Malignant colorectal polyps

Luis Bujanda, Angel Cosme, Ines Gil, Juan I Arenas-Mirave

INTRODUCTION

Adenomatous polyps are tumors of benign neoplastic epithelium with variable potential for malignancy. The adenoma-carcinoma sequence is well known and it is accepted that more than 95% of colorectal cancers arise from adenomas. The World Health Organisation (WHO) classifies adenomas into tubular (less than 20% villous architecture), tubulovillous and villous, with approximately 87% of adenomas being tubular, 8% tubulovillous and 5% villous. Only 5% of adenomas are in danger of becoming malignant. The probability of high grade dysplasia and of carcinomatous transformation increases with polyp size, especially when they are larger than 1 cm, they have a villous component, there are many polyps or the age at diagnosis is more than 60 years. The neoplasia is considered to be advanced when polyps are 1 cm or more in diameter, there is a villous component or a high degree of dysplasia. More than 25% of advanced polyps and colon cancers are located in the area

Abstract

Nowadays, the number of cases in which malignant colorectal polyps are removed is increasing due to colorectal cancer screening programmes. Cancerous polyps are classified into non-invasive high grade neoplasia (NHGN), when the cancer has not reached the muscularis mucosa, and malignant polyps, classed as T1, when they have invaded the submucosa. NHGN is considered cured with polypectomy, while the prognosis for malignant polyps depends on various morphological and histological factors. The prognostic factors include, sessile or pedunculated morphology of the polyp, whether partial or en bloc resection is carried out, the degree of differentiation of the carcinoma, vascular or lymphatic involvement, and whether the polypectomy resection margin is tumor free. A malignant polyp at T1 is considered cured with polypectomy if it is a pedunculated polyp (Ip of the Paris classification), it has been completely resected, it is not poorly differentiated, the resection edge is not affected by the tumor and there is no vascular or lymphatic involvement. The sessile malignant polyp (Is of the Paris classification) at T1 is considered not cured with polypectomy. Only in some cases (e.g. older people with high surgical risk) local excision (polypectomy or endoscopic submucosal dissection or conventional endoscopic mucosal resection) is considered the definitive treatment.

Key words: Favorable histology; Follow-up; Malignant polyps; Non-invasive high grade neoplasia; Treatment

Peer reviewers: Yutaka Saito, Professor, Division of Endoscopy, National Cancer Center Hospital, 5-1-1, Tsukiji, Chuo-ku, Tokyo, 104-0045, Japan; Dr. Freddy Penninckx, Professor, Department of Abdominal Surgery, University Clinic Gasthuisberg, Herestraat 49, 3000 Leuven, Belgium

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proximal to the splenic flexure. Mixed polyps also have the ability to become malignant, as does hyperplastic polyposis syndrome.

**EPIDEMIOLOGY**

The prevalence of cancerous polyps in series of endoscopically removed polyps is between 0.2% and 11%[^4-7]. Nowadays, the number of cases in which malignant polyps are removed is increasing due to screening programmes. In an asymptomatic population of people over 50 years old who underwent direct colonoscopy, there was a 0.8% prevalence of adenocarcinoma of which 50% were carcinoma *in situ* or in stage 1[^8,9]. During screening programmes, adenocarcinomas have been detected in between 3% and 4.6% of those who undergo colonoscopy following a positive immunological faecal occult blood test result[^10,11]. In 2006, Rubio et al[^12] reported 10 patients with hyperplastic polyposis coli syndrome and a review of the literature showed that 50% (74/147) of patients with hyperplastic polyposis coli syndrome developed colorectal cancer (CRC).

**HISTOLOGY**

Carcinoma *in situ*, intramucosal carcinoma, high-grade dysplasia or intraepithelial neoplasia is the stage at which there is no involvement of the muscularis mucosa. In general, this tumor stage does not cause metastasis. It is classified as pTIs or Stage 0 in the TNM staging system. These terms are defined as non-invasive high grade neoplasia (NHGN) in the Vienna classification[^3]. Carcinoma *in situ* or high-grade dysplasia or intraepithelial neoplasia corresponds to a carcinoma that is restricted to the epithelial layer without invasion into the lamina propria. Intramucosal carcinoma is a carcinoma characterised by invasion into the lamina propria.

When the carcinoma spreads to the submucosa, the polyp is considered to have become malignant, being able to spread to lymph nodes or distant sites. The tumors that affect the submucosa are classified as T1 and correspond to Stage I of the TNM staging system. This term is defined as submucosal carcinoma in the classification of Vienna[^2] or malignant polyp.

