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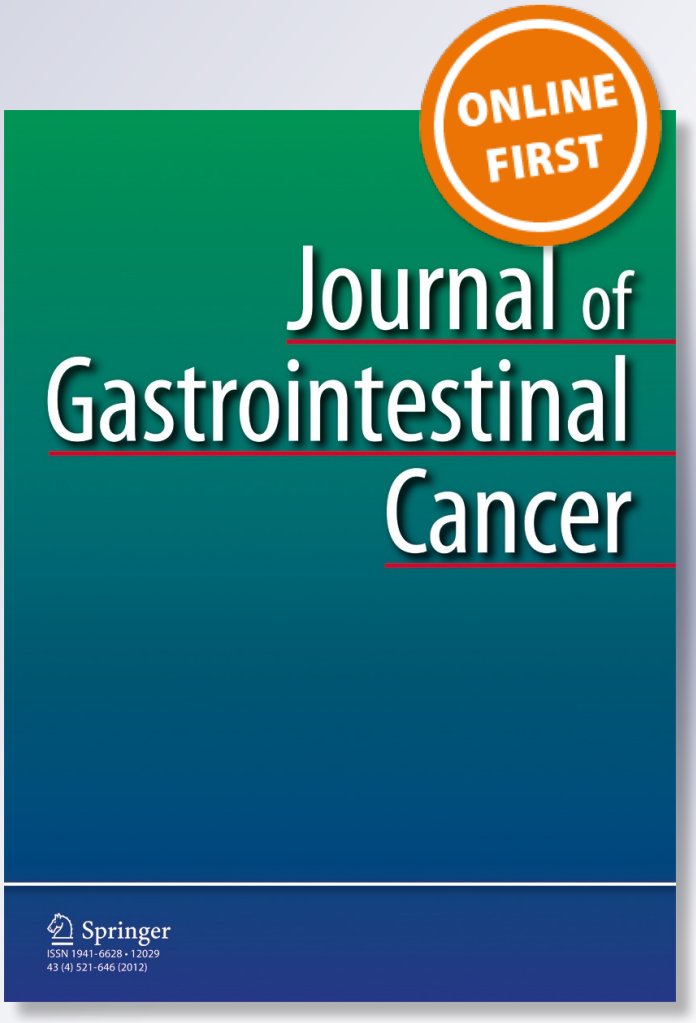

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REVIEW ARTICLE

Colorectal Cancer Emergencies

Andy Barnett · Anna Cedar · Faisal Siddiqui · Daniel Herzig · Emilie Fowlkes · Charles R. Thomas Jr.

Abstract
Introduction Colorectal cancer (CRC) is a common type of malignancy encountered in the United States. A significant proportion of patients with CRC will seek emergency medical care during the course of their illness and treatment.
Background Emergent presentations can be the result of either local tumor invasion, regional progression, or therapeutic techniques. Specific complications of CRC which present emergently include rectal bleeding, abdominal pain, and bowel obstruction. Less common issues encountered include malignant ascites, neutropenic enterocolitis, and radiation enteropathy.
Conclusion The care of CRC patients in the setting of an acute severe illness typically requires the joint efforts of the emergency medical team in consultation with surgical, medical, and radiation oncology. A high degree of suspicion for the typical and atypical complications of CRC is important for all clinicians who are responsible for the care of these patients.

Keywords Cancer emergencies · Colorectal cancer

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Introduction

Colorectal cancer (CRC) is the second leading cause of cancer death for men and women in the USA today, with 150,000 new cases and 50,000 deaths each year [1]. Many of these patients will present with acute or emergent symptoms related to their malignancy. Acute presentations can occur as the initial event, during the course of the disease, or at the end of life. In the early stages, patients will present with symptoms of local and invasive malignancy. For those who have been diagnosed and are undergoing treatment, there are a host of complications associated with chemotherapeutic, radiation, and surgical treatments. In the later stages of disease, the patient with CRC may suffer from metabolic and infectious complications or symptoms in need of palliation. This overview covers the acute and emergency issues involved in the care of the patient with CRC at all stages of the disease.

Presentation of Symptomatic Malignancy

CRC may be detected early through asymptomatic screening tests or as a result of a diagnostic workup for symptomatic disease. Screening methods currently recommended by the US Preventive Services Taskforce include flexible sigmoidoscopy, barium enema, annual fecal occult blood testing, and colonoscopy [2]. Despite the relative merits of each of these strategies, approximately 40 % of the population does not complete any screening. A significant number of

patients will ultimately be diagnosed with CRC only after they present symptomatically into the healthcare system from local or advanced disease. Symptomatic disease tends to be a later stage and may not be curable.

Up to 33 % of patients who were ultimately diagnosed with CRC initially presented with an acute condition [3]. Patients presenting to the emergency department and requiring surgery within 72 h of admission had more advanced disease than patients who underwent elective surgery longer after the diagnosis. Patients requiring an acute operation had an 11 % 30-day mortality and 42 % 2-year survival compared with 5 % 30-day mortality and 65 % 2-year survival in elective operations for CRC.

Acute Lower GI Bleeding

Acute lower GI bleeding (LGIB) is defined as bleeding whose source is distal to the ligament of Treitz. Initial evaluation should try to distinguish distal sources from those proximal to the ligament of Treitz, which occurs three times more often than LGIB [4]. A cross-sectional survey by Talley et al. identified a 15.5 % lifetime prevalence of LGIB in adults [5]. Longstreth et al. estimated an annual incidence rate of hospitalization for LGIB to be 20.5/100,000 adults [6]. Between the third and ninth decades of life, this rate increased 200-fold [7] (Figs. 1 and 2; Tables 1 and 2).

CRC is the cause of LGIB in 8 to 26 % of cases [6, 8, 9]. Bleeding caused by CRC is thought to result from erosion of the mucosal surface and rarely causes brisk hemorrhage [9]. Nevertheless, up to 50 % of CRC patients will have LGIB [10]. Concurrent abdominal symptoms are present much more often when LGIB is due to cancer [11]. However, bleeding may be a relatively early symptom, and patients with bleeding may seek care earlier in the course of their disease [12].

For those patients presenting to the ED with LGIB, initial treatment is directed at resuscitation. Hemodynamic monitoring, establishment of large-bore intravenous access and crystalloid resuscitation is aimed at stabilization of the acute presentation. Transfusion should be considered based on clinical findings rather than initial hematocrit, which can be inaccurate in the setting of a brisk bleed. Particularly concerning findings include continued active bleeding and continued signs of hypoperfusion, tachycardia, or hypotension after administration of 2 l of crystalloid. The threshold to transfuse should be lower in elderly patients who are less likely to tolerate a hypovolemic state. Assessment and correction of other metabolic and electrolyte abnormalities and coagulopathy is included in the initial management. Nasogastric tube placement may be needed to evaluate for an upper GI source of bleeding [13, 14]. Patients who fail to respond to an initial crystalloid challenge should be admitted to the intensive care unit and be considered for blood transfusion and emergent interventional measures. Early consultation with a surgeon should also be requested. Localization of bleeding by angiography or endoscopy should be attempted before surgical treatment whenever possible. Indications for surgical intervention include hemodynamic instability despite vigorous resuscitation with more than 6 units of blood products; inability to stop hemorrhage with endoscopic techniques; recurrent bleeding after initial stabilization; recurrent hemorrhage associated with shock; ongoing slow bleeding requiring more than 3 units of blood products per day [7].

