Management of Rectal Polyps

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Abstract

Keywords

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Colorectal cancer is one of the most common causes of cancer and cancer morbidity in the United States. In comparison to colon polyps, rectal polyps pose a unique challenge. Advances in endoscopic techniques have allowed for more thorough rectal adenoma detection and removal; however, there remains a concern over piecemeal resection and negative resection margins. Advances in transanal excision techniques, such as transanal endoscopic microsurgery, have been proposed for the removal of benign polyps as well as some early stage rectal cancers, with emphasis on proper patient selection. This review will discuss the current endoscopic and surgical considerations of both benign and malignant rectal polyps.

Colorectal cancer (CRC) is the third leading cause of cancer morbidity in the United States, with rectal cancer accounting for approximately 40,000 new cases annually.¹ There is clear evidence that CRC can be prevented by detecting and removing adenomatous polyps using screening colonoscopy, as discussed in “Colonic Polyps: Diagnosis and Surveillance” by Drs Huck and Bohl (on pp. 296–305) and “Colonic Polyps: Treatment” by Drs Huang and Sarin (on pp. 306–314).² As discussed in detail in article, “Polyp Genetics” by Drs Klos and Dharmarajan (on pp. 289–295), this is largely based on our knowledge of the adenoma to carcinoma sequence of colorectal carcinogenesis, or the “loss of heterozygosity” hypothesis, by which accumulations of mutations result in the malignant transformation of adenomas to carcinomas. As a result, all colorectal adenomas should be completely removed to determine an accurate diagnosis and exclude/prevent malignancy. Current adenoma detection rates (ADR) in those over age 50 are estimated to be 21 to 28%.³ These polyps can often be removed endoscopically; however, there remains controversy as to what defines an adequate endoscopic resection margin and the estimated risk of lymph node metastasis if malignant. Large polyps can be difficult to endoscopically resect en bloc, which results in piecemeal removal and the inability to adequately assess margins.⁴ Unfortunately, this is a common situation in the case of rectal polyps and represents a subset of patients where deciding on

further treatment is challenging as the physician attempts to determine the risk of residual disease and/or possible lymph node involvement in the case of a malignant rectal polyp.

Traditionally, the inability to endoscopically resect a rectal polyp or the identification of malignancy in an endoscopically resected polyp indicated the need for radical surgical resection with either a low anterior resection or abdominoperineal resection combined with total mesorectal excision (TME). With the evolution of transanal surgical techniques, the National Comprehensive Cancer Network (NCCN) has stated that some patients may be candidates for local excision of early rectal cancer with transanal excision (TAE) or transanal endoscopic microsurgery (TEM), with or without systemic therapy.³ There still remains debate over proper patient selection for local excision, oncologic equivalency, and recurrence rates when compared with radical resection. The goal of this article is to review the present literature regarding the approach to rectal polyps and their endoscopic and surgical considerations.

Endoscopic Considerations for Rectal Polyps

Similar to colon polyps, rectal polyps are typically asymptomatic and often detected on screening colonoscopy. However, rectal polyps may also present with symptoms such as bleeding, mucous leakage, prolapse through the anus or in the case

of a large villous adenoma of the rectum, may present with diarrhea and electrolyte abnormalities. Although most polyps are benign, the incidence of detecting a malignant polyp in a polypectomy specimen, defined as carcinoma invading through the muscularis mucosa and into the submucosa (T_1), increases with polyp size and has been reported as high as 40% in polyps > 2 cm. Visual signs concerning for malignancy at the time of endoscopy included ulceration, induration, friability, and the inability to lift the polyp from the underlying submucosa. For the aforementioned "high risk" polyps and more difficult to resect sessile polyps in the lower third of the rectum, resection is best performed after locoregional staging. However, recent data suggest that the accuracy of an endoscopists' visual assessment with regard to lesion size, morphology, and overall suspicion of malignancy is suboptimal with only 61% of endoscopists able to accurately identify a lesion with invasive carcinoma as being malignant. Additionally, more than half of endoscopists incorrectly classified at least one in four benign adenomas as malignant.⁵ The utilization of chromoendoscopy and narrow band imaging (NBI) has been proposed to help discriminate between neoplastic and nonneoplastic lesions.⁶ Chromoendoscopy uses contrast dyes, such as methylene blue or indigo carmine, to coat and stain the colonic or rectal mucosa allowing for more detailed detection of mucosal structural variation and morphology. NBI utilizes reflective light of varying wavelengths to improve visibility of blood vessels and microcapillary architecture of the mucosa. Data comparing chromoendoscopy with conventional colonoscopy demonstrates an increased ADR with chromoendoscopy as well as improvement in the detection of dysplasia in those with inflammatory bowel disease (IBD).^{7,8} However, most of the additional polyps identified are diminutive (< 5 mm), and this technique has had limited routine incorporation into practice outside of IBD patients. Conversely, studies comparing NBI technology with conventional white light colonoscopy remain mixed with regard to improved adenoma detection and decreased adenoma miss rates and as such, studies are ongoing as to the best incorporation of NBI into daily practice.⁹⁻¹¹

