https://doi.org/10.48047/AFJBS.6.2.2024.2569-2584

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Surgical Guidelines for Management of Right Colon Cancer

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Article History

Volume 6, Issue 2, Apr-Aug 2024

Received: 10 August 2024

Accepted: 31 August 2024

Published: 31 August 2024

doi: 10.48047/AFJBS.6.2.2024.2569-2584

Abstract: Symptoms are common and prominent late in colon cancer when the prognosis is poor but are less common and less obvious early in the disease. The classic warning signs include loss of appetite, loss of weight, worsening constipation, alternating bowel habits, blood in the stool, decrease in stool caliber, and nausea or vomiting. Treatment options for colon cancer depend on the stage of the tumor that is, how far it has spread or how deeply it is affecting the intestinal wall and other tissues. In general, patients with colon cancer receive post-operative chemotherapy if the lymph nodes are positive. Treatment is also determined by the patient's age, medical history, overall health, and tolerance for specific medications and therapies. Surgery is the only curative modality for localized colon cancer (stage I-III) and potentially provides the only curative option for patients with limited metastatic disease in liver and/or lung (stage IV disease). The general principles for all operations include removal of the primary tumor with adequate margins including areas of vascular and lymphatic drainage. An open colectomy is the most common surgical procedure employed when treating colon cancers. The surgery is performed through a laparotomy incision where a part of the colon with the cancer and a small segment of normal colon on either side of the cancer are removed. Laparoscopic lobectomy is minimally invasive technique is an approach to resect a part of the colon and nearby lymph nodes and may be an option for some earlier stage cancers. Instead of making one long incision in the abdomen, the surgeon makes several smaller incisions.

Keywords: *Management of Right Colon Cancer*

1.Introduction

Symptoms are common and prominent late in colon cancer when the prognosis is poor but are less common and less obvious early in the disease. The classic warning signs include loss of appetite, loss of weight, worsening constipation, alternating bowel habits, blood in the stool, decrease in stool caliber, and nausea or vomiting [1].

Partial obstruction occasionally paradoxically produces intermittent diarrhea as stool moves beyond the obstruction. Proximal cancers rarely produce bleeding because the blood becomes mixed with stool and chemically degraded during colonic transit [2].

Signs:

A palpable abdominal mass is a rare finding that suggests advanced disease. Hypoactive or high-pitched bowel sounds suggest gastrointestinal obstruction. Rectal examination, including fecal occult blood testing (FOBT), is important in the evaluation of possible colon cancer. Other physical findings, including peripheral lymphadenopathy, especially a Virchow's node in the left supraclavicular space; hepatomegaly from hepatic metastases; and temporal or intercostal muscle wasting from cancer cachexia. Very rare findings with colon cancer include a Sister Mary Joseph node caused by metastases to a periumbilical node, and a Blumer's shelf caused by perirectal extension of the primary tumor [3].

Laboratory abnormalities:

Anemia, however, is very common, so that only a small minority of patients with anemia have colon cancer. Iron deficiency anemia of undetermined etiology, however, warrants evaluation for colon cancer, particularly in the elderly. In general, cancer patients have a high prevalence of hypoalbuminemia. Studies suggest that albumin is a negative acute phase reactant rather than a nutritional marker [4].

Since its initial description in 1965 by Gold and Freedman, Carcinoembryonic antigen (CEA) has been the most extensively investigated tumor marker for colon cancer. CEA is present in normal adult tissues in addition to malignant tissues, but very low levels normally are seen in the blood from healthy individuals with normal concentrations of 2.5 to 5.0 ng/ml. Although 80% or more of patients with advanced colonic adenocarcinoma have circulating CEA, the CEA assay should not be used as the sole diagnostic test for suspected carcinoma [5]. Preoperative serum CEA levels in diagnosed colorectal carcinoma are elevated in 40% to 70% of patients. Preoperative serum CEA concentrations correlate inversely with the grade of the carcinoma and directly with the pathologic stage and is an independent prognostic factor for recurrence. The CEA is elevated in 95% of patients with well-differentiated lesions, while it is elevated in as few as 30% of those with poorly differentiated adenocarcinomas. The higher the preoperative CEA level, the higher the stage and the greater the likelihood of a postoperative recurrence. Currently the CEA level is assessed preoperatively as a prognostic factor and predictor of recurrence and postoperatively for follow up and detection of recurrence. More over its level is used for assessment of the response to chemotherapy for metastatic colon cancerpatients [5].

Screening

Methods that are used to detect colon cancer are recently being introduced to screen for colon cancer either by one or a combination of tests

Tests that detect adenomatous polyps and cancer [6]: Flexible sigmoidoscopy every 5 years, Colonoscopy every 10years, Double-contrast barium enema (DCBE) every 5 years,or, Computed tomographic colonography (CTC) every 5 years.

Tests that primarily detect cancer [6]: Annual guaiac-based fecal occult blood test (FOBT) with high test sensitivity for cancer, or nAnnual fecal immunochemical test (FIT) with high test sensitivity for cancer, or Stool DNA (sDNA) test with high sensitivity for cancer, interval uncertain.

