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SURGERY

VOLUME 16



Roshan Lall Gupta's

Recent Advances in SURGERY

Editor
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Chapter

Management of Colon Cancer: Changing Trends, Recent Advances and Current Practices

Vikram Kate, R Kalayarasan, S Suresh Kumar, Sajal Rai, N Ananthakrishnan

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INTRODUCTION

Recent trends in published literature on colon cancer worldwide have shown several important and significant changes from what was existing information on this topic earlier. These advances have included changes in perception of epidemiology focusing not only an awareness of increasing incidence worldwide but a better perception of the differences between right and lefts sided colonic cancers which have therapeutic implications, changes in suggestions for preoperative workup impacting management decisions, a movement from open to minimally invasive and robotic surgery with reviews of oncological outcomes, greater clarity on approach to obstructed colonic cancers presenting as emergencies, a better understanding of approach to patients with stage IV disease at presentation including timing and role of surgery for metastatic disease with better neoadjuvant and adjuvant care, a greater awareness of the role and limitations of monoclonal antibodies in targeted therapy and some research which may impact the diagnosis and management of these cancers in future.

All these have been summarized in this chapter with particular emphasis on what is new, what is still in a phase of evaluation and how the diagnosis and care of these cancers is likely to be impacted by these advances.

EPIDEMIOLOGY: CHANGING TRENDS

A recent trend observed in the United States is a decrease in the incidence of cancer in people more than 50 years of age compared to those less than 50 years.[1] Hence in 2018, the American Cancer Society has recommended reducing the age for colorectal cancer screening down to 45 years.[2] Recent epidemiological studies have shown an increase in the incidence of right colon cancer.[3] Right and left colon cancer have distinct histopathology,

Table 1: Differences between right-and left-sided colon cancer.

S. No	*Characteristics*	*Right colon cancer*	*Left colon cancer*
1.	Age	Older > younger age group	Younger > older age group
2.	Sex	Females > males	Males > females
3.	Histology	Sessile serrated adenomas, poorly differentiated mucinous adenocarcinoma	Tubular, villous adenocarcinoma
4.	Morphology	Flat type that makes detection during screening difficult	Polypoid type that facilitates detection during screening colonoscopy
5.	Mutation	Microsatellite Instability (MSI)-high and mismatch repair deficient tumors	Chromosomal instability (CIN)-high tumors
6.	Immunogenicity	High with T cell infiltration	Low
7.	Response to adjuvant therapy	Due to high antigen load respond well to immunotherapy	Respond well to conventional chemotherapy and targeted therapy
8.	Site of metastases	Peritoneal	Liver and lung
9.	Prognosis	Relatively poor. However, early stage (stage I and II) tumors have better prognosis compared to similar stage tumors of left due to high MSI observed in these stage tumors	Relatively better especially in late stage (stage III and IV) tumors

molecular pathway and prognosis.[3-5] These differences are summarized in Table 1.

PREOPERATIVE INVESTIGATIONS

Colonoscopy versus Computed Tomography Colonography

Colonoscopy is the preferred investigation for diagnosis of colon cancer since it permits direct visualization of the tumor, detects synchronous lesions, facilitates removal of polyps and allows a biopsy from the tumor. A randomized study from the UK Special Interest Group in Gastrointestinal and Abdominal Radiology (SIGGAR) in which 1610 patients with symptoms suggestive of colorectal cancer were randomly assigned to colonoscopy (n = 1072) or computed tomography (CT) colonography (n = 538).[6] The need for an additional colonic investigation to detect colorectal cancer or large (>1 cm) polyps was used as the primary endpoint. Both investigations had a similar yield to detect colorectal cancer or large polyps (10.7% vs. 11.4%). However, patients undergoing CT colonography more often required additional colonic investigations (30% vs. 8%).[6] Procedural acceptance is

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more with CT colonography as it is noninvasive. However, this advantage is offset by the need for additional colonoscopy in the CT colonography group. Currently, CT colonography is primarily indicated in patients with incomplete colonoscopy due to a non-obstructive cause. CT colonography cannot replace incomplete colonoscopy in patients with obstructed left colon cancer as both procedures require bowel preparation.[7,8] Use of fecal tagging to facilitate CT colonography in patients with a loaded colon is associated with poor sensitivity and specificity.

