Chapter 17
Rectal Cancer

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Abstract Rectal cancer is a disease in which cancer cells form in the tissues of the rectum; colorectal cancer occurs in the colon or rectum. Adenocarcinomas comprise the vast majority (98%) of colon and rectal cancers; more rare rectal cancers include lymphoma (1.3%), carcinoid (0.4%), and sarcoma (0.3%).The incidence and epidemiology, etiology, pathogenesis, and screening recommendations are common to both colon cancer and rectal cancer.

The incidence of colorectal cancer rose dramatically following economic development and industrialization. The majority of colorectal cancers still occur in industrialized countries. Currently, the incidence of rectal cancer in the European Union is 15–25 cases/100 000 population per year and is predicted to increase further in both genders. High body mass index, body or abdominal fatness and diabetes type II are seen as risk factors. Longstanding ulcerative colitis and Crohn's disease affecting the rectum, excessive consumption of red or processed meat and tobacco as well as moderate/heavy alcohol use increase the risk.

The usual pathogenesis of colorectal cancer is an adenomatous polyp that slowly increases in size, followed by dysplasia and finally cancer. Screening for colorectal cancer is valuable because early detection and removal of premalignant adenomas or localized cancer can prevent cancer or cancer-related deaths.

Although radical resection of rectum is the mainstay of therapy, surgery alone has a high recurrence rates. A multidisciplinary approach that includes colorectal surgery, medical oncology, and radiation oncology is required for optimal treatment of patients with rectal cancer. Therefore, determination of optimal treatment plan for patients with rectal cancer involves a complex decision-making process.

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Rectal cancer recurs in 5–30% of patients, usually in the first year after surgery. Tumor stage, grade, number of lymph node metastasis, lymphovascular involvement, signet cell appearance, achievement of negative radial margins, and distance from the radial margin are important prognostic indicators of local and distant recurrences.

Keywords Rectal cancer · Chemotherapy · Radiotherapy

17.1 Introduction

Rectal cancer is a disease in which cancer cells form in the tissues of the rectum. Although the incidence of distal (rectal and lower sigmoid) cancers has declined, with a concurrent increase in more proximal colon cancers, approximately one quarter of colorectal cancers are located in the rectum. For many years, almost all patients with rectal cancer underwent abdominoperineal resection with a permanent colostomy. Today, this approach is rarely required. The successful treatment of patients with rectal cancer involves optimal surgical technique, and frequently adjuvant chemoradiotherapy. This combined modality approach will maximize cure, minimize the risk of a subsequent symptomatic local/pelvic recurrence, and maintain quality of life. Such multimodality approaches are applicable to patients with rectal cancers at or below the peritoneal reflection. This designation generally represents cancers below 12 cm from anal verger. Tumors in the upper rectum or rectosigmoid are treated by surgical resection, and adjuvant therapy is based on the colon cancer paradigm.

17.2 Epdimiology

Colon and rectal cancer incidence was negligible before 1900. The incidence of colorectal cancer has been rising dramatically following economic development and industrialization. Currently, the incidence of rectal cancer in the European Union is 15–25 cases/100 000 population per year and is predicted to increase further in both genders [1]. High incidences of colon and rectal cancer cases are identified in the US, Canada, Japan, parts of Europe, New Zealand, Israel, and Australia. Low colorectal cancer rates are identified in Algeria and India. The majority of colorectal cancers still occur in industrialized countries. Importantly, both colon and rectal cancer incidences, as well as mortality rates in the US, have been decreasing for the last two decades, from 66.3 per 100,000 population in 1985 to 45.5 in 2006 [2]. The rate of decrease accelerated from 1998–2006 (to 3% per year in men and 2.2% per year in women), in part because of increased screening, allowing the detection and removal of colorectal polyps before they progress to cancer. The lifetime risk of developing a colorectal malignancy is approximately 6% in the general

US population. This decrease is due to a declining incidence and improvements in both early detection and treatment.

However, in contrast to the decline in rectal cancer incidence rates in persons age 55 and older, which began in the mid-1970s, rates of rectal cancer in younger persons have been rising. From 1974 to 2013, in persons age 20–39 years, and since 1980 in adults age 30–39 years, rectal cancer incidence rates have increased 3.2% per year. In those age 40–54 years, rates have increased by 2.3% annually since the 1990s. Currently, adults born circa 1990 have quadruple the risk of rectal cancer compared with those born circa 1950 [3].

17.3 Etiology

The etiology of colorectal cancer is unknown, but colorectal cancer appears to be multifactorial in origin and includes environmental factors and a genetic component. Diet may have an etiologic role, especially diet with high fat content. Approximately 75% of colorectal cancers are sporadic and develop in people with no specific risk factors. The remaining 25% of cases occur in people with significant risk factors–most commonly, a family history or personal history of colorectal cancer or polyps, which are present in 15–20% of all cases. Other significant risk factors are certain genetic predispositions, such as hereditary nonpolyposis colorectal cancer (HNPCC; 4–7% of all cases) and familial adenomatous polyposis (FAP; 1%); and inflammatory bowel disease (IBD; 1% of all cases).

17.3.1 Environmental Factors

17.3.1.1 Diet

A high-fat, low-fiber diet is implicated in the development of colorectal cancer. Specifically, people who ingest a diet high in unsaturated animal fats and highly saturated vegetable oils (eg, corn, safflower) have a higher incidence of colorectal cancer. The mechanism by which these substances are related to the development of colorectal cancer is unknown.

Saturated fats from dairy products do not have the same carcinogenic effect, nor do oils containing oleic acid (eg, olive, coconut, fish oils). Omega-3 monounsaturated fatty acids and omega-6 monounsaturated fatty acids also appear to be less carcinogenic than unsaturated or polyunsaturated fats. In fact, recent epidemiologic data suggest that high fish consumption may provide a protective effect against development of colorectal cancer. Long-term diets high in red meat or processed meats appear to increase the risk of distal colon and rectal cancers [4, 5].

The ingestion of a high-fiber diet may be protective against colorectal cancer. Fiber causes the formation of a soft, bulky stool that dilutes carcinogens; it also

decreases colonic transit time, allowing less time for harmful substances to contact the mucosa. The decreased incidence of colorectal cancer in Africans is attributed to their high-fiber, low-animal-fat diet. This favorable statistic is reversed when African people adopt a western diet. Meta-analysis of case-controlled studies found that reduction in colorectal cancer risk occurs with increasing intake of dietary fiber [4].

Increased dietary intake of calcium appears to have a protective effect on colorectal mucosa by binding with bile acids and fatty acids. The resulting calcium salts may have antiproliferative effects, decreasing crypt cell production in the mucosa. A double-blind placebo-controlled study showed a statistically significant reduction in the incidence of metachronous colorectal adenomas [6]. Other dietary components, such as selenium, carotenoids, and vitamins A, C, and E, may have protective effects by scavenging free-oxygen radicals in the colon.

17.3.1.2 Alcohol

Alcohol intake of more than 30 g daily has been associated with increased risk of developing colorectal carcinoma, with risk of rectal cancer greater than that of colon cancer. Risk appears greater with beer than with wine [7]. Specifically, Kabat et al found that daily beer consumption of 32 ounces or more increases the risk of rectal cancer in men (odds ratio 3.5) [8].

17.3.1.3 Tobacco

Smoking, particularly when started at a young age, increases the risk of colorectal cancer [9]. Possible mechanisms for tumor development include the production of toxic polycyclic aromatic amines and the induction of angiogenic mechanisms due to tobacco smoke. A study by Phipps et al found that smoking is also associated with increased mortality after colorectal cancer diagnosis, especially among patients with colorectal cancer with high microsatellite instability [10].

17.3.2 Cholecystectomy

Following cholecystectomy, bile acids flow freely, increasing exposure to the degrading action of intestinal bacteria. This constant exposure increases the proportion of carcinogenic bile acid byproducts. A meta-analysis by Giovannucci et al revealed an increased risk of proximal colon carcinoma following cholecystectomy. Although a large number of studies suggest the increased risk of proximal colon cancer in patients following cholecystectomy, the data are not compelling enough to warrant enhanced screening in this patient population. [11]

17.3.3 Hereditary Factors

The relative risk of developing colorectal cancer is increased in the first-degree relatives of affected patients. For offspring, the relative risk is 2.42 (95% CI: 2.20–2.65); when more than one family member is affected, the relative risk increases to 4.25 (95% CI; 3.01–6.08). If the first-degree family member is younger than 45 years at the time of diagnosis, the risk increase is even higher [12].

