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OPINION REVIEW

- 6619** How to avoid overtreatment of benign colorectal lesions: Rationale for an evidence-based management
Bustamante-Balén M

REVIEW

- 6632** Mucosal imaging in colon polyps: New advances and what the future may hold
Young EJ, Rajandran A, Philpott HL, Sathananthan D, Hoile SF, Singh R
- 6662** Acute liver injury in COVID-19 patients hospitalized in the intensive care unit: Narrative review
Polyzogopoulou E, Amoiridou P, Abraham TP, Ventoulis I
- 6689** Alterations of the gut microbiota in coronavirus disease 2019 and its therapeutic potential
Xiang H, Liu QP

MINIREVIEWS

- 6702** Microbiota in the stomach and application of probiotics to gastroduodenal diseases
Koga Y
- 6716** Liver injury in COVID-19: A minireview
Hu WS, Jiang FY, Shu W, Zhao R, Cao JM, Wang DP
- 6732** Obstructive and secretory complications of diverting ileostomy
Tsujinaka S, Suzuki H, Miura T, Sato Y, Shibata C
- 6743** Role of the combination of biologics and/or small molecules in the treatment of patients with inflammatory bowel disease
Balderramo D

ORIGINAL ARTICLE

Basic Study

- 6752** Interleukin-34 deficiency aggravates development of colitis and colitis-associated cancer in mice
Liu ZX, Chen WJ, Wang Y, Chen BQ, Liu YC, Cheng TC, Luo LL, Chen L, Ju LL, Liu Y, Li M, Feng N, Shao JG, Bian ZL
- 6769** Dickkopf-related protein 1/cytoskeleton-associated protein 4 signaling activation by *Helicobacter pylori*-induced activator protein-1 promotes gastric tumorigenesis via the PI3K/AKT/mTOR pathway
Luo M, Chen YJ, Xie Y, Wang QR, Xiang YN, Long NY, Yang WX, Zhao Y, Zhou JJ

LETTER TO THE EDITOR

- 6788** The potential role of the three-dimensional-bioprinting model in screening and developing drugs

Deng CL, Wu B

ABOUT COVER

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How to avoid overtreatment of benign colorectal lesions: Rationale for an evidence-based management

Marco Bustamante-Balén

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Abstract

Implementing population-based screening programs for colorectal cancer has led to an increase in the detection of large but benign histological lesions. Currently, endoscopic mucosal resection can be considered the standard technique for the removal of benign lesions of the colon due to its excellent safety profile and good clinical results. However, several studies from different geographic areas agree that many benign colon lesions are still referred for surgery. Moreover, the referral rate to surgery is not decreasing over the years, despite the theoretical improvement of endoscopic resection techniques. This article will review the leading causes for benign colorectal lesions to be referred for surgery and the influence of the endoscopist experience on the referral rate. It will also describe how to categorize a polyp as complex for resection and consider an endoscopist as an expert in endoscopic resection. And finally, we will propose a framework for the accurate and evidence-based treatment of complex benign colorectal lesions.

Key Words: Colorectal polyps; Endoscopic mucosal resection; Colorectal surgery

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Core Tip: Despite endoscopic treatment being of choice for the treatment of large benign colorectal neoplasms, many lesions are still being referred to surgery. Problems in identifying a polyp as complex to resect, too much self-confidence of the endoscopists, and the lack of a referral pathway may be causes underlying this situation. The organization of a structured referral network may be the main step to reducing the overtreatment of benign lesions. Decisive support from Medical Societies and Public Administration is warranted to set up this paradigm change.

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INTRODUCTION

The implementation of population-based screening programs for colorectal cancer (CRC) has led to an increase in the detection of large lesions with benign histology. For example, in a French study of a population screening program based on fecal occult blood testing, 5% of the polyps found were larger than 3 cm[1]. Many of these patients are asymptomatic and of intermediate age, and removal of the lesions should be performed with the goal of maximum efficacy (complete resections, few recurrences) and maximum safety (few adverse effects). Traditionally, most polyps considered "large" were biopsied and then referred to surgery for segmental resection of the colon. However, in recent years, with the improvement of endoscopes and the development of new techniques, endoscopic treatment can be considered the treatment of choice. However, too many benign lesions are still being referred to surgery, with associated morbidity and increased costs. In this review, we will justify the selection of endoscopic therapy as the treatment of choice, dig into the main causes for referring benign lesions to surgery, and propose an organizational solution for this situation. Most of the evidence that will be reviewed here focuses on endoscopic mucosal resection (EMR) because is the endoscopic technique of choice in most instances, while other endoscopic techniques [e.g., endoscopic submucosal dissection (ESD) or full-thickness resection] are indicated for a more specific type of lesions.

WHY SHOULD ENDOSCOPIC RESECTION AND NOT SURGERY BE THE THERAPY OF CHOICE FOR THE TREATMENT OF BENIGN COLONIC LESIONS?

