Laparoscopic Lymphadenectomy for Colorectal Cancers: Concepts and Current Results

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Introduction

The mainstay management for colon cancer remains surgery. The pathological findings in the specimen are the most important predictor of further treatment and survival. Cancer staging depends upon the assessment of primary tumor [T], lymph node metastasis [N], and distant metastasis [M] and these variables are most important for pathologists and treating clinicians.

Nodal metastasis plays a crucial role in determining prognosis, management, and survival of colorectal cancer patients and consists of an important parameter in contemporary prognostic staging systems particularly the widely used tumor node metastasis [TNM] system proposed by the UICC/AJCC. The 5-year survival rates range between 70% and 80% in node negative disease, with the corresponding values in node positive disease being 30%–60%. Adjuvant chemotherapy improves the survival in node positive disease. Occult lymph node disease is present in 20%–30%

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cases which is apparently present in completely excised disease [1, 2]. Adjuvant chemotherapy is beneficial in such a subset of cases when identified. Some of the other prognostic variables over and above TNM which might affect disease spread, recurrence and eventually benefit from adjuvant chemotherapy in colorectal cancers are: (a) venous invasion, (b) perineural invasion, (c) tumour perforation, (d) serosal involvement and (e) incomplete resection [1, 2]. Incomplete resection particularly refers to both primary tumor and nodal resection. Therefore, to obtain an accurate staging a conscientiousness effort is required both by surgeons and pathologists alike.

This chapter further discusses the nodal staging and the concept of adequate lymphadenectomy in right and left sided colonic tumours and rectum with an emphasis on the techniques of adequate lymphadenectomy.

Nodal Staging

American Joint Committee on Cancer [AJCC] 6th edition suggested a range of 7–14 LNs that should be obtained. The corresponding 7th and 8th editions in their respective sections stated that it is important to obtain and examine at least 12 LNs [3–7]. Even if less than the suggested number of LNs is identified, actual N stage rather than Nx should be provided. The factors which highly impact LN recovery include

I. Patient age
II. Gender and body habitus
III. Immune response to neo adjuvant treatment
IV. Tumor site and size
V. Length of colon resected
VI. Experience of surgeon
VII. Diligence and experience of a pathologist.

CAP [College of American pathologists] malignancy convention proposes that if less than 12 LNs are found, the specimen should be reconsidered for examination methods using lymph node enhancement techniques. In contrast to the sixth version, the seventh release further partitions N1 into N1a, N1b, and N1c; and N2 into N2a and N2b. N1c is a recently presented class in the seventh release, which is characterized by Tumour deposits (TD's) in subserosa, mesentery, or nonperitonealized pericolic or perirectal/mesorectal tissue with no local nodal metastasis. The eighth version does not have critical changes in N staging definitions in contrast to the seventh version. The master board endeavored to explain a few issues that have stayed testing in past versions, like TDs and micrometastasis.

Techniques of Colorectal Lymphadenectomy

Current Concepts

As mentioned, adequate lymphadenectomy remains the most important prognostic determinant for overall and disease-free survival. In the last three decades, the concept of lymphadenectomy in colorectal cancers has been revolutionized. The concept came more into practice with evolving minimal access surgery and centres across the world performing laparoscopic and robotic surgery. After two decades of the utilization of laparoscopic approach for colorectal surgeries, many randomized trials and systemic reviews have shown that the laparoscopic approach for colon malignancy is related with quicker recovery and less morbidity in contrast with the standard open methodology without influencing oncologic results [8–15].

Complete Mesocolic Excision [CME] and Central Vascular Ligation [CVL] with D3 Lymphadenectomy for Right Sided Colonic Cancers

Western Concept of Right Sided Colonic Cancers Lymphadenectomy Hohenberger et al. promulgated the idea of complete mesocolic excision as the standard operative procedure for colonic malignancy with an emphasis that CME with CVL decreases local recurrence and improves survival rates particularly in stage III cancers [16]. Subsequent literature from different parts of the world likewise showed comparable critical decrease in local recurrences and improvement of oncological radicality [17–19].