So, for individuals who carry an increased or high risk of developing colorectal cancer such as persons with prior history of polyps, prior history of colorectal cancer, family history of colon cancer or history of inflammatory bowel diseases, screening should start at an earlier stage than the age of 45 years and be more frequent and more stringent. Those genetically diagnosed or suspected of having hereditary familial syndromes such as HNPCC or FAP should be treated as having a high risk of developing colon and rectal cancer and should adhere to a more intense surveillance protocol [7].

Methods to screen for colorectal cancer:

Fecal Occult Blood Test (FOBT): This test checks for hidden blood in fecal material (stool). Currently, two types of FOBT are available. One type, called guaiac FOBT, uses the chemical guaiac to detect heme in stool. Heme is

the iron- containing component of the blood protein hemoglobin. The other type of FOBT, called immunochemical FOBT, uses antibodies to detect human hemoglobin protein in stool. Studies have shown that FOBT, when performed every 1 to 2 years in people ages 50 to 80, can help reduce the number of deaths due to colorectal cancer by 15 to 33 percent [8].

Procto-Sigmoidoscopy: In this test, the rectum and lower colon are examined using flexible sigmoidoscope During sigmoidoscopy, precancerous and cancerous growths in the rectum and lower colon can be found and either removed or biopsied. Studies suggest that regular screening with sigmoidoscopy after age 50 can help reduce the number of deaths from colorectal cancer [9].

Colonoscopy: In this test, the rectum and entire colon are examined using a video-colonoscope. During colonoscopy, precancerous and cancerous growths throughout the colon can be found and either removed or biopsied, including growths in the proximal part of the colon, where they would be missed by sigmoidoscopy [10].

Virtual Colonoscopy (also called computerized tomographic colonography): In this test, special software is used to produce pictures of the colon and rectum. A computer then assembles these pictures into detailed images that can show polyps and other abnormalities

Because it is less invasive than standard colonoscopy and sedation is not needed, virtual colonoscopy may cause less discomfort and take less time to perform. As with standard colonoscopy, a thorough cleansing of the colon is necessary before this test [11].

Double Contrast Barium Enema (DCBE): In this test, a series of x-rays of the entire colon and rectum are taken after the patient is given in enema with a barium solution and air is introduced into the colon The barium and air help to outline the colon and rectum on the x-rays. Research shows that DCBE may miss small polyps. It detects about 30 to 50 percent of the cancers that can be found with standard colonoscopy [12].

Characteristics of Colorectal Cancer in Egypt: Relative frequency 10-12%. High male predominance 3:1. More than 1/3 under age 45 (early onset). Large tumor size 4.5 cm. Rectal 51%, poor histology 58%. Associated bilharzial colitis 12%. Associated polyps 5%. Sporadic, HNPCC [12]

B- Treatment of right colon cancer:

Treatment options for colon cancer depend on the stage of the tumor that is, how far it has spread or how deeply it is affecting the intestinal wall and other tissues. In general, patients with colon cancer receive post-operative chemotherapy if the lymph nodes are positive. Treatment is also determined by the patient's age, medical history, overall health, and tolerance for specific medications and therapies [13].

Surgical treatment:

Surgery is the only curative modality for localized colon cancer (stage I-III) and potentially provides the only curative option for patients with limited metastatic disease in liver and/or lung (stage IV disease). The general principles for all operations include removal of the primary tumor with adequate margins including areas of vascular and lymphatic drainage [14].

a) Open Colectomy:

An open colectomy is the most common surgical procedure employed when treating colon cancers. The surgery is performed through a laparotomy incision where a part of the colon with the cancer and a small segment of normal colon on either side of the cancer are removed. Usually, approximately one fourth to one third of the colon is removed but is subject to the exact size and location of the cancer. Nearby lymph nodes are removed at this time. Removing as many lymph nodes as possible for examination is important to determine proper staging and post-operative treatment of the disease [15].

b) Laparoscopic Colectomy:

This minimally invasive technique is an approach to resect a part of the colon and nearby lymph nodes and may be an option for some earlier stage cancers. Instead of making one long incision in the abdomen, the surgeon makes several smaller incisions [15].

► Advantages and Disadvantages of Laparoscopic Colon Surgery:

Conventional open surgery is associated with significant morbidity and long convalescence. The advantages of laparoscopic colon surgery (LCS) in comparison with open surgery have been suggested with respect to decreased morbidity, decreased pain, faster recovery, shorter hospital stay and possibly reduced immunosuppression [15].

Table (6): Advantages and disadvantages of LCS [16]

One of the important advantages of LCS is the decreased intensity and duration of pain sensation. In the Clinical Outcomes of Surgical Therapy (COST) study grouptrial, patients in the laparoscopic arm required parental and oral analgesics for a shorter period of time [17]. In another randomized control trial (RCT), significantly less morphine was used in the laparoscopic groups only on the first postoperative day. It has been demonstrated that well managed pain control supports respiratory function and lowers the risk of complications [18].

In colorectal surgery, the major modalities of postoperative pain control are patient- controlled analgesia, opioids, non-steroidal anti-inflammatory drugs, and epidural analgesia. Some studies show that pain control, patient satisfaction and bowel function are improved after abdominal surgery under epidural analgesia [19].