Computed Tomography of Chest in Colon Cancer

Contrast enhanced CT abdomen and pelvis is the primary investigation for staging in patients with colon cancer. CT is more sensitive to detect distant spread than regional lymph node metastasis or depth of tumor infiltration. Since 2007, the National Comprehensive Cancer Network (NCCN) guidelines for colon cancer recommend chest CT in addition to abdomen and pelvis CT although, the role of routine chest CT in colon cancer patients remains controversial.[9] Kim et al. retrospectively reviewed CT chest findings in 319 consecutive colon cancer patients without liver metastasis and with a normal chest X-ray.[10] Lung metastasis was detected in only 6.3% of patients without liver metastasis and a negative chest X-ray. CT-detected lymph node metastasis was identified as the risk factor for lung metastasis.[10] Also, routine chest CT may result in increased detection of incidental and indeterminate lung nodules requiring further evaluation thereby delaying definitive therapy.[11] Based on current evidence routine CT chest is not recommended in colon cancer patients with no liver metastasis and is selectively indicated only in patients with advanced T and N stage tumor.[12]

Role of Positron Emission Tomography-Computed Tomography in Colon Cancer

Positron emission tomography-computed tomography (PET-CT) is more sensitive than conventional CT in detecting metastatic disease. However, its additional value in staging of colon cancer is not well defined. In the current NCCN guidelines, PET-CT is not recommended for the primary staging of colon cancer in patients without any evidence of distant metastasis on conventional CT abdomen and pelvis.[9] As PET-CT scan is usually done without contrast and multiple slicing, it does not obviate the need for additional contrast-enhanced CT and it is primarily indicated in patients with doubtful metastatic lesions on contrast-enhanced CT.[9,12]

The role of PET-CT in patients with liver metastasis is not clearly defined. Ruers et al. randomized 150 patients with colorectal liver metastases selected for hepatic resection to triple-phase contrast-enhanced CT only or CT

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plus a separate PET scan.[13] The authors reported that the addition of PET significantly reduced the number of non-therapeutic laparotomies (28% vs. 45%). However, in another trial by Moulton et al., 404 patients with potentially resectable liver metastases were randomized to triple-phase contrast-enhanced CT only or PET-CT.[14] Of the 263 patients randomized to the PET-CT arm the extent of surgery was modified in only 8% of patients. More importantly, the addition of PET-CT avoided non-therapeutic laparotomy in only 2.7% of patients leading to the conclusion that the addition of PET-CT to conventional CT alone did not result in a frequent change in surgical management.[14] However, in this study, a significant proportion of patients received neoadjuvant chemotherapy that is known to reduce the yield of fluorodeoxyglucose positron emission tomography (FDG-PET) by reducing the metabolic activity of the metastatic tumor. NCCN guidelines recommend that PET-CT should be performed before planned curative resection for liver metastasis.[9] PET-CT is also used in the postoperative surveillance of patients with rising serum carcinoembryonic antigen (CEA) level and non-diagnostic conventional imaging evaluation following primary treatment and in detecting synchronous tumors in patients with obstructed left colon cancer.[15,16]

PREOPERATIVE MANAGEMENT

Mechanical Bowel Preparation

Proposed advantages of bowel preparation include easy bowel handling, aesthetic surgical field and the ability to palpate a small tumor or polyps. It also facilitates intraoperative colonoscopy if needed. The potential disadvantages are that presence of liquid stools secondary to incomplete bowel preparation might increase the risk of contamination and secondly patient discomfort associated with mechanical preparation. Multiple randomized controlled trials (RCTs) and meta-analysis have concluded that mechanical bowel preparation has no significant effect in reducing the incidence of surgical site infection or anastomotic complications and in many enhanced recovery after surgery (ERAS) protocols for colon cancer, mechanical bowel preparation has been omitted.[17,18] A limitation in the majority of these RCTs is that oral antibiotic prophylaxis was not administered along with mechanical bowel preparation. Administration of mechanical bowel preparation alone without oral antibiotics has no significant effect on colonic bacterial count. Mechanical bowel preparation by reducing the volume of feces facilitates delivery of oral antibiotics to the colonic mucosa.[19-21] An updated meta-analysis published in 2018 concluded that oral antibiotic prophylaxis, in combination with mechanical bowel preparation and parenteral antibiotics, is superior to mechanical bowel preparation and

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parenteral antibiotic prophylaxis alone in reducing surgical site infection in elective colorectal surgery.[22] The role of mechanical gut preparation, therefore, remains controversial.