The term pseudo-invasion refers to the presence of glands without invasion of the muscularis mucosa. These lesions have no malignant potential and should be treated in a similar way to adenomas[^13]. However, this phenomenon can be mistaken for invasive carcinoma by an inexperienced pathologist. Pseudo-invasion usually occurs in large polyps (>1cm), especially those with long stalks, and is most commonly found in polyps of the sigmoid colon. Islands of adenomatous epithelium are displaced through the muscularis mucosa and are found within the submucosa of the stalk. The displaced glandular tissue usually has rounded, not infiltrative, contours, carries with it a small amount of lamina propria, and is cytologically identical to the overlying adenomatous component. Haemorrhage and haemosiderin deposition are commonly seen and are a clue to diagnosis. In addition, inflammation and granulation tissue can be found. Cystic dilatation of the displaced glands with mucin distention is also not uncommon in pseudo-invasion because mucin produced by the entrapped glands has no means of reaching the lumen. Occasionally, rupture of dilated glands occurs with acellular mucin extravasation and there is a subsequent inflammatory response. Distinction from mucinous (colloid) carcinoma is important and can be difficult. Specifically, in mucinous carcinoma, the mucin pools contain malignant cells, a feature lacking in pseudo-invasion. For these reasons it is highly recommended that level sections and second opinions are obtained in cases of polyps with potential pseudo-invasion[^14].

All adenomas have some degree of dysplasia, be it high or low. However, low and high grade dysplasias are artificial subdivisions of a spectrum; there is no definition of “high-grade”. Indeed, the WHO book on tumors of the digestive system, does not contain a list of criteria for high-grade dysplasia in adenomas[^15,16]. However, in general, high-grade dysplasia entails more substantial changes and includes carcinoma *in situ*. Among these changes we consider architectural alteration, often resembling the glandular arrangement of adenomas and cytologic abnormalities, principally cellular and nuclear pleomorphism, nuclear hyperchromatism, loss of nuclear polarity, and marked stratification of nuclei. Other authors have considered as features of high grade dysplasia: loss of normal glandular architecture, hyperchromatic cells with multilayered irregular nuclei and loss of mucin, high nuclear/cytoplasmic ratio, marked nuclear atypia with prominent nuclei and focal cribriform patterns. Not all these features are necessarily present to the same degree in all dysplastic epithelia, while low-grade dysplasia manifests these same changes but to a lesser degree[^3,16].

**PROGNOSTIC FACTORS**

Many factors have been associated with a higher probability of residual disease or recurrent carcinoma.

**Morphology**

Morphology is described as polypoid (pedunculated or sessile) and nonpolypoid (flat or ulcerated) subtypes according to the Paris classification[^17]. The endoscopist should be alert to some features that are suggestive of possible malignancy. These features include the size, the presence of depressed ulceration, irregular contours, deformity, a short and immobile stalk and the inability to elevate a sessile polyp when a submucosal bleb is formed. Nonpolypoid colorectal neoplasms have a greater association with carcinoma (NHGN or submucosal invasive carcinomas) compared with polypoid neoplasms, irrespective of size[^1]. Attempts at diagnosis in such suspicious lesions, as well as in flat or depressed lesions, can be carried out using chromoendoscopy and magnification techniques that can highlight abnormalities of glandular cytoarchitecture, while also revealing information concerning the extent of submucosal invasion[^18,19]. Kudo et al[^20] developed
Type of resection

When *en-bloc* removal of a polyp is performed, it is possible to assess the depth of infiltration of the tumor cells and whether the margin is affected. Pedunculated malignant polyps are easily removed using a loop snare. However, this technique frequently results in piecemeal removal when applied to sessile and flat malignant polyps. Nevertheless, around one-third of malignant polyps are removed in this way[21]. *En-bloc* removal is advantageous because it allows full histological evaluation of the complete resection and is associated with lower recurrence rates than piecemeal removal[22]. Endoscopic submucosal dissection (ESD) has been found to be particularly useful for the removal of sessile or flat adenomatous lesions. It has an advantage over other endoscopic techniques in that it allows *en-bloc* removal of large (> 2 cm) colonic lesions. In ESD an electrosurgical cutting device is used to carefully dissect the deeper layers of the submucosa to remove neoplastic lesions in the mucosa. In a meta-analysis it was found that ESD *en-bloc* resection is achieved in 84.9% of lesions, and clear vertical and lateral margins are achieved in 75.3% of cases[24].