Regarding the personal history of colorectal cancer or polyps: Of patients with colorectal cancer, 30% have synchronous lesions, usually adenomatous polyps. Approximately 40–50% of patients have polyps on a follow-up colonoscopy. Of all patients who have adenomatous polyps discovered via a colonoscopy, 29% of them have additional polyps discovered on a repeat colonoscopy one year later. Malignancy develops in 2–5% of patients. The risk of cancer in people who have had polyps removed is 2.7–7.7 times that of the general population [13].

17.3.4 Genetic Disorders

17.3.4.1 Familial Adenomatous Polyposis (FAP)

FAP is an autosomal dominant inherited syndrome that results in the development of more than 100 adenomatous polyps and a variety of extra-intestinal manifestations. The defect is in the APC gene, which is located on chromosome 5 at locus q21. The disease process causes the formation of hundreds of intestinal polyps, osteomas of bone, desmoid tumors, and, occasionally, brain tumors. Individually, these polyps are no more likely to undergo malignant transformation than are polyps in the general population. The increased number of polyps, however, predisposes patients to a greater risk of cancer. If left untreated, colorectal cancer develops in nearly 100% of these patients by age 40. Whenever the hereditary link is documented, approximately 20% of FAP cases are found to be caused by spontaneous mutation.

17.3.4.2 Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

HNPCC is an autosomal dominant inherited syndrome that occurs because of defective mismatch repair genes located on chromosomes 2, 3, and 7. Patients have the same number of polyps as the general population, but their polyps are more likely to become malignant. These patients also have a higher incidence of endometrial, gastric, thyroid, and brain cancers.

The revised Amsterdam criteria are used to select at-risk patients (all criteria must apply): (1) Three or more relatives who are diagnosed with an HNPCC-associated cancer (colorectal, endometrium, small bowel, ureter, or renal pelvis);

(2) One affected person is a first-degree relative of the other 2; (3) One or more cases of cancer are diagnosed before age 50 years; (4) At least 2 generations are affected; (5) FAP has been excluded; (6) Tumors have undergone a pathology review.

17.3.5 Inflammatory Bowel Disease

The malignant pathway in these patients does not involve any adenoma-carcinoma sequence. Cancer risk increases with duration of disease. After 10 years, the incidence of colorectal cancer in ulcerative colitis (UC) is approximately 1% per year. Patients should be evaluated for dysplastic changes via an annual colonoscopy. Dysplasia is a precursor of cancer and when present, the risk of cancer is 30%.

The incidence of colorectal cancer in patients with Crohn's disease is 4–20 times greater than that of the general population. Cancer occurs in patients with disease of at least 10 years' duration. The average age at cancer diagnosis, 46–55 years, is younger than that of the general population. Cancers often develop in areas of strictures and in de-functionalized segments of intestine. In patients with perianal Crohn's disease, malignancy is often present in fistulous tracts. Patients with Crohn's colitis should undergo the same surveillance regimen as those with UC.

17.4 Clinical Presentation

All patients should undergo a complete history (including a family history) and assessment of risk factors for the development of rectal cancer. Many rectal cancers produce no symptoms and are discovered during digital or proctoscopic screening examinations.

Bleeding is the most common symptom of rectal cancer, occurring in 60% of patients. Bleeding often is attributed to other causes (eg, hemorrhoids), especially if the patient has a history of other rectal problems. Profuse bleeding and anemia are rare. Bleeding may be accompanied by the passage of mucus, which warrants further investigation.

Change in bowel habits is present in 43% of patients; change is not evident in some cases because the capacity of a rectal reservoir can mask the presence of small lesions. When change does occur it is often in the form of diarrhea, particularly if the tumor has a large villous component. These patients may have hypokalemia, as shown in laboratory studies. Some patients experience a change in the caliber of the stool. Large tumors can cause obstructive symptoms. Tumors located low in the rectum can cause a feeling of incomplete evacuation and tenesmus.

Occult bleeding is detected via a fecal occult blood test (FOBT) in 26% of all cases. Abdominal pain is present in 20% of the cases. Partial large-bowel obstruction may cause colicky abdominal pain and bloating. Back pain is usually a late sign caused by a tumor invading or compressing nerve trunks. Urinary symptoms may also occur if the tumor is invading or compressing the bladder or prostate.

Malaise is a nonspecific symptom and present in 9% of rectal cancer cases. Bowel obstruction due to a high-grade rectal lesion is rare, occurring in 9% of all cases. Pelvic pain is a late symptom, usually indicating nerve trunk involvement, and is present in 5% of all cases. Other manifestations include emergencies such as peritonitis from perforation (3%) or jaundice, which may occur with liver metastases (<1%).

17.5 Laboratory Studies

Routine laboratory studies should include a complete blood count (CBC); serum chemistries, including liver and renal function tests; and a carcinoembryonic antigen (CEA) test. A cancer antigen (CA) 19-9 assay, if available, may also be useful to monitor the disease.

Screening CBC may demonstrate a hypochromic, microcytic anemia, suggesting iron deficiency. The combined presence of vitamin B-12 or folate deficiency may result in a normocytic or macrocytic anemia. All men and postmenopausal women with iron deficiency anemia require a GI evaluation.

Liver function tests are usually part of the preoperative workup. The results are often normal, even in patients with metastases to the liver.

Perform a CEA test in all patients with rectal cancer. A baseline level is obtained before surgery and a follow-up level is obtained after surgery. If a previously normalized CEA begins to rise in the postoperative period, this suggests possible recurrence. A CEA level higher than 100 ng/mL usually indicates metastatic disease and warrants a thorough investigation.

Perform FOBT yearly by testing 2 samples from each of 3 consecutive stools. If any of the 6 sample findings is positive, recommend that the patient have the entire colon studied via colonoscopy or flexible sigmoidoscopy. FOBT has significant false-positive and false-negative rates.

Fecal immunochemical testing uses a monoclonal antibody assay to identify human hemoglobin. This test is more specific for lower GI tract lesions. The presence of the globin molecule is indicative of bleeding in the colon and rectum because the globin molecule is broken down during passage through the upper GI tract. This test is probably the wave of the future in fecal occult blood testing and may serve as screening in certain populations. FIT has comparable sensitivity for the detection of proximal and distal advanced neoplasia [14].

17.6 Screening for Colon and Rectal Cancer

The process of malignant transformation from adenoma to carcinoma takes several years. The purpose of screening is to eradicate potential cancers while they are still in the benign stage of the adenoma-carcinoma sequence. Screening also increases the likelihood of discovering existing cancers while they are still in the early stage.

Screening techniques include the following:

- Guaiac-based fecal occult blood test (FOBT): Perform FOBT yearly by testing 2 samples from each of 3 consecutive stools. If any of the 6 sample findings is positive, recommend that the patient have the entire colon studied via colonoscopy or flexible sigmoidoscopy. FOBT has significant false-positive and false-negative rates.
- Stool DNA screening (SDNA): SDNA screening is done using polymerase chain reaction of sloughed mucosal cells in stool. This test evaluates for genetic alterations that lead to the cancer formation. Compared with no testing, SDNA testing is cost effective and has high sensitivity for invasive cancer.
- Fecal immunochemical test (FIT): Fecal immunochemical testing uses a monoclonal antibody assay to identify human hemoglobin. This test is more specific for lower GI tract lesions. The presence of the globin molecule is indicative of bleeding in the colon and rectum because the globin molecule is broken down during passage through the upper GI tract. This test is probably the wave of the future in fecal occult blood testing and may serve as screening in certain populations. FIT has comparable sensitivity for the detection of proximal and distal advanced neoplasia [14].
- Rigid proctoscopy: Rigid proctosigmoidoscopy can be performed without an anesthetic, allows direct visualization of the lesion, and provides an estimation of the size of the lesion and degree of obstruction. This procedure is used to obtain biopsies of the lesion, assess ulceration, and determine the degree of fixation. The rigid proctoscopy is proven to be a highly reproducible method of determining the level of rectal cancer and does not depend on the operator and on the technique. Therefore, it gives an accurate measurement of the distance of the lesion from the anal verge; the latter is critical in deciding which operation is appropriate. The anal verge should be used as preferred landmark because the lowest edge of the rectal cancer and the anal verge can be visualized simultaneously during rigid proctoscopy evaluation. In conclusion, the level of rectal cancer must be confirmed by rigid proctoscopy [15].
- Flexible sigmoidoscopy (FSIG): Perform this test every 5 years. Biopsy any lesions identified, and perform a full colonoscopy. With flexible sigmoidoscopy, lesions beyond the reach of the sigmoidoscope may be missed. FSIG introduces significant variability for the level of rectal cancer and level of rectum itself. Therefore, FSIG should not be used to determine the level of the rectal cancer

[15]. Screening with flexible sigmoidoscopy is associated with significant decreases in the incidence of colorectal cancer (in both the distal and proximal colon) and in colorectal cancer mortality (distal colon only) [16].

