

# Surgical Management of Nonpolypoid Colorectal Lesions and Strictures in Colonic Inflammatory Bowel Disease



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## KEYWORDS

- Colorectal cancer • Inflammatory bowel disease • Dysplasia
- Nonpolypoid colorectal neoplasm • Stricture • Ulcerative colitis • Crohn's disease

## KEY POINTS

- Patients with inflammatory bowel disease and dysplasia have pathologic characteristics and risks that differ from those of patients with sporadic carcinomas.
- Surgical interventions need to be more aggressive than in sporadic cases.
- An algorithm for management strategies for lesions and strictures in Crohn's disease and ulcerative colitis needs to be developed.
- A better understanding of the risks and benefits of surgical procedures for dysplasia in Crohn's disease and ulcerative colitis is required.

## BACKGROUND

Colorectal cancer (CRC) arising in inflammatory bowel disease (IBD) accounts for only 1% to 2% of all general CRC cases per year. However, as CRC results in 15% of all IBD deaths, cancer screening requires special vigilance in this group. Particularly concerning is the fact that cancers in patients with ulcerative colitis and Crohn's disease often present not as mass lesions but as dysplasia, strictures, or diffuse dysplasia.

The risk of CRC in ulcerative colitis (UC) has been well studied. Most reliable risk factors associated with an increased risk of CRC in UC are related to the extent and duration of the disease. The risk for CRC development is lower before 8 to 10 years after onset of symptoms (3%); however, thereafter the risk increases by approximately

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Relationships: None.

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1% per year. Various studies have shown risks of CRC in UC ranging from 5% to 20% at 20 years of the disease.<sup>1-3</sup> By the fourth decade of UC disease, the risk of developing CRC is as high as 56 times higher than that of the general population.<sup>4</sup> In 2012, a large Danish population-based study demonstrated decreasing rates of CRC in UC over the last 30 years. This decrease is due possibly to the improved medical treatment of the disease in addition to surveillance of dysplasia.<sup>5</sup>

The rates of CRC in Crohn's disease seem to mirror those of UC.<sup>6,7</sup> Crohn's patients have a 5- to 20-fold increase in risk for CRC in comparison with the general population.<sup>7,8</sup> The absolute cumulative frequencies of CRC after 20 years of disease in both UC and Crohn's disease are similar at 8% and 7%, respectively.<sup>9</sup> Because of this similarity, despite the publication of fewer data regarding CRC in Crohn's disease, guidelines and recommendations have been developed for Crohn's patients extrapolating from the body of evidence on UC.

### DYSPLASIA AS A PREDICTOR

The mutation pathway to CRC in IBD is postulated to be distinct from the adenoma-carcinoma sequence seen in sporadic colon cancers. Duration and extent of disease are both associated with higher rates of dysplasia and malignancy. IBD-associated cancer often develops in younger patients, and is more likely to be diffuse, extensive, multifocal, and mucinous, compared with the population with sporadic colorectal cancer.<sup>10-12</sup> Cancer in Crohn's disease is more likely to be right-sided and associated with ileal/right-sided inflammation.<sup>9</sup>

Furthermore, IBD patients with colon cancer have historically been shown to have synchronous dysplasia at distant sites from the cancer, suggesting the potential for a field defect rather than an isolated mutation. A review from more than 2 decades ago that included 10 prospective studies with a total of 1225 UC patients demonstrated cancer in 43% of patients with biopsy-proven high-grade dysplasia (HGD). Nineteen percent of patients with low-grade dysplasia (LGD) also had a coexistent cancer.<sup>13</sup> Dysplasia distant to the primary carcinoma has also been shown in 23% to 70% of patients with Crohn's disease.<sup>8</sup> Indeed, the reported risks of synchronous lesions have been variable, as high as 71% for synchronous dysplasia and ranging from 17% to 43% for synchronous cancers.<sup>13-19</sup>

Interpretation of the data on synchronous cancers should, however, be made with caution, owing to the significant limitations during that era in the sensitivity of the fiberoptic technology in detecting dysplasia or cancer at index colonoscopy. Furthermore, surveillance of patients with dysplasia was not standardized (eg, performed without chromoendoscopy or image enhancement at various intervals, or in the endoscopic removal techniques). The true incidence of synchronous colorectal cancer in the setting of dysplasia, as well as the true natural history of endoscopically invisible dysplasia, is thus not known.