Three major imaging modalities—endoscopy, angiography, and tagged-red-blood-cell (RBC) scan—may be employed in the diagnosis of LGIB. Endoscopy can be difficult in the absence of a bowel prep, but this modality may identify the site of bleeding in 74 to 89 % of cases [13, 15, 16]. Angiography has a sensitivity of 42 to 86 % but interventional procedures may have a higher rate of bowel ischemia than endoscopic techniques, so some clinicians reserve this test for situations where endoscopy is not feasible or nondiagnostic [13, 16]. Tagged-RBC scanning can

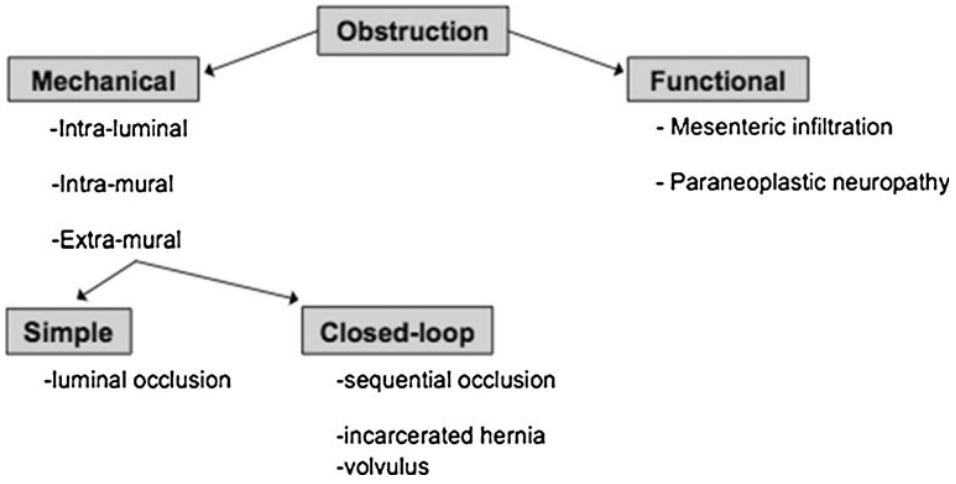

Fig. 1 Categorizing a malignant bowel obstruction. (With permission from: Ilgen JS, Marr AL [41])

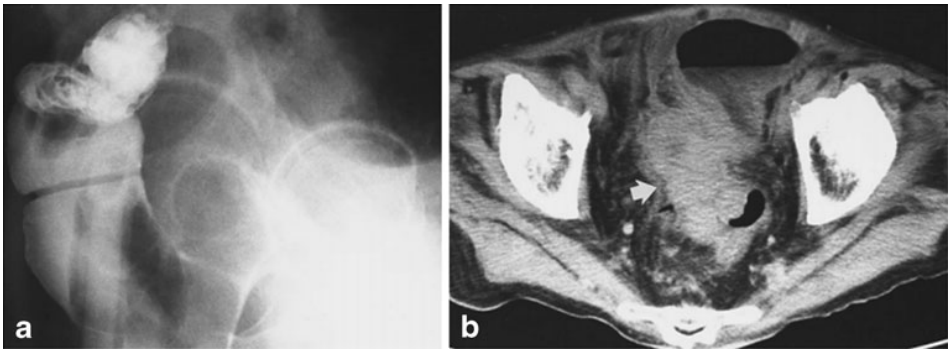

Fig. 2 False-negative CE. **a** Rectal spot film from incomplete misinterpreted barium enema where the patient could not retain the barium. **b** CT demonstrates large bulky tumor mass with infiltration of surrounding fat (*arrow*). (With permission from: Frager D, Rovno HD, Baer JW, Bashist B, Friedman M [23])

detect bleeding rates for as low as 0.1 to 0.4 ml/min but has a lower diagnostic yield ranging from 26 to 72 % [13, 16]. Because it can detect a lower rate of bleeding than angiography, it is useful to screen patients with a tagged-RBC scan before proceeding with angiography. Especially in the setting of metastatic disease, interventional radiologic treatments may provide effective treatment of hemorrhage without the need for a laparotomy, sparing the patient from a recovery period and hastening the initiation of the best treatment for systemic disease, chemotherapy.

Malignant Bowel Obstruction

Malignant bowel obstruction (MBO) may be mechanical or functional [17]. Mechanical MBO includes lesions that physically obstruct the lumen of the intestine. This obstruction can be complete or incomplete. Malignancy is the most common cause of large bowel obstruction, but the differential diagnosis includes adhesive disease, hernia, volvulus, and extrinsic obstruction [18]. Closed-loop obstruction can occur in setting of multiple tumors or a competent ileocecal valve, placing the patient at risk for ischemia and translocation of bacteria across the intestinal wall. High mortality is associated with closed loop obstruction associated with malignancy [19–21] (Figs. 3 and 4; Table 3).

Functional bowel obstruction in the setting of malignancy can include anything that causes adynamic ileus. Examples include reduced colonic motility resulting from narcotic pain medication and impaired colonic motility from direct neurovascular invasion of malignant tissue.

Patients with large bowel obstruction typically present with progressive worsening of abdominal pain, distension, tympany, and ultimately nausea and vomiting. The definitive diagnosis of large bowel obstruction is suggested on plain radiograph and can be confirmed with computed tomography (CT) scan or water-soluble contrast enema [22–25].

Surgical consultation is required, with treatment decisions individualized. Patients presenting with obstruction who have no evidence of metastatic disease should be considered for curative therapy. With complete obstruction, operative intervention may be needed. Obstruction from tumors in the rectum may respond to chemoradiation if the

Table 1 Causes of lower GI bleeding. From: Lo BM [14]

Upper GI bleed
Diverticulitis
GI carcinoma
Angiodysplasia
Arteriovenous malformations
Mesenteric ischemia
Ischemic colitis
Meckel diverticulum
Hemorrhoids
Infectious colitis
Inflammatory bowel disease
Polyps
Radiation colitis
Rectal ulcers
Trauma
Foreign bodies
Carcinoma
Prostate biopsy sites
Endometriosis
Dieulafoy lesions
Colonic varices
Portal hypertensive enteropathy

Table 2 Diagnosis of obstruction. From: Frager D, Rovno HD, Baer JW, Bashist B, Friedman M [23]

	% CT	% CE	p[a]
Sensitivity	96	80	0.045
Specificity	93	100	NS
Accuracy	95	81	0.047
Positive predictive value	96	100	NS
Negative predictive value	93	16.7	0.0004