- Combined glucose-based FOBT and flexible sigmoidoscopy: Theoretically, the combination of these two tests may overcome the limitations of each test.
- Double-contrast barium enema (DCBE): Although barium enema is the traditional diagnostic test for colonic polyps and cancer, the United States Preventive Services Task Force (USPSTF) did not consider barium enema in its 2008 update of colorectal cancer screening recommendations. The USPSTF noted that barium enema has substantially lower sensitivity than modern test strategies and has not been studied in trials of screening trials; its use as a screening test for colorectal cancer is declining [17].
- CT colonography (CTC): Virtual colonoscopy (CTC) was introduced in 1994. After bowel preparation, the thin-cut axial colonic images are gathered in both prone and supine positions with high-speed helical CT scanner. Then, the images are reconstituted into a 3-dimensional replica of the entire colon and rectum. This provides a good visualization of the entire colon, including the antegrade and retrograde views of the flexures and haustral folds. Because this is a diagnostic study, patients with positive findings should undergo colonoscopic evaluation the same day.
- Fiberoptic flexible colonoscopy (FFC): FFC is recommended every 5–10 years. Colonoscopy allows full visualization of the colon and excision and biopsy of any lesions. The likelihood is extremely low that a new lesion could develop and progress to malignancy between examinations.

Signs and symptoms in patients with average risk for colon and rectal cancer who should be screened include the following: (1) No symptoms and age 50–75 years; (2) No symptoms requesting screening; (3) Change in bowel habits; (4) Rectal and anal bleeding; (5) Unclear abdominal pain; (6) Unclear iron-deficiency anemia.

Each screening test has unique advantages. They have been shown to be cost-effective and have associated risks and limitations. Ultimately, patient preferences and availability of testing resources guide the selection of screening tests. The main disadvantage of the structural tests is their requirement for bowel preparation. The primary advantage of structural tests is that they can detect polyps as well as cancer. Conscious sedation is usually used for colonoscopy. FSIG is uncomfortable, and screening benefit is limited to sigmoid colon and rectum. Risks for colonoscopy, DCBE, and CTC may rarely include perforation; colonoscopy may also be associated with bleeding. Positive findings on FSIG, DCBE, and CTC usually result in referral for colonoscopy. The advantages of the stool tests are that they are noninvasive, do not require bowel preparation, and are more readily available to patients without adequate insurance coverage or local resources.

17.7 Histologic Findings

Histopathologic features such as poor differentiation, lymphovascular and/or perineural invasion, T4 tumor stage, and clinical findings such as obstruction or perforation, and elevated preoperative CEA levels are all associated with increased recurrence rates and worse survival [18].

17.8 Staging

17.8.1 Dukes Classification

In 1932, Cuthbert E. Dukes, a pathologist at St. Mark Hospital in England, introduced a staging system for rectal cancer. His system divided tumor classification into 3 stages, as follows:

- Those limited to the rectal wall (Dukes A);
- Those that extended through the rectal wall into extra-rectal tissue (Dukes B);
- Those with metastases to regional lymph nodes (Dukes C).

This system was modified by others to include subdivisions of stages B and C, as follows:

- Stage B was divided into B1 (ie, tumor penetration into muscularis propria) and B2 (ie, tumor penetration through muscularis propria);
- Stage C was divided into C1 (ie, tumor limited to the rectal wall with nodal involvement) and C2 (ie, tumor penetrating through the rectal wall with nodal involvement).
- Stage D was added to indicate distant metastases.

17.8.2 Tumor, Node, Metastasis (TNM) System

This system was introduced in 1954 by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (IUAC). The TNM system is a universal staging system for all solid cancers that is based on clinical and pathologic information. Each category is independent. Neither the Dukes nor the TNM system includes prognostic information such as histologic grade, vascular or perineural invasion, or tumor DNA ploidy.

17.8.3 TNM Classification for Cancer of the Colon and Rectum (AJCC) (Table 17.1)

Primary tumor (T) includes the following:

- TX – Primary tumor cannot be assessed or depth of penetration not specified
- T0 – No evidence of primary tumor
- Tis – Carcinoma in situ (mucosal); intraepithelial or invasion of the lamina propria
- T1 – Tumor invades submucosa
- T2 – Tumor invades muscularis propria
- T3 – Tumor invades through the muscularis propria into the subserosa or into non-peritonealized pericolic or perirectal tissue
- T4 – Tumor directly invades other organs or structures and/or perforates the visceral peritoneum

Regional lymph nodes (N) include the following:

- NX – Regional lymph nodes cannot be assessed
- N0 – No regional lymph node metastasis
- N1 – Metastasis in 1–3 pericolic or perirectal lymph nodes
- N2 – Metastasis in 4 or more pericolic or perirectal lymph nodes
- N3 – Metastasis in any lymph node along the course of a named vascular trunk

Distant metastasis (M) include the following:

- MX – Presence of metastasis cannot be assessed
- M0 – No distant metastasis
- M1 – Distant metastasis

The TNM stage – dependent 5-year survival rate for rectal carcinomas is as follows [18]:

- Stage I – 90%
- Stage II – 60–85%
- Stage III – 27–60%
- Stage IV – 5–7%

Table 17.1 Comparison of AJCC definition of TNM staging system to Dukes classification

Rectal Cancer Stages		TNM Staging	Dukes Staging	5-Year Survival
Stage I		T1-2 N0 M0	A	>90%
Stage II	A	T3 N0 M0	B	60–85%
	B	T4 N0 M0		60–85%
Stage III	A	T1-2 N1 M0	C	55–60%
	B	T3-4 N1 M0		35–42%
	C	T1-4 N2 M0		25–27%
Stage IV		T1-4 N0-2 M1		5–7%

17.9 Medical Care

A multidisciplinary approach that includes surgery, medical oncology, and radiation oncology is required for optimal treatment of patients with rectal cancer.

Determination of optimal treatment plan for patients with rectal cancer involves a complex decision-making process. Strong considerations should be given to the intent of surgery, possible functional outcome, and preservation of anal continence and genitourinary functions. The timing of surgical resection is dependent on the size, location, extent, and grade of the rectal carcinoma. The number of lymph nodes removed (12 or more; minimum, 10) at the time of surgery impacts staging accuracy and prognosis. The first step involves achievement of cure because the risk of pelvic recurrence is high in patients with rectal cancer and locally recurrent rectal cancer has a poor prognosis. Functional outcome of different treatment modalities involves restoration of bowel function with acceptable anal continence and preservation of genitourinary functions. Preservation of both anal and rectal reservoir function in treatment of rectal cancer is highly preferred by patients. Sphincter-saving procedures for rectal cancer are now considered the standard of care [19].

- Factors influencing sphincter preservation: surgeon training, surgeon volume, neoadjuvant chemoradiotherapy.
- Factors associated with difficult sphincter preservation: male sex, morbid obesity, preoperative incontinence, direct involvement of anal sphincter muscles with carcinoma, bulky tumors within 5 cm from the anal verge.
- Patient selection for local excision: lesions located in low rectum (within 8–10 cm), lesions occupying less than one third of the rectal circumference, mobile exophitic or polypoid lesions, lesions less than 3 cm in size, T1 lesions, low grade tumor (well or moderately differentiated), negative nodal status (clinical and radiographic).
- Disadvantages of abdominoperineal resection: need for permanent colostomy, significantly higher short-term morbidity and mortality, significantly higher long-term morbidities, higher rate of sexual and urinary dysfunction.