According to a prospective study that was designed to examine the feasibility and safety of laparoscopic resection in high risk patients with colorectal cancer; laparoscopic resection of colorectal cancer can achieve excellent results even in "high risk" patients and is associated with significant reductions in length of stay compared with open resection [20].

Major abdominal surgery has been shown to result in significant postoperative immunosuppression. Open surgery causes a reduction in lymphocyte and neutrophil chemotaxis, natural killer cell activity, lymphocyte and macrophage interactions. It is estimated that after major open abdominal surgery immune function is suppressed for six to nine days. Laparoscopic surgery, which is associated with less patient trauma through smaller incisions and less postoperative pain is associated with less immunosuppression, compared with open, surgery [21].

A major advantage of laparoscopic surgery lies in the magnification that is offered by the endoscopic camera which enables greater surgical precision and better identification of tissue structures. This important issue may potentially lead to greater standardization of the surgical approach and technique [22].

The major disadvantage of laparoscopic colectomy is increased operative time. As opposed to most other laparoscopic procedures, laparoscopic colorectal surgery requires dissection in more than one quadrant and there is need for intraoperative repositioning of instruments, ports, and personnel. The colonic mesentery includes numerous large vessels and vascular control requires considerable time and quite often much more cost than do other procedures [23].

The surgeon’s experience is important, and there is a significant learning curve for laparoscopic colectomy. Operative time, rate of conversion, blood loss, and incidence of complications decreases significantly, proportional to the greater the number of procedures performed by the operating surgeon [24].

Non-surgical treatment:

a) Systemic Chemotherapy:

5-Fluorouracil remains the backbone of chemotherapy regimens for colon cancer, both in the adjuvant and metastatic setting. In the past years, it was established that combination regimens provide improved efficacy and prolonged progression-free survival in patients with metastatic colon cancer. In addition to 5-fluorouracil, oral fluoropyrimidines such as capecitabine (Xeloda) and tegafur are increasingly used as monotherapy or in combination with oxaliplatin (Eloxatin) and irinotecan (Camptosar). Some of the standard combination regimens employ prolonged continuous infusion of fluorouracil (FOLFIRI, FOLFOX) or capecitabine (CAPOX, XELOX, XELIRI) [25].

The standard therapy for patients with stage III and some patients with stage II colon cancer for the last 2 decades consisted of fluorouracil in combination with adjuncts such as levamisole and leucovorin. This approach has been tested in several large randomized trials and has been shown to reduce individual 5-year risk of cancer recurrence and death by about 30% [26].

Though information on results of adjuvant therapy in stage II and III colon cancer is limited, a data set assembled by the Adjuvant Colon Cancer Endpoints group with fluorouracil- based adjuvant therapy concluded that adjuvant chemotherapy provides significant disease-free survival benefit because it reduces the recurrence rate particularly within the first 2 years of adjuvant therapy but with some benefit in years 3-4 [27].

b) Radiotherapy:

While radiation therapy remains a standard modality for patients with rectal cancer, the role of radiation therapy is limited in colon cancer. It does not have a role in the adjuvant setting, and in metastatic settings, it is limited to palliative therapy for selected metastatic sites such as bone or brain metastases. More selective ways of administering radiation therapy such as stereotactic radiotherapy (CyberKnife) and tomotherapy extend indications for radiotherapy in further management of colon cancer [28].

C- Technique of CME with CVL:

Laparoscopic CME with CVL is based on resection of the colon within its intact and inviolate mesocolon with high tie ligation, so to improve the quality of the resection specimen produced; up-to-date anatomo-embryological concepts are analyzed in detail, focusing on the latest studies of the mesenteric organ, its dissection by mesofascial and retrofascial cleavage planes, and questioning the need for a new terminology in colonic resections. The impact on local recurrence, disease-free and overall survival is reviewed. Current literature about laparoscopic CME with CVL demonstrated better quality of the surgical specimen produced and significant survival advantage when compared to standard non-mesocolic resections, stressing the importance of meso-resectional surgery, especially when performed with minimally invasive techniques: higher surgical quality, faster recovery and better immunological response may in fact contribute to better long term oncologic outcome [29].

At the end of the 19th century, Emil Theodor Kocher was the first to theorize oncologic resections based on removal of the involved organ along with its lymphatic drainage; this concept was shortly after substantiated for rectal and colonic cancer respectively.

Yet, the real revolution in oncologic surgery was performed seventy years later who introduced the concept of total excision of the mesorectum (TME), the primitive embryological dorsal mesentery of the rectum: Dissection in the mesorectal plane yields an intact fascial-lined specimen containing all the vasculo-lymphatic pathways and lymph nodes, and reduces the risk of an involved circumferential resection margin (CRM).

The embryological right plane of dissection, graded by the pathologist, has been shown to be independently related to the risk of local recurrence, disease free and overall survival, so to promptly became the central part of any multimodal treatment of rectal cancer [30].

translated the concept of TME to colonic cancer, noting that traditionally more favorable oncologic results of colon neoplasia was eventually overtaken by rectal cancer: Multimodal strategies, not yet applied to colonic tumors, and a more radical surgical approach performed along embryonic planes of development with higher quality specimens, produce better oncologic outcome; thus, CME with CVL was theorized, standardized and eventually validated.