Preoperative Fasting

The standard practice in elective colonic surgery is preoperative fasting from midnight of the day prior to surgery. However, multiple studies have shown that intake of fluids up to 2 hours before surgery does not increase the risk of aspiration and may accelerate postoperative recovery.[23] It reduces preoperative thirst, hunger, anxiety and allows the patients to undergo surgery in a metabolically fed state.[24] Preoperative carbohydrate loading minimizes postoperative insulin resistance, negative nitrogen balance, protein loss, maintains lean body mass and muscle strength.[25] However, milk-based fluids should be avoided as they tend to reduce gastric emptying.[26] Similarly, the safety of oral fluids in diabetics, who are at high risk of gastroparesis, is not conclusively proven.[25]

Current ERAS society guidelines are clear fluids should be allowed up to 2 hours and solids up to 6 hours before induction of anesthesia.[18] Specific safety measures should be taken at the time of induction of anesthesia in those patients in whom gastric emptying may be delayed. A routine use of preoperative oral carbohydrate treatment is recommended. In diabetic patients, preoperative oral carbohydrate treatment can be given along with the diabetic medication, although evidence for this recommendation is low.[18]

Prophylaxis against Deep Vein Thromboembolism

Patients with colon cancer are at high risk of deep vein thrombosis with a fatal pulmonary embolism. Mechanical prophylaxis with compression stockings and intermittent pneumatic compression device is strongly recommended.[27] Pharmacological prophylaxis with low molecular weight heparin should be given to these patients.[18,28] In patients receiving low molecular weight heparin, the timing should be adjusted so that epidural catheter is not placed or removed within twelve hours of the last dose of heparin.[18,27,28]

SURGERY FOR COLON CANCER

Principle of Optimal Colonic Cancer Surgery

Total mesorectal excision (TME) for rectal cancer which has improved the oncological outcome was based on the concept that sharp dissection between the visceral or mesorectal fascia and parietal or endopelvic fascia ensures complete removal of a tumor with the draining lymphatics and lymph nodes.[29] The rectal TME plane extends to the sigmoid and descending

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colon and further from the descending colon, it extends to the pancreas and around the spleen on the left side. On the right side, it extends to include the head of the pancreas, duodenum, ascending colon, cecum and the root of the mesentery.[30] The concept that mesorectum and mesocolon are continuous structures was proved in a recent histological and electron microscopy study.[31] In colon cancer like rectal cancer, lymphatics follow the arteries supplying that portion of the colon and run along the mesocolon, which is in turn covered by visceral fascia on both sides like an envelope. Identification of this plane is easy in sigmoid and transverse colon cancers as they have a distinct mesocolon. In ascending and descending colon, the mesocolic fascia is closely opposed to the retroperitoneal fascia.

The main component of complete mesocolic excision (CME) is to identify the distinct plane between the mesocolic fascia and retroperitoneal fascia by sharp dissection. This plane is marked by a single layer of fascia (Toldt's fascia) (Figs. 1A to C). A good CME prevents the breach in mesocolic fascia and the potential tumor spread. The second important component is to identify and ligate the feeding arteries at the origin to ensure maximal harvest of the regional lymph nodes. The third component of CME is a dissection of the pericolic lymph nodes at least 10 cm on either side of tumor (10 cm rule) as longitudinal lymphatic spread is rarely seen beyond 10 cm.[32] This technique ensures the integrity of mesocolon and improves lymph node yield and thereby survival in colon cancer. In open surgery, lateral to medial approach is used for CME whereas in the laparoscopic and robotic surgery a medial to lateral approach is preferred.[30]

