CHAPTER 13
Complications of colon cancer

In 2016, the Association of Coloproctology of Great Britain and Ireland (ACPGBI) published a joint paper with the Association of Upper Gastrointestinal Surgery and the Association of Surgeons of Great Britain and Ireland on the future of emergency surgery. This paper was followed by a 2018 publication by the Royal College of Surgeons of England on high risk in general surgery, which raised the bar.[1,2]

Recent publications have shown that outcomes for patients with acute colon and rectal disease are better when treated by specialist colorectal surgeons. A national audit on laparotomies published in 2017 revealed that almost 50% of all emergency laparotomies are performed for colorectal pathology.[3]

The emergency presentation of CRC can occur as an initial event establishing the diagnosis, during the course of the disease as a consequence of some type of treatment, or as an end-of-life event. CRC emergency represents 20% of cases in most publications. The main presentation is obstruction (up to 80%), followed by perforation (20%) and less commonly by bleeding.[4]

Emergency surgery is associated with a worse prognosis, high levels of morbidity and mortality, and lower overall survival. This could be due to the association of emergency presentation with older age, lower socioeconomic status, comorbidities, more advanced stage of the disease, and fewer treatments with curative intent.

The treatment objectives in these situations include avoiding the negative impact of complications (sepsis, death), achieving the best possible control of the tumor, and ensuring a rapid recovery so that systemic treatment can be started.

Perioperative mortality from emergency surgery continues to decline in European Union countries. However, in the United Kingdom, 90-day mortality after emergency surgery for CRC is approximately six times higher than that after elective surgery (11.5 vs. 2%).[2]

Colon cancer obstruction

Diagnosis

Diagnostic modalities for CRC obstruction include plain abdominal X-ray, ultrasound, and contrast-enhanced CT of the abdomen and pelvis. However, performing an X-ray may lead to a delay in decision-making, such as performing a CT scan to establish a definitive diagnosis, with local and remote staging of the disease, which favors surgical tactics. When CT is inconclusive, in some stable patients in whom obstruction is not detected, colonoscopy may be useful for etiologic diagnosis by allowing biopsy to be performed, or for treatment with a stent. However, CT scan is not mandatory when the diagnosis is conclusive and surgical treatment is established as the initial plan.[2,4]

Recommendation: For the diagnosis of colon cancer obstruction, contrast-enhanced CT of the abdomen and pelvis is the modality of choice. Evidence 3B.[4]

Stent treatment

International guidelines establish that treatment with self-expanding metal stents is the modality of choice for colon cancer obstruction, because it reduces the ostomy rate, hospital stay, in-hospital mortality, the rate of admission to the intensive care unit and the time to start chemotherapy.[1,5]

The use of endoprostheses as a bridge to surgery has short-term benefits, as it allows emergency management by relieving mechanical obstruction, improving the patient's clinical condition and allowing correct staging and planning of definitive treatment. The tactic of choice should be early planned resection with a greater possibility of laparoscopic surgery and primary anastomosis and lower rates of ostomy and morbidity and mortality.[6,7]

The use of a stent as a bridge to surgery has short-term benefits, since by relieving mechanical obstruction it allows the patient's clinical condition to be improved, the disease to be staged and the definitive treatment to be adequately planned.. After stent placement, the tactic of choice is early resection with a greater possibility of laparoscopic surgery and primary anastomosis, and lower rates of ostomy, morbidity and mortality.

The use of stents has increased due to their lower immediate morbidity and mortality compared with emergency surgery. The short-term success rate ranges from 80% to 90%.[8,9] Success tends to be higher for stents placed as a bridge to surgery than for palliative stents.[10,11] The Dutch colorectal audit demonstrated a technical success rate of 87.4% and a clinical success rate of 79.7%.[12]

The use of stents is contraindicated in the presence of perforation or peritonitis. This contraindication particularly affects the group of patients receiving antiangiogenic therapy with bevacizumab, in whom the risk of perforation during treatment is higher. This risk does not appear to be increased in patients receiving other therapeutic agents such as cetuximab.[12–15]

Stents can also be used in patients with colonic obstruction due to extraluminal malignancy and peritoneal carcinomatosis, although with a lower success rate, greater technical difficulty and a higher complication rate.