The concept of complete excision of the involved organ along with its primitive mesentery, associated to central ligation of the supplying blood vessels, is progressively gaining acceptance as the next step towards a modern surgical oncology; surgical resection of the primitive embryological mesenterium is in fact pivotal for optimal local clearance [31].

Furthermore, CVL allows for an extensive lymph node dissection along the feeding vessels, with significant effect on regional recurrence and systemic dissemination, as shown by improved survival in stage I-III colonic cancers treated with enhanced lymph node harvesting [31].

The rationale behind: There are three essential components of CME with CVL:

1. Development of a mesofascial or retrofascial plane to mobilize an intact and inviolate mesocolon as an intact package.

2. CVL with high tie to maximize the vertical lymph node dissection (central spread).
3. Adequate length of bowel to remove pericolic lymphnodes, maximizing the longitudinal lymph node harvesting (longitudinal spread).

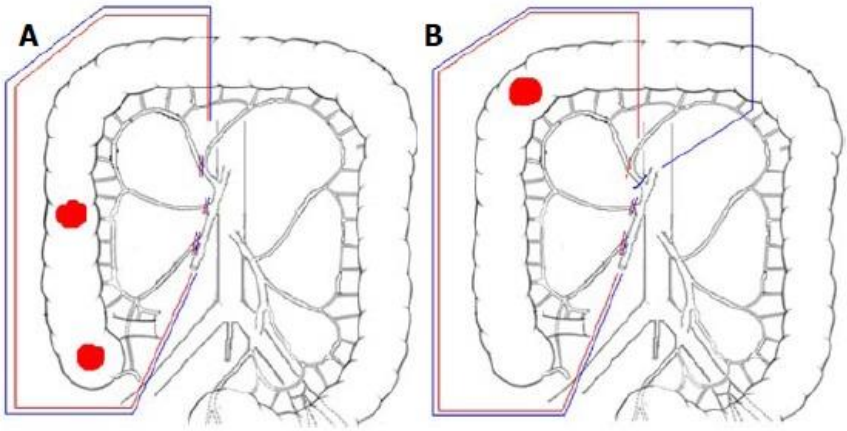

Figure (1): Schematic drawing illustrating the difference between extent of colon resection and lymph node harvesting between D3 right hemicolectomy accordingly to 2010 JSCCR guidelines (red lines) and complete mesocolic excision with central vascular ligation accordingly to Hohenberger's rules (blue lines).
A: Cancer located in the caecum or ascending colon.
B: Cancer located in the right (hepatic) flexure.

CME allows for removal of the entire envelope of the primitive dorsal mesentery along the anatomo-embryological avascular cleavage planes, and is therefore fundamental for a true radical R0 resection, as the meso contains the whole potential routes of metastatic spread through lympho-vascular, neuro-perineural and fibro-fatty tissues [32].

The mesocolon must be excised as an intact, inviolate package as any breach of its surface and underlying structures threatens the radial margin and disrupts the lymphatic network of the meso-structure with consequent spillage of neoplastic cells within the surgical field, enhancing the risk of local recurrence. This concept stresses further the need for a correct surgical plane of resection to maximize the local clearance, exactly the same way we conceptually perform TME for rectal cancer: To reduce the risk of an involved CRM and minimize the risk of local failure [32].

CVL is essential in obtaining an adequate regional control and impact on survival. The latest 2010 JSCCR guidelines recommends D2 dissection for clinically early stages colorectal cancers and D3 dissection for more advanced disease: Impressive results in terms of local recurrence and patients survival have been reported [33].

Also by Western authors who claim CME with CVL for right colonic cancer as oncologically effective as D3 right hemi-colecomy performed in Eastern Countries. CVL could be crucial in micro-metastatic clearance of central nodes, which are frequently missed by routine histological examination, and thus responsible for loco-regional recurrence and systemic dissemination [33].

For cancers located in the hepatic flexure and proximal transverse colon, possibly because of an embryological coalescence of mesenteric fascia, metastatic nodes incidence of about 5% for subpyloric station and about 4% for right gastroepiploic arcade has been reported: Central transection of middle colic vessels, ligation of right gastroepiploic vessels at the origin, 10 to 15 cm of greater omentectomy off the tumor and removal of subpyloric nodes could be beneficial, especially in advanced stages (clinically T3c-d and T4),

Blending CME with CVL is thus the logical step to ensure the best loco-regional control: CME maximizes the local clearance of the surgical field both increasing the chance for an uninvolved CRM and limiting any neoplastic spillage; CVL enhances regional control, removing apical nodes along the surgical trunk of the superior mesenteric vein (SMV), preventing regional recurrence and systemic dissemination: This is probably plausible for cancer without spread beyond the primitive meso-structure, as macroscopic involvement of apical nodes carries a poor outcome, independently from the extension of the surgical resection [34].

Quality of the surgical specimen:

1- Plane of dissection:

Laparoscopic CME with CVL, when performed in the right mesocolic plane, produces high quality surgical specimens. A grading system was developed in the CLASICC trial, with the aim to compare laparoscopically assisted surgery with open resection for colorectal cancer [29]:

1. Mesocolic plane of resection ("good" plane of surgery; intact, inviolate mesocolon with a smooth peritoneal-lined surface).
2. Intramesocolic plane of resection ("moderate" plane of surgery; irregular breaches in the mesocolon, none reaching down to the muscularis propria of the viscus).
3. Muscularis propria plane ("poor" surgical plane; disruption of the mesocolon down to the muscularis propria).