EMR can currently be considered the standard technique for the removal of benign lesions of the colon due to its excellent safety profile and good clinical results. Large series of patients, especially from the Australian endoscopic resection group, support this claim. Moss *et al*[2] performed a prospective evaluation of all patients referred for EMR of polyps ≥ 20 mm. In this cohort of particularly complex polyps, complete resection was achieved in a single session in 89.2% of patients with a recurrence rate of 20.4%. This recurrence was mostly minute and easily treated endoscopically. As for adverse effects, the same group reported a clinically significant bleeding frequency of 6.0%, of which only 44% required endoscopy and only one case required embolization[3]. The proportion of deep mural damage or perforation was only 3% and 0.6%, treated in all cases by endoscopic methods[4].

At least two meta-analyses confirm these results. The first, which evaluated the endoscopic management of lateral spreading tumors, and which analyzed separately EMR and DSE, reported a proportion of complete resections for the former of 99.5%, and a proportion of recurrences of 12.6%, most of which were manageable endoscopically. In terms of adverse effects, there was an aggregate proportion of perforation of 1.2% and bleeding of 9.6%[5]. In the second meta-analysis, the proportion of surgeries attributable to complications of EMR was less than 1%[6]. Therefore, we have an effective and safe endoscopic technique for the treatment of benign colon lesions.

The therapeutic alternative to endoscopic resection is surgery, which has classically been the treatment of choice. However, even with current techniques, surgery is not free of complications. The overall rate of adverse effects at 30 days is between 14% and 25% in the most modern series (Table 1)[7-10]. In general, the proportion of adverse effects is higher in open surgery, and as the age of the patient increases[7,8,10]. Surgery is also associated with a non-negligible risk of mortality which, although it is usually somewhat less than 1% (Table 1), in patients > 80 years of age can reach almost 3%[7].

No randomized studies are comparing both therapeutic strategies and such a study is unlikely to be performed due to ethical problems. One way to overcome this is the use of propensity score matching. Wickham *et al*[11] evaluated 95 patients referred because of endoscopically unresectable colorectal lesions and compared them to 190 propensity score-matched controls. Endoscopic resection was achieved in 66 (70%) of patients with a reduced hospital stay, a lower unplanned 30-day readmission rate, and fewer postoperative complications (4.2% *vs* 33.9%; $P < 0.001$) compared to surgery. Another attempt to make this comparison has been made using theoretical models. Ahlenstiel *et al*[12] compared the theoretical mortality of colon surgery, calculated using a proprietary Association of Surgeons of Great Britain and Ireland score, with the actual mortality from EMR of benign lesions in a cohort of 1,061 patients. While the theoretical mortality from surgery was 3.3%, there were no deaths in the first 30 days after EMR. The NNT to prevent one death was only 30. A recent Dutch study, using a microsimulation system and taking into account fatal complications of surgery, compared expert endoscopic resection of benign lesions *vs* laparoscopic surgery. Referral to an expert reduced from 2.1 surgeries for

Table 1 Main recent series on the morbidity and mortality of surgery for benign colorectal lesions

Ref.	Year	Country	Data source	N	Mortality (%)	Colostomy/ Ileostomy (%)	Major adverse event (%)	Readmission (%)	Surgical re-intervention (%)
Peery <i>et al</i> [7]	2018	USA	National Inpatient Sample ¹	12.732	0.7	2.2	14.0	7.8	3.6
Zogg <i>et al</i> [8]	2016	USA	National Inpatient Sample ¹	68.462 ²	-	-	14.7	-	1.0
de Neree <i>et al</i> [9]	2019	Netherlands	Systematic Review	139.897	0.7	-	24.0	-	0-8.9
Ma <i>et al</i> [10]	2019	USA	National Inpatient Sample ¹	262.843	0.8	-	25.3	-	-

¹All-payer inpatient healthcare database.²Overall colon surgery (not only colorectal epithelial lesions): % of adverse events are specific for surgery of benign colorectal lesions.

benign polyps/1000 individuals to 0.2/1000 reducing also the number of deaths[13]. Some observational studies performed in Eastern countries and focused on ESD confirm that the latter has a shorter hospital length stay, an inferior 30-day readmission rate, and a lower complication rate[14,15].

Furthermore, endoscopic treatment is cost-effective compared to surgery. At least four studies in different countries and contexts have compared endoscopic resection with surgery in terms of cost-effectiveness (Table 2). All agree that endoscopic resection (EMR or ESD) is cost-effective compared to surgery, and this difference widens if the complications of surgery are taken into account[13,16-19]. The development of adverse effects after surgery has been associated with a 106% increase in the average length of stay and a 91% increase in the average cost of hospitalization[10].

Therefore, and this is reflected in the clinical practice guidelines[20,21], it seems clear that endoscopic treatment should be the first-choice treatment for benign colonic lesions, provided that quality standards are maintained[21].

