Endoscopic Management of Colon and Rectal Cancer

WILLIAM R. BRUGGE, MD

Colorectal cancer is an important problem in the United States, with over 130,000 new cases and 55,000 deaths each year. There is strong evidence that screening for colorectal cancer can decrease mortality and incidence of colorectal cancer. Published guidelines recommend that all asymptomatic, average-risk U.S. citizens more than 50 years of age should be encouraged to undergo screening for colorectal cancer. Those at higher risk should be offered more intensive screening and follow-up surveillance. It is estimated that widespread adoption of these recommendations could reduce mortality from colorectal cancer by more than 50 percent. Successful screening and prevention of colon cancer are increasingly being realized through the use of colonoscopy and associated endoscopic procedures.

DIAGNOSTIC TESTS FOR COLON CANCER AND POLYPS

Colonoscopy is the primary diagnostic test for detecting colorectal cancer and its precursors. Current endoscopic techniques provide high-quality digital images of the entire colon using flexible colonoscopes that are capable of diagnosing and removing malignant and premalignant lesions of the colon. The examinations are often performed in the outpatient setting by gastroenterologists or surgeons, and the procedure usually requires 30 to 60 minutes. Patients are prepared with a colonic purge using polyethylene glycol or sodium phosphates.1 Nursing staff assist by providing anesthesia, patient monitoring, and therapeutic procedures. Intravenous sedation and analgesia are often provided to the patients to improve tolerance.2

Colonoscopy is a highly accurate test for detecting and diagnosing colon cancer whether it is performed as a screening or diagnostic test. In a large retrospective series, colonoscopy had an overall sensitivity of 95 percent for detecting colon cancer.3 The test, however, is dependent on the expertise and training of the endoscopist. When gastroenterologists perform the examination, the sensitivity is 97 percent, compared to 87 percent when practitioners who are not gastroenterologists perform the examination. The most common cause of a missed diagnosis of colon cancer is an incomplete examination of the colon. The miss rates for polyps are higher, particularly for small polyps, and are also dependent on the expertise and training of the endoscopist.4

The complications of colonoscopy may be related to the discomfort of the procedure, perforations, or bleeding after polypectomy. The discomfort associated with colonoscopy is variable in intensity and frequency and, in select patients, little or no sedation or analgesia is required.5 Pelvic adhesions, sigmoid diverticular disease, and a younger age increase the risks of pain associated with colonoscopy. Serious complications consist of bleeding or perforation and occur in less than 0.2 percent of patients.2 There are, however, no recent large series assessing the risks of colonoscopy using current technology. Bleeding may be noted in up to 2 percent of patients but requires admission or transfusion in less than 0.5 percent of patients.6 Perforations during diagnostic colonoscopy are most commonly located in the sigmoid colon and usually consist of lacerations that require surgical repair.7 Small perforations as a result of polyp removal may be managed surgically or medically.
Flexible sigmoidoscopy uses a small diameter fiberoptic or video scope, similar to colonoscopes, but the examination is limited to the left colon and often to the sigmoid colon. Flexible sigmoidoscopy may be performed by a wide range of health care providers using less expensive equipment. Although the preparation for sigmoidoscopy is similar to colonoscopy, the procedure is quite different. Since the examination lasts only a few minutes and there is much less discomfort, intravenous sedation is rarely used. Without the need for intravenous sedation, there is little need for nursing assistance, and the cost is considerably less. Although polyps may be removed during flexible sigmoidoscopy, this should be done only after the entire colon has been examined by colonoscopy.

Barium enemas can also be used as a screening test or, more commonly, as a diagnostic test. In the past, barium enemas were more often employed than colonoscopy in the diagnostic evaluation of colon cancer. Barium enemas are not, however, as sensitive as colonoscopy for the detection of colon cancer. The use of double-contrast barium enemas will improve the diagnostic rate only slightly, from 82 to 85 percent. The cancers found by barium enemas are larger and more advanced than the cancers diagnosed with colonoscopy. When an abnormality is seen on barium enema, colonoscopy is often used to diagnose or remove the lesion.