NS not significant

[a] Determined by the Fisher exact test, two tailed

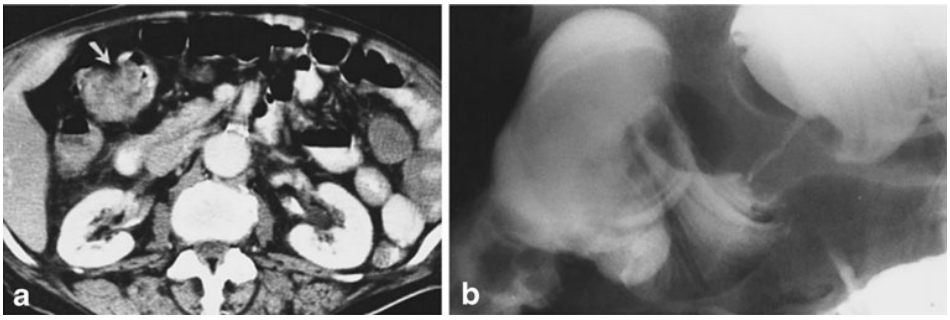

Fig. 3 False-negative CT. **a** CT was interpreted as no obstruction. The hepatic flexure (*arrow*) was considered unremarkable albeit stool filled. **b** Spot film from second barium enema reveals annular carcinoma at the hepatic flexure, which was confirmed at surgery. (With permission from: Frager D, Rovno HD, Baer JW, Bashist B, Friedman M [23])

risk of perforation is low and nutritional support can be provided. While there has been interest in colonic stenting for the relief of malignant obstruction, the risk of perforation limits its use in the curative treatment setting. However, in the presence of metastatic disease, it may prevent an operation and allow the initiation or continuation of systemic chemotherapy. Regardless of the specific approach, these cases tend to have a relatively high associated morbidity and mortality when compared with non-emergent interventions [26, 27].

Malignant Intussusception

Intussusception is defined as the telescoping of a proximal segment of bowel (intussusceptum) into an adjacent distal segment (intussuscipiens), usually resulting in a mechanical obstruction. In adults, intussusception is a rare cause of bowel obstruction and accounts for only 5 % of all cases of obstruction [28]. In a study of 60 consecutive patients with intussusception, Goh et al. found that 60 % of those patients with intussusception of the large bowel had a pathologic lead point that was malignant, suggesting that malignancy should be considered in all adults presenting with obstruction due to intussusception [29, 30]. In a study of 72 consecutive patients with intussusception, Chiang et al. found that of the patients with large bowel intussusception, 63 % were due to a malignant tumor (mostly adenocarcinoma or lymphoma) at the lead point [31]. From a management standpoint, large bowel intussusception usually results in bowel resection, due in part to the higher likelihood of a malignant lesion at the lead point [32, 33]. CT scan is the preferred method of diagnosis in the emergency setting due to its high sensitivity, its ability to distinguish pathologic from nonpathologic lead points, and its utility in aiding surgical planning [34–36] (Figs. 5 and 6; Table 4).

Bowel Perforation

Bowel perforation is a known complication of CRC and often presents with severe abdominal pain. Perforations are categorized as either free, in which the bowel contents are spilled into the abdominal cavity, or contained, where contiguous organs wall off the area. CRC predisposes patients to perforations due to multiple mechanisms. Intraluminal neoplasms can cause intrinsic bowel obstructions, resulting in perforation. Metastases to the colon can result in either extrinsic or internal colonic obstruction, also leading to perforation. Tumor lysis syndrome causes a loss of gastrointestinal wall integrity. Immunocompromised patients are also at risk of colitis

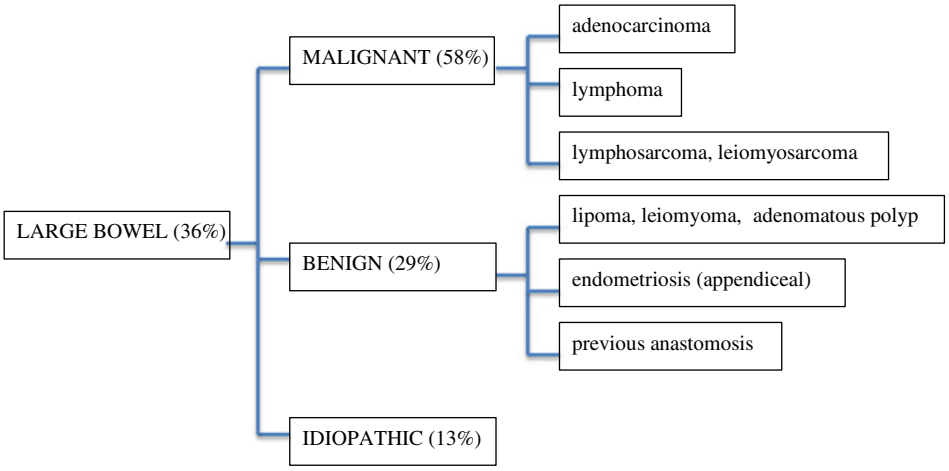

Fig. 4 General causes of intussusception in adults. Based on eight series, on an overall number of 1,048 cases. In the small intestine, the majority of cases are due to benign causes, therefore reduction before resection is recommended when possible. In the colon, the leading causes are malignant tumors, thus reduction only is a less reasonable strategy. (With permission from: Begos DG, Sandor A, Modlin IM [28])

Table 3 Number of colon and rectal cancer patients with the most frequently reported initial symptoms or symptom complexes by stage. From: Korsgaard M, Pedersen L, Sorensen HT, Laurberg S [12]

Initial symptoms or symtom complexes	Colon cancer patients (n=456)		Rectal cancer patients (n=277)	
	Nonadvanced stage 224 (49)	Advanced stage 232 (51)	Nonadvanced stage 145 (52)	Advanced stage 132 (48)
Rectal bleeding and monosymptomatic	30 (64)	17 (36)	34 (69)	15 (31)
Rectal bleeding and other symptoms	44 (59)	30 (41)	56 (55)	45 (45)
Change in bowel habits, including constipation and diarrhea	17 (41)	24 (59)	28 (52)	26 (48)
Abdominal pain and monosymptomatic	18 (41)	26 (59)	2 (67)	1 (33)
Vague symptoms, including abdominal pain	46 (43)	62 (57)	3 (27)	8 (73)
Anemia and monosymptomatic	3 (60)	2 (40)	0 (0)	0 (0)
Anemia and other symptoms	25 (52)	23 (48)	4 (80)	1 (20)
Other symptoms	41 (46)	48 (54)	18 (33)	36 (67)

Percentages in brackets

secondary to neutropenic enterocolitis (NEC) as well as atypical infections, such as cytomegalovirus and *Candida* or *Clostridium difficile*, all of which can cause bowel wall damage, necrosis, and ultimately perforation [37]. Additionally, other types of tumors, such as chronic lymphoid leukemia and lymphomas sometimes invade the colon wall and lead to perforation [38].

The presentation of a free perforation may demonstrate classic findings of peritonitis, including generalized tenderness, involuntary guarding and rebound tenderness; however, contained perforations may have findings that are more subtle and localized [39].