2- Extent of resected bowel

For resectable colonic carcinoma, the oncologically optimal surgical procedure is a curative (R0) colectomy with adequate proximal and distal resection bowel margins, and en- bloc complete removal of the respective to the resected segment mesocolon (Complete Mesocolic Excision - CME) with all regional lymph nodes [35].

Based on the fact that potential involvement of pericolic lymph nodes does not extend the 8 cm proximal and distal to the tumor baring bowel segment, bowel resection margins should be at least 10 cm, unless this is restricted by the exact location of the tumor or/and type of colectomy [36].

As a general rule, proximal ligation and division of the vascular stems supplying the specimen to be resected (CVL) ensures CME and the highest possible retrieved number of lymph nodes [37].

Surgical radicality:

Target criteria of CME for oncologic radicality includes:

(a) Preservation of visceral fascia without injuring themesocolon. (b) Complete removal of the regional lymphatic vessels andlymph nodes. (c) Division of the supplying arteries close to their origin (ileocolic artery, ICA), right colic artery, right branch of the middle colic artery). (d) Complete removal of the lymphatic tissue along theright side of the superior mesenteric vein (SMV) from approximately 3 cm distal to the ileocolic vein (ICV) up to the GPCT with division of all veins running from the mesocolon into the GPCT (SRCV and RCV). (e) Preservation of the GPCT including the pancreatic contributoriesand the veins that merge into the SMV (e.g. MCV). [38]

D3 dissection is recommended for advanced coloncancer with cT3/4 or cN + according to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines. In Japanese D3 dissection, pericolic, intermediate, and main lymphnodes are removed along with CME. demonstrated the optimal Japanese D3 dissection in right hemicolectomy and reportedthat 5-year disease-specific survival of patients with stagesI, II, and III cancer were 100.0%, 94.5%, and 85.0%, respectively [39].

The oncological validity of Japanese D3 for colon cancer has also been demonstrated byseveral studies in the past, similar to CME/CVL. According tothe interesting study employing 4034 patients with stage III coloncancer (right = 1618, left = 2416) , the right-sidedcancers more frequently invaded main lymph nodes than left-sidedlesions and the proportion of patients witha skipped pattern of lymphatic spread was higher in right than in left colon cancer . D3 would be required for clinical stage II/III right-sided colon cancer.

Besides the oncological aspects, feasibility and safety are also important issues. CME/CVL or D3 is considered technically more difficult than non-CME/CVL or D2. According to the Copenhagen Complete Mesocolic Excision

Study (COMES) by Danish Colorectal Cancer Group, intraoperative injury to other organs was more common in CME operations (including more superior mesenteric vein injuries. On the other hand, the multicenter RCT in Russia revealed that the 30-day postoperative morbidity rate was 47% in the D2 group and 48% in the D3 group, so Postoperative recovery, complication and readmission rates did not differ between the groups. Thus, the feasibility and safety of CME/CVL or D3 is still controversial [40].

As proposed , optimal D2 lymphadenectomy (removal of pericolic and intermediate nodes to the right side of the SMV) with standard high ligation as a minimum standard and selective CVL (D3 lymphadenectomy) in selected patients, suchas cN + disease, would be an ideal stance for colon cancer at the moment.

Ideal surgical report:

The ideal surgical report for colorectal cancer should provide all of the diagnostic, staging, prognostic, and technical aspects of the procedure that may influence outcome.

Documentation should include the following [41]:

1. Preoperative treatments, including chemotherapy, radiation therapy, and immunotherapy.
2. The site, size, and adherence of the primary tumor(s); obstruction or perforation if present.
3. Staging for metastatic disease (liver, peritoneum, omentum, or ovaries) and nonmesenteric lymph nodes (celiac, portohepatic, periaortic, or iliac), the extent and means (manual, bimanual, or sonographic) of liver exploration, the presence or absence of ascites and whether fluid was sent for cytologic examination, the description of any compromise of the exploration due to adhesions or concomitant disease(s), the site of biopsy of any areas suspected of having metastatic disease, the rationale if a biopsy specimen of the metastatic disease was not obtained.
4. The site and treatment of any metastatic disease.
5. The presence or absence of mesenteric lymph nodes (enlarged or firm) suspected of having disease, the site of any suspected lymph nodes left after the procedure is completed and the site of biopsy of any suspected lymph node outside the mesenteric resection.
6. The extent of resection, including level of transected feeding vessel(s), description of removal of adjacent structures or organs.
7. Any departure from an en bloc resection, any spillage of tumor or stool, site of placement of clips to aid in radiation therapy.
8. Any frozen sections submitted for examination, other interaction with a pathologist.
9. Clinical classification of tumor resection as R0, R1, or R2.

Ideal pathological report:

The histology report must include [35]:

A. Gross description: It involves length of surgical specimen, tumor size (3 dimensions) distance from proximal or distal margin, depth of invasion, tumor perforation, other lesions not related with the tumor (Crohn's disease, ulcerative colitis, adenomatous polyp, familial adenomatous polyposis), and total number of lymph nodes. The distance of direct tumor spread outside the muscularis propria should be recorded and the area in which tumor spreads closest to the lateral resection margin should also be identified macroscopically.