17.10 Surgical Care

Patient-related, tumor-related, treatment- related, and surgeon-related factors influence the ability to restore intestinal continuity in patients with rectal cancer.

17.10.1 Transanal Excision

The local transanal excision of rectal cancer is reserved for early-stage cancers in a select group of patients. The lesions amenable for local excision are small (< 3 cm in size), occupying less than a third of a circumference of the rectum, preferably exophytic/polypoid, superficial and mobile (T1 and T2 lesions), low-grade tumors (well or moderately differentiated) that are located in low in the rectum (within 8 cm of the anal verge). There should also be no palpable or radiologic evidence of enlarged mesenteric lymph nodes. The likelihood of lymph node involvement in this type of lesion ranges from 0–12% [19, 20]. A study by Peng et al found that local excision in early stage rectal cancer may result in high local recurrence rates. The authors recommend only using this procedure in highly selective groups of patients, specifically those with a tumor size of 2.5 cm or smaller [21].

Local excision is increasingly used to treat stage I rectal cancers despite its inferiority to total mesorectal excision, which is the current standard of care. In a study of all rectal cancer patients in the National Cancer Data Base from 1998 through 2010, researchers found that local excision was used to treat 46.5% of the patients with T1 tumors and 16.8% of those with T2 tumors. For patients with T1 cancer, local excision rates increased from 39.8% in 1998 to 62.0% in 2010. For patients with T2 cancers, rates increased from 12.2% to 21.4% [22].

Preoperative ERUS should be performed. If nodes are identified as suggestive of cancer, do not perform transanal excision. The lesion is excised with the full thickness of the rectal wall, leaving a 1-cm margin of normal tissue. The defect is usually closed; however, some surgeons leave it open. Unfavorable pathologic features such as positive resection margins, lymphovascular invasion, lymph node metastasis, perineural invasions, and recurrent lesion at follow-up evaluations mandate salvage resection. Usually, an abdominal perineal resection or proctosigmoidectomy with coloanal anastomosis is performed as a salvage resection following failure of local excision [20].

The advantages of local excision include rapid recovery, minimal effect on sphincter function, and relatively low perioperative morbidity and mortality. Recovery is usually rapid. The 5-year survival rate after transanal excision ranges from 65–100% (these figures include some patients with T2 lesions). The local recurrence rate ranges from 0–40%. Patients with lesions that display unfavorable histologic features but are excised completely may be treated with adjuvant radiation therapy.

Cancer recurrence following transanal excision of early rectal cancer has been studied by Weiser et al. [23] Failures due to transanal excision are mostly advanced local disease and are not uniformly salvageable with radical pelvic excision. These patients may require extended pelvic dissection with en bloc resection of adjacent pelvic organs such as the pelvic side wall with autonomic nerves, coccyx, prostate, seminal vesicle, bladder, vagina, ureter, ovary, and uterus. The long-term outcome in patients with recurrent rectal carcinoma who undergo radical resection is less favorable than expected, relative to the early stage of their initial rectal carcinoma [23].

In summary, the treatment of T1 and T2 rectal cancers continues to be challenging. Local excision is associated with higher rate of recurrence, especially in T2 lesions. Ultimately, 15–20% of patients may experience recurrence. When local recurrence is detected, patients usually have advanced disease, requiring extensive pelvic excisions. Therefore, strict selection criteria are essential when considering local excision. All patients should be informed of the risk of local recurrence and lower cure rates associated with recurrence [19, 23, 24].

17.11 Endocavitary Radiation

This radiotherapy method differs from external-beam radiation therapy in that a larger dose of radiation can be delivered to a smaller area over a shorter period. Selection criteria for this procedure are similar to those for transanal excision. The lesion can be as far as 10 cm from the anal verge and no larger than 3 cm. Endocavitary radiation is delivered via a special proctoscope and is performed in an operating room with sedation. The patient can be discharged on the same day.

A total of 6 application of high-dose (20Gy–30 Gy), low-voltage radiation (50 kV) is given over the course of 6 weeks. Each radiotherapy session produces a rapid shrinkage of the rectal cancer lesion. An additional booster dose can be given to the tumor bed. The overall survival rate is 83%, although the local recurrence rate as high as 30% [20].

17.12 Transanal Endoscopic Microsurgery (TEM)

Transanal endoscopic microsurgery is another form of local excision that uses a special operating proctoscope that distends the rectum with insufflated carbon dioxide and allows the passage of dissecting instruments. This method can be used on lesions located higher in the rectum and even in the distal sigmoid colon. Transanal endoscopic microsurgery has not come into wide use yet because of a significant learning curve and a lack of availability.

17.13 Sphincter-Sparing Procedures

Procedures are described that use the traditional open technique. All of these procedures, except the perineal portions, can also be performed using laparoscopic techniques, with excellent results. The nuances of the laparoscopic technique used are beyond the scope of this discussion. A study by Li et al found that laparoscopic and open surgery for middle and lower rectal cancer are associated with similar long-term outcomes. The study shows the value of technical experience when performing

laparoscopic surgery and encourages the use of this surgery by experienced teams [25]. Long-term results from the UK Medical Research Council trial of laparoscopically assisted versus open surgery for colorectal cancer showed no differences between groups in overall or disease-free survival or recurrence rates [26].

17.13.1 Low Anterior Resection (LAR)

LAR is generally performed for lesions in the middle and upper third of the rectum and, occasionally, for lesions in the lower third. Because this is a major operation, patients who undergo LAR should be in good health. They should not have any preexisting sphincter problems or evidence of extensive local disease in the pelvis.

Patients will not have a permanent colostomy but should be informed that a temporary colostomy or ileostomy may be necessary. They also must be willing to accept the possibility of slightly less-than-perfect continence after surgery, although this is not usually a major problem.

Other possible disturbances in function include transient urinary dysfunction secondary to weakening of the detrusor muscle. This occurs in 3–15% of patients. Sexual dysfunction is more prominent and includes retrograde ejaculation and impotence. In the past, this has occurred in 5–70% of men, but recent reports indicate that the current incidence is lower [27].

The operation entails full mobilization of the rectum, sigmoid colon, and, usually, the splenic flexure. Mobilization of the rectum requires a technique called total mesorectal excision (TME). TME involves sharp dissection in the avascular plane that is created by the envelope that separates the entire mesorectum from the surrounding structures. This includes the anterior peritoneal reflection and Denonvilliers fascia anteriorly and preserves the inferior hypogastric plexus posteriorly and laterally. TME is performed under direct visualization. Mesorectal spread can occur by direct tumor spread, tumor extension into lymph nodes, or perineural invasion of tumor [15, 24, 27].

TME yields a lower local recurrence rate (4%) than transanal excision (20%), but it is associated with a higher rate of anastomotic leak (11%). For this reason, TME may not be necessary for lesions in the upper third of the rectum. The distal resection margin varies depending on the site of the lesion. A 2-cm margin distal to the lesion must be achieved. For the tumors of the distal rectum, less than 5 cm from the anal verge, the minimally accepted distal margin is 1 cm in the fresh specimen. Distal intra-mural spread beyond 1 cm occurs rarely. Distal spread beyond 1 cm is associated with aggressive tumor behavior or advanced tumor stage [15].

The procedure is performed with the patient in the modified lithotomy position with the buttocks slightly over the edge of the operating table to allow easy access to the rectum [24]. A circular stapling device is used to create the anastomosis. A double-stapled technique is performed. This entails transection of the rectum distal to the tumor from within the abdomen using a linear stapling device. The proximal resection margin is divided with a purse-string device.

After sizing the lumen, the detached anvil of the circular stapler is inserted into the proximal margin and secured with the purse-string suture. The circular stapler is inserted carefully into the rectum, and the central shaft is projected through or near the linear staple line. Then, the anvil is engaged with the central shaft, and, after completely closing the circular stapler, the device is fired. Two rings of staples create the anastomosis, and a circular rim or donut of tissue from the proximal and distal margins is removed with the stapling device.

According to a study by Maurer et al, the introduction of TME has resulted in an impressive reduction of local recurrence rate. TME appears to have improved survival in patients without systemic disease [28].