WHAT IS THE SITUATION IN ACTUAL CLINICAL PRACTICE?

Several studies from different geographic areas agree that many benign colon lesions are still referred to surgery. In a French study conducted in a population-based screening program with fecal occult blood test, out of 4,251 patients with at least one polyp, 4.1% were referred to surgery[1]. In a study conducted in the USA, 47% of colorectal lesions sent for surgery were benign polyps[22]. In the aforementioned study by Zogg *et al*[8] the mean number of annual colectomies performed for benign pathology in the United States was around 22,000. A study of the British CRC screening program showed that, in the period from 2006 to 2009, 21.7% of the polyps sent for surgery were directly operated on, without a prior endoscopic attempt. Depending on the centers, the use of surgery as the first therapeutic option varied between 7% and 36%[23]. Finally, a recent Australian survey study showed that 16.7% of respondents would send directly to surgery a 45 mm benign polyp[24]. Saade *et al*[25], in a retrospective review of 144 patients with surgical resection for benign colorectal polyps found that 82% were referred for surgery without attempting an endoscopic resection. Of those, 22% had polyps < 2 cm, a size that should be resected en bloc by an average endoscopist[21].

But in addition, the rate of referral to surgery is not decreasing over the years, despite the theoretical improvement in endoscopic resection techniques. In a retrospective review of a national surgical database also in the United States, it was found that the incidence rate of surgery for benign polyps increased significantly over time, from 5.9 *per* 100,000 patients in 2000 to 9.4 *per* 100,000 patients in 2014, while during this same period the rate of surgery for CRC decreased. This increase was significantly greater in urban academic hospitals, which is just where one would expect it to decrease[26]. A Dutch study reviewed a national database of anatomic pathology reports looking for all cases of benign colon lesions removed by surgery. They showed that the ratio of the number of resections for benign lesions to the total number of colonoscopies performed was significant and remained constant over the last decade (2005-2015), ranging from 0.37 to 0.26[27].

Table 2 Cost-effectiveness studies, endoscopic therapy vs surgery

Ref.	Year	Country	Endoscopic technique	Design	Comparison	Costs analyzed	Results
Swan <i>et al</i> [19]	2009	Australia	EMR	Observational monocentric	Endoscopy <i>vs</i> surgery, Considering surgery without major complications	Direct costs including a 1-day hospital stay for EMR, Loss of utility not considered	EAC: \$2051 pp, SAC: \$9041
Jayanna <i>et al</i> [16]	2016	Australia	EMR	Observational multicentric	Endoscopy <i>vs</i> surgery, Considering surgery with and without complications	Direct costs including hospital stay and adverse events, 1 st surveillance endoscopy	EAC: \$4668 pp, SAC: \$12720, If surgery 7.5% complications -> SAC: \$45530
Law <i>et al</i> [17]	2016	USA	EMR	Decision analysis tree (hybrid Markov model)	Endoscopy (resection + surveillance, surgery if recurrence at 12 mo) <i>vs</i> laparoscopic surgery, Considering complications in both arms	Direct costs, Loss of utility considered, QALY, Sensitivity analysis	EAC: \$5570 pp, Endoscopy QALY: 9.64, SAC: \$18717 pp, Surgery QALY: 9.58, Laparoscopy is cost-effective if complete EMR < 75.8%, EMR adverse events rate > 12% and laparoscopy cost < \$14,000
Dahan <i>et al</i> [18]	2019	France	ESD	Observational monocentric	Endoscopy <i>vs</i> surgery, Considering complications in both arms	Direct costs including hospital stay and endoscopy costs	EAC: €3190, SAC: €8490
Buskermolen <i>et al</i> [13]	2022	Netherlands	Non-specified	Microsimulation screening analysis (MISCAN-colon)	Surgery <i>vs</i> attempted removal by an expert endoscopist, Considering complications in both arms	Direct costs, Loss of utility considered, QALY, Sensitivity analysis	EAC: €60,200, SAC: €72,700, Endoscopy QALY: 33.1/1000 individuals, Surgery QALY: 32.9/1000 individuals

EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosa dissection; QALY: Quality adjusted life years; EAC: Endoscopy average cost; SAC: Surgical average cost; pp: Per patient.

WHAT IS THE MAIN REASON THAT BENIGN LESIONS ARE STILL BEING SENT DIRECTLY FOR SURGERY? THE ENDOSCOPIST FACTOR.

Le Roy *et al*[1] evaluated different variables related to referral to surgery. Size, location, and histology (villous component and high-grade dysplasia) were influential. The most relevant factor was size > 20 mm. These data have been confirmed in a recent meta-analysis, in which the most frequent causes of referral to surgery were polyp location (right colon), size (median size = 4 cm), and sessile morphology [9].