Imaging can help identify perforation, but is not always accurate in distinguishing surgical from nonsurgical cases. In patients with nontraumatic acute abdominal pain, a three-view abdominal series has a sensitivity of 30 %, specificity of 88 %, accuracy of 56 %, and negative predictive value of 51 % for perforation [37, 40]. CT scan can aid in the diagnosis of perforation based on findings, such as free air, pneumatosis intestinalis, portal venous air or air at the site of intestinal obstruction [41], abscess or focal collection of extramural fluid next to perforation site, mesenteric stranding, bowel wall thickening, and leakage of luminal contrast material at the site of perforation [42]. Helical CT scans

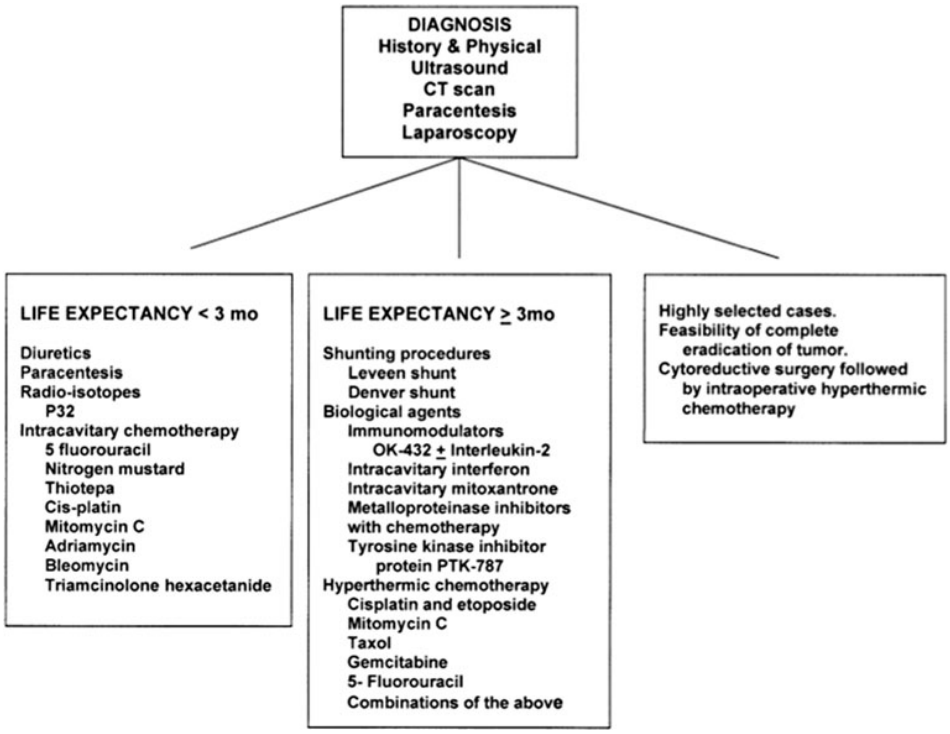

Fig. 5 Algorithm for the therapeutic approach of malignant ascites. The primary factor determining the mode of therapy for ascites is prognosis. Other factors include tumor type, tumor bulk, response before chemotherapy, and the general condition of the patient. (With permission from: Adam RA, Adam YG [44])

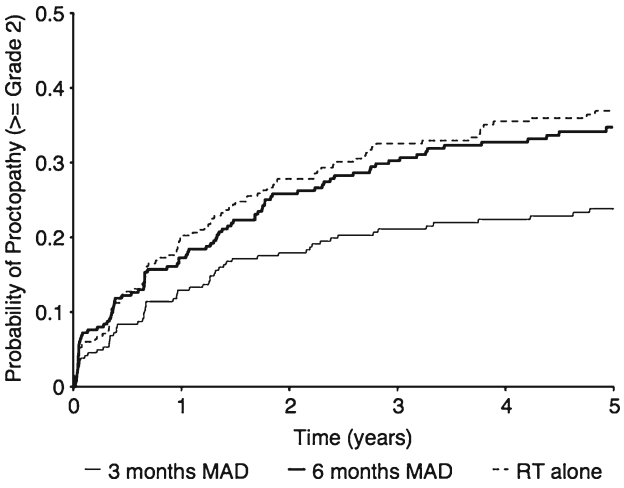

Fig. 6 Time to delayed proctopathy at Gd2 or greater levels from 90 days after starting radiotherapy to 5 years by trial arm. (With permission from: Christie D, Denham J, Steigler A et al. [50])

have a sensitivity of 95–98 %, specificity of 95–97 %, and accuracy of 95 % in detecting perforation. The performance is maximal when oral and IV contrast agents are used. Ultrasound can identify nontraumatic hollow viscous organ perforations with 93–100 % sensitivity and 64–99 % specificity, with outcomes dependent on operator skill and ease of the scan due to patient factors such as obesity [37, 43].

Perforation of the bowel can lead to significant morbidity and mortality, partly because the immunocompromised state can delay symptoms [41]. The mortality rate of secondary peritonitis after perforation is 30–50 % [37]. Perforation can be either free or contained. Free perforation is likely to be a terminal event without surgical intervention. Perforated tumors are at least stage II but can still be treated with curative intent after complete staging. Resuscitation and intravenous antibiotics followed by prompt surgical intervention is warranted. The tumor should be resected when feasible; however, the creation of an anastomosis may not be feasible or prudent in the setting of significant contamination, poor bowel quality, or hemodynamic instability. Contained perforations may present with a phlegmon or abscess. In the stable patient, clinical staging should be completed. In the absence of metastatic disease, complete resection of the tumor, en bloc with adjacent involved organs is the ideal method of controlling the perforation. If metastatic disease is identified, consideration may be given to stabilizing the patient and providing antibiotics with or without percutaneous drainage. However, since chemotherapy may lead to significant septic complications, resection is often advisable even in the setting of metastatic disease.

Table 4 Preoperative radiographic studies in the diagnosis of malignant intussusception. From: Azar T, Berger DL [32]

Examination	% of patients	Accuracy (%)
KUB/upright	71	0
UGI	24	21
Abdominal CT	22	78
Barium enema	22	54
Abdominal ultrasound	5	0

KUB kidney, ureter, and bladder, *UGI* upper gastrointestinal, *CT* computed tomography

Malignant Ascites

Malignant ascites is defined as a collection of proteinaceous fluid containing cancer cells within the peritoneal cavity [44]. About 10 % of all patients with ascites have malignant ascites. Most often, malignant ascites are due to ovarian, endometrial, breast, colonic, gastric, and pancreatic carcinomas, with ovarian cancer being the most common source. Of patients with CRC, 4 % will develop malignant ascites during the course of their disease. The development of malignant ascites carries with it a poor prognosis; the median survival after recognition of this finding is 5.7 months [45, 46]. Detrimental prognostic factors include low serum albumin, low serum protein, and liver metastases. CRC metastasizes to the liver more than any other type of cancer [45] (Fig. 7).