**DIAGNOSTIC FINDINGS ON COLONOSCOPY**

There is a wide range of endoscopic findings that diagnose colon cancer with colonoscopy (Figure 6–1). The most common lesion is a large, irregular mucosal mass that may obstruct the lumen of the colon. This endoscopic finding is nearly always diagnostic of colon cancer. In this setting, endoscopic biopsies are superfluous, but often done to provide a conclusive tissue diagnosis. Other endoscopic findings that suggest a malignancy are large irregular polyps, villous lesions, and small flat-mass lesions.

Adenomas are the most common premalignant finding encountered during colonoscopy. Adenomas range in size from 2 mm to several centimeters and, when they appear on a stalk, they are referred to as pedunculated polyps (Figure 6–2). They are readily removed during colonoscopy using cautery applied through a snare. Polypectomy is performed for two reasons, for diagnostic purposes and for the prevention of malignant transformation of a polyp. The ability of colonoscopy to detect adenomas is dependent on the size of the adenoma and colonoscopic techniques. The overall miss rate for detecting all adenomas is approximately 24 percent. For adenomas larger than 1 cm, the miss rate is less than 6 percent. The missed adenomas tend to be in the right colon where the accumulation of stool may obscure the presence of a polyp.

The origin of colon polyps is not well understood. Endoscopically, a precursor to the adenoma has been identified using magnifying endoscopy. Aberrant crypt foci are commonly seen in patients with adenomas, and the number of foci and dysplastic changes are more common in patients with colon cancer. Although clinical significance of aberrant crypt foci has not been determined, the number of aberrant crypts is reduced by the use of aspirin. The use of spray dyes on the colon mucosa during magnification colonoscopy may assist in the detection of small adenomas or flat cancers. This technique can also assist in making the diagnosis of polyposis syndromes because of the ability to visualize small mucosal polyps.

Small adenomas in the left colon may be an early indicator of colon cancer. Nearly one-third of patients with a left-sided small adenoma have a right-sided adenoma and 6 percent have a colon malignancy. The presence of a large adenoma in the left colon increases the risk of an adenoma on the right colon by 57 percent. The current recommendation is for all patients with the finding of a left-sided adenoma to undergo a colonoscopy. However, patients with a single diminutive adenoma less than 5 mm in the left colon rarely have a significant right-sided lesion. The risk of a right-sided lesion is increased by age, having more than one polyp, and a family history of colon cancer.

Malignant polyps are polyps resected with histologic evidence of malignancy within the polyp (Figure 6–3). Those with a favorable histology, grade I or II carcinoma with negative resection margins, have a good prognosis, and surgical resection is often not required. In contrast, patients with advanced malig-
nant polyps should undergo surgical resection (Figure 6–4). Some of the criteria used to predict residual malignancy include high-grade adenocarcinoma, lymphatic invasion, or stalk invasion. As many as 42 percent of patients with advanced malignant polyps will have evidence of metastases, will have residual malignancy at the resection site, or will develop recurrent malignancy.

Large, flat, villous tumors are a challenge to the endoscopist. Endoscopically, they are seen as a carpet-like lesion often covering a large surface area. They are difficult to remove endoscopically, and superficial biopsies may miss areas of malignancy. The risk of malignancy is between 2 and 50 percent in these types of polyps and, despite numerous biopsies, documentation of malignancy may not be possible; therefore, surgical or aggressive endoscopic excision is often recommended for apparently benign villous adenomas.

Hyperplastic polyps are small benign polypoid lesions that are commonly encountered in the rectum (Figure 6–5). They rarely grow larger than 5 mm in diameter or cause bleeding. Because there is essentially no potential for malignant degeneration, they are often not removed except for diagnostic purposes. It is difficult to accurately differentiate between adenomas and hyperplastic polyps based on the endoscopic appearance. The confusion between

Figure 6–1. Colonoscopic examples of colon cancers. A, Early but invasive colon cancer. B, Colon cancer invading the wall of the colon. C, Flat colon cancer involving half of the circumference of colon lumen. D, Circumference colon cancer.
Figure 6–2. Pedunculated adenomatous polyp. A, Colonoscopic view of a 1-cm adenoma with a stalk. B, Placement of a snare for polyp resection. C, Polypectomy site.