Recommendation 1: Self-expanding metal stents for the treatment of colon cancer obstruction can be used for palliation and as a bridge to surgery. Evidence IA.
Recommendation 2: Self-expanding metal stents should not be used in the presence of perforation, peritonitis, or systemic toxicity and are relatively contraindicated in patients treated with antiangiogenic agents. Evidence IIIC.[2]

Technical risks

There is debate about recurrence and poorer survival secondary to stenting, due to the dissemination of tumor cells and perforations. Some randomized studies have shown a worse oncologic prognosis with higher mortality. Other studies report higher recurrence in this group of patients. Guidelines do not recommend its routine use, reserving it for patients with metastatic disease or poor general condition and high risk of operative mortality. There is a wide variation between the different recommendation guidelines, so it is suggested that this treatment be selected individually for each patient.[2–4]

A recent meta-analysis of randomized controlled trials compared stenting with emergency surgery and found an overall higher risk of recurrence in the stenting arm (37 vs. 25.9%).[16] One retrospective study and two systematic reviews found equivalent 5-year oncologic outcomes.[17] The Dutch colorectal audit demonstrated equivalent 3-year oncologic outcomes in patients with left-sided colon cancer obstruction, with the stenting arm having a higher perforation rate, higher recurrence (18 vs. 11%; $p = 0.432$), worse 3-year DFS (49 vs. 59.6%; $p = 0.717$), and worse OS (61 vs. 75.1%; $p = 0.529$), but no statistical significance was found in any case.[18]
Balloon dilation prior to stent placement is not recommended because it may result in worse oncologic outcomes secondary to perforation.[2]

Recommendation: Self-expanding metal stents appear to be oncologically as safe as emergency surgery. Locoregional recurrence at 3 and 5 years and OS are comparable between these two groups. The risk of stent perforation represents a high risk of local recurrence. Evidence IA.[3]

Complications

Short- and long-term complications secondary to stent placement have been reported in up to 30%. The main complications include perforation (up to 12%), placement failure, migration and restenosis. Less frequent are pain, bleeding, tenesmus, fistula, late perforation, incontinence and hyperthermia. Reobstruction can be treated with the placement of a new stent.[19,20]

Stent perforation may be clinically evident, identified by the guidewire, or silent (microperforation). According to recommendations of the endoscopic audit group, the incidence of perforation should not be greater than 10%, ideally less than 5%. In recently published studies it ranges between 1.6 and 5%, reflecting greater training in the technique.[21,22]

Recommendation: The technical success rate in stent placement for obstructive colon cancer should exceed 90%. Evidence IA.[2]

Palliation

A 2011 Cochrane review demonstrated improved clinical outcomes of emergency surgery compared with stenting in a palliative setting.[23] However, subsequent studies have shown that stenting has significant benefits in terms of quality of life, with reduced ostomy rate, hospital stay, time in the intensive care unit, time to initiation of chemotherapy, and morbidity and mortality.[24]

It has therefore become the technique of choice for left-sided colonic obstructions. In contrast, stenting for right-sided colonic obstructions is technically more challenging, and the recommendation for its implementation depends on the training of each group. The ASCRS recommends considering stenting as a palliative treatment for right-sided obstructions.[4]

A diverting colostomy may be an alternative to stenting in patients with left-sided colonic obstruction. A recent Dutch population-based study compared initial stoma with decompressive stenting and demonstrated that ostomized patients have a higher rate of laparoscopic resection (57 vs. 9%; $p < 0.001$), more primary anastomoses (88 vs. 41%; $p < 0.01$), lower 90-day mortality (1.7 vs. 7.2%; $p = 0.03$), improved 3-year survival (79 vs. 73%; HR 0.36, 95% CI 0.20–0.65), and a lower rate of permanent ostomies (22 vs. 42%; $p < 0.001$).[25]