The pathophysiology of malignant ascites is multifactorial and incompletely understood, involving an imbalance between the production of peritoneal fluid and its absorption. The cancer can directly invade the peritoneum and is known as peritoneal carcinomatosis [41]. Cancer cells can also cause venous and lymphatic obstruction. Portal vein thrombosis has infrequently been found to cause ascites in association with colon cancer [47]. The neoplastic tissue leads to increased production of peritoneal fluid, and tumor vasculature has increased permeability, supplying fluid to the peritoneal space. The fluid of malignant ascites typically has high protein

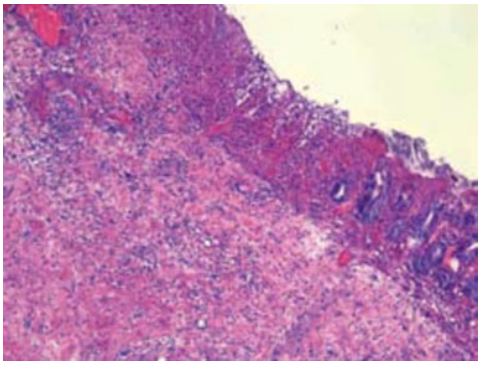

Fig. 7 Photomicrograph of colonic resection specimen, taken with a light microscope (HE, ×10). The image shows mucosa and submucosa. There is partial mucosal necrosis with significant loss of tissue architecture in the mucosa. In the lower right part of the picture, the mucosa is more intact. The submucosa shows fibrosis and a patchy chronic inflammation in the form of aggregates of lymphocytes. (With permission from: Larsen A, Reitan JB, Aase ST, Hauer-Jensen M [58])

content, causing oncotic pressure to pull fluid into the peritoneal cavity [48]. Also, decreased intravascular protein levels occur in malignancy, exacerbating the oncotic pressure gradient of the peritoneal fluid. Theoretically, low intravascular volume will then cause hormone imbalances, leading to increased renin and aldosterone with a subsequent decrease in urinary output [46] and systemic fluid retention.

Diagnosis of malignant ascites begins with a history and physical exam. Significant fluid accumulation is often notable on physical exam, manifested by abdominal distension and sometimes a positive fluid wave test. Ultrasound and abdominal CT scans detect ascites if the volume of fluid accumulation is greater than 100 ml. The differential diagnosis for ascites includes cirrhosis, congestive heart failure, nephrosis, tuberculosis, pancreatitis, malignancy, and peritonitis from pyogenic organisms [44]. Ascitic fluid analysis assists in distinguishing among these pathologies and includes cell count and differential, cytology, ascitic fluid total protein, and serum-ascites albumin gradient. Cytology is positive in almost 100 % of patients with peritoneal carcinomatosis, which make up about two thirds of those with malignant ascites. Patients without peritoneal carcinomatosis have negative cytology, so the overall sensitivity of cytology alone for detecting malignant ascites is 58–75 % and is diagnostic 50–60 % of the time [46]. Other tests improve diagnostic accuracy. Testing the peritoneal fluid for sialic acid has 82 % accuracy in differentiating malignant from nonmalignant ascites. Telomerase is found in 81 % of malignant ascites, with a sensitivity of 76 % and specificity of 96 %. When human gonadotropin-beta is combined with cytology, the diagnostic yield is 90 %. Carcinoembryonic antigen (CEA) combined with cytology yields a diagnostic accuracy of 85 % [44].

Complications of malignant ascites include those associate with multiple paracenteses, including secondary peritonitis, hypotension, pulmonary embolism, renal impairment, adhesions, bleeding, leakage of peritoneal fluid, and rapid re-accumulation of fluid [48]. Spontaneous bacterial peritonitis can also occur, though it is rare in the setting of malignant ascites [49].

The goal of treating malignant ascites is palliation due to the poor prognosis associated with this condition. Curative therapy very rarely occurs, but treatment can improve quality of life for many patients. A wide variety of approaches exists; efficacy depends on type of malignancy, location of primary tumor and metastases, size, progression, number of abdominal surgeries, and general health as well as other factors [44]. Response to therapy is not standardized, but based on evaluation of symptoms, such as pain, dyspnea, and debilitating swelling.

Medical treatment is the first option in selected patients. It provides relief in about 40 % of patients overall and is particularly effective in those with hepatic metastases. Medications used typically are spironolactone plus a loop diuretic, such as furosemide, or bumetanide. Another option is therapeutic paracentesis, which provides temporary relief in 90 % of patients although the need for repeat procedures occurs on average every 10.4 days [46]. Complications of paracentesis include secondary peritonitis, visceral and vascular injury, hypoproteinemia, and hypotension. Incomplete taps occur due to fluid loculations, which are often the result of adhesions caused by multiple or extensive abdominal surgeries [44].

Permanent drains can be placed to treat malignant ascites. Two types are used: nontunneled catheter (pigtail catheter) and secure tunneled catheter (Pleurx catheter). Drains are indicated in patients with a life expectancy of longer than 2–3 months and control ascites for an average of 52 days in 83–100 % of patients. Complications of placement include peritonitis, sepsis, hypotension, and catheter occlusion. The complication rate is 7.5 % for Pleurx catheters, which is comparable to large volume paracentesis. Pigtail catheter complication rate is 30 %. Peritoneovenous shunts are placed to drain peritoneal fluid from the peritoneum to the vena cava. Control of ascites is obtained in 78 % of patients, though patients with ovarian and breast cancer respond better than those with gastrointestinal cancers. The flow of malignant cells to systemic blood is a theoretical concern, although it is usually clinically insignificant and only infrequently seeds the cancer in distant locations [44, 46].

Other treatments for malignant ascites are emerging, including intraperitoneal chemotherapy, intraperitoneal hyperthermic chemotherapy, cytokine therapy, infectious agents as costimulatory immunotherapy, monoclonal antibodies, corticosteroid therapy, radioisotopes, octreotide, and biologic agents, such as VEGF and matrix metalloproteinase inhibitors. Additional investigational studies are needed to assess their efficacy and safety [44, 46].

Complications of Treatment

Curative Therapy

In those who can be stabilized from their emergency presentation, all patients should be considered for curative therapy. Staging includes a full colonoscopy, serum testing for CEA, a two-view radiograph of the chest, and usually CT of the abdomen and pelvis for colon cancer. Staging for rectal cancer adds local tumor staging by endoscopic ultrasound or magnetic resonance imaging with a rectal cancer staging protocol, and the option of CT scan of the chest. Patients with metastatic disease may still be treated with curative intent when there is resectable oligometastatic disease to the liver and or lungs.

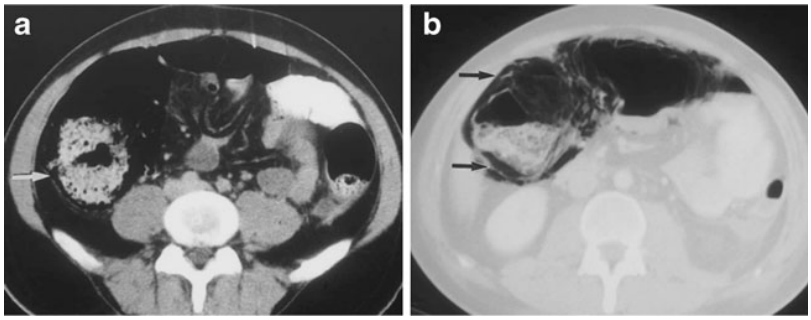

Fig. 8 CT scans obtained in a 29-year-old neutropenic man with acute lymphoblastic leukemia treated with chemotherapy and complicated by NEC. The patient developed abdominal pain, tenderness, and fever. **a** Transverse contrast-enhanced CT scan shows pneumatosis intestinalis involving the cecum (*arrow*). **b** Transverse contrast-enhanced CT scan obtained more superiorly, at lung windows (width, 1,500 HU; center, −400 HU), shows the pneumatosis extending into the transverse colon (*arrows*). The patient fully recovered with conservative therapy. (With permission from: Kirkpatrick ID, Greenberg HM [51])

Colon cancer in the absence of metastatic disease is treated with resection followed by chemotherapy for most stage III patients and selected stage II patients. Stage II patients with tumor penetrating to the visceral peritoneum or other adjacent organs usually receive adjuvant treatment after surgery. Additionally, stage II colon cancer patients who may have been candidates only for surgery may receive adjuvant chemotherapy if they have adverse features on histopathology. Stage III patients usually require adjuvant chemotherapy after surgery.

