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REVIEW

Current strategies for malignant pedunculated colorectal polyps

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Abstract

Despite significant advances in imaging techniques, the incidence of colorectal cancer has been increasing in recent years, with many cases still being diagnosed in advanced stages. Early detection and accurate staging remain the main factors that lead to a decrease in the cost and invasiveness of the curative techniques, significantly improving the outcome. However, the diagnosis of pedunculated early colorectal malignancy remains a current challenge. Data on the management of pedunculated cancer precursors, apart from data on nonpolypoid lesions, are still limited. An adequate technique for complete resection, which provides the best long-term outcome, is mandatory for curative intent. In this context, a discussion regarding the diagnosis of malignancy of pedunculated polyps, separate from non-pedunculated variants, is necessary. The purpose of this review is to provide a critical review of the most recent literature reporting the different features of malignant pedunculated colorectal polyps, including diagnosis and management strategies.

Key words: Pedunculated colorectal polyps; Malignant colorectal polyp; Early colorectal cancer; Polypoid early colon cancer; Advanced adenoma; Depth of invasion; Colorectal cancer; Polypectomy; Colorectal surgery; Early colorectal carcinoma

Core tip: Colorectal cancer has the highest chance of curability as long as it is detected at an early stage, before lymph node metastasis, or as a premalignant lesion. However, few relevant studies address pedunculated polyps separately from nonpolypoid type lesions, often resulting in a source of bias. The objective of this paper is to offer an up-to-date overview, particularly on the management of malignant pedunculated polyps.

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INTRODUCTION

Colorectal cancer (CRC) is one of the most common cancers worldwide. Of all gut malignancies, it has the highest chance of curability as long as it is detected at an early stage – either as a premalignant lesion or before lymph node metastasis. In European national screening programs, approximately 17% of cancers detected were pT1 CRCs, and the risk of developing advanced neoplasia following polypectomy was estimated at 0.6%[1].

Most reports focus on sessile or flat lesions of the colorectum, while few studies discuss the management of pedunculated cancer precursor lesions. Studies often combine data for both sessile and pedunculated polyps. Moreover, submucosal invasion is presented in the literature as absolute depth, disregarding the presence of the stalk[2], resulting in further bias. In particular, describing the macroscopic appearance of pedunculated lesions and the final histopathological diagnosis often remain challenging. At first sight, pedunculated lesions can easily be treated endoscopically; however, no large-scale reports exist to establish the real risk of lymph node metastasis stratified by depth of invasion. Additionally, an adequate technique for complete resection is mandatory for curative intent, providing the best long-term outcome. In this respect, a discussion regarding the diagnosis of malignancy inside pedunculated, separate from nonpedunculated, polyps is necessary. A clear distinction between head and stalk invasion of malignant cells is also required.

LITERATURE SEARCH

The aim of this article was to address strategies for diagnosis, staging, and risk stratification of patients with malignant pedunculated colorectal polyps (MPCP), as well as to provide a critical review of the literature regarding their management, to summarize their current state and to consider future perspectives. The literature search was conducted with PubMed and included full-text articles, up-to-date guidelines and recent abstracts with obvious conclusions as well as additional relevant publications by using the reference lists of the identified articles as a starting point. The following keywords were used: "pedunculated colorectal polyps", "malignant colorectal polyp", "early CRC", "polypoid early colon cancer", "early diagnosis", "staging", and "depth of invasion", alone or in various combinations.

DEFINITIONS, CLASSIFICATIONS AND HISTOPATHOLOGICAL CHARACTERISTICS

By definition, a malignant polyp – either sessile or pedunculated, consists of cancer cells that invade the submucosa through the muscularis mucosae without crossing the submucosa, regardless of lymph node status and without distant metastasis (T1NxMo)[3]. The term "early colorectal carcinoma" can also be used[4].

An advanced adenoma is defined as a lesion of at least 10 mm with villous components or high-grade dysplasia[5,6]. Currently, "high-grade dysplasia" is a term used for adenomas in which there is mucosal invasion without extension below the muscularis mucosae[7]. According to the recommendations of the World Health Organization (WHO), this term is preferable to "intramucosal carcinoma"[7,8]. The reason is that focal cancer that has not yet invaded through the muscularis mucosae is considered to have no risk of spreading to the lymph nodes because no lymphatic channels are located superficially to the muscularis mucosae[7]. The patients in this situation are considered to be safe candidates for endoscopic resection.