The concept of complete mesocolic excision (CME) with central vascular ligation (CVL), paralleling the concept of total mesorectal excision (TME) described by Professor RJ Heald [20], entails dissection of entire mesocolon in the embryonic planes of fusion. In the intaruterine period, the colon along with its vascular supply and lymphatics is suspended in a dorsal mesentery, which subsequently fuses with the retroperitoneum in the region of caecum, ascending and descending colon. Thus, an avascular plane exists between the mesocolon and the retroperitoneum (Fig. 1). It is important to note that the peritoneal bilayer covering the mesocolon envelopes the entire colon and is not merely limited to the pelvis. The aim of CME with CVL technique is to separate these two planes and excise the tumour along with the colon, the mesocolon with its accompanying lymphatic and vascular supply in totality, ensuring an intact visceral fascial layer is maintained. It can be achieved by sharp dissection between the visceral and the parietal peritoneal layers. Appropriate knowledge of anatomy of the mesocolon as well as adequate surgical expertise is desirable for the purpose.

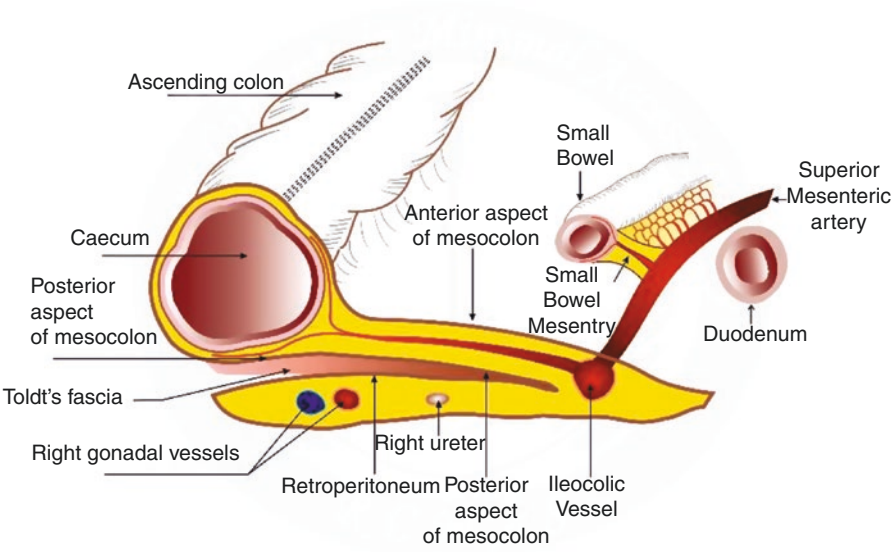

Fig. 1 Schematic representation of right colon with its mesocolic anatomy

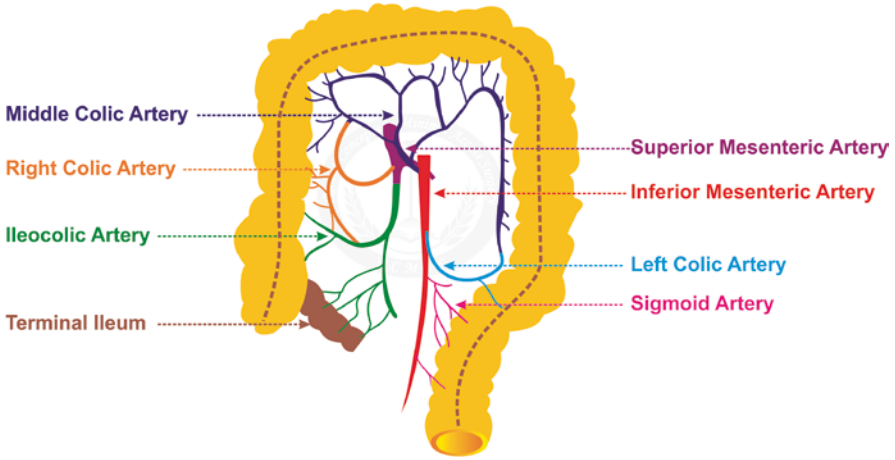

Fig. 2 Schematic diagram showing blood supply of right and left colon

The essence of CME-CVL or D3 lymphadenectomy is the ligation of the ileocolic vein, right colic vein, Henle trunk, and middle colic vein at their point of drainage into the superior mesenteric vein (SMV). Corresponding with venous ligation, the ileocolic artery, right colic artery, and middle colic artery are divided from their origin on the superior mesenteric artery (SMA) (Fig. 2). CME-CVL is a technically

demanding procedure due to the complex anatomy of the region and explicit knowledge of vascular anatomy (SMV and SMA) is vital to avoid iatrogenic complications. As regards oncological adequacy, this procedure is almost equivalent to eastern concept of Japanese D3 lymphadenectomy.