Rectal cancer treatment options are more individualized based on tumor stage and location. Options include transanal excision of early stage low rectal cancers. For locally advanced disease, preoperative chemoradiation followed by resection is a typical strategy which may or may not preserve the anal sphincters.

Radiation Enteropathy

Radiation treatment (RT) for abdominal and pelvic malignancies frequently exposes small bowel to irradiation. Typically, cancers are treated with tumor-directed RT. However for locoregional disease control, subclinical or microscopic malignant disease is often treated with larger volume of radiation, which includes lymph nodes in the tumor drainage pathway. Radiation exposure to small and large bowel can occur in the setting of extraintestinal malignancies, such as cervical cancer and prostate cancer [50–53] (Figs. 8 and 9).

Etiology of intestinal toxicity is modulated by extent of endothelial damage, activation of intestinal immune system and the enteric nervous system. Acute or early injury is modulated by cell death leading to breakdown in mucosal barrier with bacteria and toxic agents gaining access to subepithelial tissue leading to immune response [54]. Acute response to radiation leads to tissue remodeling causing intestinal fibrosis. This often leads to chronic effects characterized by mucosal atrophy and vascular sclerosis leading to malabsorption, dysmotility, intestinal obstruction, perforations, and fistula formation [55, 56].

Incidence and severity of toxicity depends on treatment related factors such as radiation dose, volume of bowel irradiated, dose fractionation, concurrent chemotherapy, and a history of previous abdominal surgeries. Other non-treatment related factors, such as irritable bowel syndrome, diabetes, collagen vascular disease (scleroderma), and tobacco smoking increase the incidence of toxicity [57].

Early symptoms of radiation toxicity to the bowel are nausea, abdominal pain and diarrhea, with nausea being the earliest indicator of injury. Typically, the early symptoms resolve within 2–4 weeks. Chronic symptoms usually present after a latency period which can last from 6 months to 3 years. Delayed toxic injury to the small bowel is characterized by malabsorption and resultant malnutrition. In contrast, radiation damage to colon manifests as intermittent diarrhea and constipation. Intestinal wall fibrosis leads to

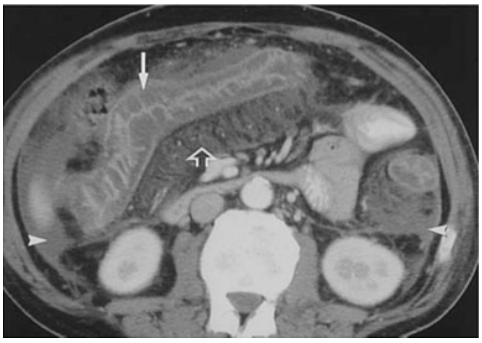

Fig. 9 Transverse contrast-enhanced CT scan obtained in a 41-year-old neutropenic man with non-Hodgkin lymphoma of the neck treated with chemotherapy. The patient developed abdominal pain, fever, and diarrhea. CT scan demonstrates marked colonic wall thickening (*solid arrow*) with nodularity, trapping oral contrast material between the thickened folds. Marked mesenteric stranding (*open arrow*) is present, along with ascitic fluid in the paracolic gutters (*arrowheads*). Results of stool tests were positive for *C. difficile* toxin. (With permission from: Kirkpatrick ID, Greenberg HM [51])

stricture formation leading to ischemic bowel complications causing fistulae or ultimately necrosis. This may present as a surgical emergency for repair of obstruction, fistula or necrotic bowel. Long-term prognosis after surgical intervention is poor since the patient may be malnourished delaying healing and requiring long-term parenteral nutrition [58, 59]. Acute radiation injury to the rectum presents with diarrhea, rectal pain and bleeding. Subsequent colonoscopy frequently reveals telangiectasia in irradiated bowel.

Rectal cancer patients who receive neoadjuvant chemoradiation often receive radiation to the entire pelvis, which includes small and large bowel, rectum, bladder, and reproductive organs. Radiation to the intestinal tissue often causes diarrhea, pain and rectal bleeding. Radiation to the bladder may cause an irritable bladder wall which may manifest as increased urinary urgency and frequency. Long-term effects of pelvic radiation include the risk of intrinsic bowel wall weakness, fistula, and perforation as well as decreased capacity of the bladder. Additionally for female patients, there is an increased risk of vaginal dryness and constriction. Newer anti-angiogenic therapies used with radiation therapy may also cause ischemia and increased bowel injury [60].

Acute GI radiation toxicity is managed symptomatically with anti-diarrheal or anti-nausea medications. Patients who do not respond to first-line anti-diarrheal medication should be considered for octreotide [61]. Acute rectal symptoms such as pain or minor bleeding may be relieved with steroid suppositories. Delayed radiation enteropathy may require surgical intervention for obstruction, perforation, fistula formation, bleeding, or malabsorption [62, 63].

Neutropenic Enterocolitis

NEC is also known by its old name as typhlitis. As the name suggests, it is associated with neutropenia secondary to chemotherapy. It is estimated that 5 % of patients receiving chemotherapy are ultimately diagnosed with NEC [64, 65]. NEC may also present in patients with aplastic anemia, cyclic neutropenia, or in those who are immunocompromised for other reasons.

The pathophysiology of NEC is complex—involving intestinal mucosal injury due to chemotherapy complicated by immunocompromised status and neutropenia. This results in polymicrobial infection due to bacterial invasion which may progress from ulceration, edema, hemorrhage to necrosis and perforation if not diagnosed and treated quickly [66]. Symptoms onset is usually 2–3 weeks after cytotoxic chemotherapy then there is onset of neutropenia. Patients who present with shock or severe abdominal pain may have bowel wall perforation [67]. Imaging studies such as CT, abdominal ultrasound, or abdominal X-rays should be considered. Bowel wall thickening, secondary to edema or hemorrhage, on radiographic imaging is the main diagnostic finding. Diagnostic laparoscopy may be considered to confirm the diagnosis. Barium enema or colonoscopy is generally contraindicated. Laboratory results show profound neutropenia (ANC less than 500). Blood cultures and stool cultures may confirm the diagnosis [68].

Patients with mild to moderate symptoms should be treated with broad-spectrum antibiotics and bowel rest. Supportive care with intravenous fluids, nutrition and blood products is essential to manage the patient. Antibiotic coverage for *C. difficile* and fungal infections should be considered [69]. Surgical consultation should be obtained in severe cases. Although, the risk of mortality with operations for NEC is high, early intervention may lead to reduced mortality.