The anastomotic leak rate with this technique ranges from 3–11% for middle-third and upper-third anastomosis and to 20% for lower-third anastomosis. For this reason, some surgeons choose to protect the lower-third anastomosis by creating a temporary diverting stoma. This is especially important when patients have received preoperative radiation therapy. The rate of stenosis is approximately 5–20%. A hand-sewn anastomosis may be performed; if preferred, the anastomosis is performed as a single-layer technique. The leak and stenosis rates are the same.

In R0 resection, the inferior mesenteric artery (IMA) should be excised at its origin, but this rule is not mandated by available supportive evidence. Patients with non–en-bloc resection, positive radial margins, positive proximal and distal margin, residual lymph node disease, and incomplete preoperative and intra-operative staging would not be considered to have complete resection of cancer (R0 resection) [15]. Patients with R1 and R2 resection are considered to have an incomplete resection for cure. Incomplete R1 and R2 resection does not change the TNM stage but affects the curability [15]. In a 2012 multicenter, randomized controlled trial, mesorectal excision with lateral lymph node dissection was associated with a significantly longer operation time and significantly greater blood loss than mesorectal excision alone [29].

17.13.2 Colo-anal Anastomosis (CAA)

Very distal rectal cancers that are located just above the sphincter occasionally can be resected without the need for a permanent colostomy. The procedure is as already described; however, the pelvic dissection is carried down to below the level of the levator ani muscles from within the abdomen. A straight-tube coloanal anastomosis (CAA) can be performed using the double-stapled technique, or a hand-sewn anastomosis can be performed transanally [27].

The functional results of this procedure have been poor in some patients, who experience increased frequency and urgency of bowel movements, as well as some incontinence to flatus and stool. An alternative to the straight-tube CAA is creation of a colonic J pouch. The pouch is created by folding a loop of colon on itself in the shape of a J. A linear stapling or cutting device is inserted into the apex of the J, and

the stapler creates an outer staple line while dividing the inner septum. The J-pouch anal anastomosis can be stapled or hand sewn.

An alternative to doing the entire dissection from within the abdomen is to begin the operation with the patient in the prone jackknife position. The perineal portion of this procedure involves an intersphincteric dissection via the anus up to the level of the levator ani muscles. After the perineal portion is complete, the patient is turned to the modified lithotomy position and the abdominal portion is performed. Either a straight-tube or colonic J-pouch anal anastomosis can be created; however, both must be hand sewn [27].

The advantages of the J pouch include decreased frequency and urgency of bowel movements because of the increased capacity of the pouch. A temporary diverting stoma is performed routinely with any coloanal anastomosis.

17.13.3 Abdominal Perineal Resection (APR)

APR is performed in patients with lower-third rectal cancers. APR should be performed in patients in whom negative margin resection will result in loss of anal sphincter function. This includes patients with involvement of the sphincters, preexisting significant sphincter dysfunction, or pelvic fixation, and sometimes is a matter of patient preference. (Table 17.2).

A 2-team approach is often used, with the patient in modified lithotomy position. The abdominal team mobilizes the colon and rectum, transects the colon proximally, and creates an end-sigmoid colostomy. The perineal team begins by closing the anus with a purse-string suture and making a generous elliptical incision. The incision is carried through the fat using electrocautery. The inferior rectal vessels are ligated and the anococcygeal ligament is divided. The dissection plane continues posteriorly, anterior to the coccyx to the level of the levator ani muscles.

Then, the surgeon breaks through the muscles and retrieves the specimen that has been placed in the pelvis. The specimen is brought out through the posterior opening, and the anterior dissection is continued carefully. Care must be taken to avoid the prostatic capsule in the male and the vagina in the female (unless posterior vaginectomy was planned). The specimen is removed through the perineum, and the wound is irrigated copiously. A closed-suction drain is left in place, and the perineal wound is closed in layers, using absorbable sutures. During this time, the abdominal team closes the pelvic peritoneum (this is not mandatory), closes the abdomen, and matures the colostomy [27].

Table 17.2 Acceptable minimal distal and proximal resectional margins for rectal cancer [14]

Resection margins	Proximal resection margin (cm)	Distal resection margin (cm)
Ideal margins	5 cm or more	2 cm or more
Minimally acceptable margins	5 cm or more	1 cm or more

In patients who have rectal cancer with adjacent organ invasion, en bloc resection should be performed in order to not compromise cure. This situation is encountered in 15% of rectal cancer patients. Rectal carcinoma most commonly invades the uterus, adnexa, posterior vaginal wall, and bladder. The urinary bladder is the organ most commonly involved in locally advanced rectal carcinoma. Extended, en bloc resection may involve partial or complete cystectomy [15, 27]. In women, rectal carcinoma also commonly invades the uterus, adnexa, and posterior vaginal wall.

Inadequate sampling of lymph nodes may reflect non-oncologic resection or inadequate inspection of pathologic specimens. The use of more extended pelvic lymphadenectomy has been studied for rectal cancer. Extended lymphadenectomy involves removal of all lymph nodes along the internal iliac and common iliac arteries. This procedure has been associated with significantly higher sexual and urinary dysfunction without any additional benefit in local recurrence especially in patients with adjuvant radiotherapy [30].

17.13.4 Treatment of Colorectal Cancer with Liver Metastasis

Chemotherapeutic regimens for liver metastasis including systemic and intrahepatic administration have only had limited benefit. Systemic chemotherapy had 18–28% response rates. However, one meta-analysis found that carefully selected patients with metastatic colorectal cancer may benefit from preoperative chemotherapy with curative intent [31]. It is well accepted that liver resections in selected patients are beneficial. Overall, 5-year survival rates following surgical resection of liver metastasis vary from 20–40%. A study by Dhir et al found that among patients undergoing hepatic resection for colorectal metastasis, a negative margin of 1 cm or more had a survival advantage [32].

17.14 Adjuvant Medical Care

Although radical resection of rectum is the mainstay of therapy, surgery alone has a high recurrence rates. The local recurrence rate for rectal cancers treated with surgery alone is 30–50%. Rectal adenocarcinomas are sensitive to ionizing radiation. Radiation therapy can be delivered preoperatively, intraoperatively, or postoperatively and with or without chemotherapy.

Tumor stage, grade, number of lymph node metastasis, lymphovascular involvement, signet cell appearance, achievement of negative radial margins, and distance from the radial margin are important prognostic indicators of local and distant recurrences. Low anterior (LAR) or abdominal-perineal resection (APR) in conjunctions with total mesorectal excision (TME) should be performed for optimal surgical therapy. A study by Margalit et al found that patients older than 75 years had difficulty tolerating combined modality chemotherapy to treat rectal cancer.

They required early termination of treatment, treatment interruptions, and/or dose reductions [33].

17.15 Adjuvant Radiation Therapy

Preoperative radiation therapy has many potential advantages, including tumor down-staging; an increase in resectability, possibly permitting the use of a sphincter-sparing procedure; and a decrease in tumor viability, which may decrease the risk of local recurrence. Preoperative radiation therapy works better in well-oxygenated tissues prior to surgery [27, 34]. Postoperatively, tissues are relatively hypoxic as a result of surgery and may be more resistant to radiotherapy. If patients have postoperative complications, there may be delay in initiating adjuvant therapy. Preoperative radiation therapy also minimizes the radiation exposure of small bowel loops due to pelvic displacement and adhesions following surgery. In a study of patients with locally advanced rectal cancer, a higher dose of radiation delivered using an endorectal boost increased major response in T3 tumors by 50% without increasing surgical complications or toxicity [35].

The disadvantages of preoperative radiation therapy include delay in definitive resection, possible loss of accurate pathologic staging, possible over-treatment of early-stage (stage I and II) rectal cancer, and increased postoperative complications and morbidity and mortality rates secondary to radiation injury. Preoperative radiation therapy decreases the risk of tumor recurrence in patients with stage II or III disease; however, this does not translate into a decrease in distant metastases or an increase in survival rate. Some recent reports cite an increase in survival; however, this is still the minority opinion.

In sum, preoperative radiotherapy may be effective in improving local control in localized rectal cancer but is only of marginal benefit in attainment of improved overall survival; it does not diminish the need for permanent colostomies and it may increase the incidence of postoperative surgical infections; it also does not decrease the incidence of long-term effects on rectal and sexual function [36]. The authors recommend preoperative chemoradiation therapy in patients with large bulky cancers and with obvious nodal involvement [27].