Polypectomy resection margin

It is essential that the pathologist identifies the stalk or the depth of the diathermy burn. The risk of relapse ranges from 0% to 2% in malignant polyps with a margin of resection greater than 1 mm. When the resection margin is also involved, or is less than 1 mm, the percentage of relapse ranges between 21% and 33%[25]. Most authors believe that a resection margin of $\geq$ 2 mm is safe and that in such cases the probability of residual disease or recurrent carcinoma is low[4,5,25,26]. However, whether the requisite distance from cancer to margin of resection should be $> 1$, $> 2$, or $> 3$ mm or only a clear margin of excision is still under debate.

| Table 1 Pit pattern classification |
|-----------------------------------|
| Type of lesion | Description |
|----------------|-------------|
| Type 1         | Round pits  |
| Type 2         | Stellar or papillary pits |
| Type 3 L       | Large tubular or roundish pits |
| Type 3 S       | Small tubular or roundish pits |
| Type 4         | Branch-like or gyrus-like pits |
| Type 5         | Non-structural pits |

Evaluation of the fine surface structure (pit pattern) of the mucosa. Lesions with type 1 and 2 pit patterns are nontumorous epithelial tissue, that is normal, inflammatory, or hyperplastic tissue. Tumorous lesions have type 3 S, 3 L, 4 and/or 5 pit patterns. Lesion 3 L and 4 are typical of the protruded type of tumor, whereas type 3 S and 5 are typical of the depressed type of tumor.

Level of invasion of adenocarcinoma into the polyp

Haggitt et al[28] assigned anatomic regions (levels) of invasion to each malignant polyp. In this study, level 1 described invasive adenocarcinoma limited to the polyp head; level 2 included neck involvement; level 3 corresponded to adenocarcinoma cells in the stalk; and level 4 to invasion, adenocarcinoma cells infiltrating the submucosa at the level of the adjacent bowel wall (Figure 1). In this system, invasive adenocarcinoma in a sessile polyp by definition had level 4 invasion. However, precise histological evaluation of Haggitt’s level may be difficult, especially the differentiation between Haggitt’s level 1 and 2, and 2 and 3. Properly marked and orientated specimens are essential. Some authors conclude that only patients with level 4 invasion require resection[29]. More recently, some authors have proposed an additional histological classification system based on the grade of cell differentiation at the lesion margins and on the size and depth of invasion of the submucosa. Accordingly, the degree of submucosal invasion has been classified into three types based on the depth of invasion. When less than one-third of the submucosa is invaded the stage is sm1, and if more than two-thirds is invaded the stage is sm3, while stage sm2 is intermediate with invasion of cancer into the middle third. Sm1 is when the depth of invasion is less $\leq 1$ mm or 1000 µm from the muscularis mucosae[30]. It has been shown that penetration of cancerous cells into the lower third of the

The prognosis correlates with the histological grade[31]. Grade 3 of differentiation is seen in 5.7% to 9.2% of patients with polyps and the risk of residual lesions or relapse in these cases is of the order of 36%-38%[25]. In most cases, grade 3 differentiation is associated with invasive adenocarcinoma cells $\leq 1$ mm from a clearly visualized margin.

Stage of differentiation

Four grades were considered. Grade 1 corresponded to a well-differentiated intestinal-type adenocarcinoma and is composed of well-formed glands with open lumina or with more than 95% glandular differentiation. Grade 2 was moderately differentiated intestinal-type adenocarcinoma containing solid nests showing only focal glands or with 50%-95% glandular differentiation. In the case of Grade 3, the carcinoma is poorly differentiated intestinal-type, signet ring cell or mucinous adenocarcinoma, composed of hyperchromatic cells arranged into solid sheets and forming absorptive glands. These tumors have between 5% and 50% glandular differentiation. Undifferentiated tumors which have less than 5% glandular differentiation correspond to Grade 4. Medullary carcinomas with high microsatellite instability are classified as undifferentiated carcinomas. The prognosis correlates with the histological grade[31]. Grade 3 of differentiation is seen in 5.7% to 9.2% of patients with polyps and the risk of residual lesions or relapse in these cases is of the order of 36%-38%[25]. In most cases, grade 3 differentiation is associated with invasive adenocarcinoma cells $\leq 1$ mm from a clearly visualized margin.