Hohenberger et al. reported that CME with central vascular ligation (CVL) reduced recurrence rate from 6.5% to 3.2% in 1329 patients of colon cancer operated from 1978 to 2002.[30] Bertelsen et al. in a retrospective study compared the oncological outcomes of 364 patients who underwent CME with 1031 patients who underwent non-CME colonic resection.[33] The 4-year disease-free survival rate was significantly higher in the CME Group (85.8% vs. 75.9%, P = 0.001) with multivariate analysis identifying CME surgery as an independent prognostic factor. Other studies have also shown that CME with CVL is associated with higher lymph node yield, R0 resection rate and overall survival.[34,35]

CME with CVL versus D3 Dissection

The Japanese Society for Cancer of the Colon and Rectum recommends D2 lymph node dissection for tumors restricted to submucosa and D3 lymph node dissection for tumor reaching muscularis propria or in patients with clinical evidence of lymph node metastasis irrespective of the depth of invasion.[36] For the right colon cancer in D2 dissection, the ileocolic vessels are tied to the right of superior mesenteric vessels without removing the lympho-adipose tissue over the superior mesenteric vessels whereas in D3

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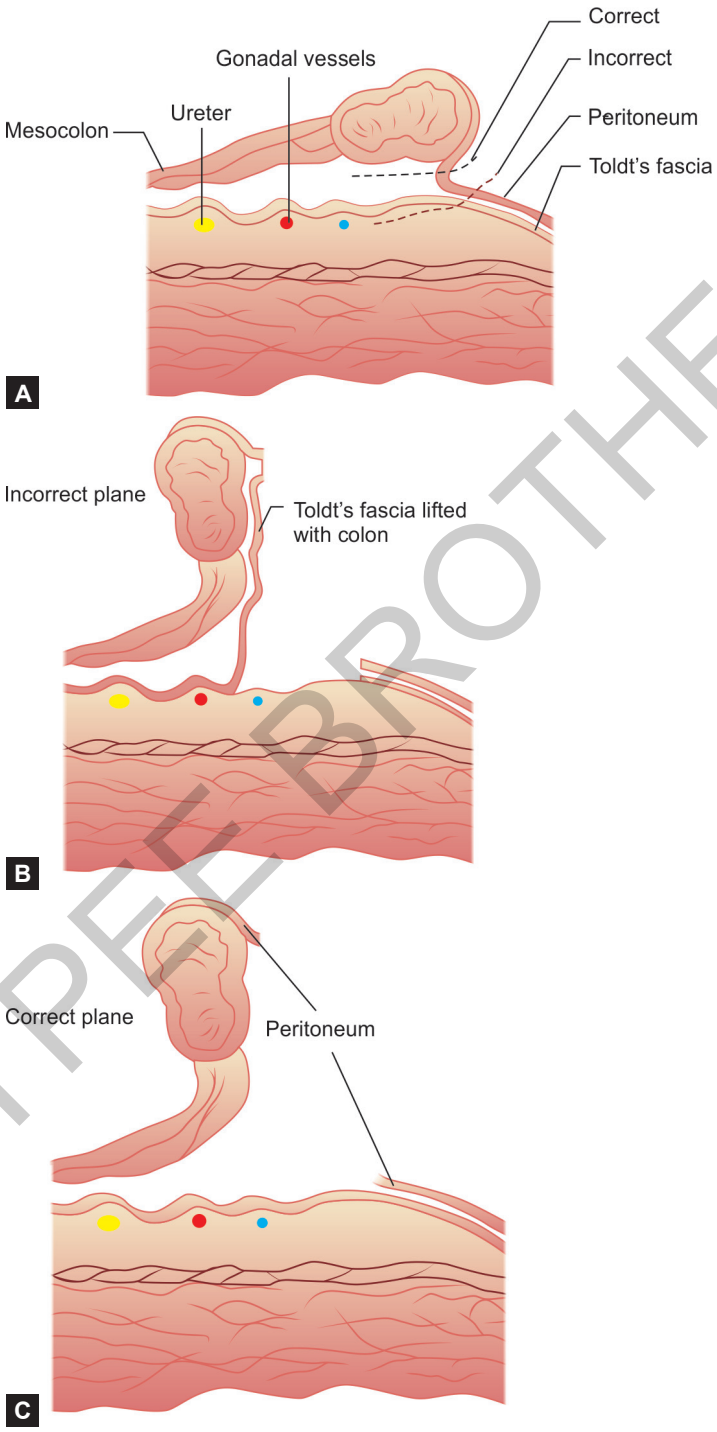

Figs. 1A to C: Plane for complete mesocolic excision (A). Lifting of Toldt's fascia increases the risk of injury to retroperitoneal structures (B). The correct plane is superficial to Toldt's fascia (C).