The advantages of postoperative radiation therapy include immediate definitive resection and accurate pathologic staging information before beginning ionizing radiation. The disadvantages of postoperative radiation therapy include possible delay in adjuvant radiation therapy if postoperative complications ensue; no effect on tumor cell spread at the time of surgery; and decreased effect of radiation in tissues with surgically-induced hypoxia. Published randomized trials suggest that preoperative or postoperative radiation therapy appears to have a significant impact on local recurrence but does not increase survival rates [27]. A study by Ng et al found that statin use during and after adjuvant chemotherapy did not result in improved disease-free survival, recurrence-free survival, or overall survival in patients with stage III colon cancer [37].

17.15.1 Intraoperative Radiation Therapy

Intraoperative radiation therapy is recommended in patients with large, bulky, fixed, unresectable cancers. The direct delivery of high-dose radiotherapy is believed to improve local disease control. Intraoperative radiation therapy requires specialized, expensive operating room equipment, limiting its use.

17.15.2 Adjuvant Chemotherapy

Chemotherapy options for colon and rectal cancer have greatly expanded in recent years, but the efficacy of chemotherapy remains incomplete and its toxicities remain substantial. Combination therapy with use of as many drugs as possible is needed for maximal effect against rectal cancer. (Table 17.3).

The most useful chemotherapeutic agent for colorectal carcinoma is 5-fluorouracil (5-FU), an antimetabolite. The prodrug, 2-deoxy-5-floxuridine (5-FUDR), is rapidly converted to 5-FU and is used for metastatic liver disease by continuous intrahepatic infusion. Fluorouracil is a fluorinated pyrimidine, which blocks the formation of thymidylic acid and DNA synthesis. Clinically, it offers good radiosensitization without severe side effects, although diarrhea can be dose limiting and, if severe, life-threatening. 5-FU has been used in conjunction with radiation (combined modality) therapy before surgery (neoadjuvant), as well as after surgery.

Stage I (T1-2, N0, M0) rectal cancer patients do not require adjuvant therapy due to their high cure rate with surgical resection. High-risk patients, including those with poorly differentiated tumor histology and those with lymphovascular invasion, should be considered for adjuvant chemotherapy and radiotherapy. The new NCCN guidelines recommend combination therapy with infusional fluorouracil, folinic acid, and oxaliplatin (FOLFOX) as reasonable for patients with high-risk or intermediate-risk stage II disease; however, FOLFOX is not indicated for good- or average-risk stage II rectal cancer [38, 39]. FOLFOX is associated with neuropathy and one long-term study confirmed that although overall neurotoxicity did not significantly increase after a median of 7 years, specific neurotoxicity (numbness and tingling of the hands and feet) remained elevated [40].

Patients with locally advanced rectal cancer (T3-4, N0, M0 or Tany, N1-2, M0) should receive primary chemotherapy and radiotherapy. The combination of preoperative radiation therapy and chemotherapy with fluorouracil improves local control, distant spread, and survival. The basis of this improvement is believed to be the activity of fluorouracil as a radiosensitizer. Surgical resection can be done 4–10 weeks after completion of chemotherapy and radiotherapy.

A study by Kim et al found that postoperative complications were associated with both omission of and delay in chemotherapy. Timely initiation of chemotherapy, defined as before 8 weeks postoperatively, was a factorable prognostic factor for overall and recurrence-free survival [41].

Table 17.3 Colorectal chemotherapeutic regimens

Colon and rectal cancer common chemotherapy regimens	
FOLFOX (Every 2 weeks)	Oxaliplatin 85 mg/m2 day 1
	Leucovorin 200 mg/m2 day 1
	5-FU 400 mg/m2 IV Bolus day 1 and 2
	5-FU 600 mg/m2 IV Infusion day 1 and 2 (22 h)
FOLFOX 4 (Every 2 weeks) (4 cycles)	Oxaliplatin 85 mg/m2 day 1
	Leucovorin 200 mg/m2 day 1
	5-FU 400 mg/m2 IV Bolus day 1 and 2
	5-FU 2400 mg/m2 IV Infusion day 1 (46 h)
mFOLFOX 6 (Every 2 weeks) (4 cycles)	Oxaliplatin 85 mg/m2 day 1
	Leucovorin 400 mg/m2 day 1
	5-FU 400 mg/m2 IV Bolus day 1 and 2
	5-FU 1200 mg/m2 IV Infusion day 2 days
CapeOX (Twice daily × 14 days) (Every 3 weeks)	Oxaliplatin 130 mg/m2 day 1
	Capecitabine 850 mg/m2 PO BID for 14 days
FOLFIRI (Every 2 weeks)	Irinotecan 165 mg/m2 day 1
	Leucovorin 200 mg/m2 day 1
	5-FU 400 mg/m2 IV Bolus day 1 and 2
	5-FU 600 mg/m2 IV Infusion day 1 and 2 (22 h)
FOLFOXIRI (Every 2 weeks)	Irinotecan 180 mg/m2 day 1
	Oxaliplatin 85 mg/m2 day 1
	Leucovorin 200 mg/m2 day 1
	5-FU 3200 mg/m2 IV Infusion day (48 h)
Bevacizumab	5–10 mg/kg IV every 2 weeks with chemotherapy
Cetuximab	400 mg/m2 IV day 1, then 250 mg/m2 IV weekly

Use of FOLFOX or the combination of folinic acid, fluorouracil, and irinotecan (FOLFIRI) is recommended in treatment of patients with stage III or IV disease.

17.15.3 Adjuvant Chemoradiation Therapy

In patients with resectable stage II and III resectable rectal cancer, preoperative chemoradiation enhances the pathological response and improves local control; however, it does not improve either disease-free or overall survival [42]. A study by Ebert et al of colorectal cancer genetics and treatment found a link between hypermethylation of transcription factor AP-2 epsilon (TFAP2E) and clinical nonresponsiveness to chemotherapy in colorectal cancer [43].

17.15.4 Radioembolization

A prospective, multicenter, randomized phase III study by Hendlisz et al compared the addition of yttrium-90 resin to a treatment regimen of fluorouracil 300 mg/m2 IV infusion (days 1–14 q8wk) with fluorouracil IV alone. Yytrium-90 was injected intra-arterially into the hepatic artery. Findings showed that the addition of radioembolization with yytrium-90 significantly improved time to liver progression and median time to tumor progression [44].

17.16 Prevention

On December 22, 2010, the US Food and Drug Administration approved the use of quadrivalent human papilloma virus (HPV) vaccine (Gardasil) for prevention of anal cancer and associated precancerous lesions in people aged 9–26 years. HPV is associated with about 90% of anal cancer. In a study of homosexual males, HPV vaccine was shown to be 78% effective in prevention of HPV 16- and 18-related anal intraepithelial neoplasms.

17.17 Prognosis

Overall 5-year survival rates for rectal cancer are as follows:

- Stage I, 90%
- Stage II, 60% to 85%
- Stage III, 27% to 60%
- Stage IV, 5% to 7%

Fifty percent of patients develop recurrence, which may be local, distant, or both. Local recurrence is more common in rectal cancer than in colon cancer.

- Disease recurs in 5–30% of patients, usually in the first year after surgery.
- Factors that influence the development of recurrence include surgeon variability, grade and stage of the primary tumor, location of the primary tumor, and ability to obtain negative margins.
- Surgical therapy may be attempted for recurrence and includes pelvic exenteration or APR in patients who had a sphincter-sparing procedure.
- Radiation therapy generally is used as palliative treatment in patients who have locally unresectable disease.

Questions & Answeres

1. **Why Is Colorectal Cancer Increasing in Younger Patients?**

Colorectal cancer (CRC) has long been considered an older person's disease. But a new American Cancer Society (ACS) report challenges that notion with findings that point to a dramatic rise in CRC among younger individuals.

Three in 10 CRC diagnoses now occur among people younger than 55 years, the report found, and rates among young and middle-aged adults have returned to what they were for people born around 1890. Someone born in 1990 now has double the risk for colon cancer and quadruple the risk for rectal cancer compared with someone born around 1950, lead author, Rebecca Siegel, MPH, from the ACS in Atlanta, Georgia, told Medscape Medical News in a recent interview.