Pedunculated polyps are recognized by their stalk of variable lengths that is attached to the colonic mucosa[9]. They are described endoscopically in the Paris international classification as 0-Ip lesions. Although it has been reported to anticipate high-grade dysplasia and even invasive carcinoma, interobserver variability associated with the Paris classification has not been studied[10]. Class 5 of Kudo's pit pattern classification, characterized by an unstructured or excavated surface, demarcated depressed areas, loss of lobulation and stalk swelling, has been shown to correlate with the diagnosis of malignancy[11,12]. A large multicenter cohort study emphasized the difficult diagnosis, as there has been a lack of agreement on the diagnosis of MPCP in a high percentage of cases[13].

The level of invasion of the stalk further dictates management, from a minimally invasive endoscopy to an invasive surgical resection. MPCP should be discussed separately from nonpedunculated polyps to obtain accurate conclusions. If in the case of a sessile polyp, the cancer cells travel a short distance to become invasive and metastatic, should the stalk length be considered a favorable prognostic factor as a first barrier through the advanced cancer pathway?

Haggitt *et al*[14] classified the level of invasion in a pedunculated malignant polyp as follows: Level 1: invasive adenocarcinoma limited to the polyp head (invading through the muscularis mucosae); Level 2: neck involvement; Level 3: carcinoma cells in the stalk; and Level 4: carcinoma cells infiltrating the submucosa at the level of the adjacent bowel wall. The Haggitt line is the imaginary border drawn as the baseline to distinguish between head invasion and stalk invasion. A low risk of local recurrence or metastasis was deduced when the level of invasion was under 4. Although many studies[15-17] reported a correlation between Haggit level, lymph node invasion risk and outcome, there are currently no consensus guidelines to be included in the pathology report of a malignant polyp.

FACTORS PREDICTING LYMPH NODE STATUS IN MALIGNANT PEDUNCULATED COLORECTAL POLYPS

Even if pedunculated polyps are generally considered to have fewer lymph node metastases, variable morphology and length of the stalk can lead to problematic measurement of the depth of the submucosal invasion and to further controversies (Table 1).

In a recent systematic review and meta-analysis of histopathological factors influencing the risk of lymph node metastasis in early CRC[2], a separate analysis of pedunculated polyps from sessile tumors was not possible because of insufficient data. They concluded that in early CRC, a depth of invasion of more than 1 mm in the submucosa by the primary tumor, poorly differentiated cancers, the presence of tumor budding and lymphovascular invasion were significantly associated with lymph node involvement.

Moreover, Kitajima *et al*[15] previously found a rate of lymph node metastasis of zero in head invasion cases (the deepest portion of invasion limited to above the baseline) and in stalk invasion cases with a depth of submucosal invasion < 3000 μm (MPCP with the level 2 line according to Haggitt's classification used as the baseline and depth of submucosal invasion measured to the deepest portion in the submucosa).

In a large retrospective cohort study[16], the authors concluded that MPCP diagnosed as head invasion by the pathologist can be safely treated by endoscopic polypectomy alone. They included 383 patients with pathologically proven adenocarcinoma spread through the muscularis mucosae into the submucosa but without extension to the muscularis propria. The invasion depth was classified into two groups by using the upper limit of level 2 according to Haggitt's classification as the baseline for all lesions. When an endoscopy was suggestive of submucosal invasion into the polyp stalk, those patients were managed directly by surgery with lymph node dissection. Thus, they found a lymph node involvement rate and recurrence rate of 3.5% (8/230; 95%CI: 1.5%–6.7%) and 0.3% (1/340; 95%CI: 0.01%–1.6%), respectively. The incidence of metastasis to the lymph nodes and recurrence rate were 0% (0/101; 95%CI: 0.0%–3.6%) and 0%, respectively, (0/219; 95%CI: 0.0%–1.7%) for the lesions with head invasion, compared with 6.2% (8/129; 95%CI: 2.7%–11.9%) and 0.8% (1/121; 95%CI: 0.02%–4.50%), respectively, for stalk invasion. A total of 29% of lesions with head invasion were lymphovascular invasion positive, while 38% of stalk invasion lesions were lymphovascular invasion positive. Finally, the authors noted no significant difference in any other factors (such as tumor size, tumor differentiation grades, or even lymphovascular invasion) except for the depth of invasion (stalk invasion) between lymph node metastasis positive and negative groups.