The management of a malignant polyp following endoscopic removal is difficult due to the possibility of residual malignancy and the risk of lymph node involvement. Prior studies on malignant rectal polyps, especially those in the lower third of the rectum, have shown a higher predisposition for lymph node spread compared with those of the proximal colon and rectum.¹² Therefore, it is paramount to assess individual risk factors for lymph node metastasis after endoscopic resection of a malignant polyp. We know from early studies by Haggitt et al that the level of tumor penetration is of critical importance in determining the risk of lymph node positivity. In 1985, Haggitt et al described a classification system for level of invasion of pedunculated malignant polyps such that levels 1, 2, and 3 reflect invasion of malignancy into the submucosa but limited to the head, neck, and the stalk of a pedunculated polyp, respectively. Levels 1 to 3 were associated with a low risk ($\sim 1\%$) of lymph node metastasis.¹³ Conversely, Haggitt level 4 reflects cancer invading the submucosa below the stalk of a pedunculated polyp, or invasion into any submucosa of a sessile polyp, and is

associated with lymph node metastasis in up to 25%. In the early 1990s, Kudo et al and Kikuchi et al further stratified sessile polyps beyond Haggitt level 4, refining the depth of submucosal invasion into three levels: Sm1, Sm2, and Sm3 based on invasion into the upper, middle, and lower third of the submucosa, respectively.^{14,15} In the study by Kikuchi et al, Sm3 was the only independent predictor of lymph node metastasis, and subsequent studies confirmed that invasion into the lower third of the submucosa (Sm3) represents a higher risk of lymph node metastasis of about 23%.¹² These data remain of utmost importance in the rectum where pedunculated lesions are unusual and sessile lesions are more common.

The ability to determine the level of submucosal invasion (Sm level) of cancer in a rectal polyp can be impossible if the endoscopically resected specimen only contains a portion of the thickness of the submucosa, or if polypectomy techniques such as diathermy and piecemeal removal preclude accurate pathological assessment. While there is still much debate as to what constitutes a positive endoscopic resection margin, with definitions ranging from a margin of 2 mm down to the presence of gross tumor at the margin, there is a general consensus that a correlation exists between a positive endoscopic resection margin and the risk of lymph node metastasis and/or recurrence.^{3,16} In recent data from Memorial Sloan-Kettering Cancer Center, a total of 143 patients underwent colectomy after a prior endoscopic polypectomy with identification or suspicion of invasive disease.¹⁷ They identified residual cancer (in the colonic wall and/or lymph nodes) in 19% of surgical specimens and concluded that a positive polypectomy margin, defined as a margin of < 1 mm, is a predictor of residual disease. Interestingly, in the patients for whom the polypectomy margin status could not be determined (30%), the rate of residual disease was the same as in those with a positive polypectomy margin. None of the patients with a negative polypectomy margin had residual disease. This suggests that an unknown resection margin should be combined with known positive margins when discussing the risks for possible residual malignant disease after polypectomy, and thus the need for further resection.

Often times a malignant polyp will have more than one risk factor for lymph node metastasis and/or recurrence. In addition to depth of invasion and endoscopic resection margin, several studies have shown that tumor differentiation, lymphovascular invasion (LVI), actual measurement of depth of submucosal invasion, and tumor budding each represent individual risk factors for residual disease after polypectomy.¹⁸ How these factors combine to create a cumulative risk of residual disease is still relatively unknown as each factor carries with it variable risk. It is generally accepted that high-risk polyps constitute those characterized by poor differentiation, the presence of LVI and deep submucosal invasion.