However, the assessment of the relative importance of these factors when deciding whether to perform endoscopic or surgical resection is highly subjective and dependent on the endoscopist. In fact, in the study by Le Roy *et al*[1] great variability was found among endoscopists when referring the patient to surgery, a difference that was maximal for polyps > 20 mm (0 to 46.6%). These results were confirmed in a study in which 154 endoscopists of different expertise (residents, gastroenterologists, surgeons, and experts in polyp resection) responded to a survey on how to treat 6 polyps presented in video format. Endoscopists specializing in complex resections referred the patient to surgery at a significantly lower percentage than other specialists (3.1% *vs* 13.3% non-specialists endoscopists *vs* 17.2% surgeons). In the univariate analysis that took into account the size of the polyp, its location, the patient's ASA, and the type of specialist, the fact that the endoscopist was not a specialist in the resection of complex polyps was the only variable related to the probability of referring the patient to surgery [odds ratio (OR) 4.93, 95% CI (1.5-16.26)][28].

This variability in clinical practice has direct practical consequences. A retrospective review of the Dutch pathology registry reviewed the medical reports of patients referred for surgery for benign polyps over 9 years. Three expert endoscopists reviewed the records to assess whether the patient could have benefited from endoscopic treatment. The conclusion was that 73% of the cases could have been treated endoscopically. This referral to surgery as a primary elective treatment was more frequent in county hospitals than in tertiary referral centers[29]. In other words, the endoscopist is perhaps the most influential factor in whether a patient is referred for surgery, and experience in complex resections seems to be the fundamental characteristic.

IS IT EFFECTIVE TO REFER THE PATIENT TO AN ENDOSCOPIST WITH EXPERTISE IN COMPLEX ENDOSCOPIC RESECTIONS?

The possibility of reducing surgeries if the patient was referred to an expert endoscopist has also been demonstrated in practice. In one study, 58 patients referred to surgery for colorectal polyps were collected. An expert endoscopist re-evaluated these lesions in a new colonoscopy to decide whether endoscopic resection was possible. Of these 48 could be resected endoscopically although 5 of them underwent surgery later either because of malignancy in the specimen (4 cases) or recurrence (1 case). In any case, surgery could be avoided in 43 (74.1%)[30]. Other studies of similar design agree that surgery is avoidable in 30-70% of cases when the polyp is reviewed by an expert endoscopist, including up to 26% of lesions with previously attempted resection[31-33].

WHY IS AN EXPERT ENDOSCOPIST MORE EFFECTIVE?

The main advantage of an experienced endoscopist when removing complex lesions is that he or she will have a higher proportion of complex resections with a lower frequency of adverse effects.

Few studies are comparing the results of EMR in terms of efficacy according to the experience of the endoscopist. The St. Marks group evaluated the proportion of successful resection between a group of expert and non-expert endoscopists. Experts were successful in 76% of cases while non-experts were successful in only 40%[34]. A retrospective study showed that the performance of resection by an expert endoscopist was protective against incomplete resection in the presence of other risk factors for incomplete resection [adjusted OR 0.13, 95% CI (0.04-0.41)][35]. The CARE study demonstrated that the rate of incomplete resection in polyps that, in the judgment of the endoscopist, were assumed to be completely removed was high (10.1%), increased with polyp size, and was highly dependent on the endoscopist. These findings suggest that technical skill in complex resections is not universal[36].

The experience of the endoscopist is also a key factor for adverse effects. In a study of 97,091 colonoscopies performed on an outpatient basis, the OR for bleeding or perforation increased significantly when the endoscopist performed fewer than 300 colonoscopies per year[37]. In a similar study of 24,509 endoscopies, the complication rate was significantly higher for endoscopists performing fewer than 200 procedures per year [RR 2.95% CI (1.1-3.7)][38]. Finally, a study of 2,315,126 colonoscopies confirmed that endoscopists performing fewer than 300 colonoscopies per year had a higher rate of bleeding and perforation[39].

HOW DO WE KNOW THAT AN ENDOSCOPIST IS AN EXPERT? THE EGO OF ENDOSCOPISTS.

Some of the studies evaluating the rate of surgery for benign polyps have found that this rate is higher in urban teaching hospitals, hospitals that often have experts or units specialized in endoscopic resection[7]. There may be too much self-confidence in the endoscopist (e.g., "if I cannot resect this lesion, nobody can") or there may be some feeling of shame in referring a lesion to a colleague.

The endoscopists' perception of their expertise is often not supported by objective criteria. This fact was elegantly highlighted in a study in which 268 surveys were conducted among endoscopists asking them, among other things, about their experience in resection and their surgical referral practices. Eighty-one (30%) of them considered themselves capable of performing complex resections on lesions that could perfectly well have been referred to surgery. However, of this group of "experts" 17% had never removed a polyp > 5 cm and 32% did not perform more than 20 EMRs per year. In other words, a significant number of endoscopists considered themselves experts in resection when there was no objective evidence of this. And this had consequences for patient management because endoscopists who considered themselves non-experts tended to send patients to another colleague, while "experts" more frequently sent them to surgery (26% vs 68%)[40].

