparison between resections performed at the ICV and the rest of the colon showed that ICV lesions were more difficult to adequately access and position for resection (62.3% vs. 34.5%; $P = 0.003$). EMR was less often attempted at the	Low quality. ICV lesions are more challenging to access and position for resection compared with EMR practice in non-ICV locations. This increases both the complexity of resection and the procedure duration. When performed in expert centers, complete adenoma clearance is achievable, and surgery can be avoided in the majority. These data suggest that evaluation of ICV lesions by a tertiary center that specializes in EMR should be considered before a decision to commit to surgery is made.

					ICV, and lower en bloc resection (8.5% vs. 16.3%; *P* = 0.15) and overall success rates (83.0% vs. 92.4%; *P* = 0.022) were achieved. Adverse event rates were similar between the two groups.	
Moss, 2015 [42]	Prospective observational cohort To quantify recurrence at 4 months (early) and 16 months (late) following successful wide-field endoscopic mucosal resection (WF-EMR) To identify associated risk factors and clinical significance.	WF-EMR for the treatment of sessile or laterally spreading coloniclesions ≥20 mm, referred for WF-EMR to seven academic endoscopy units.	All patients with a sessile or laterally spreading colonic lesions ≥20 mm in size referred for WF-EMR to seven academic endoscopy units.	EMR success rates, early (4 months) recurrence rate, late (16 months) recurrence rate, risk factors associated with recurrence, and clinical significance of recurrence, complication rate	1134 consecutive patients were enrolled when 1000 successful EMRs were achieved, of whom 799 have undergone surveillance colonoscopy at 4 months (SC1). 670 were normal. Early recurrent/residual adenoma was present in 128 (16.0%, 95%CI 13.6%–18.7%). One case was unknown. The recurrent/residual adenoma was diminutive in 71.7% of cases. On multivariable analysis, risk factors were lesion size >40 mm, use of argon plasma coagulation, and intraprocedural bleeding. Of 670 with normal SC1, 426 have undergone surveillance colonoscopy at 16 months (SC2), with late recurrence present in 17 cases (4.0%, 95%CI 2.4%–6.2%). Overall, recurrent/ residual adenoma was successfully treated endoscopically in 135 of 145 cases (93.1%, 95%CI 88.1%–96.4%). If the initial EMR was deemed successful and did not contain submucosal invasion requiring surgery, 98.1% (95%CI 96.6%–99.0%) were	Low quality. Following colonic WF-EMR, early recurrent/residual adenoma occurs in 16%, and is usually unifocal and diminutive. Risk factors were identified. Late recurrence occurs in 4%. Overall, recurrence was managed endoscopically in 93% of cases, therefore surgery and its associated costs can be avoided. Recurrence is not a significant clinical problem following WF-EMR, as with strict colonoscopic surveillance, it can be managed endoscopically with high success rates.

					adenoma-free and had avoided surgery at 16 months following EMR.	
Friedland, 2014 [43]	Retrospective observational cohort (December 2010–March 2013) To evaluate the outcomes of repeat colonoscopy at a tertiary care center in the USA	Repeat colonoscopy performed by an endoscopist with extensive experience in EMR, having performed more than 1000 EMR procedures.	Patients referred to a colorectal surgeon for surgical resection of a colorectal polyp without biopsy-proven cancer and without endoscopic features of deeply invasive cancer	Rate of successful endoscopic treatment.	38 lesions in 36 patients, Median lesion diameter of 40 ± 18 mm, 47% were located in the cecum or ascending colon, 55% Paris 0-Is 71% of the lesions were noncancerous and were successfully treated endoscopically and therefore surgery was avoided. In 26% of the lesions, previous removal was attempted by the referring physician but was unsuccessful. The adenoma recurrence rate was 50%, but all recurrences were treated endoscopically and none were cancerous. Two patients were admitted for overnight observation. There were no major adverse events.	Low quality. In the absence of biopsy-proven invasive cancer, it is appropriate to re-evaluate patients referred for surgical resection by repeat colonoscopy at an expert center and in this study in 71% of the referred patients surgery was avoided. This study suggests that in the absence of biopsy-proven invasive cancer, it is appropriate to re-evaluate patients referred for surgical resection by repeat colonoscopy at an expert center.
Longcroft-Wheaton, 2013 [44]	Prospective observational cohort study To evaluate polyp complexity by using a novel classification system To assess how this affects	Data were collected between 2005 and 2010 on patients referred for endoscopic resection of polyps >2 cm in size. Lesions were classified on the basis of size, morphology, site, and ease of access	All patients referred for endoscopic resection of polyps >2 cm in size. Removal of hese polyps was considered to be beyond the skills or resources of the	The endoscopic cure and complication rate by SMSA grade Cost savings of endoscopic resection over surgery	Endoscopic resection was performed on 220 patients with 220 polyps, in whom lesion size was the key indication (75%) for referral. Mean size 43 mm (range 20 –150 mm). 37% classified as SMSA 2 or 3; 63% were classified as the most challenging as SMSA 4. Complete endoscopic clearance was achieved in 90% of cases with the first endoscopic resection attempt, improving	Low quality. This study found that, although polyp size was the most commonly cited reason for referral, other lesion characteristics, including difficult access, location, and previous attempts at resection were also important factors. The SMSA scoring

	success at endoscopic resection	with the use of a novel scoring system (SMSA). EMR was performed by a single expert endoscopist. Patients were followed up endoscopically to assess clinical outcomes.	referrer.		to 96% with further endoscopic resection attempts. Complications in 18 of 220 (8.1%). Complications were affected by SMSA grade (P = 0.018). Probability of clearance at first endoscopic resection attempt was affected by lesion complexity: For SMSA 2 and 3, it was 97.5 vs. SMSA 4, 87.5% (P = 0.009). Probability of cancer was not affected by SMSA grade. For the whole cohort, endoscopic resection represented a cost saving of £726 288 ($1 123 858.05) over that of surgery.	system is easy to use and provides valuable information on the lesion complexity and success and complication rates of endoscopic resection. This study demonstrates that less complex lesions (SMSA 1–3) can be resected completely at first EMR attempt with a very low complication rate. However, SMSA 4 lesions can require more than 1 EMR attempt to achieve endoscopic clearance and are associated with higher complication rates. This can be used for service planning, training endoscopists, and providing prognostic information for patients.
Buchner, 2012 [45]	Retrospective observational cohort study, to determine the current nature of colorectal defiant polyps and the outcomes of	EMR performed by a single expert endoscopist for defiant polyps, defined as any 1 of the features such as lesion >20 mm, unfavorable location behind or over the folds, and	Patients with colorectal polyps not amenable to standard snare polypectomy were referred to a single endoscopist at a tertiary center	Complete resection rate, Complication rate, Recurrence rate	274 patients with a total of 315 defiant polyps (72% in the right side of the colon, mean size 23 mm range 8–100 mm) who were referred for attempted endoscopic resection. In 29 defiant polyps (10%), surgery was required because endoscopic resection was deemed unsuitable because of unfavorable appearance (n = 3), location (n = 9), inability to lift (n = 10), or	Low quality. Defiant polyps consist predominantly of sessile and flat adenomas including serrated adenomas. Most defiant polyps can be successfully eradicated at dedicated therapeutic colonoscopy by using

	EMR including complication and recurrence rates in procedures performed at an endoscopy referral center	flat and sessile morphology, all of which pose a challenge to standard polypectomy techniques for complete endoscopic resection.	for an attempt at curative endoscopic resection.		because of submucosal invasion on post-EMR histopathology (n = 7). Complete endoscopic eradication (R0) was achieved in 286 defiant polyps (91%). En bloc resection was performed in 153 polyps (53.5%) and piecemeal resection in 132 (46%). Histopathology revealed tubular adenomas (56.5%), 14 adenocarcinomas (4.5%). Adjunctive ablation of focal residual neoplastic tissue was applied in 69 defiant polyps (24%) to achieve R0. Procedure-related adverse events were recorded in 29 of 249 patients (11.6%). Acute bleeding occurred in 9 patients, 1 microperforation managed. Delayed bleeding was observed in 18 patients (7.2%). Among the patients who underwent follow-up surveillance colonoscopy (135 of 258 patients), residual/recurrent neoplastic tissue at the site of the previous EMR was identified in 36 (27%). Residual/recurrent neoplasia was successfully eradicated with further endoscopic resection or ablation.	adjunctive resection and ablation techniques performed by an experienced endoscopist. The R0 rate is high and the adverse event rate is low. A relatively high rate of local residual/recurrent neoplasia at the resection site underscores the importance of follow-up colonoscopy.
Kao, 2011 [46]	Retrospective observational cohort study To review the	Endoscopic excision with the inject-and-cut or inject-lift-and-cut EMR of large	Patients with large colorectal lesions deemed not amenable to endoscopic	Endoscopic success rate (the ability to completely eradicate the original or	104 patients included (46% men with a mean age of 67 years). Anatomic distribution of the lesions included the colon (68%) and rectum (32%), most commonly in the ascending	Low quality. Endoscopic excision of large colorectal polyps is a viable alternative to

	investigators' experience with endoscopic excision of large colorectal polyps in a subgroup of patients initially referred for surgical resection	colorectal lesions performed by 2 interventional endoscopists. All patients had been referred for surgical treatment because lesions had been deemed not amenable for endoscopic resection.	resection at initial colonoscopy and referred for surgical resection	recurrent lesion endoscopically at the index procedure or at reintervention), Procedure-related complications, Disease recurrence, Endoscopic re-intervention, and surgical intervention	colon (32%). Tubulovillous or villous adenoma (30%) was the most common histology. 39 patients (37%) had carcinoma. Median size of the lesions 3.0 cm (range 1–9) cm. Endoscopic success rate was 83% and was highest in patients with noncarcinoma histologic findings compared with carcinoma ($P < 0.001$). The complication rate was 7%, and all complications occurred in the ascending colon ($P = .06$). Endoscopic re-intervention occurred in 25 of 92 patients (27%). Surgical intervention was undertaken in 14% of all patients. During a mean follow-up of 14 months (median 12 months), recurrent disease was noted in 10 of 86 patients (12%) and occurred more frequently in rectal lesions ($P = 0.002$). All recurrences were eradicated endoscopically.	surgical resection in a select group of patients and can be performed safely with a good success rate.
Swan, 2009 [47]	Prospective observational cohort of 21-month period, ending in April 2008, To evaluate the safety, efficacy, and cost savings of a tertiary	For sessile lesions, a standardized EMR approach was used. Pedunculated lesions were removed, with or without pre-treatment, with an Endoloop procedure	Consecutive patients with large or complex colorectal polyps referred by other endoscopists for endoscopic removal of these polyps. Reasons for referral were	Complete resection rate, Complication rate, recurrence rate, and Potential cost savings. Actual outcomes of the cohort compared with a hypothetical analysis of surgical	174 patients (mean age 68 years), referred with 193 difficult polyps (186 laterally spreading, mean size 30 mm [range 10–80 mm]). 173 laterally spreading lesions totally excised by EMR (115 piecemeal, 58 en bloc). Invasive adenocarcinoma was found in 6 lesions treated successfully with EMR. 11 patients referred directly to surgery without an endoscopic attempt because	Low quality. Colonoscopic polypectomy performed by a TRCPS on large or difficult polyps is technically effective and safe. This approach results in major cost savings and avoids the potential complications of colonic

	referral colonic mucosal resection and polypectomy service (TRCPS) for colorectal lesions		the polyp was considered too difficult or hazardous to be removed on the basis of the endoscopists' skills or the available resources.	management.	of suspected invasive carcinoma. Recurrence rate is 10.5%. 7 pedunculated polyps >30 mm, were removed. No perforations. 20 bed-days incurred was used because of endoscopic complications. Among all patients referred, 90% avoided the need for surgery. Excluding patients who were treated surgically for invasive cancer, the procedural success was 95% (157 of 168). Using Australian cost estimates applied to the entire group, compared with cost estimates assuming all patients had undergone surgery, total medical cost savings were $6990 (US) per patient, or total savings of $1 216 231 (US).	surgery, since 87% of unnecessary surgery is avoided in this study. This type of clinical pathway should be developed to enhance patient outcomes and reduce health care costs.
Voloyiannis, 2008 [48]	Retrospective cohort study, To study the benefit from repeat colonoscopy by an experienced endoscopist before colorectal surgery for the removal of a	Repeat colonoscopy for the resection before colorectal surgery for the resection of difficult colon polyps	All patients referred for surgical treatment of difficult colorectal polyps between October 1999 and September 2005.	Success rate of endoscopic removal of difficult colon polyps to avoid surgical treatment of these polyps.	Study population, 252 patients, mean age 65 years. 80 patients underwent resection upon referral without a repeat colonoscopy. Upon resection, invasive cancers were found in 13 cases. 172 patients underwent at least one repeat colonoscopy by the colorectal surgeon. Of this group, 101 (58%) patients had successful polypectomy, thus avoiding major colectomy. The remaining 71 patients had a subsequent colon resection after at least one repeat	Low quality. Repeat colonoscopy by an experienced surgeon leads to complete removal and avoidance of major colectomy in 58% of these cases. Patients with large difficult polyps referred for resection should be considered for repeat colonoscopy before surgery.

	large or difficult colonic polyp				colonoscopy. In 26 cases the polyp site was tattooed for later localization. 9 post-polypectomy hemorrhages treated non operatively and 2 perforations.	
Lipof 2005 [49]	Prospective observational cohort study, To study the efficacy in preventing surgery of preoperative colonoscopy in patients referred for surgical treatment of benign polyps	Preoperative colonoscopy the day before surgery in patients referred for surgical treatment of benign colorectal polyps	All patients referred for surgical treatment of benign colorectal polyps between January 1999 and September 2003	Efficacy of endoscopic removal of benign colorectal polyps in avoiding surgical treatment of these polyps.	71 patients included. Average size of polyps 24 mm (range 10–60 mm). Location of the polyp as determined by preoperative colonoscopy differed from the location noted on referral colonoscopy in 9 patients (13%). Surgery was canceled in 23 patients (32%), primarily because of complete polypectomy at preoperative colonoscopy. Of the 48 who underwent surgery, 23 (47%) had a colonic tattoo placed, at the discretion of the surgeon. Lesions clearly located in the cecum were not tattooed routinely. Of the 48 patients who underwent surgery, 45 (94%) underwent laparoscopic colon resection.	Low quality. This study concludes that patients referred for surgical resection of a polyp should undergo repeat colonoscopy preoperatively, given that one-third of patients were spared unnecessary colectomy. In addition, repeat endoscopy by the operating surgeon offers an opportunity to confirm the location of the lesion and place a colonic tattoo to facilitate laparoscopic resection.
Church, 2003 [50]	Prospective observational cohort study, To determine how many polyps referred for surgery could actually be managed	All patients underwent colonoscopy before surgery to see if the polyp could be managed endoscopically.	All patients referred for surgical treatment of benign colorectal polyps between January 1989 and September	The efficacy of endoscopic removal of colorectal polyps in avoiding preventing surgical treatment of these polyps.	58 patients referred for surgical resection of colorectal polyp. Endoscopic polypectomy initially successful in 48. Of the 48, 5 needed surgery later, for a final success rate of 43/58 (74.1%) avoiding surgery. There were no deaths 4 complications of endoscopic polypectomy (3 bleeds, 1 post-	Low quality. Most polyps referred for surgical resection were successfully managed endoscopically. Patients with colonic polyps that are difficult or potentially dangerous to remove endoscopically

	endoscopically .		2002		polypectomy syndrome) 2 patients had complications of surgery. Polyps size range 1.5–8.0 cm. 7 polyps contained invasive cancer (3 needing surgical resection), 8 contained intramucosal cancer (1 operated), and 11 had severe dysplasia (3 operated). Rate of persistent polyp was 16/37 at first follow up, 7/23 at second, 1/14 at third and 0/8 at fourth.	should be sent for a second opinion before surgery is performed.
Brooker, 2002 [51]	Retrospective, observational cohort study, To determine the outcome of patients with large sessile colonic polyps diagnosed by specialist and nonspecialist colonoscopists .	Retrospective data retrieval from an endoscopy database, on: resection technique used and clinical and endoscopic outcomes in patients treated with large sessile polyps. Two colonoscopists were considered to be specialists.	All patients with a large (>2 cm) sessile polyp detected at colonoscopy from January 1995 to July 2000.	Differences between specialist and nonspecialist endoscopists in: Treatment strategy and resection methods, Outcomes of endoscopic management, Complete endoscopic success, Attempted removal of malignant sessile lesions, Complication rate, Costs of management	Overall 130 large sessile polyps were identified, 100 detected by either of two specialist endoscopists (including 14 cancers) and 30 by 14 non-specialist endoscopists (including 10 cancers). Endoscopic resection of benign polyps was attempted by experts in 80 of 86 cases (93%) and by nonexperts in 15 of 20 cases ($P = 0.03$), with successful management by endoscopy alone in 61 of 80 (76%) and in 6 of 15 cases respectively ($P = 0.01$). Complications occurred following 3 polypectomies performed by an expert (2 bleeding; 1 pain, one) and 1 by a non-expert (bleeding). Estimated end-cost of management by specialists was less than half of that by non-specialists.	Low quality. Endoscopic resection of large sessile colonic polyps is feasible in the majority of patients and should be considered as first-line therapy. Prompt referral to a specialist endoscopist may improve outcomes by avoiding operation or enabling complete excision at a single endoscopy session.