Endoscopic techniques such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) were introduced to allow for en bloc polyp resections and overcome the consequences of piecemeal polypectomy. However, for polyps ≥ 2 cm, EMR may be inadequate and result in piecemeal dissection and recurrence rates of up to 11%.^{18,19} ESD poses a technical challenge and is time consuming with a

steep learning curve resulting in decreased integration into practice. For this reason, there has been an ever increasing role for TAE in the management of advanced rectal polyps. Compared with endoscopic polypectomy, this technique allows for the full thickness polyp excision with ≥ 1 cm margins and avoids piecemeal polypectomy and its' consequences related to staging, prognosis, and recurrence. Accordingly, it provides a more complete assessment of histologic and pathological risk of residual disease, which can aid in future surgical decision making and provide a cure for benign polyps as well as some low-risk malignant polyps (well-to-moderately differentiated, absence of LVI, and no tumor budding or deep submucosal invasion).²⁰ Indeed, a recent meta-analysis comparing ESD with TEM for large rectal polyps demonstrated an increased R0 resection rate with TEM versus ESD (88.5 vs. 74.6%, $p < 0.001$) without a difference in complication rates.²¹ However, there is no randomized controlled trial to date comparing ESD with TEM.

Surgical Considerations for Malignant Rectal Polyps

While the endoscopic and surgical approaches for malignant rectal polyps and cancer have evolved over the last several decades, the most aggressive management of rectal cancer remains radical surgical resection with TME. This approach allows for complete removal of the tumor and draining lymph node basin thus allowing complete resection and accurate pathological staging. Surgical resection with TME for early-stage rectal cancer is associated with an 87% 5-year survival, but also carries a 2 to 3% mortality rate and 20 to 30% risk of morbidity.²² Conversely, complications from local TAE are considerably less. The low risk of morbidity and mortality combined with improvements in TAE techniques such as TEM and transanal minimally invasive surgery (TAMIS) have resulted in increased interest in local excision for early-stage rectal cancer.

Proponents of local excision for early-stage rectal cancer quote decreased invasiveness without the morbidity of TME, including the ability to avoid a stoma and the risk of anastomotic leak and sepsis. The basic principle of the TEM and TAMIS remains to obtain a full-thickness excision

with ≥ 1 cm margins; however, when compared with traditional TAE, both technologies allow for enhanced visualization and more precise dissection while also allowing for additional reach to higher rectal polyps up to 15 cm from the anal verge. This was demonstrated in a retrospective study out of the University of Minnesota comparing outcomes between TAE and TEM of early-stage rectal cancers (T_1 or T_2). In this study, they found that negative resection margins were better with TEM versus TAE (98 vs. 84%, $p = 0.017$).²³ Additionally, they found that tumor factors such as T stage and distance from anal verge were independent risk factors for local recurrence (LR) and disease free survival (DFS). However, determining who is a candidate for local excision remains challenging, as there are no universally accepted guidelines. Current NCCN guidelines state that local excision should be reserved for patients with favorable tumors (i.e., < 3 cm in size, T_1 , grade I/II [well- or moderate-differentiation], no LVI and negative margins).³ Further studies suggest that favorable tumors for local excision also include those without a mucinous component and mobile lesions that comprise $< 1/3$ circumference of the rectal wall. Additionally, only lesions with Sm1 and Sm2 level of submucosal invasion should be considered for local resection since deep (Sm3) invasion is associated with a 20 to 30% risk of lymph node metastasis (see ►Table 1).²²

Preoperative staging along with a detailed histological examination is important to guide treatment recommendations for invasive cancers in a rectal polyp. Imaging for potential metastatic disease (usually computed tomography of the chest, abdomen, and pelvis) as well as full colonoscopic examination, history and physical examination, and appropriate laboratory evaluation, as with more advanced cancers, may be required to fully evaluate the extent of disease. The locoregional staging of a biopsy-proven rectal cancer is generally performed with either endorectal ultrasound or high-resolution pelvic magnetic resonance imaging. Conversely, it can be very difficult to assess the T and N stage of a malignant polyp that has already been endoscopically excised. Differentiating between T_1 and T_2 cancers is difficult in all patients, and is often impossible in patients who have already had endoscopic resections. Additionally, local tissue inflammation

Table 1 Tumor characteristics for local excision of rectal cancer

Characteristics	Favorable	Unfavorable
Differentiation	Well-to-moderately differentiated	Poorly differentiated
Depth of invasion (T_1 tumors)	Sm1 or Sm2	Sm3
Size	< 3 cm $< 30\%$ circumference of rectal wall	> 3 cm $> 30\%$ circumference of rectal wall
Mucinous component	Absent	Present
Lymphovascular invasion	Absent	Present
Perineural invasion	Absent	Present
Tumor budding	Absent	Present

Abbreviations: Sm1, submucosal invasion into upper third of the submucosa; Sm2, submucosal invasion into middle third of the submucosa; Sm3, submucosal invasion into lower third of the submucosa.

after endoscopic resection can contribute to the identification of false-positive nodal disease.