In a previous study on 151 patients with colorectal polyps that included invasive carcinoma treated by resection, Nivatvongs *et al*[17] concluded that, unlike tumor size and grading, only the depth of invasion to the base of the stalk (Level 4) was associated with a high risk of lymph node metastasis (27%).

On the other hand, in another approach with patients who underwent systematic lymph node dissection, metastasis was observed in 14.6% of cases, and multivariate analysis showed that tumor budding was the only independent factor associated with lymph node metastasis[18].

Interestingly, Kimura *et al*[19] recently suggested that head invasion is not a lymph node metastasis-free condition in a study on 76 pedunculated polyps with no significant differences in the lymph node metastasis rate between "head invasion" (4/30, 13.3%) and "stalk invasion" (5/46, 10.9%). They stated that even for MPCP with "head invasion", additional surgical resection with lymph node dissection should be taken into consideration if there are other risk factors.

Indeed, the detection of tumor buds has been reported as an indication for colorectal surgery because of the high risk for lymph node metastasis. Pathologically, tumor budding is defined as single tumor cells or small clusters of four or fewer tumor cells in the tumor stroma, at the invasive front and in malignant polyps[20,21]. Widespread reporting of tumor budding has been limited in daily diagnostic practice due to a lack of consensus regarding guidelines on scoring methods[20,21]. Although some authors[8,22] consider it important that at least

Table 1 Histopathological factors predicting risk of lymph node metastases in malignant pedunculated colorectal polyps

Histopathological factors	Risk of LNM	Management
Depth of invasion in submucosa by the primary tumor of more than 1mm (Beaton *et al*[2])	High	Surgery with lymph node dissection
Poorly differentiated cancers (Beaton *et al*[2])		
Tumor budding (Beaton *et al*[2], Sohn *et al*[18], Geramizadeh *et al*[7], Graham *et al*[22])		
Lymphovascular invasion (Beaton *et al*[2])		
Depth of invasion to the base of the stalk-Level 4 Haggitt (Nivatvongs *et al*[17], Kimura *et al*[19])		
Submucosal invasion into the polyp stalk (Matsuda *et al*[16])		
Micropapillary component (Sonoo *et al*[26], by Verdú *et al*[27], Mukai *et al*[28])		
Head invasion (Kimura *et al*[19])		Surgical resection with lymph node dissection in case of additional pathological risk factors
Head invasion (Kitajima *et al*[15], Matsuda *et al*[16])	Low	Endoscopic polypectomy
Depth of submucosal invasion/stalk invasion < 3000 μm (Kitajima *et al*[15])		
Tumor size (Nivatvongs *et al*[17])		
Grading (Nivatvongs *et al*[17])		
Pseudoinvasion (Backes *et al*[13])		Confirmation of t1 colorectal cancer by a second expert pathologist

LNM: Lymph node metastases.

high-grade tumor budding (more than 10 tumor buds in any microscopic field viewed at 25X) should be recorded in the pathology report as a prognostic factor.

Invasive micropapillary carcinoma is composed of small clusters of tumor cells lying within clear stromal spaces simulating vascular channels[23,24] and is considered to be related to a high incidence of lymph node metastasis. However, its actual prevalence among early CRCs has not been reported[25,26], as a limited number of cases are reported in the literature. Similar cases of pedunculated early sigmoid colon cancer with a micropapillary component and multiple lymph node metastases were reported by Sonoo *et al*[26], Verdú *et al*[27] and by Mukai *et al*[28]. In another case of a sigmoid pedunculated polyp with a depressed surface without evidence of lymph node involvement or distant metastases on initial computed tomographic scans, the patient had local recurrence with lymph node metastases but also lung, liver, and spleen metastases at 6 months follow-up after the polypectomy[29].