Most experts don't advise CRC screening for average-risk individuals until age 50, so diagnosis of younger adults is often not on clinicians' radar. The report didn't explore the reason for the sharp increase of the condition in people under 50, but the authors speculate that it might be related to obesity, sedentary lifestyle, and lack of access to healthcare, which is often associated with later diagnosis and worse prognosis.

2. **Is laparoscopic surgery superior, inferior, or equal to open surgery for management of patients with rectal cancer?**

There is considerable controversy about the best surgical operative method for management of lower bowel cancer. It seems reasonable that in this anatomic region with limited visibility, a laparoscopic approach would allow for more complete tumor removal.

However, in the summary results from combining available published reports of randomized trials, the current overall results suggest that noncomplete tissue excision is increased by about 30% in patients undergoing laparoscopic surgery.

Is this the final word on the topic? Not at all. Surgeons need to wait until comparative randomized trials with long-term survival data are available.

3. **In patients with rectal cancer who have had a diverting ileostomy, is early closure of the ileostomy beneficial?**

In a recent randomized trial published in Annals of Surgery, the authors compared 55 patients allocated to an early closure group (8–13 days after stoma creation) with 57 patients in a late closure group (> 12 weeks). After 1 year of follow-up, an average of 1.2 complications per patients occurred in the early closure group compared with 2.9 complications per patient in the delayed closure group ($P < .001$).

Many studies have confirmed that diverting fecal flow after a low anterior resection is a beneficial procedure. However, there may be various complications associated with the diverting procedure, and these complications may be related to the duration of the ileostomy.

This randomized trial carried out in several Scandinavian centers found that early closure of the diverting ileostomy significantly reduced the total number of complications. Furthermore, early closure of the ileostomy minimized many troublesome but nonfatal complications, such as skin irritation, ulceration, and leakage, associated with the ileostomy.

As the authors point out, one potential study weakness is that only about one third of the 418 potentially available patients were eventually included in the final analysis. Nevertheless, the findings imply that for many patients, closing a diverting ileostomy soon after the original rectal excision is beneficial as well as safe.

4. **Is 'Watch-and-Wait' Safe in Selected Rectal Cancer Patients?**

New data support the "watch-and-wait" side of the ongoing debate about the best approach to treatment for patients with rectal cancer. With improved survival now being seen after initial chemoradiation, some experts are arguing for omitting surgery in lieu of observation.

In the largest patient series to date in which surgery was omitted after induction therapy, the authors found that 3-year survival was 91%, which is similar to historic survival rates among patients who receive surgery.

For patients who experienced local recurrence, the 3-year survival was 87%.

5. **Is Total Neoadjuvant Approach Promising in Locally Advanced Rectal Cancer?**

Preoperative chemotherapy in combination with chemoradiation (total neoadjuvant therapy, or TNT) appears to have advantages over traditional approaches to treating locally advanced rectal cancer, according to new research.

TNT has been developed to optimize delivery of effective systemic therapy aimed at micrometastases, Dr. Martin R. Weiser of Memorial Sloan Kettering Cancer Center, in New York City, and colleagues note in JAMA Oncology.

6. **Is Radical Surgery Needed in Rectal Cancer for All Patients?**

Do patients with rectal cancer who have responded optimally to chemoradiation need to undergo surgery as well? The answer to that is up for grabs, with strong viewpoints on both sides of the coin.

Experts arguing against surgery are urging that patients can be followed with "a wait and see" approach, but experts for surgery argue that this places patients at unnecessary risk for relapse.

The two sides of this debate are outlined in a pair of articles published online in the December 22 in JAMA Oncology. In the article, Heidi Nelson, MD, Nikolaos Machairas, MD, and Axel Grothey, MD, all from the Mayo Clinic, Rochester, Minnesota, argue that The curative contribution of surgery is substantial. However, Other institutions, the authors note, have reported the evidence that some patients do not need to undergo a radical resection is frankly undeniable. The ideal would be to compare watch and wait with standard total mesorectal excision in a randomized

clinical trial with clear long-term oncologic and functional outcome measures. But such a trial seems unlikely, the authors point out, considering the morbidity and mortality associated with the surgical procedure and the comparable oncologic and survival outcomes that have already been reported with observation.

7. **Obesity Linked to Increased Cancer Frequency in Young Adults.**

Cancer in adults younger than 50 years is occurring with more frequency. The increase may be due to obesity, according to a new study. As overweight and obesity have become a major public health problem almost everywhere around the globe, cancer in young adults is also increasing. Obesity is associated not only with an increase in the incidence of certain cancers but also with a worse prognosis for patients with cancer who are obese. In addition to its association with an increase in the incidence of cancer and worse prognoses, obesity hastens the development of cancer.

8. **Does Intensive Surveillance After Colorectal Cancer Surgery Improve Outcomes?**

Outcomes after colorectal-cancer surgery are no better with more- versus less-intensive surveillance, according to two new studies in the May 22/29 issue of JAMA. Five-year overall mortality did not differ significantly between high-frequency (13.0%) and low-frequency follow-up (14.1%), the researchers report. Similarly, there were no significant differences between the groups in five-year colorectal-cancer-specific mortality rates (10.6% vs. 11.4%, respectively) or in risk of colorectal-cancer-specific recurrence (21.6% vs. 19.4%, respectively).

9. **Total Mesorectal Excision**

Total mesorectal excision (TME) is a common procedure used in the treatment of colorectal cancer in which a significant length of the bowel around the tumor is removed. TME addresses earlier treatment concerns regarding adequate local control of rectal cancer when an anterior resection is performed. TME is indicated as a part of low anterior resection for patients with adenocarcinoma of the middle and lower rectum. It is now considered the gold standard for tumors of the middle and the lower rectum. TME is indicated as a part of low anterior resection for patients with adenocarcinoma of the middle and lower rectum. It is now considered the gold standard for tumors of the middle and the lower rectum.

10. **Early Colorectal Cancer: Missing the Clues?**

Colorectal cancer (CRC) is up significantly in those under age 50, and the increase of CRC in young adults in their 20s and 30s is alarming. Early detection is where the primary care doctor plays a critical role. When CRC-like symptoms are present, regardless of a patient's age, it is important not to dismiss them or chalk them up to more benign causes simply because the patient is under 50, 30, or, sadly, even under 20.

11. **To Drain or Not to Drain Infraperitoneal Anastomosis After Rectal Excision for Cancer.**

In a recent randomized trial published in Annals of Surgery, the authors compared 236 with drain and 233 without. The rate of pelvic sepsis, reoperation, and rate of stoma closure was similar between drain and no drain. This randomized trial suggests that the use of a pelvic drain after rectal excision for rectal cancer did not confer any benefit to the patient.

12. **Definitions of High and Low Risk With Help of MRI**

The German investigators used MRI to help differentiate high and low risk. Preoperative MRI can determine the relationship between the tumour and the mesorectal fascia (the potential resection margin). MRI done before therapy "should enable distinction between patients at low risk of LR [local recurrence] (uninvolved mrCRM that does not need preoperative CRT) and patients at high risk (involved mrCRM that requires preoperative CRT to downstage the tumour for a negative pCRM resection)."

13. **Improved Rectal-Cancer Survival Seen With Adjuvant Chemotherapy.**

Adjuvant chemotherapy is associated with improved overall survival in patients with rectal cancer and pathological complete response after neoadjuvant chemotherapy and resection, according to results from two studies of the National Cancer Database (NCDB).

14. **Colorectal Cancers on the Rise in Younger Adults.**

Expert don't know why the rates of colorectal cancer are rising among young people. a third of the cases can be attributed either to a genetic condition or family history of the disease. For the remaining two-thirds, it's unclear. Changes in diet over the last few decades as a possible explanation, Younger people today eat a lot more fast food and processed food – things we know are associated with colorectal and other kinds of cancers. Hormones and antibiotics used on livestock and found in meat and other animal products might reduce the ability of our gut bacteria to protect us from disease. There's a lot of speculation about potential underlying causes.

15. **Indications for Screening in Patients at high Risk for Colon and Rectal cancer.**

A patient's family history or personal history may indicate increased risk for colorectal cancer. Patients at high risk for colon and rectal cancer due to family history who should be included in surveillance programs include those with the following: Family history of colon and rectal cancer; First-degree relative with adenoma aged younger than 60 years; Genetic cancer syndromes; Hereditary nonpolyposis colorectal cancer (HNPCC); Familial adenomatous polyposis (FAP).