Palliative Care

Patients who are not medically fit for curative treatment or have unresectable metastatic disease should be treated with palliative intent. Palliation includes treatments that may prolong life or improve the quality of life, but will not cure the disease. Chemotherapy can lead to significant improvement in median survival, from an average of 6–8 months without treatment to 22–24 months with first-line chemotherapy. Quality issues generally relate to pain, bleeding, and obstruction. Pain is best managed medically, although locally advanced rectal cancers may be treated with additional radiation. Nerve block within the lumbar and sacral plexus can also effectively alleviate pain. Bleeding can be treated with supportive care and transfusion if the bleeding is low volume. More significant gastrointestinal hemorrhage can require more invasive treatment, including angioembolization, or possibly surgical intervention. Palliation for malignant ascites is discussed in a separate section above.

Conclusions

CRC is the 2nd leading cause of cancer death in the USA each year. While these numbers have been steadily declining over the last decade, many patients will still present with acute symptoms. These symptoms can lead to the initial diagnosis, can be a sequela of progressive malignant disease, or may be a consequence of disease treatment. The management of these urgent and emergent conditions is typically multidisciplinary and may begin with emergency medical services, but will ultimately require a team approach which includes surgical, radiation, and medical oncology consultants.

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin. 2009;59(4):225–49.
2. U.S. Preventive Services Task Force. Colon cancer screening (USPSTF recommendation). J Am Geriatr Soc. 2000;48(3):333–5.
3. Gunnarsson H, Holm T, Ekholm A, Olsson LI. Emergency presentation of colon cancer is most frequent during summer. Color Dis Off J Assoc Coloproctol GB Irel. 2011;13(6):663–8.
4. Peura DA, Lanza FL, Gostout CJ, Foutch PG. The American College of gastroenterology bleeding registry: preliminary findings. Am J Gastroenterol. 1997;92(6):924–8.
5. Talley NJ, Jones M. Self-reported rectal bleeding in a United States community: prevalence, risk factors, and health care seeking. Am J Gastroenterol. 1998;93(11):2179–83.
6. Longstreth GF. Epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1997;92(3):419–24.
7. Tavakkolizadeh A, Ashley S. Acute gastrointestinal hemorrhage. In: Sabiston DC, Townsend CM, editors. Sabiston textbook of surgery: the biological basis of modern surgical practice. Philadelphia: Elsevier; 2012.
8. Farrands PA, Taylor I. Management of acute lower gastrointestinal haemorrhage in a surgical unit over a 4-year period. J R Soc Med. 1987;80(2):79–82.
9. Rossini FP, Ferrari A, Spandre M, et al. Emergency colonoscopy. World J Surg. 1989;13(2):190–2.
10. Adelstein BA, Macaskill P, Chan SF, Katelaris PH, Irwig L. Most bowel cancer symptoms do not indicate colorectal cancer and polyps: a systematic review. BMC Gastroenterol. 2011;11:65.
11. Douek M, Wickramasinghe M, Clifton MA. Does isolated rectal bleeding suggest colorectal cancer? Lancet. 1999;354(9176):393.
12. Korsgaard M, Pedersen L, Sorensen HT, Laurberg S. Reported symptoms, diagnostic delay and stage of colorectal cancer: a population-based study in Denmark. Color Dis Off J Assoc Coloproctol G B Irel. 2006;8(8):688–95.
13. Zuccaro Jr G. Management of the adult patient with acute lower gastrointestinal bleeding. American College of Gastroenterology. Practice Parameters Committee. Am J Gastroenterol. 1998;93(8):1202–8.
14. Lo BM. Lower Gastrointestinal Bleeding. In: Tintinalli JE, Stapczynski JS, editors. Tintinalli's emergency medicine: a comprehensive study guide. New York: McGraw-Hill; 2011. p. 2120. xl.
15. Davila RE, Rajan E, Adler DG, et al. ASGE Guideline: the role of endoscopy in the patient with lower-GI bleeding. Gastrointest Endosc. 2005;62(5):656–60.
16. Schuetz A, Jauch KW. Lower gastrointestinal bleeding: therapeutic strategies, surgical techniques and results. Langenbeck's Arch Surg/Deut Gesellschaft Chir. 2001;386(1):17–25.
17. Anthony T, Baron T, Mercadante S, et al. Report of the clinical protocol committee: development of randomized trials for malignant bowel obstruction. J Pain Symptom Manag. 2007;34(1 Suppl):S49–59.
18. Peterson M. Large intestine. In: Rosen's emergency medicine: concepts and clinical practice. Philadelphia: Elsevier; 2006. p. 1332–4.
19. Dixon JA, Nichols RL, Hunter Jr DC. Strangulation obstruction of the intestine. early detection. Arch Surg. 1964;88:527–32.
20. Leffall LD, Syphax B. Clinical aids in strangulation intestinal obstruction. Am J Surg. 1970;120(6):756–9.
21. Saltzstein EC, Marshall WJ, Freeark RJ. Gangrenous intestinal obstruction. Surg Gynecol Obstet. 1962;114:694–700.
22. Finan PJ, Campbell S, Verma R, et al. The management of malignant large bowel obstruction: ACPGBI position statement. Color Dis Off J Assoc Coloproctol G B Irel. 2007;9 Suppl 4:1–17.
23. Frager D, Rovno HD, Baer JW, Bashist B, Friedman M. Prospective evaluation of colonic obstruction with computed tomography. Abdom Imaging. 1998;23(2):141–6.
24. Megibow AJ. Bowel obstruction. Evaluation with CT. Radiol Clin N Am. 1994;32(5):861–70.
25. Sinha R, Verma R. Multidetector row computed tomography in bowel obstruction. Part 2. Large bowel obstruction. Clin Radiol. 2005;60(10):1068–75.
26. Tekkis PP, Kinsman R, Thompson MR, Stamatakis JD. The Association of Coloproctology of Great Britain and Ireland study of large bowel obstruction caused by colorectal cancer. Ann Surg. 2004;240(1):76–81.
27. Tilney HS, Lovegrove RE, Purkayastha S, et al. Comparison of colonic stenting and open surgery for malignant large bowel obstruction. Surg Endosc. 2007;21(2):225–33.
28. Begos DG, Sandor A, Modlin IM. The diagnosis and management of adult intussusception. Am J Surg. 1997;173(2):88–94.
29. Goh BK, Quah HM, Chow PK, et al. Predictive factors of malignancy in adults with intussusception. World J Surg. 2006;30(7):1300–4.
30. Takeuchi K, Tsuzuki Y, Ando T, et al. The diagnosis and treatment of adult intussusception. J Clin Gastroenterol. 2003;36(1):18–21.
31. Chiang JM, Lin YS. Tumor spectrum of adult intussusception. J Surg Oncol. 2008;98(6):444–7.
32. Azar T, Berger DL. Adult intussusception. Ann Surg. 1997;226(2):134–8.
33. Wang LT, Wu CC, Yu JC, Hsiao CW, Hsu CC, Jao SW. Clinical entity and treatment strategies for adult intussusceptions: 20 years' experience. Dis Colon Rectum. 2007;50(11):1941–9.
34. Gayer G, Zissin R, Apter S, Papa M, Hertz M. Pictorial review: adult intussusception—a CT diagnosis. Br J Radiol. 2002;75(890):185–90.
35. Warshauer DM, Lee JK. Adult intussusception detected at CT or MR imaging: clinical-imaging correlation. Radiology. 1999;212(3):853–60.
36. Kim YH, Blake MA, Harisinghani MG, et al. Adult intestinal intussusception: CT appearances and identification of a causative lead point. Radiogr Rev Publ Radiol Soc North Am Inc. 2006;26(3):733–44.
37. Langell JT, Mulvihill SJ. Gastrointestinal perforation and the acute abdomen. Med Clin Am. 2008;92(3):599–625. viii–ix.
38. Lalani M, Rhee JC, Gutkin DW, Matin K, Ahmad J. Uncommon presentations of some common malignancies: case 3. Chronic lymphocytic leukemia involving the colon and presenting with perforation. J clin Oncol Off J Am Soc Clin Oncol. 2005;23(6):1315–7.
39. Taylor S, Watt M. Emergency department assessment of abdominal pain: clinical indicator tests for detecting peritonism. Eur J Emerg Med Off J Eur Soc Emerg Med. 2005;12(6):275–7.
40. Mackersie AB, Lane MJ, Gerhardt RT, et al. Nontraumatic acute abdominal pain: unenhanced helical CT compared with three-view acute abdominal series. Radiology. 2005;237(1):114–22.
41. Ilgen JS, Marr AL. Cancer emergencies: the acute abdomen. Emerg Med Clin North AM. 2009;27(3):381–99.
42. Spencer SP, Power N. The acute abdomen in the immune compromised host. Cancer Imaging Off Publ Int Cancer Imaging Soc. 2008;8:93–101.
43. O'brien M. Acute abdominal pain. In: Tintinalli JE, Stapczynski JS, editors. Tintinalli's emergency medicine: a comprehensive study guide. New York: McGraw-Hill; 2011. p. 2120. xxxix.
44. Adam RA, Adam YG. Malignant ascites: past, present, and future. J Am Coll Surg. 2004;198(6):999–1011.