Eastern Concept of Right Sided Colonic Cancers Lymphadenectomy The Japanese Society for Cancer of the Colon and Rectum (JSCCR) classification groups the nodes associated with lymphatic drainage of colon into three groups.

- The main lymph nodes are situated at the source of the main feeding artery.
- Intermediate lymph nodes lie between the initial and terminal branch of the main artery
- Pericolic lymph nodes are stationed between the terminal branch of the main feeding artery and the colonic wall [21, 22].

In D2 lymphadenectomy the pericolic and intermediate groups lymph nodes are removed. D3 lymphadenectomy entails dissection of the main lymph nodes in addition to D2 lymphadenectomy. Thus, the western concept of CME-CVL is essentially comparable to definition of D3 lymphadenectomy by the JSCCR. However, in D3 dissection duodenal kocherization, and removal of the gastroepiploic and infrapyloric lymph nodes is not mentioned which has been described as a component of CME with CVL [21, 22].

The JSCCR guidelines recommend D3 lymphadenectomy for advanced T categories (T3/4) or node positive (N+) disease and D2 lymphadenectomy for early node negative cancers (T1N0). Whereas performance of either a D3 or D2 lymphadenectomy is suggested for T2N0 disease. Therefore, D3 lymphadenectomy is essentially recommended for stage II or III colon cancer in tertiary care centers.

Total Mesorectal Excision [TME]

The notion of total mesorectal excision [TME] for rectal cancer has been the most revolutionary concept that has evolved during the last three decades. Multiple studies noted a decrease in local recurrence to the tune of 6%–12%, and a 53%–87% improvement in 5-year survival after incorporation of TME [23–25].

In TME the rectum, along with its surrounding mesorectum comprising of lymphovascular fatty tissue (the first area of drainage of tumour cells), is excised using precise, sharp dissection in an avascular potential space between the visceral mesorectal fascia and parietal endopelvic fascia the so called “Holy plane” a term introduced by Heald [26]. TME minimizes the chances of leaving behind residual tumor and preserves nerve fibres which supply the urinary bladder, prostate, and vagina (Fig. 3).

The essence of the TME hypothesis is that lymph nodes randomly distributed within the mesorectum, which are not visible or palpable, are completely removed. The size of the normal lymph nodes in mesorectum in about 80% of cases is <3 mm.

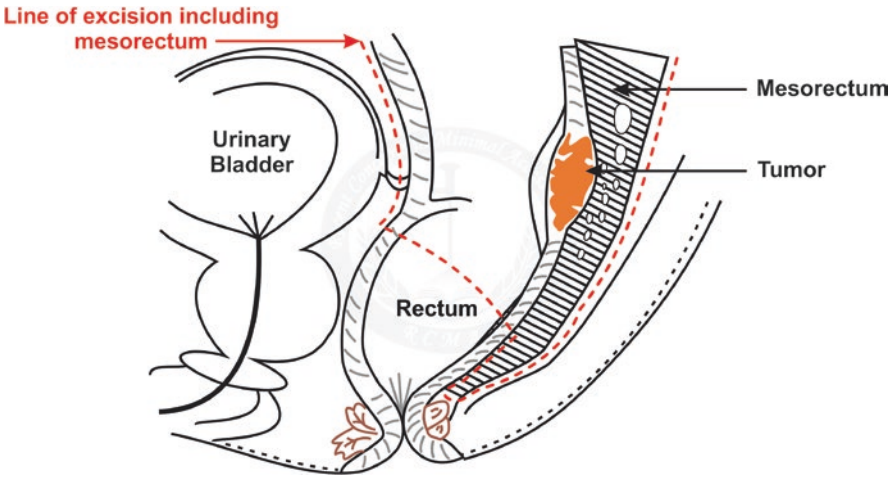

Fig. 3 Schematic diagram showing the "Holy plane of Heald"

Most lymph nodes in the mesorectum are located posteriorly, and 90% of the posterior lymph nodes lie within the upper half of the upper 2/3 of the rectum [27].