Figure 6–3. Examples of malignant polyps. A, Malignant sessile polyp that could not be resected endoscopically. B, Small adenoma that when resected contained carcinoma in situ in the short stalk. C, Malignant pedunculated polyp without invasion of the stalk.
these types of polyps often requires biopsies or polyp removal, a time-consuming and costly requirement. Magnifying colonoscopy provides high-resolution images of polyps and their surface characteristics and may improve the ability to diagnose adenomas.20 Recently, fluorescence endoscopic imaging has been used in an attempt to differentiate between adenomas and hyperplastic polyps. The rate of decay of laser-induced autofluorescence can distinguish adenomas from nonadenomas.21 With the use of photosensitizers, 77 percent of hyperplastic polyps can be correctly differentiated from adenomas.22 More advanced imaging techniques have been reported to diagnose adenomas and detect dysplasia within a polyp.23 The presence of hyperplastic polyps in the rectum is not highly predictive of proximal adenomas and should not be the sole indication for colonoscopy.24,25 Biopsy of rectal polyps can differentiate between adenomas and hyperplastic polyps, and the finding of a rectal adenoma is a frequent basis for proceeding with colonoscopy.26 Although patients with hyperplastic polyps do not require colonoscopy, there are reports that patients with hyperplastic polyps are more likely to develop adenomas in the future.27

Flat adenomas are an unusual type of colonic tumor. These tumors are often small, flat, translucent, and not easily seen with traditional colonoscopy.28 Recently, the use of dye sprays in combination with high-resolution video endoscopy has enabled endoscopists to identify and diagnose these lesions. Although they were originally identified in Japan, they are more frequently being described in Western countries in association with hereditary nonpolyposis colon cancer.28 The risk of malignancy is propor-

Figure 6–4. Algorithm for polypectomy treatment decision criteria.

Figure 6–5. Hyperplastic polyp. A, Colonoscopic view of a small, smooth, hyperplastic polyp. B, Forceps biopsy of a hyperplastic polyp. C, Endoscopic removal is often achieved with forceps biopsy.
tional to the size of the polyp. Lesions greater than 1 cm have a 2 percent risk of adenocarcinoma while 12 percent have high-grade dysplasia. These polyps are commonly missed on routine examination. The finding of a central depression is associated with invasive malignancy.

Carcinoid tumors occur commonly in the rectum (Figure 6–6). They are usually small and smooth, and often are confused with adenomas. They are readily diagnosed with histology of the resected polyp. If the tumor is superficial and completely resected, the prognosis is very good.

**ENDOSCOPIC DETECTION OF COLON CANCER**

The endoscopic screening of large populations for colorectal cancers has traditionally been done with flexible sigmoidoscopy. The technique is widely available in the United States and is relatively simple and inexpensive. The examinations, however, are limited to the lower 30 cm of the colon in 33 percent of patients because of pain or difficulty in passage of the sigmoidoscope through the sigmoid colon. The examination may be performed by a physician or a trained nurse practitioner with similar miss rates for adenomas. This type of screening is limited by the concerns over undetected right-sided colon cancer. Although flexible sigmoidoscopy may be used in conjunction with stool occult blood testing, it should not be the sole test used to evaluate patients with occult bleeding.