the pit pattern classification for colon polyps with six classes of surface pattern depicted by magnifying endoscopy after indigo-carmine dye (Table 1). Class 5 of this pit pattern classification or an unstructured surface has been shown to correlate well with a diagnosis of malignancy, and can provide important additional information prior to endoscopic treatment. However, endoscopic ultrasound using high frequency transendoscopic miniprobe currently appears to be the most accurate method for defining submucosal or further bowel wall invasion, enabling direct referral for surgical intervention in those cases with deeper infiltration who are at the greatest risk of lymphatic spread[21].
submucosa (sm3) of sessile lesions is associated with a greater risk of lymphatic spread than only mild penetration\(^{27-32}\). Research based on large patient series has shown a 1%-3% risk for lymph node metastases in sm1 cancers, 8% in sm2 cancers and 23% in sm3 cancers\(^{31}\).

However, two problems exist in measuring submucosal invasion (SM) depth; how to measure SM depth in a lesion whose muscularis mucosae could not be identified, and how to determine SM depth in tumors demonstrating morphological differences. To solve the first problem, when the muscularis mucosae could not be identified due to carcinomatous invasion, Kitajima et al\(^{33}\) (Figure 2) in a Japanese collaborative study defined the superficial aspect of submucosal invasive colorectal carcinoma (pedunculated, nonpedunculated with muscularis mucosae identified and nonpedunculated without muscularis mucosae identified) and measured SM depth from this baseline to the deepest portion of invasion. For pedunculated, submucosal invasive colorectal carcinoma, the level 2 proposed by Haggitt was used as baseline (neck of the adenoma or junction between adenoma and stalk). In these cases the rate of lymph node metastasis was 0% when stalk invasion was < 3 mm or 3000 \(\mu m\). For nonpedunculated polyps without muscularis mucosae identified, the superficial aspect was used as baseline and the vertical distance from this line to the deepest portion of invasion represented SM depth. In nonpedunculated polyps, the superficial aspect was used as baseline and the vertical distance from this line to the deepest portion of invasion was determined (bidirectional arrow grey).
**Lymphatic invasion**

The presence or absence of lymphatic invasion by cancer is defined as tumor cells within a true endothelial-lined channel in the absence of red blood cells\[^{34}\]. The risk of lymphatic spread from a malignant polyp has been estimated by histological study of resected specimens. Since lymphatics do not penetrate much beyond the muscularis mucosae, focal cancer that has not invaded through this layer appears to present little or no risk of lymph node spread\[^{35,36}\]. A plexus of lymphatic channels is normally found in the superficial submucosa and within the muscularis mucosae, with rare extensions into the lamina propria (mucosa) limited to the region at the base of the crypts. The near absence of lymphatics within the mucosa has been proposed as the reason for the observed lack of malignant potential (lymph node metastasis) observed in polyps showing only intramuscular carcinoma. However, this theory has been challenged by studies using more sensitive techniques to detect lymphatic vessels. Studies using the relatively new antibody D2-40 (Dako, Carpinteria, CA, USA), which stains lymphatic but not blood vessel endothelium, have shown that lymphatics undergo proliferation and are present in the stalk and mucosa of adenomas and early invasive cancers. In malignant polyps, lymphatic channels are often present near nests of infiltrating tumors\[^{36,37}\]. From a practical point of view, detecting lymphatic invasion by expert pathologists using light microscopy is difficult. There are no recognised guidelines for establishing the presence of lymphatic invasion (for example, the number of sections or immunostains needed to identify lymphatic vessels). For example, in a study in which five pathologists assessed the lymphatic invasion of 140 malignant polyps, they agreed (4 out of 5 observers) on only 17 cases. The intra- and inter-observer variability in the interpretation of samples received among even the most expert histopathologists can be high and often leads to diagnostic uncertainties which inevitably results in a more cautious therapeutic approach being taken\[^{38}\]. True lymphatic invasion is rare, although retraction of tissue creating an artificial space around tumor cells is common in paraffin sections. The use of immunohistochemistry for D2-40 may help identify lymphatic channels. However, its use is not yet routine, and technical issues such as loss of a suspicious focus in level sections limits the usefulness of special stains in this setting. The presence of lymphatic invasion in a malignant polyp has been proposed by some researchers as an indication for colectomy. However, few malignant polyps with lymphatic invasion have been reported, and most of them have had positive margins, Grade 3 invasive adenocarcinoma (as defined above), or both\[^{39}\]. Approximately 12% to 16% of all polyps have lymphatic invasion, and in these cases, the risk of relapse or residual lesions ranges between 17% and 39%.