Ultimately, the concern with local excision of early rectal cancer is the risk of oncologic inadequacy in the pursuit of a treatment with decreased morbidity and mortality. Indeed, initial retrospective data examining the results with TAE demonstrated higher LR rates of approximately 18% for T₁ tumors and 30% for T₂ tumors.^{24,25} This was compared with the accepted standard of approximately 8% LR after TME. One of the first and largest studies comparing TAE with TME from You et al, studied over 35,000 patients in the National Cancer Database to determine oncologic outcomes between the two surgical techniques.²⁶ They found a lower 30-day morbidity with local excision (5.6%) versus surgical resection (14.6%, $p < 0.001$); however, local excision failed to achieve an R0 resection in 4.5% compared with 0.81% in those who underwent TME ($p < 0.001$). This subsequently corresponded to a higher LR rate and decreased DFS but did not translate into a difference in overall survival at 8 years for T₁ lesions. More long-term data are now emerging with a recent retrospective study demonstrating an overall LR rate of 18% at 10 years in T₁ lesions previously resected with local excision.²⁷ Risk factors for LR include Sm3 depth of invasion, presence of LVI, and a positive resection margin. The data regarding TEM proves more promising with data from a randomized controlled trial comparing TEM with TME for T₁ lesions showing no difference in LR or survival at 5 years, suggesting good oncologic outcomes using TEM for early-invasive cancers.²⁸ In fact, with careful selection of low risk T₁ tumors, local excision with TEM, and an R0 resection results in similar LR rates as conventional surgical resection.²⁹ However, despite increasing data regarding local excision of early rectal cancer, data remain variable as most reports are single institution with heterogeneous groups of various T stages, histologic factors, and/or additional therapeutic measures which again reinforce the need for more standardized patient selection parameters.

In an effort to improve local control and disease recurrence after local excision as well as expand patient selection to those with T₂ tumors, research has explored the strategy of local excision following neoadjuvant therapy. In 2008, Lezoche et al published their 5-year follow-up data from their randomized controlled trial comparing local excision with TEM to surgical TME of T₂ lesions with favorable histology treated with neoadjuvant chemoradiation.³⁰ Their data showed no difference in morbidity or mortality and demonstrated similar short- and long-term oncologic outcomes at 84 months after local excision compared with radical surgical resection. Subsequent meta-analysis and review of T₂ tumors undergoing local excision after neoadjuvant therapy confirm these data.²⁹ While these data suggest acceptable outcomes for local excision of T₂ lesions after neoadjuvant therapy, the addition of neoadjuvant therapy before local excision comes at a price. Data suggest that the addition of neoadjuvant chemoradiation before local excision increases morbidity anywhere from 10 to 60%, with bleeding and wound dehiscence being the most frequent complications.^{31,32}

Interestingly, the data by Lezoche et al also found that 32% of patients in the TEM group and 29% of patients in the radical

resection group experienced a complete pathological response following neoadjuvant therapy (ypCR). They noted that none of the patients with ypCR experienced a recurrence and failures, either local or systemic, were in patients that did not respond to radiotherapy. This is similar to data from the ACOSOG-z6041 trial, which reported an approximately 40% ypCR on their 3-year follow-up of patients with T₂N₀ lesions who underwent chemoradiation followed by TEM.³³ This suggests that the risk of LR strictly correlates with postneoadjuvant pathological staging and that there may be a role for TEM as an appropriate alternative treatment to TME in those with a ypCR following neoadjuvant chemoradiation therapy. However, most studies reporting on TEM after ypCR are small, single institution retrospective studies with varying treatment regimens and the inclusion of heterogeneous pathological populations. Concern also still remains regarding the ability to accurately stage rectal cancers, both pre- and postneoadjuvant therapy, especially relating to lymph node involvement as well as correlating clinical response with pathological response. Thus, conclusions on the role of local excision after neoadjuvant chemoradiation therapy, regardless of ypCR, remains debated and TME remains the standard of care.