Colonoscopy is often performed in patients who have been identified as being at high risk for development of colorectal cancer. Several risk factors have been identified, including family history, age, and a history of left-sided polyps. Left-sided polyps are often used as predictors of right-sided polyps. Hyperplastic polyps in the left colon are not highly predictive of adenomas or malignancies in the right colon. The use of a left-sided adenoma as a sign of right-sided cancer has recently been examined by Rex and colleagues. In patients with right-sided cancers, only 34 percent had left-sided lesions. In fact, only 25 percent had any adenomas. Other studies have also documented that a significant percentage of patients with proximal colon cancers have no left-sided sen-

![Figure 6–6. Rectal carcinoid. An example of a small rectal carcinoid.](image)
was compared to groups of patients not undergoing colonoscopic polypectomy. The frequency of colon cancer was reduced 88 to 90 percent through the use of colonoscopy and polypectomy. Compared to a general population of low-risk patients not undergoing colonoscopy, the rate of colon cancer was reduced by 76 percent. Similar reductions in the rate of colon cancer have been reported in the United States veteran population undergoing colonoscopies.\textsuperscript{44} In the United Kingdom, a threefold increase in the incidence of rectal cancer was observed in patients undergoing incomplete resection of rectal adenomas during rigid sigmoidoscopy compared to the general population.\textsuperscript{45} With widespread use of colonoscopy and polypectomy, rectal cancers have been diagnosed at an earlier stage in France, and there has been a dramatic improvement in the survival rate.\textsuperscript{46}

The effectiveness of colonoscopic surveillance in high-risk groups has been examined in several different populations. The effectiveness of surveillance colonoscopy in patients with hereditary polyposis was compared to prophylactic colectomy.\textsuperscript{47} In patients with hereditary nonpolyposis colorectal cancer (HNPCC), colonoscopy was found to increase life expectancy by 13.5 years using a decision analysis model. When quality of life measures were used, colonoscopy was found to offer the optimal approach to reducing the risk of malignancy in HNPCC. In addition, the use of colonoscopic surveillance was found to be cost effective in patients diagnosed with mutated mismatch repair gene associated with HNPCC.\textsuperscript{48} In patients at risk for familial adenomatous polyposis (FAP), decision analysis has demonstrated that sigmoidoscopy is more cost effective than genotyping for establishing a diagnosis if small numbers of high-risk family members are examined.\textsuperscript{49} Sigmoidoscopy is also the preferred technique for following patients with FAP in whom a subtotal colectomy has been performed.\textsuperscript{50} Similar findings of effectiveness for surveillance have also been demonstrated in high-risk patients with chronic ulcerative colitis.\textsuperscript{51} Adenomas detected in patients with ulcerative colitis can be resected endoscopically without fear of underlying malignancy.\textsuperscript{52} Malignancies found arising in the setting of colonoscopy tend to be smaller, less invasive, and associated with better survival than those patients not undergoing surveillance colonoscopy.\textsuperscript{53,54}

A family history of adenomas or cancer has recently been examined as a risk factor for colon cancer. The risk of cancer varies with the age of diagnosis in the relative. In a recent study, 12 percent of patients who had relatives with colon cancer had adenomas, 25 percent of which were proximal and not detectable with sigmoidoscopy.\textsuperscript{55} Colonoscopic surveillance in patients with a first-degree relative who has an adenoma has been retrospectively examined.\textsuperscript{56} The risk of colorectal cancer discovered during colonoscopy was 1.7 times that of patients without a family history of an adenoma. When a first-degree relative of less than 50 years had an adenoma, the relative risk was even greater, 4.3 times. For further discussion of colon and rectal cancer screening, refer to Chapter 4 “Colorectal Prevention and Early Detection.”

Iron deficiency anemia and occult bleeding are risk factors for colon cancer and should be evaluated with colonoscopy, particularly in elderly patients. In a recent series, 32 percent of patients were found to have a colonic lesion at the time of colonoscopy.\textsuperscript{57} In contrast, the yield of colonoscopy in premenopausal women with iron deficiency anemia and no evidence of chronic blood loss is very low.\textsuperscript{58}

The accuracy of colonoscopy for the detection of polyps has been examined using several techniques. Tandem colonoscopy, repeating colonoscopy immediately after an initial examination, will detect a significant number of polyps, although usually small. Follow-up colonoscopy by the same endoscopist or a different one will detect an additional 8 or 11 percent of polyps.\textsuperscript{4} Most of the polyps missed during colonoscopy are less than 1 cm in diameter and without evidence of malignancy.