Inappropriately mischaracterizing oneself as an expert endoscopist directly affects patient management in three key ways: (1) The endoscopist will initiate a resection that he or she cannot complete, and complications are possible; (2) If resection is not attempted the patient is more likely to be sent to surgery than a more expert colleague; and (3) As a consequence of the previous two, the patient is more likely to be incorrectly sent to surgery.

The definition of some objective criteria to classify an endoscopist as an expert in resections could help in this situation, reassuring the less-experienced endoscopist to refer the lesion to a better-prepared endoscopist. However, there are no established criteria to identify the expert endoscopist in performing EMR, perhaps due to the lack of structured training for this technique.

WHAT LESIONS SHOULD BE REFERRED AND TO WHOM? HOW TO TRANSFORM SUBJECTIVITY INTO OBJECTIVITY

As we have seen, the assessment of the difficulty of resection of a particular polyp depends primarily on polyp factors (size, morphology, location, suspicion of submucosal invasion, *etc.*) that may seem rather subjective in their evaluation. It seems logical, therefore, to develop systems that are as objective as possible to define which polyp should be sent to an expert endoscopist, in such a way as to help endoscopists of varying degrees of experience to make the decision. On the other hand, it seems necessary to have criteria for evaluating endoscopists to define, as objectively as possible, what is an expert endoscopist, aimed to easily identify referral specialists. Finally, the expertise of the individual endoscopist is not enough. His or her work environment must allow for comprehensive treatment of benign colon lesions, with the use of different resection techniques depending on the case, and must have sufficient casuistry to maintain the skills acquired. In this section, we will review these three sides of the management of large colorectal lesions: The complex polyp, the expert endoscopists, and the reference endoscopy unit.

The “complex” polyp

To avoid or at least reduce individual subjectivity in the assessment of the difficulty of resection, objective evaluation criteria are necessary. A group of experts, following the Delphi methodology, defined a score to classify the theoretical difficulty in the resection of colon polyps. This score (“SMSA” scoring system) has four parameters (Site, Morphology, Size, and endoscopic Access), and assigns different scores to the values adopted by each one. Thus, a polyp > 4 cm, with a flat morphology, located in the right colon, and with difficult access obtains the highest score (17 points). All polyps scoring > 12 points are considered level 4, and appropriate for truly expert endoscopists[41].

The British Society of Gastroenterology (BSG) suggests other lesion’s objective features that anticipate a complex resection, grouped into three areas: Increased risk of malignancy evidenced by optical diagnosis, increased risk of incomplete resection, and increased risk of adverse effects (Table 3). Notably, the experience of the endoscopist is included as a criterium for defining a complex polyp because of an increased risk of adverse events[42]. The definition of a complex polyp, therefore, involves a judicious and sensible evaluation of the endoscopist’s expertise.

The categorization of a polyp as complex involves more than the difficulty in its removal. The management of a complex polyp may also need, to some extent, and depending on the lesion’s characteristics, the need for expert, interdisciplinary management. In this sense, the European Society of Gastrointestinal Endoscopy (ESGE) recommends sending the lesion to be evaluated in an expert center, besides the aforementioned criteria, when superficial submucosal invasion is suspected[21].

The “expert” endoscopist

The level of experience required of endoscopists to resect polyps is not objectively defined. The ASGE guidelines indicate that all endoscopists should be able to resect pedunculated or sessile polyps < 2 cm [43], but resection of complex polyps requires special skill, specific learning, and experience, and it seems unreasonable to expect this from all centers[44].

The most objective criterion could be the number of resections performed. However, this particular number has not been defined yet. Several studies place the experience necessary to perform EMR with adequate quality standards between 100 and 125 resections[45,46]. Other authors, based on a retrospective study of a new EMR unit for 4 years, suggest a number of 30 EMRs per year, but the SMSA level of their lesions was not described [47]. This figure seems a bit low when dealing with SMSA level 4 Lesions. The BSG broadly suggests that the number of resections per year should be enough to maintain acceptable quality and safety standards, but also indicates that there is no evidence to recommend a specific figure[42]. Regarding ESD, there is also a high variability in the reported number of cases needed to achieve proficiency ranging from 20 to 250 cases[48]. To maintain proficiency, the ESGE curriculum recommends performing at least 25 cases per year[49].

Some more objective methods to evaluate polypectomy competency have been developed, like the Direct Observation of Competence Skills (DOPyS). This instrument assesses several items, like optimal polyp position, determining the full extent of the lesion, polypectomy technique, *etc.* Using this tool Duloy *et al*[50] described significant variation in polypectomy competency rates (30% to 90%) with rates decreasing for larger polyps. However, it has not been designed specifically for EMR. The BSG has proposed auditable indicators to assess the ability of endoscopists to perform EMR, focusing on efficacy (% recurrences), safety (% complications), and annual case volume (Table 3)[42].