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dissection for right colon cancer, the ileocolic vessels are divided at the origin after clearing the lympho-adipose tissue over the superior mesenteric vessels and exposing them.[37] With respect to the level of vascular ligation, both CME with CVL and D3 dissection are similar.[37] However, the longitudinal length of the specimen is shorter in patients undergoing D3 dissection compared to CME with CVL as Japanese studies have shown that the longitudinal lymphatic spread is rarely seen beyond 10 cm from the tumor.[32,37] Hence, the number of mesenteric nodes removed is more in CME with CVL compared to D3 dissection.[37] Both CME with CVL and D3 dissection result in comparable oncological specimens and outcomes that are superior to conventional colon surgery.[37] Hence, the current recommended treatment for locally advanced colon cancer is either CME with CVL or D3 dissection.

Open versus Laparoscopic Surgery for Colon Cancer

In one of the earliest RCTs, Milsom et al. reported that patients who underwent laparoscopic colectomy (n = 55) had less postoperative pain, pulmonary complications and earlier return of bowel function compared to open colectomy (n = 54).[38] However, in malignancy, more than the short-term benefits it is important to document oncological equivalence. Since the follow up was relatively short (1.5 years) in their study evidence was insufficient to document oncological safety.

The oncological safety of laparoscopic colectomy was documented in an RCT reported by Lacy et al.[39] At a median (range) follow-up of 43 (27–85) months, there was no difference in the overall survival of patients who underwent laparoscopic and open colectomy. However, disease-specific survival was better in the laparoscopy group possibly due to reduced surgical stress and less tumor manipulation during laparoscopic colectomy.[39] Other RCTs also documented the oncological safety of laparoscopic colectomy.[40,41] Port site recurrence is not increased after laparoscopic colectomy with the incidence of port site recurrence being similar to the reported rates of incision site recurrence after open colectomy (0.8–1%).[39-41]

Since the introduction of the concept of CME with CVL for colon cancer, there is a renewed debate whether these could be safely accomplished using a laparoscopic approach. Also, the safety of laparoscopic surgery in locally advanced colon cancer (stage II and III) remains controversial. Recently Kitano et al. reported the results of an open-label, multi-institutional, randomized, two-arm phase 3 trial involving 1057 patients from 30 hospitals in Japan.[41] Similar five-year overall survival in both groups (90.4% vs. 91.8%) confirmed the feasibility and oncological safety of laparoscopic D3 dissection (like CME with CVL) for colon cancer. The excellent survival in both groups also documented the superiority of D3 dissection compared to conventional surgery.

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While the oncological safety of laparoscopic surgery has been documented, its role in patients with T4 cancer remains controversial. In the JCOG0404 trial, patients with T4 tumors who underwent laparoscopic surgery had inferior survival compared to the patients who underwent open colectomy possibly due to increased tumor manipulation and violation of the no-touch principle.[41] The feasibility and oncological safety of resecting T4 tumors without adjacent organ involvement have been shown in a few retrospective or prospective non-randomized trials.[42,43]