45. Ayantunde AA, Parsons SL. Pattern and prognostic factors in patients with malignant ascites: a retrospective study. Ann Oncol Off J Eur Soc Med Oncol/ESMO. 2007;18(5):945–9.
46. Chung M, Kozuch P. Treatment of malignant ascites. Curr Treat Options in Oncol. 2008;9(2–3):215–33.
47. Scoffield JL, Humphreys WG, Clarke JC. Acute presentation of ascites in association with colon cancer. Ulster Med J. 1998;67(2):137–8.
48. Becker G, Galandi D, Blum HE. Malignant ascites: systematic review and guideline for treatment. Eur J Cancer. 2006;42 (5):589–97.
49. Makharia GK, Sharma BC, Bhasin DK, Singh K. Spontaneous bacterial peritonitis in a patient with gastric carcinoma. J Clin Gastroenterol. 1998;27(3):269–70.
50. Christie D, Denham J, Steigler A, et al. Delayed rectal and urinary symptomatology in patients treated for prostate cancer by radiotherapy with or without short term neo-adjuvant androgen deprivation. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2005;77(2):117–25.
51. Kirkpatrick ID, Greenberg HM. Gastrointestinal complications in the neutropenic patient: characterization and differentiation with abdominal CT. Radiology 2003;226(3):668–674.
52. Danielsson A, Nyhlin H, Persson H, Stendahl U, Stenling R, Suhr O. Chronic diarrhoea after radiotherapy for gynaecological cancer: occurrence and aetiology. Gut. 1991;32(10):1180–7.
53. Eifel PJ, Levenback C, Wharton JT, Oswald MJ. Time course and incidence of late complications in patients treated with radiation therapy for FIGO stage IB carcinoma of the uterine cervix. Int J Radiat Oncol Biol Phys. 1995;32(5):1289–300.
54. Hauer-Jensen M, Wang J, Denham JW. Mechanisms and modification of the radiation response of gastrointestinal organs. In: Milas L, Ang KK, Nieder C, editors. Modification of radiation response: cytokines, growth factors, and other biological targets. Heidelberg: Springer; 2002. p. 49–72.
55. Carr KE. Effects of radiation damage on intestinal morphology. Int Rev Cytol. 2001;208:1–119.
56. Fajardo LF. Alimentary tract. In: Pathology of radiation injury. New York: Masson Publishing; 1982. p. 47–76.
57. Denham JW, Hauer-Jensen M. The radiotherapeutic injury—a complex 'wound'. Radiother Oncol J Eur Soc Ther Radiol Oncol. 2002;63(2):129–45.
58. Larsen A, Reitan JB, Aase ST, Hauer-Jensen M. Long-term prognosis in patients with severe late radiation enteropathy: a prospective cohort study. World J Gastroenterol WJG. 2007;13(26):3610–3.
59. Regimbeau JM, Panis Y, Gouzi JL, Fagniez PL. Operative and long term results after surgery for chronic radiation enteritis. Am J Surg. 2001;182(3):237–42.
60. Lordick F, Geinitz H, Theisen J, Sendler A, Sarbia M. Increased risk of ischemic bowel complications during treatment with bevacizumab after pelvic irradiation: report of three cases. Int J Radiat Oncol Biol Phys. 2006;64(5):1295–8.
61. Yavuz MN, Yavuz AA, Aydin F, Can G, Kavgaci H. The efficacy of octreotide in the therapy of acute radiation-induced diarrhea: a randomized controlled study. Int J Radiat Oncol Biol Phys. 2002;54(1):195–202.
62. Andreyev HJ, Vlavianos P, Blake P, Dearnaley D, Norman AR, Tait D. Gastrointestinal symptoms after pelvic radiotherapy: role for the gastroenterologist? Int J Radiat Oncol Biol Phys. 2005;62 (5):1464–71.
63. Denton AS, Andreyev HJ, Forbes A, Maher EJ. Systematic review for non-surgical interventions for the management of late radiation proctitis. Br J Cancer. 2002;87(2):134–43.
64. Cunningham SC, Fakhry K, Bass BL, Napolitano LM. Neutropenic enterocolitis in adults: case series and review of the literature. Dig Dis Sci. 2005;50(2):215–20.
65. Bremer CT, Monahan BP. Necrotizing enterocolitis in neutropenia and chemotherapy: a clinical update and old lessons relearned. Curr Gastroenterol Rep. 2006;8(4):333–41.
66. Rolston KV, Bodey GP, Safdar A. Polymicrobial infection in patients with cancer: an underappreciated and underreported entity. Clin Infect Dis Off Publ Infect Dis Soc Am. 2007;45(2):228–33.
67. Schnoll-Sussman F, Kurtz RC. Gastrointestinal emergencies in the critically ill cancer patient. Semin Oncol. 2000;27(3):270–83.
68. Kouroussis C, Samonis G, Androulakis N, et al. Successful conservative treatment of neutropenic enterocolitis complicating taxane-based chemotherapy: a report of five cases. Am J Clin Oncol. 2000;23(3):309–13.
69. O'brien S, Kantarjian HM, Anaissie E, Dodd G, Bodey GP. Successful medical management of neutropenic enterocolitis in adults with acute leukemia. South Med J. 1987;80(10):1233–5.