Rectal cancers very rarely spread in a downward direction intramurally, but the lymphatic spread in the mesorectum i.e. extramural spread, appears to be bidirectional (both in distal and proximal directions), within the limits of fascia of mesorectum, emphasizing the need for a complete mesorectal excision. Whereas TME is a beneficial procedure to extirpate lymphatic spread in high rectal carcinomas located >5 cm above the dentate line, the same is not noted in lower rectal neoplasms [less than 5 cm from the dentate line] wherein around 15–20% cases there is lateral nodal involvement which lies outside the confines of TME. A lateral node dissection as described below may prove beneficial in such patients.

Lateral Lymph Node Dissection [LLND]

The lymphatic drainage from the rectum below the peritoneal reflection follows two major pathways [Fig. 4]:

1. The superior rectal artery, inferior mesenteric artery, para-aortic corridor
2. Middle and inferior rectal artery, obturator, internal iliac and external iliac corridor (the lateral nodal group).

Total Mesorectal Excision [TME] involves removal of the first pathway of lymph nodes [28]. Management of the lymph node stations in the second route of drainage (the lateral nodes) has been a topic of interest lately [29]. It needs to be emphasized that the internal iliac group of nodes is classified as regional disease (Stage III) whereas the external and common iliac nodes are grouped as metastatic disease

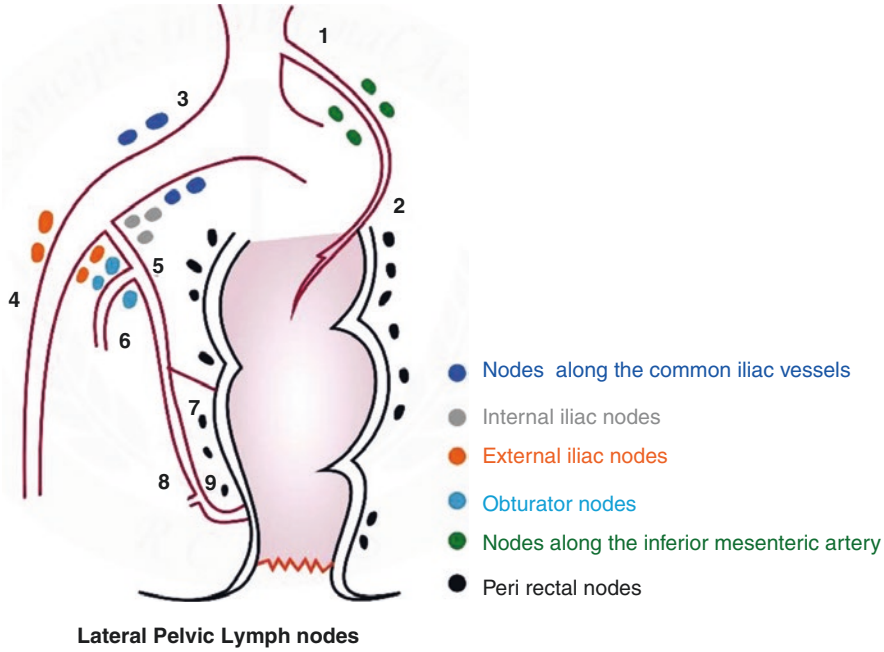

Fig. 4 Schematic diagram showing the Lateral pelvic lymph nodes. In the diagram marked vessels are 1. Inferior mesenteric artery, 2. Superior rectal artery, 3. Common Iliac artery, 4. External Iliac artery, 5. Internal Iliac artery, 6. Obturator artery, 7. Middle rectal artery, 8. Internal pudendal artery, 9. Inferior rectal artery. *(Radjindrin A (2018) Does Lateral Pelvic Lymph node matters in rectal cancer Glob Surg, 2018 doi:* https://doi.org/10.15761/GOS.1000196*)*