Table 7 Which polyps require other (non-snare) techniques, e.g. endoscopic submucosal dissection (ESD) or surgery. Preremoval criteria (size, morphology, site, access [SMSA] criteria).

First author, year [ref.]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Narrow band imaging (NBI)						
Hirata, 2007 [52]	Retrospective	NBI	n = 189 polyps (n = 20 hyperplastic, n = 109 adenomas, n = 41 high grade dysplasia (HGD)/sm1, n = 19 sm2+)	Adenoma vs. T1, Prediction of sm2+/ >1000 µm invasion	Thin vessels: 102/139 (73%) tubular adenoma, 31/139 (22%) HGD/sm1, 4/139 (3%) sm2+. Thick vessels: 5/30 (17%) TA, 10/30 (33%) HGD/sm1, 15/30 (50%) sm2+. Regular vessel pattern: 98/119 (82%) TA, 19/119 (16%) HGD/sm1. Mildly irregular: 9/38 (24%) TA, 22/38 (58%) HGD/sm1, 7/38 (18%) sm2+. Severely irregular: 12/12 sm2+.	Moderate quality. Thick and irregular vessels are predictive of T1Sm, and sm2+.

Yohida, 2011 [53]	Retrospective	Flexible spectral imaging color enhancement (FICE)/NBI (Hiroschima)	n = 28 hyperplastic, n = 115 adenomas n = 72 HGD/sm1+, n = 20 sm2+	Prediction of sm2+/ >1000 µm invasion	FICE: Type B: 43/52 (83%) adenoma, 8/52 (15%) mucosal and slightly invaded submucosal cancer (M-sSM), Type C1/2: 23/50 (46%) adenoma, 25/50 (50%) HGD/sm1+, 2/50 sm2+. Type C3: 7/7 sm2+ NBI: Type B: 28/44 (64%) adenoma, 14/44 (32%) M-sSM Type C1/2: 19/47 (40%) adenoma, 24/47 (51%) HGD/sm1+, 4/47 (9%) sm2+. Type C3: 7/8 (88%) sm2+	Moderate quality. Type C3 shows deep invasion in the majority of cases.
Wada, 2009 [54]	Prospective	NBI	n = 52 T1 cancers, n = 532 adenomas	Adenoma vs. T1, Prediction of sm2+/ >1000 µm invasion	Irregular or sparse vascular pattern: Prediction of cancer: 46/62 (74%) cancer, 17/63 (27%) adenoma, Positive predictive value (PPV) 74%; negative predictive value (NPV) 99%. Prediction of sm2+ T1 PPV 40/63 (63%); NPV 521/521 (100%)	Low quality. Irregular or sparse vascular pattern predicts the presence of T1 and deep invasion.

Oba, 2010 [55]		NBI (Hiroschima)	189 type C lesions	Prediction of sm2+/ >1000 µm invasion	Type C1: 54/96 (56%) HGD/sm1+, 5/96 (5%) sm2+ . Type C2: 15/38 (40%) HGD/sm1, 23/38 (60%) sm2+, Type C3: 4/55 (7%) HGD/sm1, 51/55 (93%) sm2+	Combination of surface pattern and microcapillary features better predict depth of invasion with good interobserver variability (k = 0.749).
Wada, 2010 [56]	Prospective	NBI, magnifying chromoendoscopy (MCE), vascular pattern	n = 1317 adenomas, n = 103 T1Sm (25 sm1, 78 sm2+)	Adenoma vs. T1, Prediction of sm2+/ >1000 µm invasion	Vascular pattern: Irregular /sparse 6/80 (7%) HGD/sm1, and 74/80 (93%) sm2+. Network/dense 19/23 (83%) HGD/sm1 and 4/23 (17%) sm2+ . Pit pattern: Vi low grade: 16/108 (15%) HGD/sm1, 7/108 (6%) sm2+, Vi high grade: 3/55 (5%) HGD/sm1, 45/55 (82%) sm2+. Vn: 25/25 (100%) sm2+	Moderate quality. MCE is slightly better in discriminating sm1 vs. sm2+ T1 CRC.
Ikematsu, 2010 [57]	Prospective	NBI vascular pattern	n = 130 type IIIA/B polyps	Prediction of cancer	Sensitivity 85%, specificity 89%, accuracy 88%, PPV 72%, NPV 96%	Moderate quality. Sano capillary pattern III can differentiate adenoma from intramucosal and invasive carcinomas.

				Prediction of sm2+/> 1000 µm invasion	Type IIIA 86/91 (95%) HGD/sm1, 5/91 (5%) sm2+, Type IIIB 11/39 (28%) HGD/sm1, 28/39 (72%) sm2+	Moderate quality. Sano capillary pattern IIIb may be useful in discriminating deep vs. superficial invasion.
Jang, 2014 [58]	Prospective	NBI and MCE	n = 85 laterally spreading tumors (LSTs) (n = 58 HGD, n = 5 sm1, n = 22 sm2+)	Prediction of sm2+/ >1000 µm invasion	NBI: Type C1: 10/13 (77%) HGD/sm1, 3/13 (23%) sm2+. Type C2: 2/4 (50%) HGD/sm1, 2/4 (50% sm2+, Type C3: 3/20 (15%) HGD/sm1 and 17/20 (85%) sm2+ Kudo Vi: 3/8 (37%) HGD/sm1, 5/8 (62%) sm2+, Kudo Vn 15/17 (88%) sm2+.	Moderate quality. NBI type C3 and Kudo Vn predict deep invasion (sm2+).
Kanao, 2009 [59]	Retrospective	NBI	289 polyps (n = 12 hyperplastic, 165 TA, 65 HGD/sm1, 47 sm2+)	Prediction of sm2+/ >1000 µm invasion	Type C1: 21/45 (47%) TA, 19/45 (42%) HGD/sm1, 5/45 (11%) sm2+. Type C2: 10/22 (45%) HGD/sm1, 12/22 (55%) sm2+. Type C3: 30/30 sm2+	Low quality. Type C3 shows deep invasion in the majority of cases and should be referred for surgery. C1/C2 cases should be analyzed further.

Oka, 2011 [60]	Retrospective	NBI	n = 698 polyps (n = 53 hyperplastic, 318 TA, 225 HGD/sm1, 102 sm2+	Prediction of sm2+/ >1000 µm invasion	Type B: 260/337 (77%) TA, 75/337 (22%) HGD/sm1. Type C1: 56/184 (30%) TA, 122/184 (67%) HGD/sm1, 6/184 (3%) sm2+. Type C2: 23/54 (43%) HGD/sm1, 31/54 (57%) sm2+. Type C3: 5/70 (7%) HGD/sm1, 65/70 (93%) sm2+	Moderate quality. Type C3: strong association with deep invasion. Type C1/C2: associated with HGD/sm1 and deep invasion (C2).
Goto, 2014 [61]	Prospective	NBI + acetic acid	45 adenomas, n = 38 HGD, n = 8 sm cancers	Adenomas vs. superficial cancers	NBI: Sensitivity 85%, specificity 60%, PPV 68%, NPV 79%. NBI + acetic acid: Sensitivity 80%, specificity 64%, PPV 70%, NPV 76%. Magnifying endoscopy plus crystal violet staining (MCE+CV): Sensitivity 83%, specificity 62%, PPV 869% NPV 78%	Low quality. NBI + acetic acid improves diagnostic accuracy of NBI alone in prediction of HGD/sm cancer.
Shibagaki, 2015 [62]	Prospective	NBI + acetic acid	116 polyps (n = 18 HGD/sm1, n = 10 sm2+	Adenomas vs. superficial cancers, Prediction of sm2+/ >1000 µm invasion	Type Vi-L: 14/29 (48%) adenoma, 14/28 (48%) HGD/sm1, 1/29 (3%) sm2+. Type Vi-H: 1/12 (8%) TA, 4/12 (33%) HGD/sm1, 7/12 (58%) sm2+. Vn: 2/2 sm2+	Moderate quality. Type Vi-L with MCE+ acetic acid + NBI predicts superficial carcinomas. Type Vi-H /Vn with MCE+ acetic acid + NBI predicts deep invasion

Hayashi, 2013 [63]	Retrospective	NBI international colorectal endoscopic (NICE) classification	Image library: n = 22 adenomas, n = 23 HGD/sm1, n = 35 sm2+	Prediction of sm2+/ >1000 µm invasion	Brown color, disrupted and missing vessels, amorphous surface pattern. 1 out of 3 present: Sensitivity 95%, NPV 96%, substantial interobserver agreement (kappa 0.7)	Low quality. NICE 3 predicts the presence of deep invasion
Chromoendoscopy						
Hurlstone, 2004 [64]	Prospective cohort	Magnifying chromoendoscopy	Polyp showing type V pit pattern (n = 47)	Prediction of sm2+/ >1000 µm invasion	Vn B/C predict deep invasion	Moderate quality. Vn(c) is a marker of deep invasion. Combined with Vn(b) it however overestimates the risk of invasion.
Kanao, 2008 [65]	Retrospective	Magnifying chromoendoscopy	Polyp showing type V pit pattern (n = 272)	Prediction of sm2+/ >1000 µm invasion	Vn predicts deep submucosal invasion	Low quality. Vn reliably predicts deep invasion. Type Vi consists of dysplasia sm1 and sm2+ and is therefore not suitable to direct strategy.
Tobaru, 2008 [66]	Retrospective	Magnifying chromoendoscopy	Polyps showing type V pit pattern (n = 99)	Prediction of sm2+/ >1000 µm invasion	Well demarcated Vi: 21/26 (80%) m-sm1, 5/26 (20%) sm2+ . Poorly demarcated Vi: 4/19 (21%) m-sm1, 15/19 (79%) sm2+; Vn: 6/6 (100%) sm2+	Moderate quality. Vn predicts deep mucosal invasion. Poorly demarcated Vi also has a high percentage of sm2+.

Ikehara, 2010 [67]	Retrospective	Polyp morphology: size, loss of lobulation, excavation, demarcated depressed area, pit pattern (noninvasive vs. invasive), stalk swelling	n = 57 pedunculated, 175 sessile, n = 147 superficial	Prediction of sm2+/ >1000 µm invasion	Sessile: *Pit pattern:* Invasive in 55/61 with deep invasion (90%), Noninvasive in 14/114 (13%) with deep invasion *Loss of lobulation:* Present in 63/92 (68%) with deep invasion Absent in 6/83 (7%) with deep invasion. Superficial: *Fullness:* Present in 66/86 with deep invasion, Absent in 11/61 with deep invasion *Pit pattern:* Invasive in 76/86 (88%) with deep invasion, Noninvasive in 1/61 (2%) with deep invasion.	Low quality. Invasive pit pattern, loss of lobulation, fullness are predictors of deep depression
Matsuda, 2008 [68]	Prospective cohort		4215 polyps (n = 3371 adenomas, n = 612 HGD, n = 52 sm1, n = 180 sm2+	Prediction of sm2+/ >1000 µm invasion	Invasive pattern: PPV 154/178 (87%), NPV 640/666 (96%)	High quality. The invasive pattern predicts the presence of deep invasions
Morphology						

Moss, 2011 [69]	Prospective cohort	Endoscopic evaluation + NBI	n = 479 polyps, n = 33 sm invasive cancer	Prediction of sm invasive cancer	Paris IIc, or IIa+c (32%), nongranular morphology (15%), or Kudo V pit pattern (56%)	Moderate quality. Depression (Paris IIc or IIa-c), nongranular pit pattern predict the presence of sm cancer
Li, 2010 [70]	Prospective cohort		Polyps showing a depression (n = 66) Star-shaped, round-shaped		Round-shaped depression is a high suspicion marker of sm CRC	Low quality. Round-shaped depression is suspicious for deep invasion
Horie, 2008 [71]	Retrospective cohort (selected still images)	Morphologic characteristics A: depression, B: irregular surface, C: ulceration/ erosion D: fold convergence E: spontaneous bleeding	111 patients n = 69 Tis, n = 42 T1 (14 sm1, 28 sm2+)	Prediction of sm2+/ >1000 µm invasion	Deep depression: odds ratio (OR) 6.6, 95%CI 0.8–56.3 Irregular surface: OR 5.6, 95%CI 1.7–19; kappa 0,23 Spontaneous bleeding: OR 4, 95%CI 1.2–13); kappa 0.56	Low quality. Deep depression, irregular surface, spontaneous bleeding are features of deep invasion

Saitoh, 1998 [72]	Retrospective cohort (selected still images)	Morphologic characteristics: Size, Color, Nature of the border, Depth of depression, Irregular surface, Converging folds	64 patients with a lesion depression (32 IIc and 32 II-a+ IIc	Prediction of sm2+/ >1000 µm invasion	Surface appearance: 1/29 m-sm1 and 26/35 sm2+, Depth of depression: 0/29 m-sm1 and 18/35 sm2+, Irregular surface in depression: 0/29 m-SM1 and 17/35 sm2+, Converging folds: 2/29 m-sm1 and 16/35 sm2+	Low quality. Expansion appearance, deep depression, irregular surface in depression, converging folds, predict deep invasion
Ikehara, 2010 [67]	Retrospective	Polyp morphology: Size, Loss of lobulation, Excavation, Demarcated depressed area, Pit pattern (noninvasive vs. invasive), Stalk swelling	n = 57 pedunculated, n = 175 sessile, n = 147 superficial	Prediction of sm2+/ >1000 µm invasion	Pedunculated: no morphologic sign was associated with deep invasion. Sessile: loss of lobulation, invasive pit pattern, Superficial: fullness and invasive pit pattern	Low quality. Invasive pit pattern, loss of lobulation, fullness are predictors of deep depression
Saito, 2001 [73]	Retrospective	Size, Depression,	n = 97 adenomas, n = 138 HGD/sm1, n = 22 sm2+	Prediction of T1Sm	Large nodule: 15/64 (23%) T1Sm, Depression: 14/25 (56%) T1Sm	Moderate quality. Large nodule and depression are predictors of T1Sm