Recommendation: Self-expanding metal stents should be the palliative treatment of choice in patients with unresectable primary disease or metastases associated with colonic obstruction. Stent placement in this group of patients is associated with a better quality of life, a shorter hospital stay, and a lower rate of ostomies, compared with palliative surgery. Evidence IA.[3]

Stent as a bridge to surgery

Emergency surgery for colon cancer obstruction has a higher incidence of morbidity and mortality, including anastomotic leak, when compared with elective surgery. These complications adversely affect oncologic outcome. International guidelines vary widely in recommending the use of stents as a bridge to surgery. Furthermore, these results are variable when comparing left-sided versus right-sided tumors. While the UK and European guidelines do not favor the use of right-sided stents, American guidelines recommend it.[4]

Most studies focus on left-sided obstruction. Meta-analyses have shown that stenting as a bridge to surgery is associated with lower morbidity, lower ostomy rate, higher number of primary anastomoses, and similar mortality rate.[11,14]

A systematic review of right-sided obstruction comparing stenting with surgery showed lower morbidity and mortality in the former group, but cautioned that most of the studies reviewed were retrospective.[26]

Recommendation: There is good evidence supporting the use of self-expanding metal stents as a bridge to definitive surgery for malignant colon obstructions distal to the splenic flexure, particularly in high-risk patients. The decision should be individualized between the patient and physician. Evidence IA. This recommendation can be applied to right-sided obstructions, although its practical application is more limited. Evidence IIIC.

Time to surgery after stent placement

The European Society of Gastrointestinal Endoscopy recommends surgery within 5 to 10 days of stent placement, although current evidence is weak.[9] With longer waiting times, a 20% increase in complications, such as migration and perforation, has been reported during this period and an increase in recurrence. Further studies are needed for a definitive conclusion on this matter.

Recommendation: In the absence of strong evidence, surgical resection appears appropriate immediately after improvement of the patient's clinical condition, radiological staging and the decision of the multidisciplinary committee. Evidence IV.

Coated stents

Coated stents are associated with a higher rate of migration in retrospective series. Migration is likely to be facilitated by less tumour growth incorporating into the stent, resulting in less anchorage. The European Society of Gastrointestinal Endoscopy and the American Society for Gastrointestinal Endoscopy do not recommend this type of stent.[9,27]

Recommendation: Uncoated stents should be used as a bridge to surgery due to reduced migration. In palliative care patients, the evidence on coated versus uncoated stents is inconclusive. Evidence IIIB.

Surgical treatment

Antegrade lavage

There is no relevant evidence on the benefit of applying antegrade lavage in obstructive colon cancer surgery. According to Mattacheo,[28] the best evidence comes from the study by Lim et al,[29] which compares lavage with manual decompression and shows a difference only in lavage time and similar results regarding time to recovery of bowel function, length of stay, surgical site infection and anastomotic dehiscence.

Antegrade lavage is performed using the appendicular orifice (post appendectomy) or an enterostomy to infuse more than 4 liters of saline solution. The fluid is recovered through a colostomy proximal to the tumor, or more commonly, through the proximal colon after the tumor has been removed. Obviously, this technique is only used in the conventional approach. Transanastomotic lavage through a corrugated tube or by colonoscopy has also been described, which requires a significant increase in operating time without considerable advantages in postoperative variables.