The current recommendations of the American Cancer Society for screening in average-risk individuals is (1) fecal occult blood testing every year combined with flexible sigmoidoscopy every 5 years, (2) double-contrast barium enema every 5 to 10 years, or (3) colonoscopy every 10 years. A digital rectal examination should be performed at the same time as sigmoidoscopy, colonoscopy, or double-contrast barium enema. The recommendations for moderate- and high-risk patients are listed in Table 6–1.
STAGING OF COLON CANCER WITH ENDOSCOPIC TECHNIQUES

Endoscopic ultrasound probes can provide local tumor and nodal staging of rectal cancers\textsuperscript{59,60} (Figure 6–7). The technique is particularly effective for the staging of superficial malignancies where the accuracy rate is more than 90 percent.\textsuperscript{61–63} Advanced malignancies are staged with much lower accuracy rates. The sensitivity for detecting lymph node metastases is 85 percent, but compromised by a low specificity rate of 72 percent. Furthermore, the accuracy of endoscopic ultrasound staging (EUS) for accurately staging small (<5 mm) malignant nodes is poor.\textsuperscript{64} Rectal EUS has also been used to document the tumor response to neoadjuvant chemoradiation.\textsuperscript{65} Ultrasound staging can also be performed using laparoscopic ultrasound instruments, which determine the depth of invasion and the presence of lymph nodes in the peritoneal cavity.\textsuperscript{66}

In large comparative trials, EUS has produced staging accuracy rates that have surpassed CT scanning and magnetic resonance imaging (MRI) using rectal coils.\textsuperscript{67,68,69} Endoscopic ultrasound staging is also less expensive than MRI of rectal cancers.\textsuperscript{67} Lymph node staging was comparable with all techniques. EUS has many advantages, including ease of use, small diameter, and low cost. The use of EUS to improve the preoperative staging of rectal cancer will improve the selection of patients for sphincter preserving surgery.\textsuperscript{70}

Endoscopic ultrasound can also be used to determine the depth of malignant invasion of a malignant polyp after resection. This may be useful when

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<th>Table 6–1: AMERICAN CANCER SOCIETY RECOMMENDATIONS FOR COLON CANCER SCREENING IN MODERATE- AND HIGH-RISK PATIENTS</th>
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<tr>
<td><strong>Risk Category</strong></td>
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<tr>
<td><strong>Moderate Risk</strong></td>
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<tr>
<td>People with single, small (&lt; 1 cm) adenomatous polyps</td>
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<tr>
<td>People with large (≥ 1 cm) or multiple adenomatous polyps of any size</td>
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<td>Personal history of curative-intent resection of colon cancer</td>
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<tr>
<td>Colorectal cancer or adenomatous polyps in first-degree relative younger than age 60 or in two or more first-degree relatives of any age</td>
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<td>Colorectal cancer in other relatives (not included above)</td>
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<td><strong>High Risk</strong></td>
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<td>Family history of familial adenomatous polyposis</td>
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<td>Family history of hereditary nonpolyposis colon cancer</td>
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<td>Inflammatory bowel disease</td>
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TCE = total colon evaluation.
Figure 6-7. Rectal cancer staging. A. Ultrasound staging schema for rectal cancer. B. Rectal ultrasound example of T1 cancer (arrow points to mass; mp: muscularis propria). C. Rectal ultrasound example of T2 cancer (arrow points to mass; mp: muscularis propria). D. Rectal ultrasound example of T3 cancer (arrow points to mass, note adjacent lymph nodes, ln). E. Rectal ultrasound example of recurrent cancer (arrow points to mass).
deciding whether surgical resection of the polypectomy site is necessary.\textsuperscript{71} Similarly, EUS can document rectal cancer recurrence with sensitivities greater than rectal examinations or sigmoidoscopy.\textsuperscript{72,73} Lymph node metastases can also be documented using EUS-guided biopsies.\textsuperscript{68} Through the use of endosonography in the colon, malignant recurrences at an anastomosis can be diagnosed using the finding of an irregular hypoechoic mass.\textsuperscript{74}