Uraoka, 2006 [74]	Retrospective	Nodules, Depression, Pit pattern		Prediction of T1sm	Laterally spreading tumor-granular (LST-G): Large nodule: PPV 14/47 (30%), Laterally spreading tumor-nongranular (LST-NG): Vn pit pattern: PPV 28/74 (38%)	Moderate quality. Large nodule in LST-Gs predicts malignancy Disturbed pit pattern predicts malignancy in LST-NG
Non-lifting						
Kobayashi, 2007 [75]	Prospective	Non-lifting vs. lifting	n = 271 polyps	Prediction of sm2+/ >1000 µm invasion	Non-lifting: PPV 16/20 (80%); NPV 241/251 (96%) Endoscopic assessment: PPV 22/25 (88%); NPV 242/246 (98%)	Moderate quality. Endoscopic assessment of deep invasion is superior to non-lifting.
Kato, 2001 [76]	Prospective	Non-lifting vs. lifting	n = 104	Prediction of sm2+/ >1000 µm invasion	Incompletely lifted: 3/15 sm2+ ; PPV, non-lifting 8/8 sm3	Low quality. Non-lifting is a sign of deep invasion
Magnifying chromoendoscopy (MCE) vs. NBI						
Sakamoto, 2011 [77]	Retrospective	MCE vs. NBI (Sano classification)	Early colorectal carcinomas (n = 72)	Prediction of m/sm1 vs. sm2+ on 72 MCE and NBI images by 2 independent reviewers	MCE: Reviewer A: sensitivity 61%, specificity 94%, Reviewer B: sensitivity 83%, specificity 78%. NBI: Reviewer A: sensitivity 61%, specificity 94%, Reviewer B: sensitivity 78%, specificity 78%, Kappa: MCE 0.63; NBI 0.44	Low quality. NBI and MCE are equal for estimating depth of early CRC

Zhang, 2015 [78]	Prospective	NBI, Acetic acid, Chromoendoscopy with crystal violet	n = 31 adenomas, n = 47 HGD/sm1, n = 34 sm2+	Prediction of sm2+/ >1000 µm invasion	Predicting deep submucosal invasion: NBI: sensitivity 30/34 (88%), specificity 66/78 (85%), PPV 30/42 (71%), NPV 66/70 (94%). Acetic acid: sensitivity 29/34 (85%), specificity 68/78 (87%), PPV 29/39 (74%), NPV 68/73 (93%). MCE+CV: sensitivity 32/34 (94%), specificity 73/78 (94%), PPV 32/37 (87%), NPV 73/75 (97%).	Moderate quality. MCE with crystal violet performs a little better than NBI or MCE +acetic acid, although difference is not statistically significant
Hayashi, 2013 [63]	Prospective	Magnifying NBI (Hiroschima) vs. MCE with crystal violet (Kudo)	n = 516 polyps,	Prediction of sm2+/ >1000 µm invasion	C3 corresponds to Vi-H (40%)/Vn (60%); C2 to Vi-L (26%)/Vi-H (74%); C1 to Vi-L (71%), Vi-H (9%) and IV (20%). 73% of type C1 were HGD/sm1, 54% of C2 were sm2+, All C3 were sm2+	Moderate quality. NBI magnifying differs from pit pattern analysis with dye with MCE + dye being more accurate. C2/C3 is associated with Vi-H/Vn
MCE vs. endoscopic ultrasound (EUS)						
Shimura, 2014 [79]	Prospective	EUS +MCE or MCE + EUS	Early CRC (n = 70)	Prediction of sm2+/ >1000 µm invasion	Vi-H, Vn strongly associated with deep invasion	Moderate quality. MCE and EUS are equal accurate in predicting depth of invasion

Matsumoto, 2002 [80]	Prospective	MCE + EUS	Early CRC, n = 50 (HGD/sm1, n = 22, sm2+, n = 28)	Prediction of sm2+/ >1000 µm invasion	Probe-based EUS: PPV 25/27(93%); NPV 20/22 (91%). MCE: PPV 11/12 (92%); NPV (54%)	Moderate quality. Probe-based EUS is better in diagnosing deep invasion

Table 8 Colonic tattooing – which lesions should be tattooed and what is the best technique and location for tattoo placement?

First author, year [ref.]	**Study design** **Study objective**	**Intervention**	**Participants**	**Outcomes**	**Results**	**Level of evidence** **Conclusion**
Elarini, 2015 [81]	Editorial	Tattooing	N/A	N/A	N/A	Very low quality. Expert opinion only. Use India ink. Suggest common standard of tattooing 1–2 cm distal to the lesion in 3 or more quadrants. Standardize documentation language in the endoscopy report regarding the tattooing performed.
Moss, 2012 [82]	Editorial	Tattooing	N/A	N/A	N/A	Very low quality. Expert opinion only. Use sterile carbon particle suspension (SCPS). Use saline bleb technique. Tattoo 3 cm downstream (anal side) of lesion. One or two tattoos to be placed at that level on opposite sides of the lumen. All lesions requiring future location should be tattooed except those in cecum, involving theileocecal valve, or in the low rectum.
Zafar, 2012 [83]	Retrospective case series To determine the relationship	Polyp size and finding of malignancy.	165 patients had 269 polypectomies.	Size of polyps, finding of malignancy, whether	Risk of invasive malignancy in a polyp was 0.7% (1/143) for endoscopic polyp size <10 mm; risk	Low quality. Recommends tattooing of all polyps ≥10 mm. This is because the risk of malignant polyp among BCSP

	between endoscopic polyp size and invasive colorectal cancer so as to inform tattooing practice for patients in the English Bowel Cancer Screening programme (BCSP).			tattoo was placed	increased to 2.4% (2/83) for polyp size was 10–19 mm, and to 13% (5/40) for polyps >20 mm; statistically significant (P = 0.001). About 23% of patients had site of tpolyp tattooed. Mean size of tattooed polyps 21 mm (range 15–50 mm).	patients increases significantly when the polyp size is ≥10 mm.
Bartels S, 2012 [84]	Retrospective, case–control study To determine whether colonoscopic tattooing can be used to refine staging accuracy by increasing the lymph node (LN) yield per specimen, and its accuracy as a sentinel LN procedure	All lymph nodes within the surgical specimen were microscopically examined for the presence of carbon particles to determine if tattooing led to a higher lymph node yield.	95 patients with colonic tattoos who had surgery, compared with 210 non-tattooed patients who had surgery.	Total number of lymph nodes retrieved, Detection rate, Sensitivity of tattooing as sentinel node procedure	Higher LN yield in patients with preoperative tattooing, median (interquartile range [IQR]) 15 (10–20) vs. 12 (9–16), (P = 0.014). Multivariable analysis: presence of carbon-containing LNs was independent predictive factor for a higher LN yield (P = 0.002). Detection rate: 71%, with median 5 carbon-containing LNs per specimen. If preoperative	Moderate quality. Preoperative colonoscopic tattooing in patients with colorectal cancer can be used to refine lymph node staging. It has acceptable accuracy rates as a sentinel mapping procedure and leads to a higher lymph node yield

					tattooing was used for sentinel node mapping, overall accuracy of predicting LN status was 94%. In the24 N1 cases, there were 4 false-negative procedures (sensitivity 83%).	
Moss, 2011 [85]	Case series of sterile carbon particle suspension (SCPS) injection-related complications	4 cases of SCPS-related complications were identified	4 patients	Clinical outcomes of these patients following SCPS tattoo injection	Clinical and endoscopic evidence that tattoo injection is not biologically inert, nor its use clinically benign. Outcomes included peritonitis without evidence of colonic perforation, endoscopic perforation during EMR due to SPCS tattoo-induced fibrosis causing fusion of the mucosa to serosal surface, and difficult EMRs due to tattoo-induced fibrosis resulting in non-lifting of the polyps.	Low quality. SCPS tattoo) is an effective dye for endoscopic tattooing. Careful consideration should be given to its use and attention paid to correct methodology. SCPS tattooing should be used for lesions requiring subsequent endoscopic or surgical location. Tattoo should be placed 3 cm downstream (anal side) of the lesion. This will limit the likelihood of inadvertent spread beneath the lesion. At this level, two to three separate injections should be performed, one in line with the lesion and at least one on the opposite side of the lumen. This is to increase the likelihood of the tattoo being visible on the antimesenteric side during surgery, thereby enhancing detection during surgery. A submucosal bleb should be created by an initial submucosal injection of

						normal saline solution, followed by tattoo injection, to reduce the incidence of inadvertent transmural injection.
Kethu, 2010 [86]	American Society of Gastrointestinal Endoscopy (ASGE) technology status evaluation report on endoscopic tattooing	Tattoo agents review	N/A	N/A	N/A	Low quality. Endoscopic tattooing is an effective means to enable subsequent endoscopic and surgical locating of luminal digestive tract lesions. India ink has been used effectively in a large number of cases over several decades. When diluted (1:100 with normal saline solution) and injected tangentially in small aliquots (0.5–1 mL), India ink tattooing is safe and long lasting. One purified carbon particle suspension is the only Food and Drug Administration (FDA)-approved agent for this indication and its ready-to-use formulation offers convenience. Indocyanine green has been used less frequently and appears to be safe but provides a less durable tattoo.
Yeung, 2009 [87]	Review To review current techniques in preoperative tumor location and methods	Literature search (Medline and Pubmed) with manual cross-referencing of all articles related to colonic	N/A	Efficacy of various methods for locating colonic tumors during	Tumor location and sensitivity by different methods: Preoperative double-contrast barium enema, 48%–90%	Low quality. India ink is a reliable method of marking tumor location within the colon as prelude to laparoscopic resection. Surgeons must, however, be aware of potential complications associated with this technique. The

	used for colonic tattooing including agents used, dosage, and potential complications.	tattooing.		laparoscopic resection.	sensitivity CT colonography: 82% sensitivity for location, but has been shown to be poor at discerning small colonic lesions (<10 mm) compared to colonoscopy Perioperative colonoscopy: estimation of lesion location (without tattooing), 86% accuracy Endoscopic tattooing is the most reliable method, with direct single injection resulting in 80% visualization of the lesion, but 98% accurate visualization with the saline bleb injection technique.	most effective method for location of colonic tumor is endoscopic tattooing before surgery, using the submucosal saline bleb injection technique.
Ono, 2009 [88]	Brief report (case series)	Tattooing resulting in subsequent difficult and hazardous endoscopic submucosal detection (ESD)	2 clinical cases	Clinical details of the 2 cases	In both cases, ESD was abandoned due to tattoo infiltration beneath the lesion, with the dense tattooing agent in the fibrous tissue oozing and, together with the	Very low quality. Avoid tattooing beneath colonic lesions, and ensure to tattoo away from the lesion.

		procedures			fibrosis, preventing determination of the correct cutting plane for ESD. Snare excision had to be used instead, resulting in piecemeal excision rather than en bloc excision in one case.	

Park, 2008 [89]	Retrospective observational study	Colonic tattooing using the saline bleb technique. SCPS tattoo placed downstream of the lesion. Tattooing at three locations circumferentially at that level, tattoos placed 120 ° apart. A 1 mL saline bleb was injected, followed by 1–1.5 mL of SCPS tattoo injection, followed by 1 mL saline to flush out the remaining SCPS in the injector needle.	63 patients	Safety and efficacy of tattooing with this technique	Tattoos were visualized intraoperatively in 62 (98.4%) of the 63 patients. Colorectal tumors were accurately located in 61 patients (96.8%). Localized leakages of ink were identified in 6 patients (9.5%) during surgery. Of these, 5 were asymptomatic. 1 had chills post colonoscopy, but this patient also had multiple polyps removed at the procedure, so the cause could have been either tattoo leakage or post polypectomy-related symptoms.	Low quality. SCPS tattoo is safe and effective using the following technique: saline bleb method, with 1–1.5 mL SCPS injection, tattoos placed downstream of lesion, and 3 injections performed 120 ° apart circumferentially around the lumen to optimize detection at surgery. This resulted in 98% visualization at surgery.
Arteaga-Gonzalez, 2006 [90]	Prospective comparative clinical observation study	Tattooing vs. conventional location methods for colorectal cancer laparoscopic surgery	47 patients with colorectal carcinomas were included in the study	Preoperative endoscopic tattooing and operative results	Visualization of the correct resection site was higher in the tattoo group (100% vs. 80.8%, $P = 0.03$) Operative time (147.3 ± 46.2 vs.	Low quality. Preoperative endoscopic tattooing improves intraoperative location of the tumor at laparoscopic colorectal surgery, as well as reducing the surgical time and reducing blood loss, compared with conventional location

					187.0 ± 52.7 minutes, $P = 0.02$) was less in the tattoo group. Blood loss (99.3 ± 82.8 vs. 163.6 ± 96.6 mL, $P = 0.03$) was lower in the tattoo group.	methods.
Askin, 2002 [91]	Observational study	Safety and efficacy of tattooing with SCPS	113 patients	Location of the lesion during surgery or endoscopic procedure Histological analysis of resected surgical specimens	118 SCPS injections in 113 patients. In the nonoperated group, 42 patients subsequently underwent colonoscopies at the authors' institution, and in all cases, tattoo was identified at the injection site. In 10 surgical patients, the tattoo was seen in all patients. In the resected surgical specimens, there was no abscess or necrosis formation.	Low quality. Tattooing with SCPS is safe and effective for identification at surgery or subsequent endoscopy.
Sawaki, 2003 [92]	Observational study	Tattooing using the saline bleb injection technique (called the two-step technique in this	18 patients	Safety and efficacy (visualization at surgery)	At surgery, all lesions were visible. There were no complications from tattooing.	Low quality. The two-step (saline bleb injection) technique is very effective and safe for colonic tattooing.

		paper)				
Fu, 2011 [32]	Retrospective observational study Compare direct India ink injection vs. novel saline bleb injection technique.	Tattooing directly or with saline bleb	91 patients 36 direct tattoo injection 55 saline bleb injection		Surgical location successful: 86% conventional 98% saline bleb Conventional technique: 2 cases of silent peritonitis and 1 reactive lymph node swelling. Saline bleb technique: 1 small leakage of India ink into the peritoneal cavity that was asymptomatic.	Low quality. Tattooing after creation of saline bleb is more effective, and was associated with fewer complications, compared with direct injection of India ink.

N/A, not available

Table 9 Submucosal injection – which solution is best? Note: Studies were human, in vivo, for endoscopic mucosal resection (EMR) of lesions predominantly ≥20 mm in size. Other studies (animal, ex vivo, lesions ≤20 mm) were not included in this evidence table.