Surgical tactics

In patients with proximal obstruction of the ascending and transverse colon, who are stable and at low surgical risk,

it is reasonable and safe to perform resection with primary anastomosis.[30,31]

The European Society of Coloproctology audited 3208 patients and found an increased rate of dehiscence in different types of stapled anastomoses in this group of patients, suggesting that a hand-sewn anastomosis is preferable in this setting.[32]

The incidence of dehiscence after emergency right hemicolectomy for obstruction varies widely between 7 and 16.4%, with a tendency to be higher in proximal than in distal anastomoses. Advanced age, ASA II-IV classification and preoperative renal damage are factors associated with a worse postoperative outcome in colon cancer obstruction. Therefore, in patients with low surgical risk or high anastomotic risk, it is reasonable not to perform a primary anastomosis and to consider resection and ileostomy.[33,34]

Elective surgery after stenting does not adversely affect oncologic outcome and reduces the rate of ostomy.[17] A meta-analysis of 8 studies with 444 patients (219 stents vs. 225 surgeries) found that 7 studies showed no difference in the rate of ostomy and 3 randomized controlled trials showed no difference in mortality or anastomotic dehiscence but did show a difference in overall morbidity. Stenting is no more advantageous than emergency surgery for left-sided colon obstruction due to malignant tumor.[34]
In left-sided obstructive cancers, multiple options exist, including primary resection and anastomosis with or without diverting stoma, or a defunctioning stoma alone. In a meta-analysis, no difference was found between one-stage resection versus two-stage or three-stage resection.[35] Primary resection and anastomosis, a technique used for many years, is safe even in selected elderly patients and should be the preferred option if the clinical condition is good.[31]

If possible, segmental resection is preferred over subtotal colectomy or extended colectomy because of its better functional results.[36] Subtotal colectomy with a minimal portion of distal ileum should be reserved for cases of proximal colonic damage due to distal obstruction or for synchronous tumors. Anastomotic leak varies between 2.2 and 12%.

The LaCes trial, which compared conventional surgery with laparoscopic surgery, showed that the latter is feasible, acceptable and safe, with a conversion rate of 39%.[37]

The proportion of emergency laparoscopic resections in the UK between 2000 and 2016 ranged from 15.1% to 30.3%, with a conversion rate of around 18.7%. This approach was associated with shorter operating time, hospital stay and mortality.[38]

In a recent study published by the Dutch Snapshot Research Group,39 between 2009 and 2016, 158 patients were selected from 2002 patients who underwent laparoscopic resection for left colon obstruction due to cancer and compared with 474 patients who underwent open surgery. Complications at 90 days were 26.6 vs. 38.4%, with no difference in mortality (5.1 vs. 7.2%). OS and DFS at 3 years were better in the laparoscopic surgery group (81 vs. 69.4% and 68 vs. 52%, respectively). They conclude that laparoscopic surgery in obstructive colon cancer decreases complications and increases survival. This study suggests that intentional emergency laparoscopic resection might improve short- and long-term outcomes in patients with left-sided obstructive colon cancer compared with emergency open resection, warranting confirmation in future studies. Adequate patient selection for intentional laparoscopic resection is required if relevant experience of the surgical team is available, to avoid emergency open resection.

Recommendation: The surgical decision should be based on the patient's physiological condition, the extraction site, and the characteristics of the proximal colon. In case of obstruction proximal to the transverse colon, resection and primary anastomosis is preferable, except in a markedly deteriorated patient, in whom the accepted treatment is resection with terminal ostomy and mucous fistula. In case of obstruction of the colon distal to the transverse colon in physiologically stable patients, resection and primary anastomosis is preferable. The presence of comorbidities and poor general condition determines resection with terminal colostomy. Evidence IIIB.[4]

Recently, it has been shown that tumor obstruction of the transverse colon can be successfully treated with a stent in selected patients. The success rate of right-sided stenting ranges from 87 to 96%.[40]

In the Japanese National Database Study of 1500 patients, emergency surgery was compared with stenting as a bridge to surgery and in the latter case a higher indication for laparoscopic surgery was observed (50 vs. 25%; $p < 0.001$), as well as a lower rate of ostomy (1.7 vs. 5.1%; $p < 0.01$) and a shorter hospital stay (13 vs. 15 days; $p < 0.001$).[41]

A 2022 systematic review and meta-analysis on emergency colectomy or stenting as a bridge to surgery for right-sided obstructive colon cancer demonstrated that stenting is associated with reduced postoperative complications and mortality.[42]

In a meta-analysis by Veld et al.[43] of 18 studies and 1518 patients, early complications were found in 13.6% with stenting and 25.5% with surgery, whereas late complications were lower with surgery (23.2 vs. 9.8%), including reobstruction (16.7%), migration (6.9%), and perforation (5%). There were 14.3% ostomies in the stenting group and 58.4% in the surgery group, and mortality was 3.9% vs. 9.4%, respectively.