Therefore, even if the initial diagnosis is an MPCP, extensive surgical resection may still be taken into consideration for tumors with a micropapillary component due to the high risk for lymph node metastasis and poor outcome.

Beyond the conclusions of these studies, immunohistochemistry for the confirmation of the difficult-to-assess lymphovascular invasion is usually reserved for equivocal cases (*e.g.*, tumors with positive margins after resection)[30].

Chicken-skin-like mucosa is an endoscopic finding described as pale yellow-speckled mucosa frequently surrounding pedunculated adenomas of the distal colon. Its clinical and pathophysiological significance have yet to be determined. Histopathologically, it represents fat accumulation in macrophages within the muscularis propria and, rarely, intestine-like microvilli. In two studies[31,32], the prevalence of chicken-skin-like mucosa was higher in carcinoma patients than in adenoma patients, and its role as a potential predictive marker of carcinogenetic progression was taken into consideration. However, it is a colonoscopic sign to search for a polyp in challenging locations. Additionally, it may serve as a potential marker of advanced pathology of colorectal adenoma in future research and might offer a better perspective on postpolypectomy management[33].

Both endoscopists and histopathologists should also pay attention to possible pseudoinvasion. A histopathological pseudoinvasion (prolapse of the adenomatous epithelium into the polyp stalk), associated with ischemic changes when the polyp stalk is twisted, can be observed more often in large pedunculated polyps, which are typically located in the sigmoid colon and rarely in the rectum[7]. Despite the lack of a gold standard diagnosis, invasive carcinoma could be distinguished from pseudoinvasion by the presence of stromal desmoplasia and high-grade dysplasia[34]. However, the exact incidence of discordant diagnosis cannot be estimated; moreover, misplaced epithelium in pedunculated polyps has a lobular contour with a rim of lamina propria, along with hemorrhage, and/or hemosiderin[35]. Biopsy-related misplacement can be even more difficult to recognize than typical pseudoinvasion in polyps with stalks[36].

Thus, because misplaced epithelium can simulate early CRC in pedunculated polyps, British guidelines currently recommend diagnostic confirmation of T1 CRC by a second expert pathologist[13].

CHALLENGES IN ENDOSCOPIC RESECTION TECHNIQUES

When we suspect a malignant pedunculated polyp, the snare should be placed as close as possible to the bowel wall to increase the chance of obtaining a cancer-free resection margin. Snare polypectomy is considered

curative when the histopathology report is favorable, but there is no consensus on the accurate assessment of negative margins. Most authors[37,38] consider polypectomy technically satisfactory, with the lowest rate of local recurrence and metastases, if the margin from the invasive component to the diathermy burn is at least 2 mm. A new study[39] reported a similar 5 -year cumulative recurrence rate between surgical and endoscopic resection (8.2% and 2.4%, respectively) for patients with MPCP and a pathological margin ⩾ 1 mm.

The site of resection should be inked with a tattoo to facilitate easy recognition if surgery is necessary; however, there is no guideline on the optimal placement of tattoos or metallic clips[40].

Unlike sessile or flat polyps, in the case of pedunculated lesions, it is easier for the pathologist to avoid a diathermy artifact of the resected specimen and to better identify eventual invasive cancer cells at the polypectomy margin due to the distance of resection from the invasive component. Many studies[16,41] have stated that pedunculated early polyp CRCs limited to the polyp head, without unfavorable histological features, could be managed by endoscopic resection alone with minimal risk of locoregional recurrence. However, in cases of unfavorable histological criteria (resection margins less than 1 mm, poor differentiation, lymphovascular invasion, invading the submucosa of the bowel wall below the stalk), endoscopy is not considered curative; therefore, surgery is recommended[40].

Generally, giant pedunculated polyps (over 30 mm) have been managed surgically; further prospective studies are needed to establish if endoscopic resection of giant MPCP represents a feasible safe procedure[42]. Recently, a prospective pilot study explored the safety and feasibility of insulated-tip knife endoscopic polypectomy for difficult giant polyps[43]. Endoscopic submucosal dissection[44] and the use of a dual knife procedure[45] were reported to be options as well, but the patient number was too small to make definitive conclusions.