The implementation of structured learning tools or courses could help to evaluate who may be competent in endoscopic resection techniques. *In vivo* and virtual tools have been described for EMR and ESD[51,52], and a formal curriculum for ESD has been developed by the ESGE[49]. However, there is not a similar curriculum for EMR training, which has essentially been limited to that obtained during residency and has repeatedly proven to be insufficient[53].

Table 3 Objective parameters for assessing lesions, endoscopists, and units

Complex polyp	Expert endoscopist	Reference endoscopy unit
SMSA score ≥ 12 (Level 4)[41]	BSG criteria[42]	BSG criteria[42]
BSG criteria[42]	500 independent colonoscopies	Ensure that endoscopists undertake a sufficient number of procedures a year to maintain acceptable standards ⁴
Increased risk of malignancy	100-125 EMR to obtain competence	
Kudo's pit pattern V	A non-defined number ¹ of EMR procedures to maintain competence	
Paris 0-IIc/0-IIa+IIc		
LST-NG/LST-Gm (dominant nodule)	Fulfilling key performance indicators	Time from referral to definitive management: < 8 wk
NICE 3/Sano III	Presence of recurrence/residual polyp at 12 mo < 10%	Geraghty <i>et al</i> [40]
Increased risk of incomplete resection/recurrence		Provided endoscopy list time for the additional workload with a dedicated list
Size ≥ 40 mm	EMR perforation rate: < 2%	Staff to include at least two endoscopists that can cover each other and endoscopy nurses with training in complex polypectomy
Difficult location (ileocecal valve, appendix, diverticulum, dentate line)	Post-polypectomy bleeding rate: < 5%	
Within an inflamed segment of the colon	DOPyS ²	
	ESGE ³ curriculum for optical diagnosis[59]	
Prior failed resection attempt	Assessing competence: ≥ 80 % accuracy for identifying submucosal invasion in large (≥ 20 mm lesions), Maintaining competence: <i>in vivo</i> audit and review of at least 10 large (≥ 20 mm) lesions within a year	Equipment: including necessary snares and hemostatic devices
Non-lifting sign		Surgeons for discussion in the MDT and case of operative treatment of adverse events
Increased risk of adverse events		
Cecum		
Endoscopist's expertise		
ESGE criteria[21]		Robust referral system including administrative staff support and tools for virtual MDT
Difficult location or poor access (ileocecal valve, periapendicular, anorectal junction)		
Prior failed resection attempts		
Non-lifting sign		
SMSA level 4		

¹Enough to maintain quality standards.²Direct Observation of Competence Skills (not specific for EMR).³For achieving competence in optical diagnosis of early colorectal cancer.⁴Review in conjunction with other key performance indicators.

BSG: British Society of Gastroenterology; EMR: Endoscopic mucosal resection; LST-NG: Non-granular lateral spreading tumor; LST-Gm: Granular mixed lateral spreading tumor; NICE: NBI International Colorectal Endoscopic classification; ESGE: European Society of Gastrointestinal Endoscopy; MDT: Multi-disciplinary team; DOPyS: Direct Observation of Competence Skills; SMSA: Site, Morphology, Size, Access.

Moreover, for increasingly larger polyps, with flat morphology, in difficult locations, or patients with previous colon pathology such as inflammatory bowel disease, the endoscopist must also master alternative mucosal resection techniques such as the underwater technique, or fragmented cold loop resection, and know how to choose between them by changing the initial resection plan. Strategies to decrease the recurrence rate, like margin ablation, margin marking, or hybrid argon plasma coagulation [54-56] should be mastered as well. Finally, an endoscopist specializing in endoscopic resection of larger lesions must also know and apply optical diagnosis (use of NICE and JNET classifications, use of dyes, use of magnification, *etc.*) to identify those that, due to a higher probability of superficial submucosal invasion, require an en bloc resection, using ESD or full-thickness resection[20,57]. And also, those that, due to a high probability of deep submucosal invasion, must be surgically removed[58]. Following, for instance, the BSG guidelines, these skills are needed to correctly classify a polyp as complex (Table 3) [42]. Mastering optical diagnosis also needs proper training and practice to obtain and maintain competence[59].

The “reference” endoscopy unit

It seems that the number of procedures is the single most important factor influencing on efficacy and safety results of an endoscopy unit specialized in complex resections. In the aforementioned Australian study on risk factors for post-polypectomy bleeding, the unit (one that had performed fewer than 75 procedures) was directly related to the likelihood of immediate post-polypectomy bleeding [adjusted OR 3.78 (2.35-6.10)] and to bleeding occurring beyond the first 48 h[60]. And immediate post-polypectomy bleeding was related to the probability of recurrence at the first endoscopic control. Other studies describe a lower rate of complications in colonoscopies performed in a hospital center than in an outpatient clinic[39]. It thus appears that units that accumulate a larger number of cases are more effective in the treatment of complex colon lesions. This has also been shown in studies on newly developing EMR units, in which the rate of complications decreased as experience time was gained[47]. The frequency of SMSA level 4 Lesions in a single institution is unlikely to be enough to maintain competency, therefore a centralized referral system seems advisable[40].