First author, year [ref.]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Moss, 2010 [94]	Randomized controlled, double-blind trial To compare normal saline with succinylated gelofusine (SG) for EMR	Submucosal injection with normal saline vs. SG	80 patients, 80 colorectal lesions ≥20 mm	Snare resections, Number of injections, Injection volume, Procedure duration, Complications	80 patients, 41 SG 39 normal saline Sydney Resection Quotient (SRQ)* median (IQR): SG 10.0 (7.5–20.0) vs. normal saline 5.9 (4.4–11.7); $P = 0.004$. Snare resections per lesion: SG 3.0 (1.0–6.0) vs. normal saline 5.5 (3.0–10.0); $P = 0.028$; Injections per lesion: SG:2.0 (1.0–3.0) vs. normal saline 3.0 (2.0–11.0); $P = 0.002$ Injection volume: SG 14.5 mL (8.5–23.0) vs. normal saline 20.0 mL (16.0–46.0): $P = 0.009$ Procedure duration SG: 12.0 min (8.0–28.0) vs. normal saline 24.5 min (15.0–36.0); $P = 0.006$.	High. Succinylated gelatin improves SRQ, reduces snare resections per lesion, injections per lesion and injection volume, and shortens procedure duration.
Uraoka, 2005 [95]	Retrospective case–control To compare normal saline with glycerol for EMR	Submucosal injection with normal saline vs. glycerol	223 patients/colorectal lesions 10–29 mm	En bloc resections, Complete resection rate, Complications, Recurrence rate	En bloc resection rate: glycerol 63.6% (70/110); normal saline 48.9% (55/113); $P < 0.05$) Complete resection rate: glycerol group 45.5% (50/110); normal saline group 24.6% (28/113); ($P < 0.01$) Associated complication rates: similar in both groups	Low. Glycerol improves the en bloc resection rate, complete resection rate. Retrospective historical control.
Bacani, 2008 [96]	Retrospective case–control	Submucosal injection	111 colorectal lesions	Complete recurrence	Complications occurred in 5/67 (8%) HPMC group and in 1/22 (5%) saline; $P > 0.2$	Low. Equivalent efficacy

	To compare normal saline to hydroxypropyl methyl cellulose (HPMC) for EMR	with normal saline vs. HPMC	89 lesions in 88 patients HPMC, 22 lesions normal saline (mean size 19–20 mm)	rate, Complications	Long-term follow-up with repeat endoscopy was available for 43 lesions and identified 35/43 to be completely excised: 20/25 (80%) HPMC-EMR; 15/18 (83%) saline EMR; $P > 0.2$]. Size of lesion was not associated with success.	and safety of saline and HPMC
Arezzo, 2009 [97]	Prospective case series	Submucosal injection with HPMC	27 flat, sessile, or laterally spreading lesions up to 60 mm (28 mm average)	Injection dose, Procedure time, En bloc resection, Complete resection, Complications, Recurrence	Mean dose of HPMC 10.2 mL (range 8–40 mL) Median procedure time 32 min (range 15–105 min). En bloc resection was achieved in 21 cases (78%). Histologically complete resection in 23 lesions No perforation was observed. 2 intraprocedural bleeding. 2 local recurrence at 3 and 12 months, endoscopically treated.	Low Small case series in humans showed acceptable outcomes with few complications.
Varadarajulu, 2006 [98]	Prospective randomized controlled trial	Submucosal injection with normal saline or 50% dextrose	52 sessile lesions in 50 patients. Mean size: 25 mm (dextrose); 22 mm (saline)	Injection volume, Number of injections, En bloc resection, Elevation persistence, Complications, Complete resection	Injection volumes were smaller with dextrose (median 7 mL vs. 5 mL; $P = 0.02$) Fewer injections were required with dextrose (median 2 vs. 1; $P = 0.003$) En bloc resection was higher with dextrose (82% vs. 44%; $P = 0.01$) Persistent elevation occurred in 96% of dextrose vs. 20% of normal saline ($P < 0.001$) No significant differences in the rates of complete resection or complications	High Several technical improvements over normal saline. Small study
Woodward,	Prospective single center	Submucosal injection	140 sessile	Sydney Resection	No statistically significant difference in SRQ	High

2015 [99]	randomized controlled trial	with normal saline or HPMC	lesions >15 mm.	Quotient (SRQ),	between groups. Possible trend to a difference in lesions <20 mm.	No difference between injectate solutions.

* Sydney Resection Quotient (SRQ) is defined as lesion size in mm divided by the number of resection pieces.

Table 10 Limits of en bloc resection.

First author, year [ref]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Bourke, 2009 [100]	Review	Endoscopic mucosal resection (EMR)/ endoscopic submucosal dissection (ESD)				
Moss, 2011 [69]	Prospective multicentric cohort	EMR for >20 mm colorectal sessile polyps	n = 479 lesions	89% complete excision 20% recurrence		
Barendse, 2012 [101]	Retrospective multicentric cohort (EMR vs. transanal endoscopic microsurgery [TEM])	EMR or TEM for large >2 cm rectal benign adenoma	n = 73 EMR (292 patients)	EMR early recurrence 31%; late recurrence after secondary treatment 13,8%		
Cai, 2014 [102]	Review	EMR, ESD, EMR with precutting, ESD with snare				
Tajika, 2011 [103]	Monocentric retrospective study	EMR vs. ESD (consecutive periods)	104 EMR vs. 85 ESD	En bloc: 83% ESD vs. 48% EMR Recurrence: 1.2% ESD vs. 15%		

				EMR		
Arebi, 2007[104]	Monocentric retrospective study	EMR large flat/sessile colorectal lesions ≥20 mm	161 piecemeal EMR	Clearance 60% after 1 EMR (95% after 6 attempts)	Recurrence 36%	
Sakamoto, 2012 [105]	Monocentric retrospective study	Circumferential incision-EMR of large colorectal lesions >20 mm	24	En bloc 67% (Rx 66%) Recurrence 0% Perforation 0%		
Barendse, 2014 [106]	Prospective data collection multicentric Netherlands cohort (non-tertiary centers)	Piecemeal EMR large rectal adenomas > 30 mm	64 patients (65 lesions)	97% procedures successful Remnants at 3 months: 10 Recurrence 16 (25%)	Complications 23%	
Conio, 2004 [107]	Retrospective study bicentric	Piecemeal EMR large colorectal lesions >20 mm (right colon)/ >30 mm (other segments)	139 polyps in 136 patients	All piecemeal resections Recurrence 22%	No delayed bleeding No perforation 5% post-polypectomy syndrome	
Kaltenbach, 2010 [108]	Review					
Serrano, 2012 [109]	Retrospective monocentric study	EMR for colorectal neoplasm >10 mm	140 EMRs in 133 patients	Size >20 mm associated with piecemeal EMR and residual lesions	Recurrence 18.9% Complication 5.7% Referral for surgery 15%	
Belberdos,	Systematic review and meta-	From >10 mm to >40 mm	33 studies	Recurrence risk: 20% after		

2014 [110]	analysis To define surveilllance interval)	Nonpedunculated		piecemeal EMR vs. 3% after en bloc resection		
Fujiya, 2015 [111]	Systematic review and meta-analysis To define superiority of ESD vs. EMR?	From >5 mm to >20 mm	9 studies EMR vs. ESD (2299 lesions)	En bloc: EMR 46% vs. ESD 91% Curative: EMR 42% vs. ESD 80% Recurrence 12% vs. ESD 0.9%	Additional surgery: EMR 5%, ESD 9%. Perforation: 1.4% EMR vs. ESD 5.7%	
Uraoka, 2006 [74]	Retrospective clinicopathologic comparison	Laterally spreading tumor-granular (LST-G) vs. LST-nongranular (NG)	511 colorectal LSTs analyzed	Risk of sm invasion lower for LST-G (mainly under main nodule/depressed area) than for LST-NG (see characteristics)	LST-G: resect main nodule in one piece LST-NG: en bloc	
Hurlstone, 2005 [112]	Retrospective monocentric study	Extensive EMR for large sessile or LST lesions in rectum	n = 62	98% cured at 16 months 8% local recurrence treated by new EMR at 3 months	8% delayed bleeding 0% perforation	
Imai, 2014 [113]	Retrospective monocentric study	LST-G uniform type vs. mixed type	n = 136 uniform n = 316 mixed	sm invasion: 1.8% in uniform vs. 15.5% in mixed (25% outside main nodule)	LST-G mixed: should be removed en bloc	
Jameel,	Retrospective monocentric	EMR for large colorectal lesions	30 lesions	22 en bloc,	No perforation,	

2006 [114]	study	(10–50 mm)		8 piecemeal Low rate of R0 resections (10/30) led to 19 complementary EMR procedures	Bleeding 2 Recurrence rate of adenoma? (0% adenocarcinoma recurrence)	
Kobayashi, 2012 [115]	Comparative (matched) historical cohorts	EMR vs. ESD for large colorectal tumors	28 ESD vs. 56 EMR	En bloc: 92.9% ESD; 37.5% EMR Time 140 min ESD; 11 min EMR Recurrence: 0% ESD; 21% EMR (91% managed endoscopically and 1 surgery)	Perforation rate: 10.7% ESD (all managed conservatively); 0% EMR Delayed bleeding 7% ESD; 1.8% EMR (not significant)	
Lee, 2012 [116]	Retrospective monocentric study	Comparison of EMR, EMR with precutting (EMR-P), and ESD for ≥20 mm colorectal tumors	140 EMR 69 EMR-P 314 ESD	En bloc: 42% EMR; 65% EMR-P; 93% ESD R0: 33%; 59%; 87%	Recurrence: EMR 26%; EMR-P 3.8%; ESD 0.8% Perforation: EMR-P 2.9%; ESD 8%	
Messman, 2014 [117]	Review (not systematic) To discuss EMR vs. ESD					
Buchner, 2012 [45]	Retrospective monocentric study	EMR for defiant polyps (8–100 mm)	315 lesions (274 patients)	En bloc 53% Piecemeal 46% If >25 mm, 16% en bloc Free margins:	Recurrent/residual neoplasia 27% Multivariate analysis: Factors associated with recurrence: size,	

				piecemeal 0%; en bloc 41%	piecemeal resection. If argon plasma coagulation (APC) used, recurrence 47%	
Belle, 2014 [118]	Retrospective monocentric study	EMR for flat lesions (>10 mm, Is, IIa-b-c), follow-up	n = 177 EMR (147 patients)	En bloc 58%; Piecemeal 24%; Piecemeal+APC 14%: 2 procedures 5%	Recurrence 16% (treated by endoscopy in 93%). Factors associated with recurrence: en bloc, immediate complication	
Saito, 2001 [73]	Monocentric retrospective study	Clinicopathologic evaluation of LST (aspect and risk of deep submucosal invasion)	n = 257 LST (EMR+surgery) Mean size 23 mm	Multivariate analysis: histologic type and depression associated with d-sm invasion		
Saito, 2010 [119]	Retrospective case-controlled study monocentric	Compare EMR with ESD outcomes	145 ESD; 228 EMR (same amount of cancers in both groups)	ESD: Longer, More en bloc resection (84 % vs. 33%), Larger specimen	Recurrence: ESD 2% vs. 14% EMR (more recurrence if not en bloc in both groups) Perforation 6% ESD vs. 1.3% EMR Delayed bleeding 1.4% ESD vs. 3.4% EMR	
Saito, 2014 [120]	Review colorectal ESD	(Partial data, multicentric study in Japan)	1029 EMR and 816 ESD	Perforation: ESD 1.6%; EMR 0.8%; $P < 0.05$ Delayed bleeding		

				ESD 2.2%; EMR: 2%; not significant		
Tanaka, 2008 [121]	Review ESD					
Terasaki, 2012 [122]	Retrospective monocentric study	ESD, hybrid-ESD, EMR, endoscopic piecemeal mucosal resection (EPMR)	269 colorectal LST >20 mm (61 ESD; 28 hybrid ESD; 70 EMR; 108 EPMR)	Recurrence in the case of curative resection: 0% ESD; 0% hybrid-ESD; 1.4% EMR, 12% EPMR (Recurrence higher if LST >40 mm treated by EPMR and if ≥3pieces)	Perforation rates: similar (0% ESD; 7% hybrid-ESD; 1.4% EMR; 1.9% EPMR)	
Wang, 2014 [123]	Meta-analysis EMR vs. Esd	Included 6 studies comparing EMR to ESD (no RCT)	1642 lesions	En bloc resection rate Histological resection rate Local recurrence rate Operation time Complications	En bloc resection rate: Higher for ESD, odds ratio (OR) 7.94 (95%CI 3.96–15.91) Histological resection rate: Not different, OR 1.65 (0.29–9.3) Local recurrence rate: lower for ESD, OR 0.09 (0.04–0.19) Operation time: higher for ESD Complications: Not different, OR 1.59 (0.92–2.73)	
Ah Soune,	Retrospective monocentric	EMR for >4	n = 26	Recurrence: 12%		

2010 [124]	study	colorectal tumors	(25 piecemeal)	Perforation: 1 1 session: 88% APC 38%		
Yoshida, 2014 [125]	Retrospective study	Dual-loop snare for EMR	n = 589 dual loop snare EMR vs. n=339 classical snare EMR	En bloc resection for lesions ≥20 mm: 64% with dual-loop snare		
Binmoeller, 2015 [126]	Prospective observational	Underwater EMR for large 2–4-cm colorectal lesions	n = 53 lesions (50 patients)	55% en bloc resection 79% of whom free margins 5% residual tissue		
Uedo, 2015 [127]	Retrospective monocentric study	Underwater EMR for large sessile polyps (15–25 mm)	n = 11	6/11 en bloc 7/11 R0		
Puli, 2009 [128]	Meta-analysis EMR	Complete cure en bloc resection by EMR		58%		

Table 11 Summary of evidence for adjunctive ablation, e.g. argon plasma coagulation (APC) or soft coagulation.

First author, year [ref.]	Study design, objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Neneman, 2006 [129]	Prospective	Argon plasma coagulation (APC) in the management of gastric and colorectal polyp remnants after polypectomy	18 patients with gastric polyps and 29 with colonic polyps Overall 22 gastric polyps and 58 colonic polyps have been detected	To assess the outcome and safety of argon plasma coagulation (APC) in the management of gastric and colorectal polyp remnants after polypectomy	Among colonic polyps there were: 17 hyperplastic, 26 tubular, 8 tubulo-villous, 4 villous adenomas and 3 inflammatory pseudopolyps. Effective destruction of remnant polyp tissue was obtained in 56 (96.4%) polyps in 27 (93.1%) patients. A significant positive correlation between the power output and the size, distal location, and villous texture of the polyp has been demonstrated. No complications other than mild abdominal distension have been encountered.	APC is an effective and safe method in the management of polyp remnants in the stomach and colon In the case of colonic polyps the application of higher electric power should be recommended in case of large-sized lesions, located in rectum and of villous texture.
Brooker, 2002 [130]	Prospective randomized	Patients with large (>1.5 cm) sessile polyps removed by piecemeal snare cautery were placed into 2 groups.	21	To evaluate the safety and efficacy of argon plasma coagulation (APC) in preventing recurrence when	There were fewer recurrences after APC in the randomized group (1/10 APC, 7/11 no APC; $P = 0.02$). In the group	In patients with apparent complete endoscopic snare resection of large adenomas, post-polypectomy application

		The first consisted of patients with polyps believed by the endoscopist to be completely excised. These patients were randomized to either no further therapy (control) or to APC of the rim and any residual mucosal or submucosal tissue in the base of the polypectomy site.		applied to the edge and base of the polypectomy site after apparently complete piecemeal resection	with initial incomplete snare polypectomy, recurrence was detected at 3 months in 6 of 13 despite APC. One patient was hospitalized with abdominal pain and minor rectal bleeding but required no intervention.	of APC reduces adenomatous recurrence.
Regula, 2003 [131]	Prospective	Patients in whom polypectomy was complete received no further treatment (polypectomy group; n = 14). When polypectomy was incomplete, additional treatment with APC was started either immediately or 1–3 months after the last polypectomy session (polypectomy + APC group, n = 63). Patients were followed (by endoscopy and biopsy) at regular intervals.	77 patients with 82 sessile colorectal adenomas (median size 2.9 cm, range 1.5–8.0 cm) underwent snare piecemeal polypectomy	Histologically proven adenoma eradication	The adenoma recurrence rate was 14% in both the polypectomy and polypectomy + APC groups. All recurrences except one occurred during the first year of follow-up and all were successfully re-treated endoscopically. A total of 69 patients in whom long-term follow-up data are available are free from adenoma at a median follow-up of 37 months (range 12–80). No major complications of endoscopic treatment occurred. In 7 cases (9%) the polyp was eventually shown to be malignant; in 2 of these patients the	APC used in combination with piecemeal polypectomy of large colorectal adenomas is an effective and safe method of therapy, provided patient selection is careful and follow-up close.

					diagnosis of cancer was delayed as a result of unsuccessful endoscopic treatment.	
Moss, 2011 [69]	Prospective, multicenter, observational study	All patients referred for EMR of sessile colorectal polyps that were 20 mm or greater in size	n = 479, mean age, 68.5 y; mean lesion size, 35.6 mm	Data analyzed on lesion characteristics and procedural, clinical, and histologic outcomes. Multiple logistic regression analysis identified independent predictors of EMR efficacy and recurrence of adenoma, based on findings from follow-up colonoscopy examinations.	Risk factors for submucosal invasion were: Paris classification 0-IIa+c morphology, nongranular surface, and Kudo pit pattern type V. The most commonly observed lesion (0-IIa granular) had a low rate of submucosal invasion (1.4%). EMR was effective at completely removing the polyp in a single session in 89.2% of patients. Risk factors for lack of efficacy included: Prior attempt at EMR (OR 3.8, 95%CI 1.77–7.94; *P* = 0.001), and Ileocecal valve involvement (OR, 3.4, 95%CI 1.20–9.52; *P* = 0.021). Independent predictors of recurrence after effective EMR: Lesion size >40 mm (OR 4.37, 95%CI 2.43–7.88;	Large sessile colonic polyps can be managed safely and effectively by endoscopy. Endoscopic assessment identifies lesions at increased risk of containing submucosal cancer. The first EMR is an important determinant of patient outcome – a previous attempt is a significant risk factor for lack of efficacy.