Pedunculated polyps have a higher risk of bleeding compared to sessile polyps[46]. Postpolypectomy bleeding is the most common complication reported in the literature, and the rate varies between 24%[47] and the more usual frequency of 3%–4%[48]. When considering referral bias, the general frequency is thought to be lower, while other complications such as postcoagulation syndrome or perforation can rarely occur[49]. The only polyp-related factor that has been constantly proven to increase the risk of delayed bleeding is the large size of the lesion[50,51]. Therefore, pretreatment of stalks in large polyps may be necessary, and a variety of techniques are available. For polyps with a head ⩾ 20 mm or a stalk ⩾ 10 mm in diameter, recent European guidelines (ESGE) have recommend pretreatment of the stalk with injection of diluted adrenaline and/or mechanical hemostasis (moderate quality evidence, strong recommendation)[52].

Endoclips

Prophylactic clipping before or after polypectomy remains controversial, with conflicting results reported in different studies[46].

Quintanilla *et al*[53] reported in a prospective randomized study of large pedunculated polyps that prophylactic clips (prior to polyp resection) did not decrease the risk of delayed bleeding after polypectomy. Technically, they suggested the use of hemoclips in the case of polyps with long and thin pedicles. However, this study was suspended early because of the high risk of morbidity in the clipping group, with higher rates of mucosal burns and perforation rather than bleeding.

Very thick and/or short stalks may be a challenge for clip placing, causing mucosal burns and risk of perforation due to the contact of the base of the polyp with the snare and the clip[54].

Indeed, prophylactic clips applied before endoscopic removal for this type of polyps were actually associated with further risk of mucosal deep erosions and perforation[55].

For MPCP resected by hot snaring, neither early nor delayed bleeding complications occurred for more than two decades during which clips were not used[56].

On the other hand, Parikh *et al*[57] concluded that prophylactic placement of hemoclips after polypectomy was a cost-effective plan for patients on antiplatelet or anticoagulation therapy.

Endoloops

The use of the endoloop can also generate technical difficulties from looping large polyps and the endoloop removal[53] to the transection by the loop of a thin stalk before the polypectomy or insufficient tightening of the loop[58]. A prospective randomized multicenter study[59] suggested that the application of a prophylactic hemoclip is as effective and safe as an endoloop in the prevention of postpolypectomy bleeding in large pedunculated colonic polyps.

Anchor clip technique

Mizukami *et al*[60] described the anchor clip device, which, placed before the resection of large polyps, constrains the base of the stalk after resection, avoiding immediate bleeding and mucosal burns.

Adrenaline injection

A prospective study on pedunculated polyps larger than 20 mm has shown that there are no differences between adrenaline injection and the use of endoloops or hemoclips in postpolypectomy bleeding prophylaxis[48], although its addition to both techniques appeared to increase the efficiency in other studies[61,62]. Recently, a prospective randomized study[63] that compared the rates of bleeding after resection following single clipping alone

and a combined method (hemoclips plus epinephrine-saline injection) concluded that large pedunculated polyps can be successfully removed *via* hot snare by using the single prophylactic clipping method.

A recent meta-analysis of three randomized controlled studies[64] that compared the efficacy of epinephrine injection and mechanical hemostasis in postpolypectomy bleeding in patients with pedunculated polyps over 20 mm demonstrated that prophylactic treatment with mechanical hemostasis is more effective than epinephrine injection for preventing overall postpolypectomy bleeding (2.2% *vs* 6.3%) and early postpolypectomy bleeding (1.1% *vs* 4.5%). The rate of delayed postpolypectomy bleeding was 1.9% in the epinephrine group and 1.1% in the mechanical group, and their implementation was not found to significantly affect the rate of delayed postpolypectomy bleeding (OR = 0.58, 95%CI: 0.13, 2.49; P = 0.46) without significant heterogeneity between the studies (P = 0.94, I^2 = 0%).

The impact of underlying comorbidities and other pedunculated polyp characteristics

The presence of comorbidity, beyond the size and location of the polyp, should also be taken into consideration when discussing further management.

Different risk factors for postpolypectomy complications, such as old age (older than 65 years of age), underlying diseases (cardiovascular or chronic renal disease), anticoagulant use, polyp size > 10 mm, a stalk size > 5 mm, polyps located on the right side of the colon, malignant polyps, use of cutting mode and low-volume endoscopists, have been described[47,64-67].