But in addition to the experience and casuistry of the units, the adequate management of complex colon lesions requires adequate infrastructure. High-definition endoscopes that allow precise optical diagnosis, electrosurgical units with automatic microprocessors, CO₂ insufflation, specific pumps for lavage channels, *etc.*[21]. They also need the availability of a variety of resection devices (snare, knives, injection substances, hemostatic, *etc.*) allowing switching resection techniques and dealing with complications. Resections of complex polyps lengthen the procedure time beyond that required for a conventional colonoscopy[61], prolongation which is closely related to the size of the polyp in question. Therefore, the unit will have to have the facility to adjust the citation slots to the performance of longer and more complex procedures. Finally, the work of this kind of unit must be integrated into a background with experienced surgeons, a multidisciplinary team for the management of complex lesions[40], and all the infrastructure (computed tomography scanning, *etc.*) to handle possible adverse events.

The BSG has also proposed measurable domains for accrediting Endoscopy Units for performing EMR (Table 3). Regarding ESD, the American Society of Gastrointestinal Endoscopy recommends setting up an “ESD cart” with the necessary equipment for the procedure and the management of adverse events. The presence of experienced nurses and technicians is also addressed[48].

IS IT TRULY EFFICIENT IN REAL PRACTICE TO REFER COMPLEX POLYPS TO EXPERIENCED UNITS?

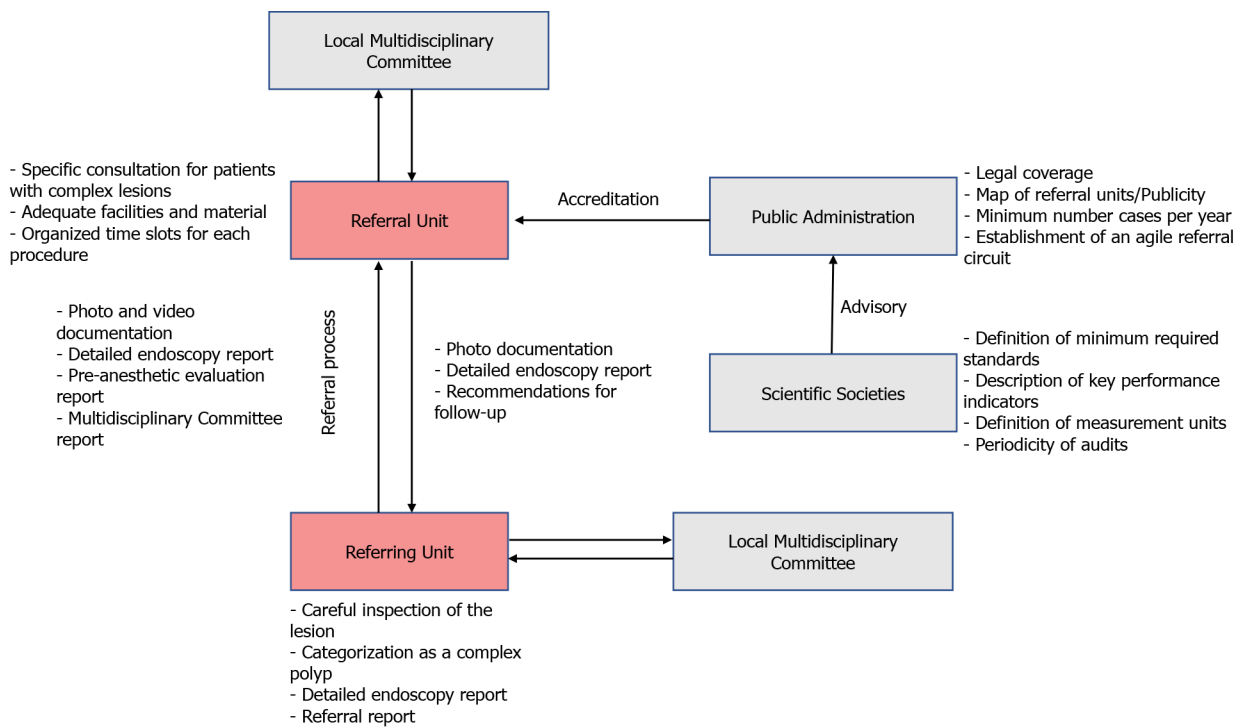
We have learned that an appropriate referral of complex polyps to an expert endoscopist increases the rate of successful endoscopic treatment and reduces adverse events compared to surgery. We have also learned how a referral endoscopy unit should be to ensure efficacy. How has this been translated onto clinical practice?