Laparoscopy versus Robotic Surgery

Robotic surgery has overcome some of the mechanical and visual constraints associated with laparoscopic surgery such as limited degree of freedom of movement, exaggerated tremors and 2D vision. Park et al. in an RCT comparing robot-assisted versus conventional laparoscopic right colectomy reported that hospital stay, surgical complications, postoperative pain score, resection margin and the number of lymph nodes harvested were similar in both groups.[44] Robot-assisted colectomy was associated with prolonged duration of surgery (195 versus 130 min; $P < 0{\cdot}001$) and higher overall hospital costs (US $12,235 versus $10,320; $P = 0{\cdot}013$) despite similar duration of hospital stay primarily due to more expensive consumables.[44] A meta-analysis of trials comparing robotic and laparoscopic colectomy confirmed that robotic colectomy did not offer a significant advantage in perioperative and postoperative outcomes compared to laparoscopic colectomy while at the same time contributing to prolonged operative duration and high cost.[45] The primary reason for the lack of benefit with robotics in colonic surgery is that robotic systems are primarily designed to enhance maneuverability, facilitate precise dissection and suturing in narrow confined spaces whereas, colonic surgery is usually a multi-quadrant operation involving a relatively large dissection area. The stable vision and ambidextrous capability of robotics facilitates vascular control and lymph node dissection. However, these potential benefits do not translate to clinical advantage in the trial setting when compared to laparoscopic surgery performed by the experienced surgeon. Hence, robotic surgery is not recommended as a superior option to minimally invasive colon surgery. However, the double console in current robotic systems facilitates learning by resident by allowing them to actively participate in the surgical procedure right from the commencement of their surgical experience and hence may shorten the learning curve.

Management of Obstructed Colonic Cancer

Resection and primary anastomosis is the preferred option for obstructing right colon cancer. Studies have shown that even in the emergency setting,

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primary anastomosis is associated with a less than 5% anastomotic leak rate.[46,47] The mobility and better blood supply of small bowel contributes to a low anastomotic leak rate in right colon cancer.[46,47] In patients with a poor general condition or prolonged obstruction, ileocolic resection with proximal ileostomy and distal colonic mucus fistula is recommended.[48] Stoma creation (ileostomy) or ileotransverse bypass is reserved for patients with unresectable tumors.[49] Percutaneous cecostomy is an option in poor risk patients although it is often associated with inadequate decompression.[50] Self-expanding metal stent (SEMS) as a bridge to elective surgery is not recommended for obstructed right colonic cancers.[51,52] However, it is an option in the palliative setting.[52]

For patients with obstructed left colon cancer, the choice lies between a single stage vs. a staged procedure and loop colostomy vs. SEMS as a bridge for elective colonic resection. As RCTs comparing various options are lacking, decision making should be based on available evidence from various retrospective and prospective non-randomized studies.

Primary Resection and Anastomosis versus Hartmann's Procedure

The German study group of colorectal carcinoma database reported that postoperative mortality was less in patients undergoing Hartmann's procedure compared to patients undergoing resection with primary anastomosis (7.2% vs. 9%) despite higher preoperative risk factors in patients undergoing the Hartmann's procedure.[53] The primary disadvantage with Hartmann's procedure is the need for a second stage procedure which requires a formal laparotomy. In contrast to rectal tumors where Hartmann's reversal is a challenging procedure due to the short rectal stump, it is a relatively straightforward option following left colectomy.

No RCT has evaluated the role of a diverting stoma in patients undergoing resection anastomosis in the emergency setting. In a series of 743 patients who underwent emergency surgery for obstructed left colon cancer, 58% of patients underwent primary resection anastomosis and 12% of patients underwent resection anastomosis with diverting stoma.[54] There was no significant difference in the rate of the anastomotic leak or the need for reoperation in both the groups.[54] In the absence of bowel preparation, leakage of the anastomosis into the peritoneal cavity will result in peritonitis. This might explain the lack of a protective effect of a diverting stoma in the emergency setting.

Based on the available evidence, use of primary resection anastomosis should be restricted to patients with uncomplicated obstructed left colonic cancer without any risk factors. Use of protective stoma is unlikely to reduce anastomotic leak rate or its severity in patients with a loaded colon. In most

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of the patients who undergo resection, end colostomy with Hartmann's procedure seems to be a reasonable option.

Subtotal Colectomy versus Segmental Colectomy

In the past, subtotal colectomy has been advocated in patients who undergo resection for obstructed left colonic cancer as it obviates the need to use an unprepared colon for the anastomosis.[55-57] Limitations with subtotal colectomy include prolonged operative time and poor functional result due to increased stool frequency. In the SCOTIA (Subtotal Colectomy versus On-Table Irrigation and Anastomosis) trial 91 patients from 12 different centers were randomized to undergo either subtotal colectomy or segmental colectomy with on-table lavage (47 vs. 44 patients).[58] There was no significant difference in the morbidity and mortality; however, functional outcomes were worse in patients who underwent subtotal colectomy.[58] In patients with loaded colon planned for segmental colectomy and anastomosis, the proximal bowel can be cleared using intraoperative colonic irrigation or manual decompression.[56-59] Both RCTs and systematic reviews of papers comparing intraoperative colonic irrigation with manual decompression have reported similar anastomotic leak rates and mortality.[59,60] However, manual decompression was simpler and took less time compared to intraoperative colonic irrigation.[60] Based on current evidence, segmental colectomy is preferred over subtotal colectomy in patients undergoing emergency resection for obstructed left colonic cancer with subtotal colectomy being reserved for patients with synchronous colonic cancer and in patients with evidence of colonic ischemia or cecal tear/perforation secondary to obstruction.[61]