Some studies suggest a better prognosis in patients whose primary tumor is resected compared to those treated with a stent without resection.[44]

In summary, the stent:
- Is a safe option, particularly for severely deteriorated patients.
- Has a high rate of early and late complications.
- May avoid unnecessary resection.
- May have a worse prognosis than surgical resection of the primary tumor.

Recommendation 1: In patients with left-sided colon obstruction and potentially curable disease, endoscopic stenting or oncologic colectomy with primary anastomosis with or without protective stoma should be individualized. Evidence IB.[4]
Recommendation 2: In markedly deteriorated patients with significant preexisting comorbidities, loop stoma alone is reasonable. Evidence IIIC.[4]
Recommendation 3: In patients with right-sided colon or transverse colon obstruction with curative disease, initial colectomy with or without anastomosis, with or without protective or definitive stoma, and/or decompression with endoscopic stenting with immediate subsequent colectomy are all valid therapeutic options. Evidence IC.[4]

Colon cancer perforation

Perforation accounts for 18.6-28.4% of all colon cancer complications. It may occur at the cancer site (65-92%) and proximal to the cancer (3-35%).[2,4] These data are based on mostly retrospective, single-center studies with corresponding bias. In population-based studies, 1.6-4.1% of all cancers presented with perforation.[5,45]

Mortality depends on the site of perforation. Perforation proximal to the tumor site in an obstructed colon leads to diffuse peritoneal contamination and septic shock, with subsequent perioperative mortality. A perforation at the tumor site results in local contamination with a lower risk of severe peritonitis, although these data are not supported by strong evidence. Mortality, reported as high as 62%, is associated with age, comorbidities, and stage IV.[46] However, more recent studies have reported perioperative mortality of between 0 and 20%.[4]

The influence of perforation on oncologic outcome has not been clearly determined. There is heterogeneity according to the site of obstruction, the site of perforation,

emergency surgery, immediate vs. delayed surgery, and other factors that lead to confusing conclusions. A worse oncologic prognosis has been reported in patients with emergency vs. elective surgery. The worse oncologic outcome would be related to perioperative mortality and advanced-stage oncologic disease.[47] However, other authors have reported a similar 5-year OS in perforated patients with complete resection compared to those without perforation. In more recent population-based studies, locally perforated cancers had a higher local recurrence (15.7 vs. 7.8%; p = 0.0021) and greater peritoneal carcinomatosis (13.8 vs. 6.3%; p = 0.036), although there was no difference in the incidence of distant metastasis (17.7 vs. 18.6%; p = 0.099). Perforation was an independent risk factor for local recurrence and peritoneal carcinomatosis (p = 0.004). However, after excluding postoperative mortality, perforation was not a significant prognostic factor in the multivariate analysis regarding survival (p = 0.54).[48] On the other hand, the Erlangen CRC registry found a lower 5-year DFS (42.9 vs. 72.8%) and lower OS (47.3 vs. 66.9%) in perforated patients, demonstrating that perforation was an independent negative prognostic factor.[49] It has also been shown in the multivariate analysis that although patients with colon cancer with local perforation had a significantly lower DFS than those with nonperforated obstructive cancers, there were no differences in OS.[49]

According to ASCRS, patients with perforation tend to have fewer primary anastomoses and higher postoperative morbidity and mortality. In addition, they have significantly lower 5-year OS and DFS, with an increased risk of metachronous peritoneal metastases. Patients with free perforation have a worse OS than those with sealed-off perforation.[4]