A recently published review and meta-analysis[68] identified cardiovascular disease, hypertension, polyp size over 10 mm, and polyp location as significant risk factors for delayed postpolypectomy bleeding, whereas pedunculated morphology, carcinoma histology, age, sex, alcohol use, smoking, diabetes and cerebrovascular disease were not.

Related to the polyp location, recent evidence[50] suggests that right-sided polyps have a significantly higher risk of bleeding and perforation in comparison with left-sided polyps, for both sessile and pedunculated polyps.

In conclusion, the effectiveness of common preventive methods is variable, and no consensus has been reached to date on the strategy to avoid postpolypectomy bleeding. Large randomized controlled trials are necessary to confirm these observations, taking into consideration more potential risk factors such as pedunculated polyp characteristics (*e.g.*, length of the pedicle) or other patient comorbidities (*e.g.*, the bleeding risk from heparin - bridging therapy in patients with high thromboembolic risk[69]). Interestingly, Shibuya *et al*[70] showed that the overall postpolypectomy bleeding rate under the new Japanese guidelines, which indicate that antithrombotic agents are not to be discontinued in cases with a high-risk of thromboembolic incidents, was not significantly higher when compared with data from previous guidelines, without particularly addressing pedunculated polyps.

STRATEGIES FOR PATIENTS ON ANTIPLATELET THERAPY OR ANTICOAGULANTS

The risk of bleeding, as the most common adverse effect of polypectomy and particularly the higher risk of bleeding of pedunculated polyps, was already described in the section "Challenges in endoscopic resection techniques". Therefore, endoscopic polypectomy is considered to be a high-risk procedure based on the risk of bleeding, which is increased by the addition of antiplatelet or anticoagulant therapy. In this group of patients, the risk of hemorrhage should be balanced against the risk of thrombosis when antiplatelet or anticoagulant therapy is discontinued.

Patients with MPCP and indication of polypectomy should be managed as summarized in Table 2, according to the most recent British Society of Gastroenterology and ESGE general recommendations[71].

ADEQUATE FOLLOW-UP AFTER RESECTION

Discussing surveillance after polypectomy can be challenging because the risks and outcomes are difficult to calculate. Generally, when the risk of the lesion seems to be low, interval surveillance is performed. For patients with a higher risk, further surgical resection is necessary, but there is no consensus on follow-up procedures and subsequent intervals for early cancer in pedunculated lesions. The management of an MPCP following endoscopic resection can generate anxiety for both the physician and patient because of possible residual cancerous cells and/or positive lymph nodes that are variable from one case to another[72]. However, further management remains balanced between the general approach of postpolypectomy surveillance of patients with high-risk adenomas[6,73,74] and the follow-up of a resected CRC with curative intent[75-77]. However, it is also based on the experience and clinical sense of the physician.

The recent recommendations of the United States Multi-Society Task Force on Colorectal Cancer endorsed by the American Society for Gastrointestinal Endoscopy[75] address only the use of colonoscopy in the follow-up of patients with resected CRC with curative intent and insist on the fact that the colorectum should be carefully cleared of synchronous neoplasia in the perioperative period, without any particular information on early cancer in pedunculated polyps.

Fortunately, pedunculated polyps are unusual

Table 2 Endoscopic polypectomy in patients on antiplatelet therapy or anticoagulants (British Society of Gastroenterology and European Society of Gastrointestinal Endoscopy Recommendations[71])

Thrombosis risk factors		High thrombotic risk	Low thrombotic risk	Post-polypectomy
Discontinuation of warfarin concerning the requirement for heparin bridging	Discontinuation of clopidogrel, prasugrel or ticagrelor	Continuing aspirin and liaising with a cardiologist about the risk/benefit of discontinuing P2Y12 receptor antagonists (high quality evidence, strong recommendation)	Continuing aspirin in patients on dual antiplatelet therapy (low quality evidence, weak recommendation)	Antiplatelet or anticoagulant therapy should be suspended up to 48 h after the procedure depending on the perceived bleeding and thrombotic risks (moderate quality evidence, strong recommendation)
Prosthetic metal heart valve in mitral position	Drug-eluting coronary artery stents within 12 mo of placement	Warfarin should be temporarily stopped and substituted with LMWH (low quality evidence, strong recommendation)	Discontinuing P2Y12 receptor antagonists 5 d before the procedure (moderate quality evidence, strong recommendation)	
Prosthetic heart valve and atrial fibrillation	Bare metal coronary artery stents within 1 mo of placement.	The last dose of DOAC should be taken at least 48 h before the procedure (very low quality evidence, strong recommendation)	Discontinuing warfarin 5 d before the procedure (high quality evidence, strong recommendation)	
Atrial fibrillation and mitral stenosis			Ensure the INR target < 1.5 prior to the procedure (low quality evidence, strong recommendation)	
< 3 mo after venous thromboembolism				