References

1. Glynne-Jones R, Wyrwicz L, Tiret E et al (2018) Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 29:iv263. https://doi.org/10.1093/annonc/mdy161
2. American Cancer Society. Cancer facts & figures, 2018. American Cancer Society 2018
3. Siegel RL, Fedewa SA, Anderson WF et al (2017) Colorectal cancer incidence patterns in the United States, 1974–2013. J Natl Cancer Inst. 2017 Aug 1;109(8)
4. Potter JD (1999) Colorectal cancer: molecules and populations. J Natl Cancer Inst 91(11):916–932
5. Chao A, Thun MJ, Connell CJ et al (2005) Meat consumption and risk of colorectal cancer. JAMA 293(2):172–182
6. Baron JA, Beach M, Mandel JS et al (1999) Calcium supplements for the prevention of colorectal adenomas. N Engl J Med 340(2):101–107
7. Ferrari P, Jenab M, Norat T et al (2007) Lifetime and baseline alcohol intake and risk of colon and rectal cancers in the European prospective investigation into cancer and nutrition (EPIC). Int J Cancer 121(9):2065–2072
8. Kabat GC, Howson CP, Wynder EL (1986) Beer consumption and rectal cancer. Int J Epidemiol 15(4):494–501
9. Tsoi KK, Pau CY, Wu WK et al (2009) Cigarette smoking and the risk of colorectal cancer: a meta-analysis of prospective cohort studies. Clin Gastroenterol Hepatol 7(6):682–688
10. Phipps AI, Baron J, Newcomb PA (2011) Prediagnostic smoking history, alcohol consumption, and colorectal cancer survival: the Seattle colon cancer family registry. Cancer 117(21):4948–4957
11. Giovannucci E, Wu K. Cancers of the colon and rectum. Schottenfeld D, Fraumeni J Cancer epidemiology and prevention. 3rd, New York Oxford University Press; 2006.
12. Johns LE, Houlston RS (2001) A systematic review and meta-analysis of familial colorectal cancer risk. Am J Gastroenterol 96(10):2992–3003
13. Burt RW (1996) Familial risk and colorectal cancer. Gastroenterol Clin N Am 25(4):793–803
14. de Wijkerslooth TR, Stoop EM, Bossuyt PM et al (2012) Immunochemical fecal occult blood testing is equally sensitive for proximal and distal advanced neoplasia. Am J Gastroenterol 107(10):1570–1578
15. Nelson H, Petrelli N, Carlin A et al (2001) Guidelines 2000 for colon and rectal cancer surgery. J Natl Cancer Inst 93(8):583–596
16. Schoen RE, Pinsky PF, Weissfeld JL, Yokochi LA, Church T, Laiyemo AO et al (2012) Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. N Engl J Med 366:2345–2357
17. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC et al (2016) Screening for colorectal cancer: US Preventive Services Task Force Recommendation Statement. JAMA 315(23):2564–2575
18. Kapiteijn E, Marijnen CA, Nagtegaal ID et al (2001) Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. N Engl J Med 345(9):638–646
19. Baxter NN, Garcia-Aguilar J (2007) Organ preservation for rectal cancer. J Clin Oncol 25(8):1014–1020
20. Rothenberger D, Garcia-Aquilar J (2005) Rectal cancer, local treatment. Current therapy in colon and rectal surgery, 2nd edn. Mosby, Philadelphia
21. Peng J, Chen W, Venook AP et al (2011) Long-term outcome of early-stage rectal cancer undergoing standard resection and local excision. Clin Colorectal Cancer 10(1):37–41
22. Stitzenberg KB, Sanoff HK, Penn DC et al (2013) Practice patterns and long-term survival for early-stage rectal cancer. J Clin Oncol 31(34):4276–4282
23. Weiser MR, Landmann RG, Wong WD et al (2005) Surgical salvage of recurrent rectal cancer after transanal excision. Dis Colon Rectum 48(6):1169–1175

24. Bullard KM, Rothenberger DA (2005) Colon, rectum, and anus. Principles of surgery, 8th edn. McGraw Hill, New York
25. Li S, Chi P, Lin H et al (2011) Long-term outcomes of laparoscopic surgery versus open resection for middle and lower rectal cancer: an NTCLES study. Surg Endosc 25(10):3175–3182
26. Green BL, Marshall HC, Collinson F et al (2013) Long-term follow-up of the Medical Research Council CLASICC trial of conventional versus laparoscopically assisted resection in colorectal cancer. Br J Surg 100(1):75–82
27. van Helmond J, Beart RW (2005) Cancer of the rectum: operative management and adjuvant therapy. Current therapy in colon and rectal surgery, 2nd edn. Mosby, Philadelphia
28. Maurer CA, Renzulli P, Kull C et al (2011) The impact of the introduction of total mesorectal excision on local recurrence rate and survival in rectal cancer: long-term results. Ann Surg Oncol 18(7):1899–1906
29. Fujita S, Akasu T, Mizusawa J et al (2012) Postoperative morbidity and mortality after mesorectal excision with and without lateral lymph node dissection for clinical stage II or stage III lower rectal cancer (JCOG0212): results from a multicentre, randomised controlled, non-inferiority trial. Lancet Oncol 13(6):616–621
30. Meredith KL, Hoffe SE, Shibata D (2009) The multidisciplinary management of rectal cancer. Surg Clin North Am 89(1):177–215
31. Quan D, Gallinger S, Nhan C, Auer RA, Biagi JJ, Fletcher GG et al (2012) The role of liver resection for colorectal cancer metastases in an era of multimodality treatment: a systematic review. Surgery 151(6):860–870
32. Dhir M, Lyden ER, Wang A et al (2011) Influence of margins on overall survival after hepatic resection for colorectal metastasis: a meta-analysis. Ann Surg 254(2):234–242
33. Margalit DN, Mamon HJ, Ancukiewicz M et al (2011) Tolerability of combined modality therapy for rectal cancer in elderly patients aged 75 years and older. Int J Radiat Oncol Biol Phys 81(5):e735–e741
34. Ceelen WP, Van Nieuwenhove Y, Fierens K (2009) Preoperative chemoradiation versus radiation alone for stage II and III resectable rectal cancer. Cochrane Database Syst Rev 2:CD006041
35. Jakobsen A, Ploen J, Vuong T et al (2012) Dose-effect relationship in chemoradiotherapy for locally advanced rectal cancer: a randomized trial comparing two radiation doses. Int J Radiat Oncol Biol Phys 84(4):949–954
36. Wong RK, Tandan V, De Silva S et al (2007) Pre-operative radiotherapy and curative surgery for the management of localized rectal carcinoma. Cochrane Database Syst Rev 2:CD002102
37. Ng K, Ogino S, Meyerhardt JA et al (2011) Relationship between statin use and colon cancer recurrence and survival: results from CALGB 89803. J Natl Cancer Inst 103(20):1540–1551
38. NCCN. Clinical practice guidelines in oncology symposium: colon, rectal and anal cancers
39. NCCN. Clinical Practice Guidelines in Oncology. Rectal Cancer V.2.2009
40. Kidwell KM, Yothers G, Ganz PA et al (2012) Long-term neurotoxicity effects of oxaliplatin added to fluorouracil and leucovorin as adjuvant therapy for colon cancer: results from National surgical adjuvant breast and bowel project trials C-07 and LTS-01. Cancer 118(22):5614–5622
41. Kim IY, Kim BR, Kim YW (2015) Factors affecting use and delay (≥8 weeks) of adjuvant chemotherapy after colorectal cancer surgery and the impact of chemotherapy-use and delay on oncologic outcomes. PLoS One 10(9):e0138720
42. Cheng X, Chen VW, Steele B et al (2001) Subsite-specific incidence rate and stage of disease in colorectal cancer by race, gender, and age group in the United States, 1992–1997. Cancer 92(10):2547–2554
43. Ebert MP, Tanzer M, Balluff B et al (2012) TFAP2E-DKK4 and chemoresistance in colorectal cancer. N Engl J Med 366(1):44–53
44. Hendlisz A, Van den Eynde M, Peeters M et al (2010) Phase III trial comparing protracted intravenous fluorouracil infusion alone or with yttrium-90 resin microspheres radioembolization for liver-limited metastatic colorectal cancer refractory to standard chemotherapy. J Clin Oncol 28(23):3687–3694