Recommendation: Patients with perforated cancer should be warned about an increased incidence of local recurrence and peritoneal carcinomatosis, but not of distant metastasis. The long-term oncologic outcome of patients treated urgently with curative intent for obstruction or perforation is equivalent. Level of evidence IIIB.[4]

The goals of emergency surgery for perforated colon cancer are to control the immediate negative impact of complications such as sepsis and death, to achieve the best possible local control of the tumor, and to ensure a prompt recovery in order to initiate systemic adjuvant therapy. The preferred treatment when possible is standard oncologic resection. Patient safety must be balanced with prompt local control of sepsis and optimization of oncologic control of the disease. Subtotal colectomy is generally indicated for patients with perforation proximal to the tumor, while perforations at the tumor site can be treated with segmental resections.

Perforated patients and those with a higher ASA classification have the lowest chance of having a primary anastomosis. This depends on the clinical condition of the patient and the balance between the risks associated with an anastomotic leak vs. those associated with an end ostomy. The anastomotic risk in patients with emergency surgery is higher than in those undergoing elective surgery and has an average incidence of 15.8%.[47,48]

In selected patients with minimal peritoneal contamination, healthy tissue, and hemodynamic stability, consideration should be given to performing an anastomosis with or without a protective stoma. The threshold for performing a staged procedure in this setting should be low, although ostomies performed in emergency situations are often not reversed. In patients with free perforation complicated by peritonitis, oncologic resection with an end stoma should be considered therapeutic.

Recommendation: Surgical tactics should be individualized taking into account physiological factors, comorbidities, and tumor characteristics. If possible, the choice is to perform an oncologic resection that includes the perforation site, with or without anastomosis, with or without diverting ostomy. In proximal perforations, simultaneous resection of the tumor and the perforation is required. Evidence IIIB.[4] In the context of a macroscopic or imminent perforation, oncologic resection is recommended, with a low threshold for performing a staged procedure. Evidence IC.[4]

Bleeding

CRC is the cause of 6.1 to 7.4% of all cases of lower gastrointestinal bleeding.[2] However, this rate may be underestimated due to the lack of diagnosis at the time of presentation and early discharge of patients without study or without diagnosis, which reaches up to a third of cases. Acute bleeding from a newly diagnosed colon cancer should initially be managed with a nonsurgical approach. Evidence IC.[4]

For the British Society of Gastroenterology, colonoscopy is the initial investigation method for minor or major acute lower gastrointestinal bleeding in stable patients. In unstable patients, CT-guided angiography is the option. The latter achieves the diagnosis of bleeding in 49.7 to 55.8% of cases. It should be performed in a triphasic manner, involving the acquisition of the arterial phase, the portal venous phase and the delayed phase.[50] In addition to the localization of bleeding, CT angiography allows locoregional assessment and staging of a potential tumor. It has been shown to be superior to nuclear medicine for the diagnosis of the bleeding site (sensitivity 85 vs. 20-60%, respectively).

Conventional angiography detects bleeding in 40-90% of patients and allows treatment with embolization, achieving cessation of bleeding in 70-90% of cases.

Emergency colonoscopy without preparation detects the site in 20-40% of patients with acute bleeding and has the advantage of being both diagnostic and therapeutic. If possible, stabilization of the patient and bowel preparation within 12 hours of admission is preferred.[51,52]

Surgery is indicated in cases of hemodynamic instability despite transfusion of 6 U of red blood cells, persistent bleeding requiring more than 3 U per day, inability to stop bleeding by an endoscopic or endovascular procedure, or recurrent episodes of low-grade bleeding.

If surgical resolution is required, resection should be performed using oncologic principles if possible. The performance of a primary anastomosis or a diverting or definitive ostomy should be individualized according to the patient's condition and the surgical team's judgment. Infrequently, in the case of unresectable neoplasms with significant bleeding, endovascular stents can be successfully placed.[2,4]

Adjuvant treatment in complicated colon cáncer

Patients with complications from colon cancer are indicated for adjuvant therapy, however, the high presence of comorbidities and prolonged hospitalization determine that only 50% receive systemic treatment.[53]

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