					$P < 0.001$) and Use of APC (OR 3.51, 95%CI 1.69–7.27; $P = 0.0017$). There were no deaths from EMR; 83.7% of patients avoided surgery.	
Tsiamoulos, 2012 [132]	Single-center, nonrandomized case series	Application of high-power APC, preceded by injection of a submucosal fluid cushion (normal saline/diluted adrenaline and/or sodium hyaluronate solution) to protect the muscle layer, was performed to augment further piecemeal EMR and polyp eradication.	Consecutive patients referred for endoscopic excision of recurrent benign colon polyps with severe submucosal fibrosis (>30% of the entire lesion).	Technical safety, success, complication and recurrence rates.	14 patients (mean age 73 years; 9 men, 5 women) with 15 recurrent colon adenomas (mean polyp size 30 mm ; 9 proximal/6 distal) Endoscopic mucosal ablation (EMA) with a mean APC power setting of 55 W was applied. Complete polyp eradication was achieved in 9 of 11 patients (82%) at first or second completed follow-up. One patient needed laparoscopic colectomy because of cancer, and 1 underwent transanal endoscopic microsurgery for benign massive recurrence. The other 3 patients with small, easily treatable recurrence (≤3 mm) were followed by	EMA appears to be a safe and easily applicable technique to assist the complete eradication of recurrent fibrotic colon polyps.

					1-year-surveillance. No perforations and no post-polypectomy syndrome were reported.	

Table 12 Management of the non-lifting polyp.

First author, year [ref.]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Uno, 1994 [133]	Prospective cohort To determine the association between the non-lifting sign and submucosal invasive cancer (SMIC)	Submucosal injection with normal saline.	157 patients, 205 colorectal lesions	"Non-lifting" with submucosal injection. Histological evidence of SMIC	12/205 lesions non-lifting (5.9%) High specificity (99%) and positive predictive value (83%) for the prediction of SMIC by non-lifting. The first published description of the lifting sign.	Moderate Non-lifting correlates with submucosal invasive disease
Ishiguro, 1999 [134]	Prospective cohort To determine the association between the non-lifting sign and depth of SMIC	Submucosal injection with normal saline.	60 patients, 60 colorectal lesions with submucosal invasion	"Non-lifting" with submucosal injection. Depth of submucosal cancer invasion.	15/60 lesions non-lifting (25.0%) Non-lifting associated with a high sensitivity (100%) and specificity (83%) for sm3 disease. Positive predictive value (PPV) 40%; negative predictive value NPV 100% Low numbers in study.	Low Lifting is not associated with sm3 disease. Non-lifting does not exclude invasion. Invasion under 1000 μm may still provide sufficient submucosa for lifting.

Kato, 2001 [76]	Retrospective cohort To determine the association between the non-lifting sign and prediction of SMIC	Submucosal injection with hypertonic saline and adrenaline	94 patients, 104 lesions	"Non-lifting" with submucosal injection. Presence and depth of submucosal cancer invasion.	11/104 lesions non-lifting. (10.6%) Sensitivity 73%, Specificity100%, PPV 100%, NPV 97%	Low Non-lifting correlates with deep (sm3) submucosal invasive disease
Kobayashi, 2007 [75]	Prospective multicenter cohort To determine the association between the non-lifting sign and prediction of SMIC	Submucosal injection with normal saline or glycerol	239 patients, 271 lesions	"Non-lifting" with submucosal injection. Presence of submucosal cancer invasion.	22/271 lesions non-lifting. (8.1%) Non-lifting: Sensitivity 61.5%, Specificity 98.4%, PPV 80.0%, NPV 96.0 % Endoscopic diagnosis with chromoendoscopy had greater sensitivity and specificity.	Moderate Non-lifting had high specificity but modest PPV and sensitivity. Chromoendoscopy assessment was superior.
Han, 2008 [135]	Retrospective cohort To determine the association between the non-lifting sign, clinical findings and depth of SMIC	Submucosal injection with normal saline	76 patients, 76 lesions. 61 underwent endoscopic resection, 15 primary surgical resection. 46 lesions had been previously biopsied or sampled.	"Non-lifting" with submucosal injection. Histological evidence of SMIC Time from lesion biopsy	15/76 lesions non-lifting (19.7%). Sm3 invasion, a history of biopsy, and the absence of adenomatous remnants were associated with non-lifting. A period of >21 days between biopsy and resection was associated with non-	Low Deep invasion, prior biopsy and lack of adenomatous remnants associated with non-lifting. Retrospective study with possibility of bias. Resection should occur promptly if biopsy has occurred.

					lifting	
Ferrara, 2010 [134]	Prospective cohort Prediction of SMIC and prediction of EMR failure.	Submucosal injection with normal saline, adrenaline and dye (methylene blue)	157 patients, 182 lesions	"Non-lifting" with submucosal injection. Histological evidence of SMIC	5/182 lesions non-lifting.(2.7%) Non-lifting sign sensitivity 100%, specificity 95.5%, PPV 38.5% and NPV 100%.	Moderate Adequate lifting associated with absence of SMIC (depth not specified)
Moss 2011[69]	Prospective multicenter cohort Prediction of SMIC and prediction of EMR failure.	Submucosal injection with normal saline or succinylated gelatin, adrenaline and dye (methylene blue or indigo carmine)	479 patients, 479 lesions.	"Non-lifting" with submucosal injection. Histological evidence of SMIC EMR technical failure.	60/479 lesions non-lifting (12.5%). EMR failure associated with previous attempts at resection. (OR 2.85 (95%CI 1.64–2.93) $P < 0.001$ Previous attempts associated with non-lifting (OR 4.96 (95%CI 3.51–7.01) $P < 0.001$.	Moderate EMR failure indirectly linked with non-lifting.

Table 13 Definition of the successful endoscopic mucosal resection (EMR) procedure and summary of evidence for dealing with incomplete resection

First author, year [ref.]	**Study design, Study objective**	**Intervention**	**Participants**	**Outcomes**	**Results**
Moss, 2011 [69]	Prospective multicenter cohort	EMR for >20 mm colorectal sessile polyps	n = 479 lesions	89% complete excision 20% recurrence	
Hong Young Mi , 2015 [137]	Retrospective study	>20 mm colorectal sessile polyps	n = 80 EMR-circumferential incision (CI)	Definition of endoscopic complete resection; histologically complete resection	
Shadid, 2012 [138]	Prospective study multicentric	Probe-based confocal laser endomicroscopy (pCLE) to predict residual adenoma on EMR scar	n = 129 scars	Accuracy of pCLE 81%	
Masci, 2013 [139]	Multicentric retrospective study	EMR for sessile or flat > 1cm colorectal polyps	n = 427 lesions	Complete resection 98% Recurrence 15% Argon plasma coagulation (APC) use 15%	Univariate analysis: use of APC associated with recurrence (hazard ratio [HR] 2.74)
Brooker, 2002 [130]	Randomized controlled trial (RCT) monocentric	Suspicion of complete resection: add APC vs. no add APC	n = 11 vs. 10	Fewer recurrences in APC group (not true if suspicion of residual tissue)	
Hurlstone,	Monocentric prospective	Magnification chromoendoscopy to	n = 684 EMR	12% single en bloc resections had	Accuracy of magnification

2004 [140]	study	predict residual adenoma after EMR		histological evidence of residual adenoma;	endoscopy to predict residual adenoma: 93%–95%
Hurlstone, 2004 [141]	Monocentric prospective study	Magnification chromoendoscopy of LSTs to characterize lesions	n = 82 LST	Flat (F)-type more in right colon, more invasive cancer	Recurrence 17% associated with granular (G)-type, and piecemeal resection
Tsiamoulos, 2002 [132]	Monocentric retrospective case series	Submucosal injection+APC	n = 14 (15 polyps)	No recurrence at 6 months in 12/14	No major complication, easy to use
Hurlstone, 2008 [142]	Monocentric prospective series	Salvage ESD in Western country for residual/recurrence polyp after EMR	n = 30	R0 83% Overall cure rate 96%	
Kim, 2012 [143]	Monocentric study	EMR for LST: risk of incomplete resection assessment	n = 493	Incomplete resection: risk: For lesions <30 mm: increased if piecemeal; In en bloc resection: increased with lesion size >30 mm	
Sakamoto, 2011 [144]	Monocentric retrospective study	Salvage EMR/ESD for residual/recurrent adenoma after endoscopic resection	n = 58 EMR n= 9 ESD	En bloc: 56% with ESD; 39% with EMR Recurrence: 0% ESD; 14% EMR	Rate of en bloc resection lower due to fibrosis

Kim, 2014 [145]	Monocentric retrospective study	Underwater (U-) EMR vs. EMR for residual/recurrent adenoma after piecemeal EMR for LST >20 mm	n = 36 UEMR vs. n = 44 EMR	In favor of UEMR: En bloc 47 vs. 15.9%; Complete endoscopic removal 89% vs. 32%; Need for APC 11% vs. 65%	Recurrence: 10% UEMR vs. 39% EMR
Tanaka, 2009 [146]	Review (non-systematic: expert opinion)	Method to reduce recurrence after EMR:	Magnifying endoscopy of the ulcer; complementary APC/heater probe if needed	0.5% residual adenoma-recurrence	
Regula, 2003 [131]	Prospective study+comparison	EMR vs. EMR+adenoma eradication by (repeated) APC sessions	n = 14 EMR n = 63 EMR+APC	Adenoma eradication: 100% EMR; 90% EMR+APC	
Elta, 2012 [147]	Editorial (expert opinion)	APC not effective in adenoma eradication			
Woodward, 2015 [99]	RCT of two snare techniques			Sydney resection quotient (SRQ) definition	
Albuquerque, 2013 [148]	RCT APC vs. no APC after complete piecemeal EMR	APC vs. no APC after complete piecemeal EMR	n = 10 vs. n = 11	2 recurrences in each group: no difference	

Table 14 Summary of evidence examining lymph node metastasis (LNM) (by study size)

First author, year [ref.]	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence, Conclusions
Studies with <200 patients						
Kitajima, 2004 [149]	Retrospective	Surgical	865 patients (725 flat/sessile; 140 pedunculated lesions)	87 LNM (10%)	Pedunculated: LNM 0% in head or stalk invasion cases with submucosal (SM) depth <3000 μm if lymphatic invasion was negative. Nonpedunculated: LNM 0% if SM depth was <1000 μm. Tumor budding and lymphatic invasion also associated	Low Large study, provides some of the stronger evidence for SM depth <1000 μm. Risk factors: Lymphatic invasion, SM invasion >1000 μm, Tumor budding
Kawachi, 2015 [150]	Retrospective multicenter	Surgical	806 patients Pedunculated lesion, 139, Nonpedunculated, 667	LNM 97 (12%)	Depth of submucosal invasion ≥1000 μm and high-grade budding associated with LNM	Low Risk factors: Depth of submucosal invasion ≥1000 μm; high-grade budding Risk score developed using 3 factors.
Suh, 2012 [151]	Retrospective	Surgical and endoscopic resections Tumors: 32	435 patients (324 with surgical resection)	LNM 42/324 (17.6%)	Poor differentiation, lymphovascular invasion, tumor budding, and the absence of underlying	Low Risk factors: Poor differentiation, Lymphovascular invasion,

		pedunculated, 344 sessile, 41 flat, 49 depressed-type			adenoma.	Tumor budding
Okabe, 2004 [152]	Retrospective	Surgical	428 (Morphology not available in some lesions. Protruded 291, Flat/depressed 41)	LNM 43 (10%)	Submucosal invasion >3000 μm, lymphovascular invasion key risk factors on multivariate analysis	Low Risk factors: Submucosal invasion >3000 μm Lymphovascular invasion
Meining, 2011 [153]	Retrospective	Surgical (some prior endoscopic resections) and endoscopic resection only	390 patients Pedunculated 184, Sessile 206	LNM 17/141 (12.1%)	Lymphatic vessel infiltration, poor grading of tumor stage, and incomplete endoscopic resection associated with poor outcome (local recurrence of tumors, metastasis, or death from colorectal cancer [CRC])	Low Risk factors: Lymphatic invasion, Poor differentiation, Incomplete endoscopic resection.
Matsuda, 2011 [154]	Retrospective	Surgical (Some prior endoscopic resections)	384 patients. Pedunculated	LNM 8/230 (3.5%)	Depth of invasion strongest predictor of LNM	Low Stalk invasion had 6.2% risk of LNM Head invasion, low risk.
Nascimbeni, 2002 [155]	Retrospective	Surgical	353 Sessile	LNM 46 (13%)	Lymphovascular invasion, sm3 depth, and location in the lower third of the rectum associated with LNM	Low Risk factors: Lymphatic or vascular invasion, sm3 depth, Location in the lower third

						of the rectum
Tateishi, 2010 [156]	Retrospective	Surgical	322 patients (Polypoid 33, sessile 289)	LNM 46 (14.3%)	Lymphatic invasion, poor tumor differentiation, and tumor budding associated with LNM.	Low All patients with LNM had at least one of lymphatic invasion, poor tumor differentiation, tumor budding, or completely disrupted muscularis mucosa. Risk factors: Lymphatic invasion, Poor tumor differentiation, Tumor budding, Disrupted muscularis mucosae
Nakadoi, 2014 [157]	Retrospective	Surgical (Some prior endoscopic resections)	322 patients Morphology not stated	LNM 38 (11.8%)	High grade tumor budding, poor differentiation, lymphatic invasion, and disrupted muscularis mucosae associated with LNM	Low Condition of muscularis mucosae associated with LNM. Risk factors: High-grade tumor budding, Poor differentiation, Lymphatic invasion, Disrupted muscularis mucosae
Yamamoto, 2004 [158]	Retrospective	Surgical	301 patients	LNM 19 (6.3%)	Submucosal invasion (sm3) and presence of lymphovascular invasion	Low Risk factors: Submucosal invasion (sm3), Presence of lymphovascular invasion