Carcinoid tumors can also be staged with linear array EUS.\textsuperscript{75} The staging of carcinoids is particularly important and has a direct bearing on the treatment. Carcinoids localized to the rectal mucosa or submucosa can be treated with local or endoscopic excision.\textsuperscript{31} Linear array endosonography and guided lymph node biopsies can accurately detect malignant nodes associated with the primary tumor with an overall staging accuracy of 90 percent.\textsuperscript{75} The prognosis for small rectal carcinoids is excellent.\textsuperscript{76}

\textbf{ENDOSCOPIC MANAGEMENT OF COLON CANCER}

Endoscopic removal of colon or rectal cancers is performed with either electrocautery or laser treatments (see Figure 6–2). Snare resection is the most commonly used technique for polyp removal and is ideal for pedunculated polyps. The stalk is transected with cautery and the polyp is retrieved. The complication rate of this technique is low, with bleeding being the most common complication.

Large sessile polyps at high risk for malignancy may have to be resected using piecemeal techniques\textsuperscript{77} (Figure 6–8). This technique requires several snare excisions through the polyp and has a complication rate of 3 percent. Although 88 percent of patients will have a successful resection, malignant recurrence and the need for surgical resection are not uncommon. Incompletely resected malignant polyps or malignant polyps with malignancy present at the resection site should be surgically removed.\textsuperscript{18} Polyps with unfavorable histology (poorly differentiated carcinoma) are associated with a greater chance of recurrence of metastasis.\textsuperscript{17} Community pathologists have a significant rate of misdiagnosis on polyp specimens and will miss 31 percent of the findings of dysplasia.\textsuperscript{78} Therefore, polyps with sus-
picious pathology should be carefully reviewed by experienced pathologists. Polyps requiring surgical removal should be marked with India ink injection during colonoscopy. The tattooing enables the surgeon to readily identify the site of the polyp at the time of resection.

Piecemeal resection can also be used for large benign sessile adenomas. Injection of saline under the sessile polyps enables the endoscopist to minimize the risk of bleeding and perforation through the muscularis propria. A success rate of 81 percent is achieved with localized adenomas and is higher than the rates seen with laser ablation of sessile adenomas. Recurrence of adenomatous tissue after piecemeal resection of large polyps has been reported in 10 to 20 percent of patients. Recurrence of benign adenomas may be effectively treated with superficial tissue coagulation. The technique appears to be particularly useful in large, flat, benign adenomas. The approach can also be used successfully for rectal carcinoids.

Superficial colonic malignancies can be resected endoscopically. Saline injection under the tumor and demonstration of the lift sign indicates a tumor that is localized to the mucosa or submucosa. This technique should be used only in patients that are not surgical candidates or when the superficial nature of the malignancy has been well established with staging.

Advanced or unresectable rectal cancers can be treated endoscopically for palliation or attempt at local control. Through laser fulguration of malignant tissue, noncircumferential rectal tumors can be eliminated for periods of up to 36 months. The use of chemotherapy and radiation in conjunction with cautery may provide prolonged tumor ablation. Fulguration is particularly effective in patients with small recurrences after surgical resection. Rectal tumors can also be injected with chemotherapeutic agents with good local tumor response. Complication rates of approximately 10 percent are noted after fulguration and include strictures, bleeding, and fistulas. The use of lasers for large benign rectal villous adenomas may be less costly than surgical resection. Endoscopically placed stents may improve the long-term patency of a malignant stricture after laser fulguration (Figure 6–9).

CONCLUSION

Effective screening for colon cancer, using colonoscopy to detect and remove premalignant polyps and early cancers, can reduce the incidence and mortality of colon cancer.

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