**Vascular invasion**

The presence or absence of venous invasion is defined as cancer in an endothelial-lined channel surrounded by a smooth muscle wall\[^{34}\]. However, it is difficult to recog-
nise venous invasion. Vascular markers, such as CD31, CD34 and factor VIII may help in assessing vascular invasion. These markers strongly stain blood vessel endothelium, and, to a lesser extent, lymphatic endothelium\[^{34}\]. The prevalence of venous invasion in malignant polyps varies greatly from one study to another, ranging from 3.5% to 39%\[^{38}\]. Often venous invasion is associated with lymphatic invasion and/or tumors which have a resection margin of less than 2 mm and/or are poorly differentiated. In contrast to the majority of studies, Talbot et al\[^{39}\] observed that venous invasion was not associated with poorer prognosis.

**Favourable and unfavourable histology and the risk of residual disease or recurrent carcinoma**

Favourable histology is defined as Grade 1 or 2 differentiated adenocarcinoma in which carcinoma cells are at least 2 mm from a clearly visualised margin, resection is carried out en bloc and there is an absence of vascular or lymphatic invasion.

The definition of unfavourable histology is when the distance between the invasive tumor and the cauterized biopsy margin < 2 mm or 2000 µm, there is piecemeal removal or tumor within the cauterized region constitutes a positive margin or a poorly differentiated tumor (Grade 3) or there is lymphatic or vascular invasion. In these cases, surgical resection is indicated because of the increased risk of lymph node metastasis or residual disease\[^{14}\]. On the other hand, in the absence of unfavourable features, polypectomy is considered curative. Specimens that do not lend themselves to proper analysis for any reason (piecemeal removal or poor orientation) sometimes result in a default decision to resect.

In 1995, Volk et al\[^{1}\] reviewed 20 studies in which 858 malignant polyps were analysed. They observed that in 89 patients (10%), there was residual disease or recurrent carcinoma. However, there were relapses or tumors in the area of the resection in only 8 (1%) patients with favourable histological criteria. Subsequent studies have also reported an incidence of less than 1%\[^{36,37}\]. Only one study described an incidence higher than 5% in malignant polyps with favourable histology\[^{41}\] and the study itself has been widely criticised and excluded from subsequent reviews\[^{38}\]. By contrast, in malignant polyps with unfavourable histology, the risk of relapse or residual lesions ranges between 10% and 39%\[^{5,14,31,41}\].

**TREATMENT**

Prior to removal of the polyp, it is difficult to know whether the polyp is malignant or not. Some features, as we have mentioned earlier, can give some indication of the degree of malignancy (Figure 3). In these cases, it is advisable to perform tattooing in order to mark the base of the resected polyp. Tattooing helps the surgeon or endoscopist to locate the base of the polyp. Regardless of the morphological characteristics, a polyp is normally removed when detected. Polypectomy should be per-
formed en bloc, since this is essential to establish and define favourable or unfavourable histological criteria. In just a few cases, only polyp biopsies are performed. This may be due to a lack of coagulation data, the polyp being difficult to remove at that point in time, or the patient being on antiplatelet drugs or anticoagulants.

NHGN regardless of their morphology, are considered to be cured with polypectomy.

The indication for a malignant polyp with sessile morphology, regardless of favourable histological criteria, is surgery, especially in patients younger than 50 years old, who tend to present fewer surgical complications. ESD has emerged as a possible technique to successfully resect malignant colonic polyps en bloc. This approach is indicated for polyps larger than 2-3 cm, involving more than one-third of the colon circumference or two haustral folds, or with a flat/depressed morphology. The technique makes it possible to treat large (>2 cm) sessile and flat polyps enabling pathological evaluation and cure in most patients. ESD is better than conventional endoscopic mucosal resection because it has higher en bloc resection and curative rates despite the longer procedure time and higher perforation associated with ESD. Also, ESD can be an alternative to surgery for older patients and for those suffering from associated conditions that contraindicate surgery. In addition, this type of resection should be considered for malignant polyps with sessile morphology, and hence, with surgical indication, regardless of histological criteria.