Table 1 Differences in the understanding and management of LLNs between the East and the West

	Western concept	Japanese concept
Regional nodes	Internal iliac nodes	Internal, external and common iliac and obturator nodes
Metastatic nodes	Common iliac, external iliac and obturator nodes	Not Applicable
Management	nCRT with RT boost to involved nodes	LLN dissection

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(Stage IV) in the TNM classification. Despite the classification radiation oncologists often treat external and common iliac nodes in rectal cancer with curative intent in concordance with treatment of regional nodes [Table 1] [30]. The lateral lymph nodes can be treated with either a radiotherapy boost or surgically by lateral lymph node dissection [30]. The Japanese guidelines for colorectal cancer [2016] recommends LLND for all rectal tumours situated caudal to the peritoneal reflection [31]. According to the JSCCR, LLND decreases intrapelvic recurrence by 50% and

offers a survival advantage of 8–9% [31]. A randomized controlled trial noted no increase in urinary dysfunction consequent to LLND though a tumor location below peritoneal reflection was proposed as a risk factor for the complication [32]. A multicentre non inferiority trial from Japan, JCOG2012, could not conclude a non-inferiority of TME alone over TME + LLND, however observed that the incidence of urinary and male sexual dysfunction was not significantly higher in the LLND group.[33] Nevertheless an increased morbidity has been observed following the procedure [32–34]. Mesorectal nodal metastasis has been proposed to be another important determinant of lateral lymph node metastasis [35].

Minimally Invasive LLND

In a study assessing feasibility of lateral pelvic lymph node dissection, when compared with the open approach the laparoscopic approach was considered safe, incurred a less blood loss, had lower hospital stay and had higher mean number of harvested nodes [35]. An autonomic nerve preserving approach for laparoscopic LLND based on vesical-hypogastric fascia and uretero-hypogastric nerve fascia has been proposed [36]. Robotic LLND has similar short-term outcomes and lymph node harvest, offering advantages in male narrow pelvis where manipulation of instruments becomes difficult in laparoscopic approach [37, 38].

Sentinel Lymph Node [SLN] Resection

The concept of sentinel lymph node biopsy [SLNB], which has significantly impacted the treatment of melanoma and breast cancer, is being investigated in colorectal cancers to enhance nodal staging accuracy especially in T1 disease. The sentinel lymph node is considered the lymph node[s] located the closest in the lymphatic mapping area. Despite a potential curative resection, 20–30% of node negative colorectal cancers develop distant metastasis presumably due to occult undetected nodal disease [39]. It has been noted that small <5 mm nodal deposits carry similar survival prognostication as >5 mm deposits emphasizing the importance of thorough examination of nodes [40]. Though yet controversial, micrometastatic deposits <2 mm may also benefit from postoperative adjuvant therapy.

Identifying patients who have tumor-negative nodes but are at high risk of regional or distant node metastasis who might benefit from adjuvant chemotherapy is challenging. The current histopathological evaluation of lymph nodes with standard Hematoxylin–Eosin [HE] pathological techniques is inadequate as large regions of the lymph nodes remains unexamined, with the subsequent risk of undetected residual micrometastases. Therefore, SLN mapping in colon cancer can help identify nodes that carry the higher risk of metastasis and such nodes can be subjected to detailed pathologic scrutiny, including more sections, immunohistochemistry and molecular diagnostic techniques thereby enhancing the staging accuracy.