For high-risk patients the decision regarding whether to proceed with colectomy or local endoscopic removal with continued colonoscopic surveillance is unquestionably complex, and requires a multidisciplinary approach.

### DYSPLASIA MANAGEMENT

#### *Endoscopically Visible Dysplasia*

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Nowadays most IBD-related dysplasia visible, following the advancements of endoscopic imaging and techniques and a deeper understanding of its appearance, and can be removed endoscopically. Furthermore, terminology for neoplasia in IBD is now being standardized to be similar to neoplasia not related to IBD (ie, polypoid

and nonpolypoid for shape; and endoscopically resectable and endoscopically nonresectable for management). Historical terms such as adenoma-like dysplasia-associated lesion or mass (DALM) and non-adenoma-like DALM, or flat dysplasia, are being abandoned because they are regarded as confusing, and conceived when dysplasia was largely thought to be invisible during an era of lower-quality endoscopic imaging and interpretation.

In fact, longitudinal studies show that isolated adenomatous polyps may be safely removed endoscopically with close follow-up, analogous to sporadic adenoma removal in the absence of colitis. Such adenomatous polyps treated with endoscopic resection alone have been found to have no increased risk for cancer, as long as there is no evidence of dysplasia in the mucosa surrounding the polyp or elsewhere in the colon.<sup>20–22</sup> Numerous biopsies of the region surrounding the area of concern are recommended in evaluating for dysplasia. If these biopsies are positive for dysplasia, local or endoscopic resection is not recommended. A lesion that occurs proximally to known areas of colitis without surrounding inflammation can be considered as sporadic adenoma, and treated endoscopically.

### ***Endoscopically Invisible or Nonresectable Dysplasia***

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Close involvement of the surgeon, gastroenterologist and pathologist in evaluating dysplasia allows for the best management choices and optimal outcomes. This section focuses on the surgical management of endoscopically invisible or nonresectable dysplasia.

First, it is recommended that a diagnosis of dysplasia (LGD or HGD) be independently confirmed by 2 experienced gastrointestinal pathologists. Controversy continues regarding the management of LGD, owing to the variation in reported rates of progression from LGD to HGD or cancer.<sup>23</sup> Patients confirmed to have endoscopically invisible multifocal LGD or repetitive endoscopically invisible unifocal LGD following evaluation by an expert endoscopist using chromoendoscopy should be counseled and given a strong recommendation for total proctocolectomy.<sup>24</sup> A decision analysis for endoscopically invisible unifocal LGD compared cost-effectiveness of enhanced surveillance with immediate colectomy, and found that immediate colectomy was associated with higher quality-adjusted life years and lower costs.<sup>24</sup> Nonetheless, patients with endoscopically invisible unifocal LGD on surveillance colonoscopy who do not wish to undergo an operation should have the area tattooed, repeat surveillance colonoscopy with chromoendoscopy performed at 3, 6, and 12 months with local and distant biopsies, and then annually.