LMWH: Low molecular weight heparin; DOAC: Direct oral anticoagulants.

in the rectum. However, rectal cancer is generally associated with a higher risk of local recurrence than other segments of the colon, and additional considerations for surveillance[77], such as endoscopic ultrasound for better detection of suspicious lymph nodes and recurrences[75], are suggested. The utility of adjuvant chemoradiation or chemoradiation alone for high-risk early rectal carcinoma remains to be elucidated[1].

In a long-term prospective study of 25 consecutive patients with MPCP treated with snare cautery polypectomy[56], the author concluded that short-term outcomes after removal appeared to be similar to those with a nonmalignant polyp. He suggested that long-term surveillance should be considered in each patient, assuming reasonable life expectancy, because the risk of additional adenomas and metachronous colon cancer persists even after the initial five years of currently recommended surveillance. In addition to the small number of patients, the location of the lesions was limited to the sigmoid or descending colon, and both standard and high-definition colonoscopes were used without calculating the accuracy of polyp detection in separate subgroups. Personal or family history of intestinal neoplasia (such as previously resected adenomas) or underlying inflammatory bowel disease was excluded from the study.

A high carcinoembryonic antigen (CEA) value may be predictive of metastatic disease[78-80]. There have been reported cases of MPCP with unfavorable histological criteria without initial local residual carcinoma or lymph node invasion but with distant metastasis even five years after surgery[11,81], so close monitoring of such patients using CEA and imaging techniques seems prudent.

To our knowledge, to date, there are no particular guidelines including optimal treatment and surveillance of subgroups, such as synchronous CRCs, malignant pedunculated polyps, multiple malignant pedunculated polyps or malignant pedunculated polyps, associated with chronic inflammatory bowel disease.

UNRESOLVED ISSUES AND AREAS FOR FURTHER RESEARCH

There is a thin line between early cancer in pedunculated polyps and invasive cancer, due either to interobserver variation in detection rate by endoscopists or histologic interpretation by pathologists. Standard snare polypectomy is appropriate for pedunculated polyps with early cancer limited to the submucosa and favorable histology. The distance from the cancer to the margin of the resection excision is still under debate. These situations lead to a challenging evaluation of the natural history of the lesions.

Treatment plans and the best strategy to avoid postpolypectomy complications for colorectal malignant pedunculated polyps lack the evidence of randomized trials. Large randomized trials on this particular topic should be included in meta-analyses that develop further guidelines to provide relevant conclusions for patients' long-term

surveillance and outcomes. More long-term information focused on patients with endoscopically removed malignant polyps, including personal or family history of intestinal neoplasia, previously resected adenomas, or underlying inflammatory bowel disease[82,83], would be valuable.

In addition to general unfavorable histological criteria, better stratification of patients with high-risk pedunculated polyps requiring surgery[84], including those with high-grade tumor budding or invasive micropapillary components as reliable predictors of lympho-hematic metastases, is necessary. On the other hand, inadequate recognition of the pseudoinvasion pitfall as a benign condition can generate overdiagnosis and subsequent overtreatment of certain lesions. In this respect, a second histological opinion seems advisable for all cases of MPCP, especially when surgery is taken into consideration.

CONCLUSION

There are still unresolved issues requiring detailed recommendations according to the patient's and polyp's risk factors to avoid an overuse of surveillance procedures. Provided future novel imaging technologies and increased pathological recognition of high-risk markers for angiolymphatic invasion will be developed, it will be easier to decide on the optimal follow-up plan and therapy.

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