Modification in Techniques of Sentinel Lymph Node Mapping

In Vivo Versus Ex Vivo Technique
The mapping can be performed *in vivo* or *ex vivo* using various substances: blue dyes, fluorescent dyes or radioactive tracers. Blue dye is the most commonly used dye both for *in vivo* and *ex vivo* techniques. The ex vivo technique can be also used in case the in vivo technique fails and has been noted to upstage the tumor in upto 12%. The results of the two techniques of mapping is reported to be similar. One advantage of the ex vivo technique is that the patient is spared from adverse reactions related to the dye but carries limitations due to the surgical disruption of the native lymphatic channels [41]. *In vivo* analysis involves injecting 1–2 mL of blue dye into the subserosa, around the tumor. The first blue-colored lymph node is removed after 5–10 min and sent separately to the pathologist. In *ex vivo* mapping, about 30 min after resection and before formalin fixation, 0.5–2 mL of blue dye is injected subserosally or circumferentially around the tumor (depends on the location of tumor i.e. above or below peritoneal reflection) and sites are massaged for five minutes to push the tracer into the lymphatic vessels. The first blue stained lymph node[s] is defined as the SLN [41]. Factors which influence the *In vivo t*echnique are: gender, age, BMI, tumor size, tumor location, previous abdominal surgery, nodal status, grade of tumour, tracer used, technique and preoperative chemoradiation [42].

Fluorescent Dye Technique Recently fluorescence navigation with Indocyanine Green [ICG] has gained popularity for *in vivo* visualization of SLN. A near infra-red imaging camera system is used in laparoscopic surgeries. The tracer can be injected subserosally or submucosally around the tumor. Advantages of the technique is that it offers real time visualization of lymph nodal compartments and aids detection of aberrant lymphatic drainage. In a study evaluating this method, 96% identification rate was noted. The main deterrent of this procedure is the high cost [43].

Immunohistochemistry and Molecular Methods for Detection of Metastasis in Lymph Nodes Use of immunohistochemistry and molecular diagnostic methods has been proposed for more accurate detection of micro metastasis in sentinel nodes. Immunohistochemical examination is more sensitive than Hematoxylin–Eosin [HE] whereas and molecular diagnostics (RTPCR/ one step nucleic acid amplification test) is more specific, and more accurate than immunohistochemistry [IHC] in detecting micrometastasis and isolated tumor cells [ITC]. The one step nucleic acid amplification test also decreases time to adjuvant chemotherapy. Ultra-staging with RT PCR demonstrated that node negative colon cancer patients who had recurrence had positive SLN [42]. Focused examination of sentinel node using CK-IHC and RT-PCR can identify micrometastases in 53% of patients whose SNs were labelled as negative by conventional histopathological techniques [44]. Among all the techniques used for the identification of the lymph nodes, the molecular one is the most expensive, but appears to provide the most accurate up staging [44].

Laparoscopic Right Colonic Resections with CVL

Though there are numerous laparoscopic techniques described in literature. The common approaches described are:

- Medial to lateral approach,
- Lateral to medial approach
- Caudo-cranial approach

We prefer the caudo-cranial approach [also called the initial retrocolic endoscopic approach IRETA APPROACH]. All procedures are done in the modified lithotomy position under general anaesthesia, and table position modified in accordance with the area to be mobilized.

Placement of Trocars Pneumoperitoneum is established with open or closed technique. A diagnostic laparoscopy is initially performed through a 10 mm/12 mm umbilical port. Subsequently the camera port is shifted to suprapubic region to facilitate viewing of the retroperitoneal tunnel that will be created. Two other ports, a 5 mm working port is placed in the region of right iliac fossa and another 5 mm port placed in the left subcostal region to retract small bowel and colon (Fig. 5). Later, the camera port can be transferred to the umbilicus for enabling better visualization during superior dissection along hepatic flexure and transverse colon. The procedure is performed in head down, right up position.