B. Microscopic description:

Histologic type: The main histologic types in WHO classification are adenocarcinoma, mucinous adenocarcinoma (>50% mucinous), signet ring carcinoma (>50% signet ring), squamous carcinoma, adenosquamous, small cell, medullary and undifferentiated carcinoma. Although most histological types do not have any proven prognostic significance there are exceptions. Signet-ring and small cell carcinomas have poor prognosis. Mucinous and medullary carcinomas, when associated with microsatellite instability (MSI), have a favourable prognosis.

Histologic grade: Currently, a 2-tiered grading system is used (low and high grade). The system is based on the proportion of gland formation and in this way the inter-observer variation is avoided. Low grade has a proportion >50% glandular formation and in this grade the well and moderately differentiated carcinomas are

included. In the high-grade category the poorly differentiated and undifferentiated carcinomas are included (<50% glandular formation).

Lymph nodes: All lymph nodes found in the surgical specimen should be sampled. A minimum of 12 lymph nodes must be found to predict the real lymph node status. The interpretation of the discrete nodules of tumor in the adipose tissue on microscopic examination is many times problematic. According to the old guideline, extramural tumor nodules measured >3 mm in diameter but lacked evidence of residual lymph node tissue were considered as positive lymph nodes. According to the updated guideline, a discrete extramural invaded nodule with smooth contours irrespective of size is considered as positive lymph node. Extramural and extranodal tumor deposits at the mesenteric fat are considered as remote metastatic disease and carry a poor prognosis.

Approaches of right colectomy:

Standardization of the procedure can help to improve the treatment outcome, even though there are several different approaches in use across the world including medial to lateral approach, lateral to medial approach, caudal to cranial approach and cranial to caudal approach.it still remains controversial which approach is superior in laparoscopic right hemi-colectomy. Besides there is newly emerging evidence favoring the cranial-to-caudal approach. We here presented a systematic review of approaches applied in laparoscopic right hemi-colectomy [42].

Complete mesocolic excision with central vascular ligation is considered to contribute to superior oncological outcomes after colon cancer surgery. For advanced right-sided colon cancer, this surgery sometimes requires lymph node (LN) dissection along the superior mesenteric vein (SMV), with division of the middle colic vessels, or their right branches at origin [42].

There are four approach for laparoscopic right colectomy:

1. Caudal to cranial approach.
2. Medial to lateral approach.
3. Lateral to medial approach.
4. Cranial to caudal approach.

Caudal to cranial approach:

First, a "yellow-white borderline" between the right mesostenium and retroperitoneum in the right iliac fossa is dissected as the entry for separation of the fusion fascial space between the visceral and parietal peritoneum. The right Toldt's fascia is dissected and expanded medial to the periphery of the superior mesenteric vein (SMV), cranial to the pancreas head, and lateral to the ascending colon. The posterior paries of ileocolic vessels (ICVs), right colic vessels (RCVs), and Henle's trunk are exposed. Second, the mesocolon between the ICV and SMV is dissected safely, and the ICV, RCV, and right gastroepiploic vessels as well as the right branch of the middle colic vessel are divided and ligated easily because of the separated retroperitoneal space. The lymph nodes along the SMV are dissected using a caudal-to-cranial approach. Third, the greater omental is dissected for full mobilization of the mesocolon containing 10 cm of normal colon distal to the lesion followed by complete mobilization of the lateral attachments of the ascending colon, extraction of specimen and anastomosis performed [43].

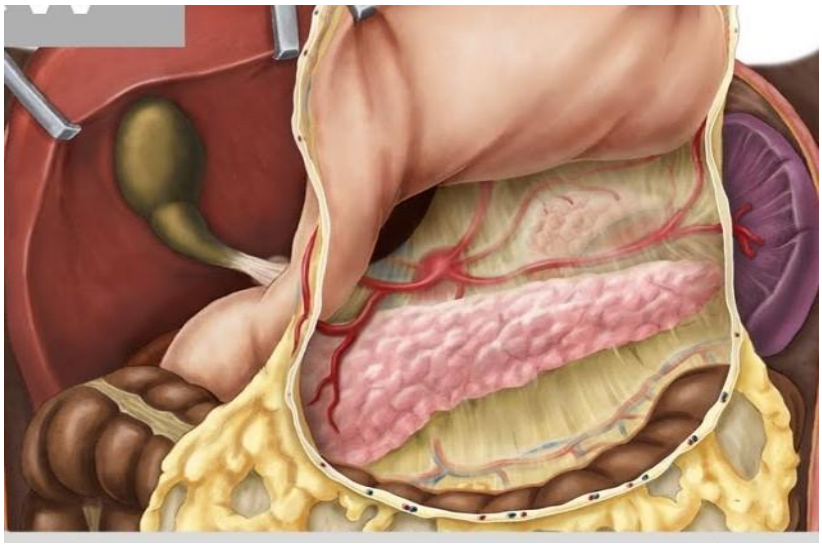

Figure (2): First step in cranial to caudal approach open omental bursa

Medial to lateral approach:

After positioning the patient right side up in steep Trendelenburg, the small bowel is retracted out of the right lower quadrant, and the greater omentum is placed in the upper abdomen, exposing the transverse colon. Optimal exposure should allow visualization of the right colon mesentery. Identify the ileocolic pedicle. This is typically done by using atraumatic graspers to elevate the ileocecal junction toward the right lower quadrant and anteriorly toward the abdominal wall, placing the mesentery under tension. The pedicle is identified as a "bow string" [44].