Ueno, 2004 [159]	Retrospective	Surgical (Some prior endoscopic resections)	292 patients. 238 sessile lesions, 54 pedunculated.	LNM 33/251 (13.1%)	Poor differentiation grade, vascular invasion, and tumor budding. Identified low, moderate and high risk groups	Low Low moderate and high risk groups for LNM. (0.7%, 20.7%, and 36.4%) Risk factors: Poor differentiation grade, vascular invasion, and tumor budding
Sakuragi, 2003 [160]	Retrospective	Surgical (Some prior endoscopic resections)	271 patients 278 lesions (181 polypoid, 51 pedunculated, 106 flat/sessile)	LNM 21 (7.7%)	Depth of submucosal invasion (>2000 μm) and lymphatic invasion associated with LNM.	Low Depth of invasion <2000 μm associated with very low LNM, 0.7%. Risk factors: Submucosal invasion >2000 μm, Lymphatic invasion
Saraste, 2012 [161]	Retrospective	Surgical	201 T1 cancers	LNM 25 (12%)	Incorporated T2 lesions. Poor differentiation and vascular invasion associated with LNM	Low T1 and T2 cancers included. Risk factors: T2 cancer, Poor differentiation, Vascular invasion
Studies with <200 patients						
Tanaka, 1995 [162]	Retrospective	Surgical	177 patients (polypoid 135, non-polypoid 42)	LNM 21 (12%)	Poorly and moderately well differentiated tumors, depressed lesions, submucosal invasion >400 μm, sessile	Low No lesions with superficial submucosal invasion and well-moderately well differentiated histology had

					lesions, lymphatic invasion correlated with LNM	LNM.
Shimomura, 2004 [163]	Retrospective	Surgical Validation cohort endoscopic resection and subsequent surgeries	171 patients (validation 60 patients) Data incomplete on polyp morphology	LNM 18 (10.5%)	Depth of invasion >1500 µm, lymphatic invasion, tumor budding, infiltrative pattern of invasion associated with LNM	Low Risk factors: Depth of invasion >1500 µm, Lymphatic invasion, Tumor budding, Infiltrative pattern of invasion Validated score on 60 patients, but only 3 LNM so limited validity
Yamauchi, 2008 [164]	Retrospective	Surgical (Some prior endoscopic resections)	164 patients, Pedunculated lesions 30, Sessile/flat 134	LNM 16 (9.8%)	Poor differentiation, tumor budding associated with LNM.	Low Risk factors: Poor differentiation, tumor budding.
Pan, 2006 [165]	Retrospective	Surgical (Some prior endoscopic resections)	162 patients 166 polyps: 110 polypoid, 56 sessile or flat	LNM 11 (6.8%)	Greater distance from muscularis mucosae to muscularis propria associated with LNM.	Low Early colorectal cancers at the fold-top or with a long distance from muscularis mucosae to muscularis propria have less tendency to metastasize to lymph nodes.
Wang, 2005 [166]	Retrospective	Surgical	159 patients	LNM 16 (10.1%)	Poor histologic grade, lymphatic invasion, inflammation around cancer, tumor	Low Risk factors: Poor histologic grade, lymphatic invasion,

					budding	Inflammation around cancer, Tumor budding
Tominaga, 2005 [167]	Retrospective	Surgical	155 patients Nonpedunculated lesions	19 LNM (12%)	Multivariate analysis showed lymphatic invasion (P = 0.014) and high grade focal dedifferentiation at the submucosal invasive front (P = 0.049) to be independent factors predicting lymph node metastasis. No lymph node metastasis was found in tumors with a depth of submucosal invasion of <1.3 mm.	Low Risk factors: Lymphatic invasion, High grade focal dedifferentiation at the submucosal invasive front No LNM with SM invasion <1.3 mm
Son, 2008 [168]	Retrospective	Surgical	147 patients Nonpedunculated lesions	30 LNM (17%)	Male sex, left colon, macroscopically depressed lesions, moderately or poorly differentiated carcinoma, depth of tumor invasion (sm2 or sm3), and presence of lymphatic tumor emboli predict LNM	Low LNM risk factors: Male sex, Left colon, Macroscopically depressed lesions, Moderately or poorly differentiated carcinoma, Depth of tumor invasion (sm2 or sm3), Presence of lymphatic tumor emboli
Butte,	Retrospective	Surgical All with	143 patients	LNM 10	Lymphovascular invasion strongest	Low

2012 [169]		previous endoscopic resections		(7.0%)	predictor of LNM	Residual tissue associated with margins of <1 mm. Risk factors: Lymphovascular invasion strong predictor of LNM.
Cooper, 1995 [170]	Retrospective	Endoscopically removed then surgery.	140 patients Pedunculated lesions 91, Sessile 13, Unknown 36	LNM 13 (9.3%)	Resection margin <1.0 mm, poor differentiation, lymphatic and/or venous invasion	Low Risk factors: Resection margin <1.0 mm, Poor differentiation, Lymphatic and/or venous invasion Prespecified histological features correlated with risk of an adverse event (recurrent and/or local cancer and/or lymph node metastasis)
Egashira, 2004 [171]	Retrospective	Surgical	140 Sessile 129, Pedunculated 11)	LNM 13 (9%)	Lymphatic invasion, cribriform-type structural atypia, venous invasion and depth of invasion >2000 µm	Low Identified risk factors formed criteria with improved specificity and accuracy over Haggitt criteria. Risk factors: Lymphatic invasion, Cribriform-type Structural atypia, Venous invasion, Depth of invasion >2000 µm.

Kawaura, 2007 [172]	Retrospective	Surgical (Some prior endoscopic resections)	122 patients Nonpedunculated lesions	20 LNM (16%)	Multivariate analysis showed that lymphatic invasion shown by D2–40 (P = 0.0415) and cascular invasion determined by Van Gieson staining predicted LNM (P = 0.0119)	Low LNM risk factors: Lymphatic and vascular invasion. LNM was absent in 25 patients with other risk factors for invasive disease but a depth of <1500 µm. In patients without risk factors, LNM was absent when invasion depth was <3000 µm
Akishima-Fukusawa, 2011 [173]	Retrospective	Surgical	111 patients 33 polypoid, 78 non-polypoid	LNM 36 (32%)	Neutrophil infiltration in cancer cells, lymphatic invasion and MMP-7 expression associated with LNM. Multiple other histopathological associations.	Low Risk factors: Lymphatic invasion, Neutrophil infiltration, MMP-7 expression
Okuyama, 2002 [174]	Retrospective	Surgical and endoscopic resections	101 T1 and T2 tumors.	LNM 14 (14%)	Only lymphovascular invasion and budding examined.	Low Risk factors: Lymphovascular invasion, Tumor budding.
Macias-Garcia, 2015 [175]	Retrospective	Surgical	97 patients sessile 47, Rectal cancers 30, ?Morphology 20)	LNM 14 (14%)	Infiltrative growth pattern, Absence of lymphoid infiltrate, Poor differentiation, Sessile morphology	Low Predictive score for LNM. Also reports on surgical outcomes – Mortality 2%. ~30% of cohort rectal cancers.

						Risk factors: Infiltrative growth pattern, Absence of lymphoid infiltrate, Poor differentiation, Sessile morphology
Choi, 2009 [176]	Prospective	Surgical and endoscopic resections	87 patients 70 pedunculated/subpendunculated, 17 sessile	LNM 9 (10.3%)	Tumor budding strongly associated with LNM	Moderate Prospective study, but low numbers. Application of a prospective strategy. Risk factors: Tumor budding.
Yasuda, 2007 [177]	Retrospective	Surgical	86 patients Polypoid 61, Sessile 25	LNM 11 (13%)	Vascular invasion, tumor budding, and submucosal invasion >2000 μm	Low No LNM for tumors <1000 μm. Risk factors: Vascular invasion, Tumor budding, Submucosal invasion >1000 μm
Ishikawa, 2008 [178]	Retrospective case–control	Surgical	71 patients Non-polypoid 41, Polypoid 30	LNM 28 (39.4%) NB: case control	Lymphatic invasion and tumor budding	Low Study focused on immunohistochemical markers to improve histological assessment. Risk factors: Lymphatic invasion (with immunostaining), Tumor budding

Kobayashi, 2012 [179]	Retrospective	Surgical (All with prior endoscopic resections)	68 patients Sessile 48, Pedunculated 20	LNM 6 (8.2%)	Moderately–poorly differentiated tumor, lymphovascular invasion	Low Study focused on outcomes following endoscopic resection. 2 patients without LNM had subsequent metastatic recurrence. Risk factors: Moderately-poorly differentiated tumor, Lymphovscular invasion
Suzuki , 2003 [180]	Retrospective	Surgical (Previous endoscopic resections excluded)	65 patients Sessile lesions	LNM 11 (17%)	In sessile polyps with Haggitt 4 invasion, width of submucosal invasion >5 mm was significantly greater in node-positive than in node-negative patients. Depth not significant. Area and differentiation also significant.	Low Risk factors: Poor differentiation, Width and area of submucosal invasion
Bayar, 2002 [181]	Retrospective	Surgical	59 patients (sessile 51, pedunculated 8)	LNM 5 (9.2%)	Vascular invasion	Low Small study. Risk factors: Vascular invasion
Rasheed, 2008 [182]	Retrospective	Surgical	55 T1 rectal cancers	LNM 7 (12.7%)	In combination with T2 lesions. Poor differentiation and vascular invasion were associated with	Low Risk factors: Poor differentiation, Vascular invasion

					LNM.	
Son, 2007 [168]	Retrospective	Surgical	48 patients 20 pedunculated, 28 sessile	7 LNM (14.6%)	Tumor budding	Low Risk factors: Tumor budding
Kim, 2008 [183]	Retrospective	Surgical with previous endoscopic resection (EMR or ESD)	44 patients Polypoid 28, Sessile 16	LNM 3 (6.8%)	Grossly incomplete resection, involved resection margin, lymphovascular invasion	Low Risk factors: Incomplete resection, involved margin, Lymphovascular invasion
Colacchio, 1981 [18$]	Retrospective	24 surgery, 15 polypectomy alone	39 Patients with invasive cancer All pedunculated.	LNM 6 (25.0%)	No statistical analysis of risk factors. Low numbers. Examined differentiation, stalk invasion, lymphatic invasion.	Low Unable to determine factors predictive of LNM from the cohort. Low numbers.

References

1 Atkin WS, Morson BC, Cuzick J. Long-term risk of colorectal cancer after excision of rectosigmoid adenomas. N Engl J Med 1992; 326: 658–662

2 Citarda F, Tomaselli G, Capocaccia R et al. Efficacy in standard clinical practice of colonoscopic polypectomy in reducing colorectal cancer incidence. Gut 2001; 48: 812–815

3 Cottet V, Jooste V, Fournel I et al. Long-term risk of colorectal cancer after adenoma removal: a population-based cohort study. Gut 2012; 61: 1180–1186

4 Loberg M, Kalager M, Holme Ø et al. Long-term colorectal-cancer mortality after adenoma removal. N Engl J Med 2014; 371: 799–807

5 Loeve F, van Ballegooijen M, Boer R et al. Colorectal cancer risk in adenoma patients: a nation-wide study. Int J Cancer 2004; 111: 147–151

6 Nishihara R, Wu K, Lochhead P et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med 2013; 369: 1095–1105

7 Winawer SJ, Zauber AG, Ho MN et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 1993; 329: 1977–1981

8 Zauber AG, Winawer SJ, O'Brien MJ et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012; 366: 687–696

9 Goldstein NS, Watts JC, Neill JS et al. The effect of electrothermal cautery-assisted resection of diminutive colonic polyps on histopathologic diagnosis. Am J Clin Pathol 2001; 115: 356–361

10 Yasar B, Kayadibi H, Abut E et al. The histological quality and adequacy of diminutive colorectal polyps resected using jumbo versus hot biopsy forceps. Dig Dis Sci 2015; 60: 217–225

11 Vanagunas A, Jacob P, Vakil N. Adequacy of "hot biopsy" for the treatment of diminutive polyps: a prospective randomized trial. Am J Gastroenterol 1989; 84: 383–385

12 Peluso F, Goldner F. Follow-up of hot biopsy forceps treatment of diminutive colonic polyps. Gastrointest Endosc 1991; 37: 604–606

13 Woods A, Sanowski RA, Wadas DD et al. Eradication of diminutive polyps: a prospective evaluation of bipolar coagulation versus conventional biopsy removal. Gastrointest Endosc 1989; 35: 536–540

14 Paspatis GA, Vardas E, Charoniti I et al. Bipolar electrocoagulation vs. conventional monopolar hot biopsy forceps in the endoscopic treatment of diminutive rectal adenomas. Colorectal Dis 2005; 7: 138–142

15 Efthymiou M, Taylor AC, Desmond PV et al. Biopsy forceps is inadequate for the resection of diminutive polyps. Endoscopy 2011; 43: 312–316

16 Jung YS, Park JH, Kim HJ et al. Complete biopsy resection of diminutive polyps. Endoscopy 2013; 45: 1024–1029

17 Lee CK, Shim JJ, Jang JY. Cold snare polypectomy vs. cold forceps polypectomy using double-biopsy technique for removal of diminutive colorectal polyps: a prospective randomized study. Am J Gastroenterol 2013; 108: 1593–1600

18 Kim JS, Lee BI, Choi H et al. Cold snare polypectomy versus cold forceps polypectomy for diminutive and small colorectal polyps: a randomized controlled trial. Gastrointest Endosc 2015; 81: 741–747

19 Gomez V, Badillo RJ, Crook JE et al. Diminutive colorectal polyp resection comparing hot and cold snare and cold biopsy forceps polypectomy. Results of a pilot randomized, single-center study (with videos). Endosc Int Open 2015; 3: E76–80

20 Weston AP, Campbell DR. Diminutive colonic polyps: histopathology, spatial distribution, concomitant significant lesions, and treatment complications. Am J Gastroenterol 1995; 90: 24–28

21 McAfee JH, Katon RM. Tiny snares prove safe and effective for removal of diminutive colorectal polyps. Gastrointest Endosc 1994; 40: 301–303

22 Paspatis GA, Tribonias G, Konstantinidis K et al. A prospective randomized comparison of cold vs hot snare polypectomy in the occurrence of postpolypectomy bleeding in small colonic polyps. Colorectal Dis 2011; 13: e345–348

23 Aslan F, Camci M, Alper E et al. Cold snare polypectomy versus hot snare polypectomy in endoscopic treatment of small polyps. Turk J Gastroenterol 2014; 25: 279–283

24 Pohl H, Srivastava A, Bensen SP et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013; 144: 74–80 e71

25 Kim HG, Thosani N, Banerjee S et al. Effect of prior biopsy sampling, tattoo placement, and snare sampling on endoscopic resection of large nonpedunculated colorectal lesions. Gastrointest Endosc 2015; 81: 204–213

26 Repici A, Hassan C, Vitetta E et al. Safety of cold polypectomy for <10 mm polyps at colonoscopy: a prospective multicenter study. Endoscopy 2012; 44: 27–31

27 Ichise Y, Horiuchi A, Nakayama Y et al. Prospective randomized comparison of cold snare polypectomy and conventional polypectomy for small colorectal polyps. Digestion 2011; 84: 78–81

28 Horiuchi A, Nakayama Y, Kajiyama M et al. Removal of small colorectal polyps in anticoagulated patients: a prospective randomized comparison of cold snare and conventional polypectomy. Gastrointest Endosc 2014; 79: 417–423

29 Yoshida N, Naito Y, Inada Y et al. Endoscopic mucosal resection with 0.13% hyaluronic acid solution for colorectal polyps less than 20 mm: a randomized controlled trial. J Gastroenterol Hepatol 2012; 27: 1377–1383

30 Muniraj T, Sahakian A, Ciarleglio MM et al. Cold snare polypectomy for large sessile colonic polyps: a single-center experience. Gastroenterol Res Pract 2015; 2015: 175959

31 Katsinelos P, Kountouras J, Paroutoglou G et al. A comparative study of 50% dextrose and normal saline solution on their ability to create submucosal fluid cushions for endoscopic resection of sessile rectosigmoid polyps. Gastrointest Endosc 2008; 68: 692–698