The Australian group was the first to demonstrate the efficacy of a referral unit for the treatment of large colorectal lesions. Out of 174 patients referred for 193 complex polyps, 90% avoided surgery with a procedural success of 95% excluding those patients with invasive cancer[19]. Another Australian retrospective study comparing the surgical rate of benign colorectal lesions before and after the introduction of a specific EMR service in a tertiary referral center showed a 56% reduction in the number of patients referred to surgery[62]. More recently, in France, a study evaluated the evolution of surgical management of benign polyps > 2 cm after the implementation of a regional referral network for the management of these lesions. This regional care network included two specialized endoscopists in the referral center with direct access by e-mail or by phone to all general gastroenterologists in the region and with twice-a-year regular meetings with general gastroenterologists. The surgical management rate of benign lesions decreased significantly after the implementation of the referral network from 14.6% in 2012 to 5% in 2017[63]. Similarly, in the Northwest of the Netherlands, a reference panel of expert endoscopists for the general endoscopist to consult was organized. Eleven centers participated and 88 patients were evaluated by the panel. Overall, 43.2% of consulting endoscopist changed their initial management strategy after consultation, and in 56 cases (63.3%), the patient was referred to another endoscopy center[64].

In conclusion, setting up a referral system for the management of complex polyps is efficient and translates into immediate clinical advantages.

HOW TO SET UP A REFERRAL ENDOSCOPY UNIT FOR THE MANAGEMENT OF COMPLEX POLYPS: PRACTICAL TIPS AND AN ORGANIZATION PROPOSAL

To achieve the objective of an adequate and comprehensive treatment of large benign colon lesions, several actors must be involved: The Administration, the Scientific Societies, the Units themselves, and



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Figure 1 Organizational proposal for the management of complex benign colorectal lesions.

finally the referring endoscopists (Figure 1).

One side of the referral network is the referral endoscopy unit. Having established the main characteristics that a referral unit must have to be considered as such, a certification system should be put in place. For instance, using criteria similar to that of the BSG plus others adapted to the specific background, periodical audits of the organization and key performance indicators should be performed. The local Endoscopy Societies should collaborate in the design of the certification protocol (definition of key indicators, measurement units, audit's periodicity, *etc.*). An example of this kind of collaborative effort, although not applied to complex resections, is the Qualiscopia initiative in Spain, which aimed to monitor and certify endoscopy units and endoscopists in quality in colorectal screening colonoscopy [65]. Ideally, the endoscopy unit has to establish an internal Quality Management Program, including the definition of a system for recording staff's initial competency and continued competency on an annual basis. Working together with the referral unit there should be a multidisciplinary team in place, made up of surgeons, oncologists, radiologists, and every specialist that could be involved in the management of complex polyps, especially when facing a deep submucosal invasion or dealing with adverse events. Finally, the referral unit should have enough administrative staff to handle the communication and documentation workload from and to the referring units. Clean communication systems should be established (e-mail, telephone, videoconference, *etc.*).

The Administration should, in agreement with the Societies, should give legal cover to the concept of Referral Unit, should establish a map of referral units according to population needs, ensure a minimum number of cases per unit to maintain competence, and should participate in the establishment of an agile regional referral circuit[21,42]. It is the Administration that should make available for all possible referring physicians a list with the accredited Units.

The other face of the referral network is the referring endoscopist. These endoscopists have to carefully evaluate and characterize the lesion using the usual classifications (NICE, Paris, *etc.*), categorize it as a "complex lesion" and decide if he/she can resect it. If not, the lesion should not be biopsied (unless an invasive carcinoma is suspected), and a tattoo should be placed not too close to the lesion[66]. Several pictures and videos should be taken. All this information should be provided in a detailed and structured endoscopy report. Ideally, a Multidisciplinary Committee (including at least an endoscopist and surgeons) should evaluate the patient and make a report that should be incorporated into the referral report.

The referral process should be detailed including clinical and administrative data from the patient, photo and video documentation of the lesion, a detailed endoscopic report including size, location, and morphology of the lesion, if biopsies were taken or if there was any resection attempt. The reason for referring the lesion should also be described. In correspondence, once the lesion has been treated in the referral unit, a thorough report of the applied treatment should be done, again with photo documentation. The technical result of this treatment (success/failure) should be provided. Finally,

recommendations for patient follow-up should be attached to the report. It is mandatory to maintain fluid communication between referring and referral units during the therapeutic process. All the steps back and forth in the referral process should be subjected to the Quality Management Program and should be auditable.

CONCLUSION

Endoscopic resection is the treatment of choice for large colorectal lesions. However, overtreatment is still an important issue in many countries. Organizing a network of specialized endoscopy units in complex resections seems to be the main approach to tackling this situation. This development should be accompanied by the organization of an accreditation system and a Quality Management Program, a process in which endoscopy units, endoscopists, Scientific Societies, and the Public Administration should be involved.

FOOTNOTES

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