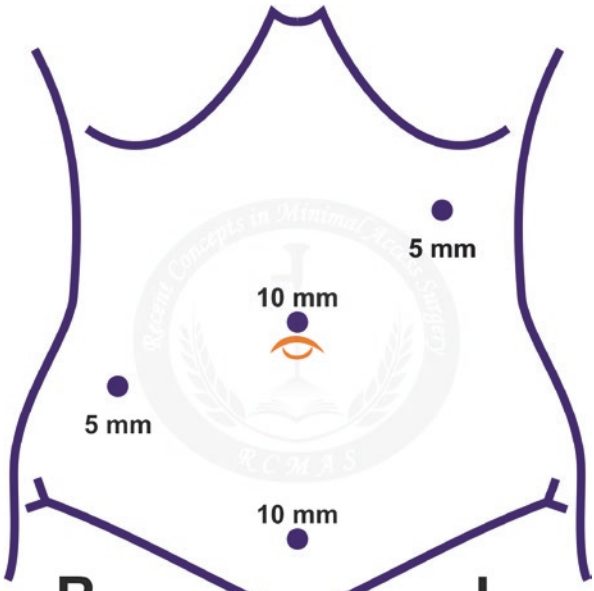

Fig. 5 Port position for right hemicolectomy

Mobilization of the Retro Colic Colon and Complete Mesocolic Excision [CME] In the initial retrocolic tunnel approach (IRETA), dissection begins with incision on the inferior border of terminal ileal mesentery (ileocolic fold) and is continued upwards laterally to behind the caecum and cranially and anteriorly in the avascular plane which separates the right ureter, right gonadal vessels and IVC posteriorly from the small bowel mesentery and retroperitonealized right mesocolon anteriorly (Fig. 1). It is important not to dissect free the lateral attachments of the colon at this stage to maintain retraction and keep open the retroperitoneal tunnel by preventing the colon from falling into the operative field. A retroperitoneal tunnel is thus created between two layers of embryologic fusion. Superiorly the dissection continues anterior to Gerota's fascia laterally, and the duodenum and pancreas cranially (Fig. 6).

Central Vascular Ligation (Figs. 7 and 8) Tenting the ileocolic mesentery by lifting it up is a useful technique that helps in identifying the ileocolic vessels which are dissected and traced to their origin from the superior mesenteric vessels and clipped. The right colic artery is thereafter addressed. It needs to be noted that it is inconsistently present. Further attention is directed to the middle colic vessels that can be identified traversing the transverse mesocolon vertically up when the transverse colon is lifted towards the abdominal wall. There are variations in drainage of

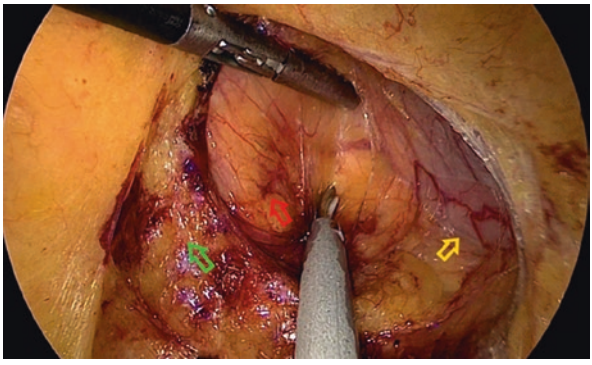

Fig. 6 Showing the right retro colic dissection creating the tunnel. The image also shows Duodenum (Yellow Arrow), Right pericolic tissue (Green arrow) and Gerota's fascia (Red arrow)

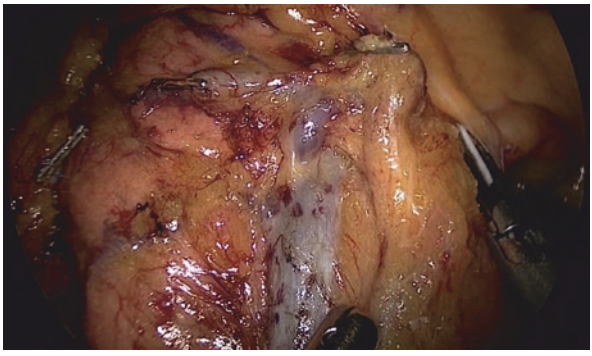

Fig. 7 D3 Right hemicolectomy dissection

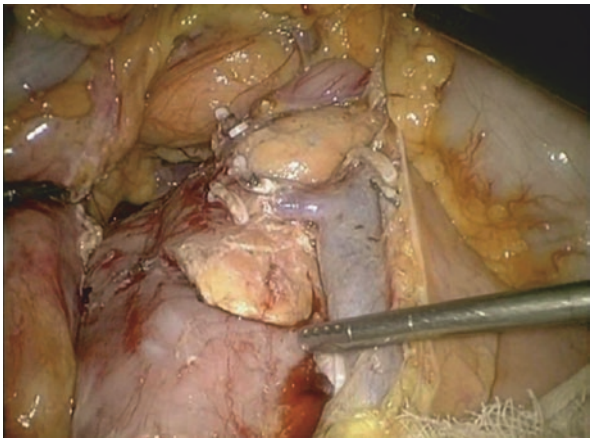

Fig. 8 Right Hemicolectomy D3 Dissection at completion

right colic and middle colic veins which may be encountered in the process. In conventional right hemicolectomy only the right branch of middle colic artery is ligated at its origin.