The dissection begins by incising the peritoneum below the pedicle, in a direction parallel to the course of the vessel. A wider incision makes this dissection easier. Using a blunt technique, the plane between the mesentery above and the retroperitoneum below is entered. The duodenum should be identified and swept down. The dissection should proceed cephalad and laterally. The plane is largely avascular. Any retroperitoneal tissues are sometimes identified by a purple appearance; use this as a marker of tissues that should be swept down. Using your left hand to provide sufficient retraction and tension is key to making this dissection efficient, safe, and complete. The ileocolic vessel is isolated and divided at its origin using an energy device, clips, or staples, ensuring the duodenum is safe from injury next, identify the rightbranch of the middle colic artery [44].

This is done by continuing the dissection as cephalad and lateral as possible, while always remaining aware of the location of the duodenum. The transverse colon mesentery should be elevated and placed under tension. The peritoneum is scored medical to the pedicle, and it is isolated at its base. After ensuring that the duodenum is safe, the vessel can be divided using energy, clips, or staples. At this point, if the medial-to-lateral dissection is adequate, the only remaining attachments are located laterally. These are dividing relatively easily with good tension-counter tension from the surgeon and assistant. Once mobilized, the colon is placed in its anatomic position [44].

A division of the small bowel mesentery at the terminal ileum may be required to allow for a safe extraction. The camera port site is extended, a wound protector is placed, and the specimen is exteriorized, ensuring that the colon remains anatomically oriented to prevent twisting of the mesentery. After ensuring the location of the tumor and adequate margins, the small bowel and distal colon are divided and an anastomosis performed using the surgeon's preference. Commonly, a side-to-side, functional end-to-end ileocolic anastomosis using a GIA stapler, and a single fire of linear stapler is used to close the common enterotomy. The viscera are returned to their anatomic locations and the fascial closure is performed in the typical fashion [44].

Lateral to medial approach:

The cecum and terminal ileum were mobilized cephalad. Dissection of the Toldt fascia from the ileocecal junction to the hepatic flexure was followed by blunt dissection to separate the mesocolon from the retroperitoneal fat. After identification of the duodenum, the hepatic flexure and transverse colon were released, thus completing right colon mobilization. Finally, the colon was ligated and anastomosis was performed begin as caecum and terminal ileum were mobilized cephalic, then dissection of told`s fascia from ileoceacal junction to hepatic flexure in avascular plane to separate mesocolon from retroperitomeal fat, after identification of duodenum and moved down to separated from transverse colon. Here, hepatic flexure and transverse colon totally mobilized thus right colon also mobilized, identification of ileo colic vessels and ligated, separation of mesocolon, specimen extracted and anastomosis performed [45].

Cranial to caudal approach:

It is a newly emerging evidence favoring in laparoscopic right colectomy as giving easy access to pancreas, early division of ARCV and middle colic vessels at origin, and easy dissection along SMV, central vessels ligation and division of middle colic vessels or its right branches. The omental bursa is first opened wide, and the gastrocolic trunk of Henle is exposed, using the right gastroepiploic vessels and the accessory right colic vein (ARCV) as landmarks. After division of ARCV, SMV and middle colic vein (MCV) are identified. After dividing MCV at its root, LN dissection along SMV is conducted in a cranial-to-caudal manner. Concurrently, the middle colic artery, or its right branch, is exposed and divided at origin. The transverse colon is then raised ventrally, and LN dissection along SMV using a cranial-to-caudal approach is again performed. The ileocolic and right colic vessels are divided at origin. The ascending and transverse mesocolon, including the pedicles, are then separated from the retroperitoneal tissues, pancreatic head, and duodenum, using a medial approach [42].

Complications of laparoscopic colorectal surgery:

Despite the many potential benefits of laparoscopic colorectal surgery, as has been reported for colorectal surgical procedures, complications are also inevitable; as the disease processes are varied and the surgical procedures are technically more complex than other laparoscopic procedures [46].

Intra-operative complications may be associated with anesthesia, laparoscopic access and complications of the operative procedure such as bleeding, bowel injury, ureteric and bladder injury and conversion. Postoperative complications include wound infection, anastomotic leakage, ileus, bleeding and port site metastasis [47].

1. Intra-operative complications

a) Anesthesia related complications:

The use of a steep Trendelenburg position and the distension of the abdomen may both reduce excursion of the diaphragm. Carbon dioxide (CO_2) can be absorbed particularly during prolonged operations. Monitoring by pulse oximetry, the use of endotracheal intubation and positive pressure assisted ventilation reduce the risk of hypercapnia to a minimum [48]. Brachial plexus injury attributed to the Trendelenburg position during prolonged laparoscopic procedures has been reported [49].

b) Trocar complications:

Abdominal access carries a definite risk of vascular and visceral injury. Many techniques used to create a pneumoperitoneum: blind Verrus needle, direct trocar insertion, optical trocar insertion and open laparoscopy. The described overall complication rates in these techniques are below 1%. Some studies revealed a higher rate of visceral injuries in the open-entry technique [50].