Loop Colostomy versus SEMS as a Bridge for Elective Colonic Resection

Both diversion colostomy and SEMS allow colonic decompression thereby facilitating bowel preparation and resection anastomosis at a second stage, besides facilitating accurate staging including evaluation for synchronous tumors. However, both the procedures have their advantages and limitations. The advantage of SEMS is that it does not require surgical decompression. Placement of SEMS is associated with complications like stent-induced perforation.[62] Patients who underwent SEMS had poor oncological outcomes.[63] Possible reasons are that the peritumoral inflammation induced by the stent may promote lympho-vascular invasion and lymph node metastasis. Also, microperforations and tumor manipulation caused by radial dilatation of SEMS, facilitates tumor dissemination.[64] RCTs and meta-analysis on stent as a bridge to surgery, report lower short-term overall morbidity.[64,65] However, it is important to remember that two RCTs on stents as a bridge to surgery had to be prematurely stopped due to a high incidence

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of complications.[66,67] Also, oncologic outcomes of the Dutch Stent-In 2 trial showed that 5 of 6 patients with a stent-related perforation experienced tumor recurrence.[68] In two meta-analysis, the long-term recurrence was more in the stent group compared to emergency surgery, although the difference did not reach statistical significance.[64,65] Hence, based on current evidence, stent as a bridge to surgery should be used only in selected poor risk candidates. Diversion colostomy is preferable over SEMS till more evidence on long-term oncological outcomes from Enteral Stents for Colonic Obstruction (ESCO) and Colo Rectal Endoscopic Stenting Trial (CREST) trials are available.

APPROACH TO PATIENTS WITH METASTATIC DISEASE

Patients suspected of having synchronous metastasis should undergo a metastatic workup including chest, abdominal and pelvic CT.[69] In selected cases potentially curable by surgical resection, a PET-CT may be considered to rule out distant metastasis.[69,70] It is currently recommended that all the patients with metastatic colon cancer should undergo genetic testing including K-ras (KRAS), neuroblastoma RAS (NRAS) and B-Raf (BRAF) mutations (which makes the patients unresponsive to cetuximab and panitumumab).[71-73] The management of metastatic colon cancer primarily depends on three factors, viz. the resectability of the primary colonic tumor, resectability of the extra-colonic organ metastasis and the presence of potentially "convertible to resectable" secondaries.[9] To consider for potentially curative surgery, the following criteria needs to be fulfilled, viz. (a) primary should be resectable with R0 resection, (b) no unstable extrahepatic or extrapulmonary metastasis and (c) likelihood of adequate function of the liver or lung after the resection of metastatic tumor.

Any surgery lesser than R0 resection such as a debulking procedure is not recommended.[9] Patients with unresectable tumors should be re-evaluated at the end of two months of neoadjuvant therapy and every two months thereafter for potential conversion to resectability.[9,74] Liver/lung metastasis can be considered for either synchronous resection of both primary and metastatic tumor or staged colectomy depending on the complexity involved in the liver/lung resection, comorbidity of the patient, expertise of the surgeon and the exposure required during the surgery. Trials have evaluated three types of management protocols with respect to timing of the resection of lung/liver metastasis.[9,74] These include the following:

1. Concurrent or staged colectomy and resection of liver/lung secondary.
2. Neoadjuvant chemotherapy with FOLFOX/CapOX for 2–3 months followed by concurrent or staged colectomy and resection of liver/lung metastasis.
3. Colectomy followed by chemotherapy with FOLFOX/CapOX for 2–3 months and resection of liver/lung secondary.

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