32 Augusto Barros R, Monteverde MJ, Federico Barros R et al. [Safety and efficacy of cold snare resection of non-polypoid colorectal lesions (0-IIa and 0-IIb)]. Acta Gastroenterol Latinoam 2014; 44: 27–32

33 Dobrowolski S, Dobosz M, Babicki A et al. Prophylactic submucosal saline-adrenaline injection in colonoscopic polypectomy: prospective randomized study. Surg Endosc 2004; 18: 990–993

34 Lee SH, Chung IK, Kim SJ et al. Comparison of postpolypectomy bleeding between epinephrine and saline submucosal injection for large colon polyps by conventional polypectomy: a prospective randomized, multicenter study. World J Gastroenterol 2007; 13: 2973–2977

35 Iishi H, Tatsuta M, Narahara H et al. Endoscopic resection of large pedunculated colorectal polyps using a detachable snare. Gastrointest Endosc 1996; 44: 594–597

36 Di Giorgio P, De Luca L, Calcagno G et al. Detachable snare versus epinephrine injection in the prevention of postpolypectomy bleeding: a randomized and controlled study. Endoscopy 2004; 36: 860–863

37 Paspatis GA, Paraskeva K, Theodoropoulou A et al. A prospective, randomized comparison of adrenaline injection in combination with detachable snare versus adrenaline injection alone in the prevention of postpolypectomy bleeding in large colonic polyps. Am J Gastroenterol 2006; 101: 2805; quiz 2913

38 Kouklakis G, Mpoumponaris A, Gatopoulou A et al. Endoscopic resection of large pedunculated colonic polyps and risk of postpolypectomy bleeding with adrenaline injection versus endoloop and hemoclip: a prospective, randomized study. Surg Endosc 2009; 23: 2732–2737

39 Ji JS, Lee SW, Kim TH et al. Comparison of prophylactic clip and endoloop application for the prevention of postpolypectomy bleeding in pedunculated colonic polyps: a prospective, randomized, multicenter study. Endoscopy 2014; 46: 598–604

40 Feagins LA, Nguyen AD, Iqbal R et al. The prophylactic placement of hemoclips to prevent delayed post-polypectomy bleeding: an unnecessary practice? A case control study. Dig Dis Sci 2014; 59: 823–828

41 Nanda KS, Tutticci N, Burgess NG et al. Endoscopic mucosal resection of laterally spreading lesions involving the ileocecal valve: technique, risk factors for failure, and outcomes. Endoscopy 2015, DOI: 10.1055/s-0034–1391732:

42 Moss A, Williams SJ, Hourigan LF et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut 2015; 64: 57–65

43 Friedland S, Banerjee S, Kochar R et al. Outcomes of repeat colonoscopy in patients with polyps referred for surgery without biopsy-proven cancer. Gastrointest Endosc 2014; 79: 101–107

44 Longcroft-Wheaton G, Duku M, Mead R et al. Risk stratification system for evaluation of complex polyps can predict outcomes of endoscopic mucosal resection. Dis Colon Rectum 2013; 56: 960–966

45 Buchner AM, Guarner-Argente C, Ginsberg GG. Outcomes of EMR of defiant colorectal lesions directed to an endoscopy referral center. Gastrointest Endosc 2012; 76: 255–263

46 Kao KT, Giap AQ, Abbas MA. Endoscopic excision of large colorectal polyps as a viable alternative to surgical resection. Arch Surg 2011; 146: 690–696

47 Swan MP, Bourke MJ, Alexander S et al. Large refractory colonic polyps: is it time to change our practice? A prospective study of the clinical and economic impact of a tertiary referral colonic mucosal resection and polypectomy service (with videos). Gastrointest Endosc 2009; 70: 1128–1136

48 Voloyiannis T, Snyder MJ, Bailey RR et al. Management of the difficult colon polyp referred for resection: resect or rescope? Dis Colon Rectum 2008; 51: 292–295

49 Lipof T, Bartus C, Sardella W et al. Preoperative colonoscopy decreases the need for laparoscopic management of colonic polyps. Dis Colon Rectum 2005; 48: 1076–1080

50 Church JM. Experience in the endoscopic management of large colonic polyps. ANZ J Surg 2003; 73: 988–995

51 Brooker JC, Saunders BP, Shah SG et al. Endoscopic resection of large sessile colonic polyps by specialist and non-specialist endoscopists. Br J Surg 2002; 89: 1020–1024

52 Hirata M, Tanaka S, Oka S et al. Evaluation of microvessels in colorectal tumors by narrow band imaging magnification. Gastrointest Endosc 2007; 66: 945–952

53 Yoshida N, Naito Y, Kugai M et al. Efficacy of magnifying endoscopy with flexible spectral imaging color enhancement in the diagnosis of colorectal tumors. J Gastroenterol 2011; 46: 65–72

54 Wada Y, Kudo SE, Kashida H et al. Diagnosis of colorectal lesions with the magnifying narrow-band imaging system. Gastrointest Endosc 2009; 70: 522–531

55 Oba S, Tanaka S, Oka S et al. Characterization of colorectal tumors using narrow-band imaging magnification: combined diagnosis with both pit pattern and microvessel features. Scand J Gastroenterol 2010; 45: 1084–1092

56 Wada Y, Kashida H, Kudo SE et al. Diagnostic accuracy of pit pattern and vascular pattern analyses in colorectal lesions. Dig Endosc 2010; 22: 192–199

57 Ikematsu H, Matsuda T, Emura F et al. Efficacy of capillary pattern type IIIA/IIIB by magnifying narrow band imaging for estimating depth of invasion of early colorectal neoplasms. BMC Gastroenterol 2010; 10: 33

58 Jang HW, Park SJ, Cheon JH et al. Does magnifying narrow-band imaging or magnifying chromoendoscopy help experienced endoscopists assess invasion depth of large sessile and flat polyps? Dig Dis Sci 2014; 59: 1520–1528

59 Kanao H, Tanaka S, Oka S et al. Narrow-band imaging magnification predicts the histology and invasion depth of colorectal tumors. Gastrointest Endosc 2009; 69: 631–636

60 Oka S, Tanaka S, Takata S et al. Clinical usefulness of narrow band imaging magnifying classification for colorectal tumors based on both surface pattern and microvessel features. Dig Endosc 2011; 23 Suppl 1: 101–105

61 Goto N, Kusaka T, Tomita Y et al. Magnifying narrow-band imaging with acetic acid to diagnose early colorectal cancer. World J Gastroenterol 2014; 20: 16306–16310

62 Shibagaki K, Amano Y, Ishimura N et al. Magnification endoscopy with acetic acid enhancement and a narrow-band imaging system for pit pattern diagnosis of colorectal neoplasms. J Clin Gastroenterol 2015; 49: 306–312

63 Hayashi N, Tanaka S, Hewett DG et al. Endoscopic prediction of deep submucosal invasive carcinoma: validation of the narrow-band imaging international colorectal endoscopic (NICE) classification. Gastrointest Endosc 2013; 78: 625–632

64 Hurlstone DP, Cross SS, Adam I et al. Endoscopic morphological anticipation of submucosal invasion in flat and depressed colorectal lesions: clinical implications and subtype analysis of the kudo type V pit pattern using high-magnification-chromoscopic colonoscopy. Colorectal Dis 2004; 6: 369–375

65 Kanao H, Tanaka S, Oka S et al. Clinical significance of type V(I) pit pattern subclassification in determining the depth of invasion of colorectal neoplasms. World J Gastroenterol 2008; 14: 211–217

66 Tobaru T, Mitsuyama K, Tsuruta O et al. Sub-classification of type VI pit patterns in colorectal tumors: relation to the depth of tumor invasion. Int J Oncol 2008; 33: 503–508

67 Ikehara H, Saito Y, Matsuda T et al. Diagnosis of depth of invasion for early colorectal cancer using magnifying colonoscopy. J Gastroenterol Hepatol 2010; 25: 905–912

68 Matsuda T, Fujii T, Saito Y et al. Efficacy of the invasive/non-invasive pattern by magnifying chromoendoscopy to estimate the depth of invasion of early colorectal neoplasms. Am J Gastroenterol 2008; 103: 2700–2706

69 Moss A, Bourke MJ, Williams SJ et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology 2011; 140: 1909–1918

70 Li X, Chen H, Gao Y et al. Prediction of histology and invasive depth of colorectal neoplasia based on morphology of surface depression using magnifying chromocolonoscopy. Int J Colorectal Dis 2010; 25: 79–85

71 Horie H, Togashi K, Kawamura YJ et al. Colonoscopic stigmata of 1 mm or deeper submucosal invasion in colorectal cancer. Dis Colon Rectum 2008; 51: 1529–1534

72 Saitoh Y, Obara T, Watari J et al. Invasion depth diagnosis of depressed type early colorectal cancers by combined use of videoendoscopy and chromoendoscopy. Gastrointest Endosc 1998; 48: 362–370

73 Saito Y, Fujii T, Kondo H et al. Endoscopic treatment for laterally spreading tumors in the colon. Endoscopy 2001; 33: 682–686

74 Uraoka T, Saito Y, Matsuda T et al. Endoscopic indications for endoscopic mucosal resection of laterally spreading tumours in the colorectum. Gut 2006; 55: 1592–1597

75 Kobayashi N, Saito Y, Sano Y et al. Determining the treatment strategy for colorectal neoplastic lesions: endoscopic assessment or the non-lifting sign for diagnosing invasion depth? Endoscopy 2007; 39: 701–705

76 Kato H, Haga S, Endo S et al. Lifting of lesions during endoscopic mucosal resection (EMR) of early colorectal cancer: implications for the assessment of resectability. Endoscopy 2001; 33: 568–573
77 Sakamoto T, Saito Y, Nakajima T et al. Comparison of magnifying chromoendoscopy and narrow-band imaging in estimation of early colorectal cancer invasion depth: a pilot study. Dig Endosc 2011; 23: 118–123
78 Zhang JJ, Gu LY, Chen XY et al. Endoscopic diagnosis of invasion depth for early colorectal carcinomas: a prospective comparative study of narrow-band imaging, acetic acid, and crystal violet. Medicine 2015; 94: e528
79 Shimura T, Ebi M, Yamada T et al. Magnifying chromoendoscopy and endoscopic ultrasonography measure invasion depth of early stage colorectal cancer with equal accuracy on the basis of a prospective trial. Clin Gastroenterol Hepatol 2014; 12: 662–668 e661–662
80 Matsumoto T, Hizawa K, Esaki M et al. Comparison of EUS and magnifying colonoscopy for assessment of small colorectal cancers. Gastrointest Endosc 2002; 56: 354–360
81 Elarini T, Wexner SD, Isenberg GA. The need for standardization of colonoscopic tattooing of colonic lesions. Dis Colon Rectum 2015; 58: 264–267
82 Moss A. Colonic tattooing: the revival of a black art? Gastrointest Endosc 2012; 76: 801–803
83 Zafar A, Mustafa M, Chapman M. Colorectal polyps: when should we tattoo? Surg Endosc 2012; 26: 3264–3266
84 Bartels SA, van der Zaag ES, Dekker E et al. The effect of colonoscopic tattooing on lymph node retrieval and sentinel lymph node mapping. Gastrointest Endosc 2012; 76: 793–800
85 Moss A, Bourke MJ, Pathmanathan N. Safety of colonic tattoo with sterile carbon particle suspension: a proposed guideline with illustrative cases. Gastrointest Endosc 2011; 74: 214–218
86 Kethu SR, Banerjee S, Desilets D et al. Endoscopic tattooing. Gastrointest Endosc 2010; 72: 681–685
87 Yeung JM, Maxwell-Armstrong C, Acheson AG. Colonic tattooing in laparoscopic surgery - making the mark? Colorectal Dis 2009; 11: 527–530
88 Ono S, Fujishiro M, Goto O et al. Endoscopic submucosal dissection for colonic laterally spreading tumors is difficult after target tattooing. Gastrointest Endosc 2009; 69: 763–766
89 Park JW, Sohn DK, Hong CW et al. The usefulness of preoperative colonoscopic tattooing using a saline test injection method with prepackaged sterile India ink for localization in laparoscopic colorectal surgery. Surg Endosc 2008; 22: 501–505

90 Arteaga-Gonzalez I, Martin-Malagon A, Fernandez EM et al. The use of preoperative endoscopic tattooing in laparoscopic colorectal cancer surgery for endoscopically advanced tumors: a prospective comparative clinical study. World J Surg 2006; 30: 605–611

91 Askin MP, Waye JD, Fiedler L et al. Tattoo of colonic neoplasms in 113 patients with a new sterile carbon compound. Gastrointest Endosc 2002; 56: 339–342

92 Sawaki A, Nakamura T, Suzuki T et al. A two-step method for marking polypectomy sites in the colon and rectum. Gastrointest Endosc 2003; 57: 735–737

93 Fu KI, Fujii T, Kato S et al. A new endoscopic tattooing technique for identifying the location of colonic lesions during laparoscopic surgery: a comparison with the conventional technique. Endoscopy 2001; 33: 687–691

94 Moss A, Bourke MJ, Metz AJ. A randomized, double-blind trial of succinylated gelatin submucosal injection for endoscopic resection of large sessile polyps of the colon. Am J Gastroenterol 2010; 105: 2375–2382

95 Uraoka T, Fujii T, Saito Y et al. Effectiveness of glycerol as a submucosal injection for EMR. Gastrointest Endosc 2005; 61: 736–740

96 Bacani CJ, Woodward TA, Raimondo M et al. The safety and efficacy in humans of endoscopic mucosal resection with hydroxypropyl methylcellulose as compared with normal saline. Surg Endosc 2008; 22: 2401–2406

97 Arezzo A, Pagano N, Romeo F et al. Hydroxy-propyl-methyl-cellulose is a safe and effective lifting agent for endoscopic mucosal resection of large colorectal polyps. Surg Endosc 2009; 23: 1065–1069

98 Varadarajulu S, Tamhane A, Slaughter RL. Evaluation of dextrose 50 % as a medium for injection-assisted polypectomy. Endoscopy 2006; 38: 907–912

99 Woodward T, Crook JE, Raimondo M et al. Improving complete EMR of colorectal neoplasia: a randomized trial comparing snares and injectate in the resection of large sessile colon polyps. Gastrointest Endosc 2015; 81: 673–681

100 Bourke M. Current status of colonic endoscopic mucosal resection in the west and the interface with endoscopic submucosal dissection. Dig Endosc 2009; 21 Suppl 1: S22–27

101 Barendse RM, van den Broek FJ, van Schooten J et al. Endoscopic mucosal resection vs transanal endoscopic microsurgery for the treatment of large rectal adenomas. Colorectal Dis 2012; 14: e191–196

102 Cai S, Zhong Y, Zhou P et al. Re-evaluation of indications and outcomes of endoscopic excision procedures for colorectal tumors: a review. Gastroenterol Rep (Oxf) 2014; 2: 27–36

103 Tajika M, Niwa Y, Bhatia V et al. Comparison of endoscopic submucosal dissection and endoscopic mucosal resection for large colorectal tumors. Eur J Gastroenterol Hepatol 2011; 23: 1042–1049

104 Arebi N, Swain D, Suzuki N et al. Endoscopic mucosal resection of 161 cases of large sessile or flat colorectal polyps. Scand J Gastroenterol 2007; 42: 859–866

105 Sakamoto T, Matsuda T, Nakajima T et al. Efficacy of endoscopic mucosal resection with circumferential incision for patients with large colorectal tumors. Clin Gastroenterol Hepatol 2012; 10: 22–26

106 Barendse R, Musters G, Fockens P et al. Endoscopic mucosal resection of large rectal adenomas in the era of centralization: Results of a multicenter collaboration. United European Gastroenterol J 2014; 2: 497–504