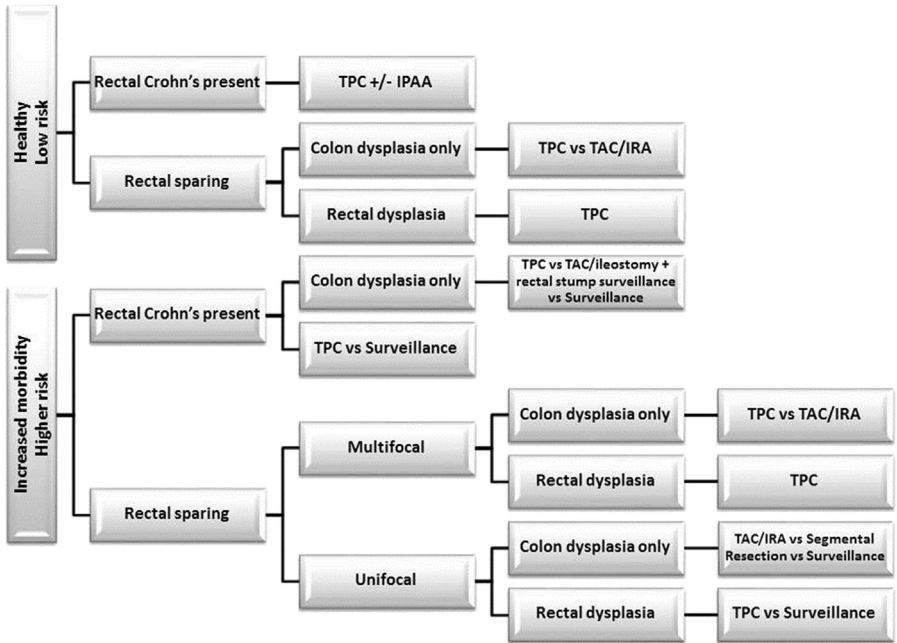
Before surgical intervention, any patient with a known dysplastic or cancerous lesions should undergo complete colonoscopy surveillance with chromoendoscopy, which allows for best evaluation of where dysplasia may exist. If dysplasia remains endoscopically invisible, a minimum of 3 biopsies every 10 cm is standard; in addition, biopsies of the rectum and anal transition zone should be performed to rule out dysplasia. Multiple biopsies should be performed in any transition zone where an anastomosis may be considered. Surgical options will be based on these findings.

### ***Surgical Options for Resection***

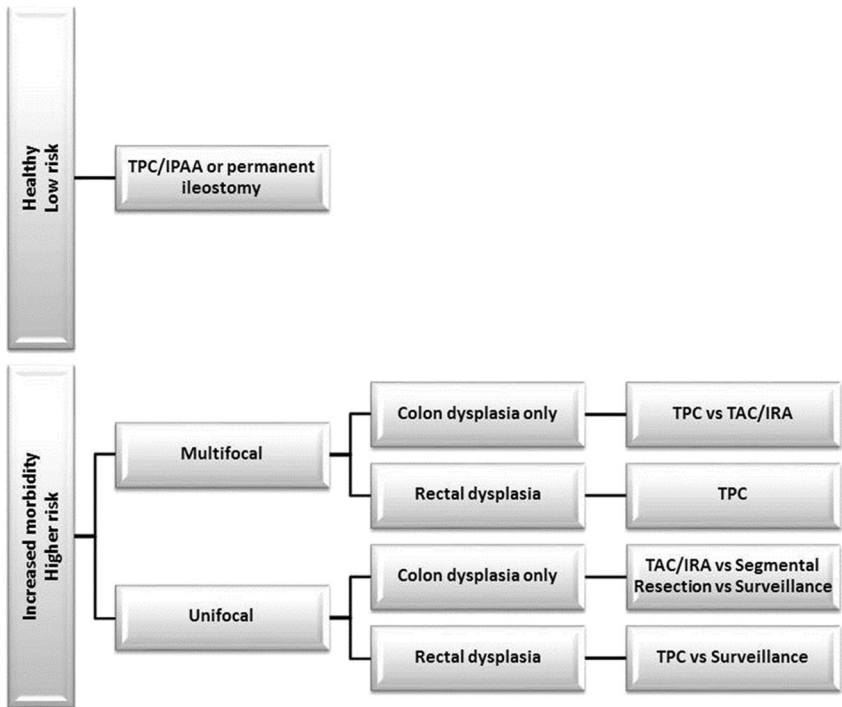
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Risks of recurrence of disease or findings of synchronous disease must be weighed against the morbidity of surgical resection. Recommendations are generally varied for Crohn's disease and UC, and also vary based on type of dysplasia, morbidities, and patient factors (Figs. 1 and 2).