Surgical treatment is also recommended for malignant polyps with pedunculated morphology which have unfavourable histological criteria (partial polyp resection, poorly differentiated carcinoma, vascular or lymphatic invasion, margin of resection <2 mm or depth of submucosal invasion is ≥3 mm from muscularis mucosae). On the other hand, for malignant polyps with pedunculated morphology but with favourable histological criteria, polypectomy is considered to be curative.

However, until now many pathology reports did not report histological criteria. For example, at the University of Minnesota between 1987 and 2000, in 83% of patients angiolymphatic vessel invasion was not reported, in 69% the depth of invasion by cancer cells was not reported and in 22% the degree of tumor differentiation was not stated. Besides the agreement among experienced pathologists was poor with respect to histological grade of differentiated carcinoma and angiolymphatic vessel invasion.

In recent years, various serum markers have been identified in an effort to establish which patients could benefit from surgical treatment and from a stricter follow-up. These markers include metalloproteinase 7, vascular adhesion proteins, vascular endothelial growth factors and cytokeratins. The majority of markers have been studied in patients operated on for colon cancer with infiltration of the muscularis propria (equivalent to or higher than T2), so these results cannot readily be extrapolated to malignant colorectal polyps.

An exception to these guidelines is patients with malignant polyps, with sessile or flat morphology, that are located in the rectum. The occurrence of distant metastases is correlated to T-stage and, after radical resection of T1 tumors, the 5-year rate of metastases is about 10%.

Figure 3 Diagnostic and therapeutic algorithm of malignant polyps.

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FOLLOW-UP

In cases of NHGN and malignant polyp with pedunculated morphology and favourable histological criteria, it is recommended that a colonoscopy be carried out three months after taking the biopsy\(^{12,24}\). If this is normal, a further check up is advised after one year, three years and five years\(^{20}\). Some authors suggest that if the results within three months are negative, subsequent monitoring should be the same as that offered to patients with non-malignant adenomas, since there is no evidence that such patients are at a higher risk of metachronous polyps or cancers than those patients with benign adenomas\(^{12,25}\). However, recent studies estimate that 11.8% of patients who have undergone polypectomy will develop a metachronous advanced adenoma and 0.6% an invasive carcinoma. Associated risk factors include age, number of polyps (5 or more), size (greater than 1 cm), villous architecture, proximal location, and being male. The odds ratio increases progressively according to the number of adenomas, it being 1.39 for those who have had 2 adenomas and 3.87 for those who have had 5 or more. Smoking, body mass index, family history of CRC, and degree of dysplasia were not found to be associated with higher risks of advanced adenoma or cancer\(^{24}\).

There have been reports of cases of malignant pedunculated polyps with unfavourable histological criteria which, despite no findings of residual carcinoma in the intestine wall or lymph node involvement, are found on follow up to have distant metastasis, even five years after surgery\(^{103}\). These data force us to consider the monitoring of such patients using serum levels of carcinoembryonic antigen and imaging techniques such as computerised tomography which would enable early detection of recurrence.

Published series of malignant colorectal polyps usually include fewer than 100 cases, and most of these are retrospective studies. Given this, it would be interesting for new prospective studies to be carried out to evaluate the progress of such patients and to establish the most suitable treatment and follow up regimens for them.

CONCLUSION

The prevalence of malignant polyps in series of endoscopically removed polyps is between 0.2% and 11%. Currently the number of cases in which malignant polyps are removed is increasing due to screening programmes. Carcinoma “in situ”, intramucosal carcinoma, high-grade dysplasia or intraepithelial carcinoma is the stage at which there is no involvement of the muscularis mucosa. These terms are defined as non-invasive high grade neoplasia in the Vienna classification. When the carcinoma spreads to the submucosa, the polyp is considered to have become malignant, being able to spread to lymph nodes or distant sites. This term is defined as submucosal carcinoma in the classification of Vienna. The definition of unfavourable histology is when the distance between the invasive tumor and the cauterized biopsy margin < 2 mm, there is piecemeal removal or tumor within the cauterized region constitutes a positive margin or a poorly differentiated tumor (grade 3) or there is lymphatic or vascular invasion. In these cases, surgical resection is indicated because of the increased risk of lymph node metastasis or residual disease. Also, the indication for a malignant polyp with sessile morphology, regardless of favourable histological criteria, is surgery. In cases of non-invasive high grade neoplasia and submucosal carcinoma with pedunculated morphology and favourable histological criteria, it is recommended that a colonoscopy be carried out three months after taking the biopsy and if this is normal, a further check up is advised after one year, three years and five years.

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