107 Conio M, Repici A, Demarquay JF et al. EMR of large sessile colorectal polyps. Gastrointest Endosc 2004; 60: 234–241

108 Kaltenbach T, Soetikno R. Endoscopic mucosal resection of non-polypoid colorectal neoplasm. Gastrointest Endosc Clin N Am 2010; 20: 503–514

109 Serrano M, Mao de Ferro S, Fidalgo P et al. Endoscopic mucosal resection of superficial colorectal neoplasms: review of 140 procedures. Acta Med Port 2012; 25: 288–296

110 Belderbos TD, Leenders M, Moons LM et al. Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: systematic review and meta-analysis. Endoscopy 2014; 46: 388–402

111 Fujiya M, Tanaka K, Dokoshi T et al. Efficacy and adverse events of EMR and endoscopic submucosal dissection for the treatment of colon neoplasms: a meta-analysis of studies comparing EMR and endoscopic submucosal dissection. Gastrointest Endosc 2015; 81: 583–595

112 Hurlstone DP, Sanders DS, Cross SS et al. A prospective analysis of extended endoscopic mucosal resection for large rectal villous adenomas: an alternative technique to transanal endoscopic microsurgery. Colorectal Dis 2005; 7: 339–344

113 Imai K, Hotta K, Yamaguchi Y et al. Should laterally spreading tumors granular type be resected en bloc in endoscopic resections? Surg Endosc 2014; 28: 2167–2173

114 Jameel JK, Pillinger SH, Moncur P et al. Endoscopic mucosal resection (EMR) in the management of large colo-rectal polyps. Colorectal Dis 2006; 8: 497–500

115 Kobayashi N, Yoshitake N, Hirahara Y et al. Matched case-control study comparing endoscopic submucosal dissection and endoscopic mucosal resection for colorectal tumors. J Gastroenterol Hepatol 2012; 27: 728–733

116 Lee EJ, Lee JB, Lee SH et al. Endoscopic treatment of large colorectal tumors: comparison of endoscopic mucosal resection, endoscopic mucosal resection-precutting, and endoscopic submucosal dissection. Surg Endosc 2012; 26: 2220–2230
117 Messmann H. Endoscopic resection: when is EMR/ESD sufficient? Recent Results Cancer Res 2014; 203: 25–30
118 Belle S, Haase L, Pilz LR et al. Recurrence after endoscopic mucosal resection-therapy failure? Int J Colorectal Dis 2014; 29: 209–215
119 Saito Y, Fukuzawa M, Matsuda T et al. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. Surg Endosc 2010; 24: 343–352
120 Saito Y, Yamada M, So E et al. Colorectal endoscopic submucosal dissection: Technical advantages compared to endoscopic mucosal resection and minimally invasive surgery. Dig Endosc 2014; 26 Suppl 1: 52–61
121 Tanaka S, Oka S, Chayama K. Colorectal endoscopic submucosal dissection: present status and future perspective, including its differentiation from endoscopic mucosal resection. J Gastroenterol 2008; 43: 641–651
122 Terasaki M, Tanaka S, Oka S et al. Clinical outcomes of endoscopic submucosal dissection and endoscopic mucosal resection for laterally spreading tumors larger than 20 mm. J Gastroenterol Hepatol 2012; 27: 734–740
123 Wang J, Zhang XH, Ge J et al. Endoscopic submucosal dissection vs endoscopic mucosal resection for colorectal tumors: a meta-analysis. World J Gastroenterol 2014; 20: 8282–8287
124 Ah Soune P, Menard C, Salah E et al. Large endoscopic mucosal resection for colorectal tumors exceeding 4 cm. World J Gastroenterol 2010; 16: 588–595
125 Yoshida N, Saito Y, Hirose R et al. Endoscopic mucosal resection for middle and large colorectal polyps with a double-loop snare. Digestion 2014; 90: 232–239
126 Binmoeller KF, Hamerski CM, Shah JN et al. Attempted underwater en bloc resection for large (2–4 cm) colorectal laterally spreading tumors (with video). Gastrointest Endosc 2015; 81: 713–718
127 Uedo N, Nemeth A, Johansson GW et al. Underwater endoscopic mucosal resection of large colorectal lesions. Endoscopy 2015; 47: 172–417
128 Puli SR, Kakugawa Y, Gotoda T et al. Meta-analysis and systematic review of colorectal endoscopic mucosal resection. World J Gastroenterol 2009; 15: 4273–4277
129 Neneman B, Gasiorowska A, Malecka-Panas E. The efficacy and safety of argon plasma coagulation (APC) in the management of polyp remnants in stomach and colon. Adv Med Sci 2006; 51: 88–93

130 Brooker JC, Saunders BP, Shah SG et al. Treatment with argon plasma coagulation reduces recurrence after piecemeal resection of large sessile colonic polyps: a randomized trial and recommendations. Gastrointest Endosc 2002; 55: 371–375

131 Regula J, Wronska E, Polkowski M et al. Argon plasma coagulation after piecemeal polypectomy of sessile colorectal adenomas: long-term follow-up study. Endoscopy 2003; 35: 212–218

132 Tsiamoulos ZP, Bourikas LA, Saunders BP. Endoscopic mucosal ablation: a new argon plasma coagulation/injection technique to assist complete resection of recurrent, fibrotic colon polyps (with video). Gastrointest Endosc 2012; 75: 400–404

133 Uno Y, Munakata A. The non-lifting sign of invasive colon cancer. Gastrointest Endosc 1994; 40: 485–489

134 Ishiguro A, Uno Y, Ishiguro Y et al. Correlation of lifting versus non-lifting and microscopic depth of invasion in early colorectal cancer. Gastrointest Endosc 1999; 50: 329–333

135 Han KS, Sohn DK, Choi DH et al. Prolongation of the period between biopsy and EMR can influence the nonlifting sign in endoscopically resectable colorectal cancers. Gastrointest Endosc 2008; 67: 97–102

136 Ferrara F, Luigiano C, Ghersi S et al. Efficacy, safety and outcomes of 'inject and cut' endoscopic mucosal resection for large sessile and flat colorectal polyps. Digestion 2010; 82: 213–220

137 Hong YM, Kim HW, Park SB et al. Endoscopic mucosal resection with circumferential incision for the treatment of large sessile polyps and laterally spreading tumors of the colorectum. Clin Endosc 2015; 48: 52–58

138 Shahid MW, Buchner AM, Coron E et al. Diagnostic accuracy of probe-based confocal laser endomicroscopy in detecting residual colorectal neoplasia after EMR: a prospective study. Gastrointest Endosc 2012; 75: 525–533

139 Masci E, Viale E, Notaristefano C et al. Endoscopic mucosal resection in high- and low-volume centers: a prospective multicentric study. Surg Endosc 2013; 27: 3799–3805

140 Hurlstone DP, Cross SS, Brown S et al. A prospective evaluation of high-magnification chromoscopic colonoscopy in predicting completeness of EMR. Gastrointest Endosc 2004; 59: 642–650

141 Hurlstone DP, Sanders DS, Cross SS. Colonoscopic resection of lateral spreading tumours: a prospective analysis of endoscopic mucosal resection. Gut 2004; 53: 1334–1339. doi: 10.1136/gut.2003.036913

142 Hurlstone DP, Shorthouse AJ, Brown SR et al. Salvage endoscopic submucosal dissection for residual or local recurrent intraepithelial neoplasia in the colorectum: a prospective analysis. Colorectal Dis 2008; 10: 891–897

143 Kim HH, Kim JH, Park SJ et al. Risk factors for incomplete resection and complications in endoscopic mucosal resection for lateral spreading tumors. Dig Endosc 2012; 24: 259–266

144 Sakamoto T, Saito Y, Matsuda T et al. Treatment strategy for recurrent or residual colorectal tumors after endoscopic resection. Surg Endosc 2011; 25: 255–260

145 Kim HG, Thosani N, Banerjee S et al. Underwater endoscopic mucosal resection for recurrences after previous piecemeal resection of colorectal polyps (with video). Gastrointest Endosc 2014; 80: 1094–1102

146 Tanaka S, Oka S, Chayama K et al. Knack and practical technique of colonoscopic treatment focused on endoscopic mucosal resection using snare. Dig Endosc 2009; 21 Suppl 1: S38–42

147 Elta GH. What is a defiant polyp and how good are we at removing them? Gastrointest Endosc 2012; 76: 264–266. doi: http://dx.doi.org/10.1016/j.gie.2012.04.450

148 Albuquerque W, Arantes VN, Coelho LG et al. Complementation by argon plasma coagulation after endoscopic piecemeal resection of large colorectal adenomas. Rev Col Bras Cir 2013; 40: 404–408

149 Kitajima K, Fujimori T, Fujii S et al. Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study. J Gastroenterol 2004; 39: 534–543

150 Kawachi H, Eishi Y, Ueno H et al. A three-tier classification system based on the depth of submucosal invasion and budding/sprouting can improve the treatment strategy for T1 colorectal cancer: a retrospective multicenter study. Mod Pathol 2015; 28: 872–879

151 Suh JH, Han KS, Kim BC et al. Predictors for lymph node metastasis in T1 colorectal cancer. Endoscopy 2012; 44: 590–595

152 Okabe S, Shia J, Nash G et al. Lymph node metastasis in T1 adenocarcinoma of the colon and rectum. J Gastrointest Surg 2004; 8: 1032–1039; discussion 1039–1040

153 Meining A, von Delius S, Eames TM et al. Risk factors for unfavorable outcomes after endoscopic removal of submucosal invasive colorectal tumors. Clin Gastroenterol Hepatol 2011; 9: 590–594

151 Matsuda T, Fukuzawa M, Uraoka T et al. Risk of lymph node metastasis in patients with pedunculated type early invasive colorectal cancer: a retrospective multicenter study. Cancer Sci 2011; 102: 1693–1697

155 Nascimbeni R, Burgart LJ, Nivatvongs S et al. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum 2002; 45: 200–206

156 Tateishi Y, Nakanishi Y, Taniguchi H et al. Pathological prognostic factors predicting lymph node metastasis in submucosal invasive (T1) colorectal carcinoma. Mod Pathol 2010; 23: 1068–1072

157 Nakadoi K, Oka S, Tanaka S et al. Condition of muscularis mucosae is a risk factor for lymph node metastasis in T1 colorectal carcinoma. Surg Endosc 2014; 28: 1269–1276

158 Yamamoto S, Watanabe M, Hasegawa H et al. The risk of lymph node metastasis in T1 colorectal carcinoma. Hepatogastroenterology 2004; 51: 998–1000

159 Ueno H, Mochizuki H, Hashiguchi Y et al. Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology 2004; 127: 385–394

160 Sakuragi M, Togashi K, Konishi F et al. Predictive factors for lymph node metastasis in T1 stage colorectal carcinomas. Dis Colon Rectum 2003; 46: 1626–1632

161 Saraste D, Gunnarsson U, Janson M. Predicting lymph node metastases in early rectal cancer. Eur J Cancer 2013; 49: 1104–1108

162 Tanaka S, Haruma K, Teixeira CR et al. Endoscopic treatment of submucosal invasive colorectal carcinoma with special reference to risk factors for lymph node metastasis. J Gastroenterol 1995; 30: 710–717

163 Shimomura T, Ishiguro S, Konishi H et al. New indication for endoscopic treatment of colorectal carcinoma with submucosal invasion. J Gastroenterol Hepatol 2004; 19: 48–55

164 Yamauchi H, Togashi K, Kawamura YJ et al. Pathological predictors for lymph node metastasis in T1 colorectal cancer. Surg Today 2008; 38: 905–910

165 Pan W, Terai T, Abe S et al. Location of early colorectal cancers at fold-top may reduce the risk of lymph node metastasis. Dis Colon Rectum 2006; 49: 579–587

166 Wang HS, Liang WY, Lin TC et al. Curative resection of T1 colorectal carcinoma: risk of lymph node metastasis and long-term prognosis. Dis Colon Rectum 2005; 48: 1182–1192

167 Tominaga K, Nakanishi Y, Nimura S et al. Predictive histopathologic factors for lymph node metastasis in patients with nonpedunculated submucosal invasive colorectal carcinoma. Dis Colon Rectum 2005; 48: 92–100

168 Son HJ, Song SY, Lee WY et al. Characteristics of early colorectal carcinoma with lymph node metastatic disease. Hepatogastroenterology 2008; 55: 1293–1297

169 Butte JM, Tang P, Gonen M et al. Rate of residual disease after complete endoscopic resection of malignant colonic polyp. Dis Colon Rectum 2012; 55: 122–127

170 Cooper HS, Deppisch LM, Gourley WK et al. Endoscopically removed malignant colorectal polyps: clinicopathologic correlations. Gastroenterology 1995; 108: 1657–1665

171 Egashira Y, Yoshida T, Hirata I et al. Analysis of pathological risk factors for lymph node metastasis of submucosal invasive colon cancer. Mod Pathol 2004; 17: 503–511

172 Kawaura K, Fujii S, Murata Y et al. The lymphatic infiltration identified by D2–40 monoclonal antibody predicts lymph node metastasis in submucosal invasive colorectal cancer. Pathobiology 2007; 74: 328–335

173 Akishima-Fukasawa Y, Ishikawa Y, Akasaka Y et al. Histopathological predictors of regional lymph node metastasis at the invasive front in early colorectal cancer. Histopathology 2011; 59: 470–481

174 Okuyama T, Oya M, Ishikawa H. Budding as a risk factor for lymph node metastasis in pT1 or pT2 well-differentiated colorectal adenocarcinoma. Dis Colon Rectum 2002; 45: 628–634

175 Macias-Garcia F, Celeiro-Munoz C, Lesquereux-Martinez L et al. A clinical model for predicting lymph node metastasis in submucosal invasive (T1) colorectal cancer. Int J Colorectal Dis 2015; 30: 761–768

176 Choi DH, Sohn DK, Chang HJ et al. Indications for subsequent surgery after endoscopic resection of submucosally invasive colorectal carcinomas: a prospective cohort study. Dis Colon Rectum 2009; 52: 438–445

177 Yasuda K, Inomata M, Shiromizu A et al. Risk factors for occult lymph node metastasis of colorectal cancer invading the submucosa and indications for endoscopic mucosal resection. Dis Colon Rectum 2007; 50: 1370–1376

178 Ishikawa Y, Akishima-Fukasawa Y, Ito K et al. Histopathologic determinants of regional lymph node metastasis in early colorectal cancer. Cancer 2008; 112: 924–933

179 Kobayashi H, Higuchi T, Uetake H et al. Resection with en bloc removal of regional lymph node after endoscopic resection for T1 colorectal cancer. Ann Surg Oncol 2012; 19: 4161–4167

180 Suzuki T, Sadahiro S, Mukoyama S et al. Risk of lymph node and distant metastases in patients with early invasive colorectal cancer classified as Haggitt's level 4 invasion: image analysis of submucosal layer invasion. Dis Colon Rectum 2003; 46: 203–208

181 Bayar S, Saxena R, Emir B et al. Venous invasion may predict lymph node metastasis in early rectal cancer. Eur J Surg Oncol 2002; 28: 413–417

182 Rasheed S, Bowley DM, Aziz O et al. Can depth of tumour invasion predict lymph node positivity in patients undergoing resection for early rectal cancer? A comparative study between T1 and T2 cancers. Colorectal Dis 2008; 10: 231–238

183 Kim JH, Cheon JH, Kim TI et al. Effectiveness of radical surgery after incomplete endoscopic mucosal resection for early colorectal cancers: a clinical study investigating risk factors of residual cancer. Dig Dis Sci 2008; 53: 2941–2946

184 Colacchio TA, Forde KA, Scantlebury VP. Endoscopic polypectomy: inadequate treatment for invasive colorectal carcinoma. Ann Surg 1981; 194: 704–707