Initial evaluation of patients includes assessment of overall medical stability, fitness for surgery, and current function. Decisions for surgery must be based on the patient's



**Fig. 1.** Surgical options for ulcerative colitis with dysplasia found on colonoscopy. IPAA, ileal pouch anal anastomosis; IRA, ileorectal anastomosis; TAC, total abdominal colectomy; TPC, total proctocolectomy.



**Fig. 2.** Surgical options for Crohn's colitis with dysplasia found on colonoscopy.

ability to undergo surgery; in some cases suboptimal procedures will be performed secondary to limited preoperative life expectancy and anticipated comorbidities from undergoing surgery. In addition, assessment of preoperative defecatory dysfunction including incidents of fecal incontinence should be evaluated. Patients with severe preoperative incontinence and difficulty with mobility may benefit most from resection with creation of stomas for functional reasons. Overall goals should be preservation of the quality of life combined with appropriate oncologic resection.

The gold standard for patients from an oncologic perspective is total proctocolectomy with perineal resection and end ileostomy. All colonic mucosa is removed, up to and including mucosa at the anorectal junction, therefore virtually eliminating the risk of colonic metaplasia and advancement to cancer. This result must be weighed against the patient's desire for intestinal continuity. Most patients would prefer to have intestinal continuity, and complete removal of the rectoanal junction would leave them with a permanent colostomy. In addition, though eliminating the risk of concurrent or future colon cancer, in patients with isolated disease or with sporadic adenoma this may not be necessary from an oncologic perspective.

For patients with UC a total proctocolectomy with ileal pouch anal anastomosis is a possibility. This operation removes the colon and colonic mucosa except a small margin at the anorectal junction, and allows for replacement of the rectum with an ileal pouch. The pouch serves as a reservoir to store stool and decrease frequency of defecation for patients. The disadvantages of this procedure include a small risk of recurrence within the rectal mucosa at the margin of the pouch, necessitating regular surveillance; and complication rates of the surgery, which are often 15% or greater and include risk of reoperation, incontinence, decreased fertility, and sexual dysfunction.<sup>25</sup> Some patients with isolated Crohn's colitis and no signs of small intestine or perianal disease may also be appropriate for total proctocolectomy with ileal pouch anal anastomosis. These patients are at higher risk of pouch complications such as fistulization, recurrence of pouch inflammation (pouchitis), and pouch failure. To consider this procedure, patients must have good sphincter function at baseline, be surgically fit, and not have signs of low rectal or anal dysplasia on screening biopsies. If HGD is found in the rectum during colonoscopy, reconstruction with ileal pouch anal anastomosis should be delayed to avoid the risk of radiation to the pouch if synchronous advanced carcinoma is found within the rectum after surgical resection. Risks of cancer in the retained rectal mucosa are generally low, reported as less than 5% at 25 years.<sup>26,27</sup> A mucosectomy, or removal of the rectal mucosa down to the anorectal ring, may be performed, but continence may be compromised in this case. In general, patients are expected to have 4 to 6 bowel movements daily, and some soilage or nighttime incontinence is not uncommon.

For patients with diffuse colonic disease but without rectal involvement, it may also be possible to consider a total abdominal colectomy with ileal rectal anastomosis. Advantages of this operation generally include preserved rectal and sexual function. The operation itself is shorter and less extensive. However, this operation does not treat dysplasia or inflammatory disease within the rectum. This area will require continued surveillance, and in patients with both Crohn's disease and UC the rates of recurrence of inflammatory disease in the rectum are as high as 60%.<sup>28</sup> This operation is contraindicated in patients with rectal or anal lesions, and considered as very high risk for patients with multifocal dysplasia. Other contraindications include patients with baseline fecal incontinence or severe rectal inflammation.

For patients who are not fit for anastomosis, or reconnection, a total abdominal colectomy with Hartmann procedure may be performed. This operation leaves the remnant rectum in place during the operation, and an end ileostomy is performed.

Advantages of this surgery include decreased time and morbidity by leaving the rectum in situ. However, risks include inflammation and risk of dysplasia within the rectum, and continued surveillance is necessary.