Direct insertion of trocar without prior pneumoperitoneum is associated with less insufflation-related complications such as gas embolism, is faster to perform and is a safe alternative. The visual entry cannula system may provide advantages over the traditional techniques but has to be fully' explored in the future [51].

c) Bowel and Vascular Injury:

There is limited data regarding iatrogenic injuries in colorectal surgery. The main fears of the surgeon are vessel injury, damage to the spleen during colorectal surgery (incidence of 0.006%), or intestinal perforation and ureteric injuries (incidence < 0.01%) [52].

d) Ureteric and Bladder Injuries:

One of the hazards of colorectal surgery is ureteric injury. The incidence of ureteric injuries during laparoscopic resections is estimated to be about 0.66%, Injuries to the ureters or the bladder occur mainly in patients undergoing oncologic resections, and those with difficult anatomic exposure, owing to previous operation, recurrent tumor or radiation therapy. Most of the injuries can be repaired by primary suture. Placement of ureteric catheterization preoperatively can reduce the incidence of this complication [53].

1. Postoperative Complications:

a) Surgical Site Infection

Colorectal surgery is associated with a high rate of surgical site infection (SSI), with overall infection rates reported to be as high as 26% [54]. There is increasing awareness of the need to reduce SSI given that development of this complication adversely affects length of hospitalization, quality of life, other post-operative outcomes and costs [55].

It has been demonstrated that; despite the presence of predisposing factors such as ASA> III, obesity, smoking, diabetes, inflammatory conditions as indication for surgery, operative time ...180 minutes and anastomosis involving the rectum; LAP approach is associated with decreased rate of SSI [56].

b) Anastomotic leak

Anastomotic leaks occur in approximately 3 to 15 percent of patients having undergone colon and rectal surgery and can lead to significant morbidity and mortality. The most important risk factor is the level of the anastomosis; low rectal anastomoses have a much higher leak rate compared with intra peritoneal colonic anastomosis. Technical considerations most often relate to tension and inadequate blood supply [57].

The anastomotic leak rate from intracorporeal laparoscopic anastomosis is not greater than that for open surgery or laparoscopic surgery with extra-corporeal anastomosis [58].

c) Port Site Metastasis:

Port-site metastasis is defined as cancer recurrence at a trocar insertion site without evidence of recurrence anywhere else [59].

Although the etiology of port-site metastasis is still unclear, the likely mechanism involves direct tumor cell contact and implantation. The initial enthusiastic application of laparoscopic techniques in colorectal surgical procedures was tempered in the early 1990s by reports of tumor implants in the laparoscopic incisions. Substantial evidence has accumulated to support that laparoscopic resection results in oncologic outcomes similar to open resection, when performed by well-trained experienced surgeons [60].

Abdominal wall recurrence after open colectomy was considered to be rare about 0.7% according to a retrospective study [61]. However, abdominal wall recurrence was reported in 2.5% of patients after open resection of colon cancer [62].

According to the consensus of the European association of endoscopic surgery (E.A.E.S.), the incidence of port site metastasis after laparoscopic colectomy is <1%. Proper surgical technique and practice reduce the likelihood of port site metastasis [63].

1. Conversion:

Laparoscopic colectomy is converted to open surgery in 14% (0- 42%) of cases. The most common causes of conversion are tumor invasion of adjacent structures or bulky tumor, adhesions, and technical failure [63].

Conversion from laparoscopy to laparotomy can be expected in a variable percentage of surgeries. Patients who experience conversion to a laparotomy may have a worse outcome than those who have a successfully completed laparoscopic procedure. In a study aimed to compare the outcomes of converted cases based on whether the case was a reactive conversion (RC) due to an intra-operative complication such as bleeding or bowel injury or a preemptive conversion (PC) due to a lack of progression or unclear anatomy, preemptive conversion is associated with a better outcome than reactive conversion. Based on this finding, it appears preferable for the surgeon to have a low threshold for performing PC rather than awaiting the need for an RC [64].

1. Non-operative complications:

The suppression of pulmonary function is a well-known sequela of abdominal surgery and following upper abdominal incisions, forced vital capacity (FVC) and forced expiratory volume in 1st second (FEV1) are reduced by almost 60% because of a refractory dysfunction of the diaphragm. Because the functional residual capacity is decreased postoperatively, small airways collapse and atelectasis occurs in most patients [65].

Pulmonary function does not recover to preoperative values within the first postoperative week after conventional abdominal surgery, and intensive physiotherapy does not prevent pulmonary dysfunction. Pneumonia is clinically apparent in more than 5% of all patients undergoing elective conventional colorectal resection and constitutes the most common general postoperative complication after conventional colorectal resection [66].

Pulmonary function is better after simple laparoscopic procedures than after conventional surgery. Postoperative recovery of pulmonary function has been shown to be quicker after laparoscopic colectomy as the measured FEV1 and FVC improved significantly faster in the laparoscopic than in the open group [67].

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