Surgical Salvage after Local Excision

Due to concern of local recurrence after local excision for early rectal cancer as well as its impact on long-term oncologic outcomes, several studies have looked at the role of surgical salvage after local excision. Early data from Weiser et al, reported that LR after local excision is often quite significant, even if an initial early stage, requiring extensive pelvic resection, and resulting in the survival of only approximately 50% at 5 years.³⁴ This is compared with an over 90% survival rate at 5 years after upfront surgical resection. More recent data out of the Mayo clinic also confirm that surgical salvage for recurrence after local excision of rectal cancer is associated with only modest success.³⁵ They show that surgical salvage is associated with only a 50% overall survival and 47% DFS at 5 years, despite an R0 resection at the time of recurrence. Unfortunately, specific pathological features of the local excision specimens were not available for all of the patients in their study. This is important as it is thought that LR of early rectal cancer after local excision is primarily associated with unfavorable pathological features. Concordantly, data show that when radical surgery is performed immediately after local excision of rectal cancer found to have pathological high risk features, outcomes such as DFS and overall survival are not compromised.^{29,36,37} In a study out of Mayo Clinic, 52 patients who underwent local excision had immediate radical surgery due to poor pathological features found on local excision. These patients were compared with case-matched controls treated by primary radical surgical resection. Of the 52 patients who underwent immediate radical surgery after local excision, they found that nodal disease was common, found in 21% in T₁ lesions. After a median follow-up of 10 years, overall and cancer-free survival were comparable without a statistically significant difference.³⁶ This and other studies suggest that adverse pathological features compromise local control and

survival after local excision. Thus, in circumstances where local excision using TEM or TAMIS results in a specimen with high-risk features such as a deep submucosal invasion (Sm3), positive LVI or perineural invasion, poor differentiation or positive margins, the local excision acts as an excisional biopsy and should be followed by immediate surgery instead of postponing surgery until the time of LR.

Surveillance of Rectal Polyps

Postpolypectomy surveillance is a large part of any endoscopic practice. Despite data from the National Polyp Study demonstrating that postpolypectomy surveillance can be deferred for at least 3 years, surveys suggest that many endoscopists choose shorter intervals for surveillance.³⁸ For benign rectal polyps, postpolypectomy surveillance follows that of the colon (as described in "Colonic Polyps: Diagnosis and Surveillance" by Drs Bohl and Huck, on pp. 296–305) such that people at high risk, those with three or more adenomas, an adenoma > 1 cm in size or with high-risk features, such as high-grade dysplasia or villous architecture, undergo repeat colonoscopy at 3 years.³⁹ Those at low risk with only one to two small, < 1 cm adenomas without high-grade features can have a repeat surveillance colonoscopy within 5 to 10 years. For those who have undergone radical surgical resection of a rectal cancer by TME, endoscopy should be performed 1 year after the surgery and then every 3 years to detect and remove new adenomas and exclude metachronous cancers. These patients should also undergo a complete history and physical examinations with a carcinoembryonic antigen (CEA) level every 3 months for the first 2 years, then every 6 months for the next 3 years.³

There are currently no standardized guidelines for surveillance after local excision of early rectal cancer. Due to the potentially high local recurrence rates seen with local excision, it seems logical that if recurrent disease is detected early, outcomes may be better. Most data regarding surveillance after local excision have been extrapolated from data that have been published as part of studies looking at LR and long-term outcomes after local excision. Most of these articles follow guidelines as above for surveillance of rectal cancer; however, they add an evaluation of the local excision site to detect any mucosal recurrence. It is the practice of the authors to evaluate the TEM site via digital rectal examination and proctoscopy every 3 months for the first 2 years followed by every 6 months for the following 3 years. This is in addition to routine CEA testing and full colonoscopic surveillance.

Conclusions

Rectal polyps present a unique challenge to the gastroenterologist and surgeon. Advances in TAE techniques (TEM and TAMIS) to remove polyps and obtain appropriate en bloc resection specimens allow for a more thorough and complete pathological evaluation. While the gold standard for rectal cancer remains surgical resection with TME, advances in local excision for early rectal cancer have changed the historical paradigm of rectal cancer treatment. However, strict patient selection is required

and extensive discussions must be had with the patient regarding risk of local recurrence if local excision is to be pursued.

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