In isolated inflammatory and dysplastic disease, or in cases of a sporadic adenoma, the most appropriate operation may be a segmental colectomy. Benefits of this operation include shorter operative times, maintenance of key portions of the colon, including possibly the ileocecal valve which may functionally decrease risks of diarrhea, and the greater part of the colon for fluid absorption. This option is restricted to patients with isolated dysplasia and those with relatively normal mucosa in terms of inflammation; surgical anastomosis necessitates functional mucosa for creation of a colon anastomosis. Patients who undergo this option must be committed to continued colonoscopic surveillance to evaluate for metachronous lesions and the risk of continued progression of inflammatory disease. Data demonstrate that up to 40% of patients with Crohn's disease will require additional colectomy at 10 years for recurrence of inflammation after segmental colectomy.<sup>29,30</sup>

All resections, whether segmental or complete proctocolectomies, should follow the principles of surgical oncology. A full lymphadenectomy and vessel resection with high ligation should be completed. Current data recommend resection of a minimum of 12 lymph nodes for segmental colectomy to ensure appropriate staging of tumors.<sup>31</sup>

In addition, good data also exist to affirm that the use of laparoscopic or minimally invasive surgery is beneficial for patients.<sup>32</sup> All of the aforementioned procedures can be performed laparoscopically in experienced hands. Contraindications to laparoscopic surgery are few and decreasing in number, but may include extensive prior adhesions, bulky mesentery, and extraluminal invasion. Benefits of laparoscopy include decreased postoperative pain and quicker return to function; moreover, laparoscopy may allow appropriate patients earlier access to definitive medical oncology treatments.

## STRICTURES

The repeated cycle of inflammation, necrosis, and ulceration, alternating with the deposition of granulation tissue during the healing phase, results in the development of raised areas of inflamed tissue that resemble polyps, called pseudopolyps, or may result in stricture formation. Such sequelae make endoscopic surveillance of dysplasia and cancer, and its management, a challenge.

Colonic strictures are more common in Crohn's disease than in UC. Colonic strictures reportedly are found in 5% to 17% of patients with Crohn's colitis.<sup>10</sup> Although data are lacking, colonic strictures have been reported in approximately 5% of UC patients. Rates of stricture occurrence seem to be improving as medical treatments allow more patients to achieve remission. Colonic strictures in any setting should be considered malignant until proven otherwise. Gumaste and colleagues<sup>33</sup> evaluated the Mount Sinai Hospital (New York) population of UC patients with strictures, and found 29% to be malignant. In Crohn's disease, despite a higher rate of stricture occurrence, the rate of malignant colorectal strictures was only 6.8%.<sup>34</sup> There is no role for stricturoplasty in the primary management of colonic strictures in IBD. Strictures found at prior anastomotic sites in Crohn's disease may be judiciously dilated to allow for endoscopic evaluation of recurrence or technical problems from the original resection. Dysplasia and carcinoma at colonic strictures cannot always be detected preoperatively.<sup>35</sup> The stricture must be able to be traversed, adequately examined, and biopsied. Even then, the risk of sampling error in a stricture can be high; a biopsied portion may demonstrate inflammation and fail to show deeper

malignancy. If malignancy cannot be excluded, oncologic resection is indicated. In UC, proctocolectomy is the only means to definitively diagnose or rule out carcinoma and to treat possible multifocal malignancy, and should be considered in the management of colonic UC stricture. Unlike UC, a segmental oncologic resection may be appropriate in Crohn's disease colorectal stricture in a patient with limited segmental disease.

## SUMMARY

Identification and treatment of dysplasia and colorectal cancer in IBD creates management challenges for the clinician. Treatment options for patients must be based on the understanding of differences in virulence between sporadic adenomas and inflammatory related dysplasia in patients with IBD. Surgical interventions should be based on patient morbidities, location and type of inflammation, and, most importantly, findings of dysplasia. Although the gold standard for oncologic resection is total proctocolectomy, many appropriate options exist that allow for intestinal continuity.

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