Mobilization of Transverse Colon and Hepatic Flexure After completion of CVL the following sequence of steps is adopted (1) lesser sac entry by dividing gastrocolic ligament along with omentectomy (2) dissection of hepatocolic ligament and mobilization of hepatic flexure of colon (3) The attachments of the mesoclon dissected from anterior surface of duodenum and pancreas (4) The ascending colon dissected from its lateral attachments to abdominal wall and retroperitoneum.

Resection of Specimen and Anastomosis If an extracorporeal anastomosis is planned the bowel is delivered through a plastic sheath, by extending the umbilical port and resection as well as anastomosis (handsewn/stapled) is performed outside (Fig. 9). In a totally laparoscopic approach, the transection of the colon and anastomosis is performed intracorporeally using Endo GIA stapler, conversion of the 10 mm port to 12 mm is needed for the purpose or initially a 12 mm umbilical port may be inserted (Fig. 10). Side to side ileo- transverse anastomosis is preferred anastomosis.

Advantages of Initial Retro Colic Approach

- There is minimal initial handling of colon thereby decreasing chances of tumor dissemination and bowel injury
- Easy creation of retroperitoneal tunnel and excellent retroperitoneal view
- The lateral attachments of the colon are dissected last thereby eliminating need for retraction of colon and preventing colon from falling into the operative field, particularly useful for bulky disease
- Easy early access to vascular pedicles near the origin

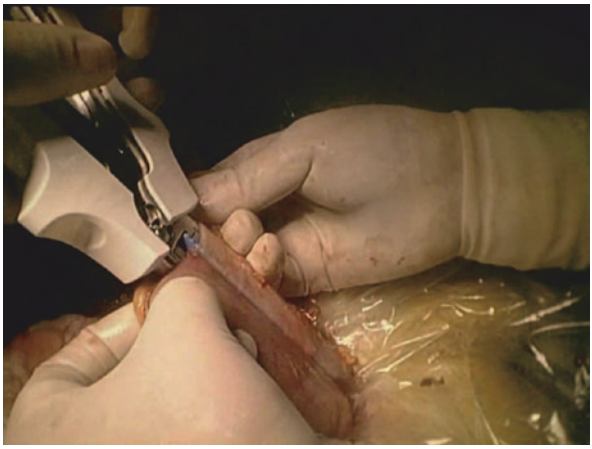

Fig. 9 Extra corporeal stappled anastomosis

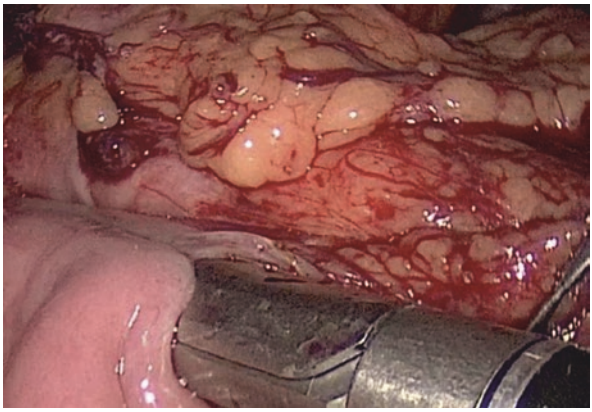

Fig. 10 Intracorporeal stappled ileocolic side-to-side anastomosis

Laparoscopic Left Sided Colonic Resections with Total Mesorectal Excision [TME]

The approaches frequently described in literature for the left colon are:

- Medial to lateral approach
- Lateral to medial approach

All procedures are done in the modified lithotomy position under general anaesthesia.

Placement of Trocars The surgeon and the camera assistant are stationed to the right of the patient. A 10mm camera port is inserted at the umbilicus. The procedure is performed with 4 or 5 ports: two 5-mm ports are introduced on either side and

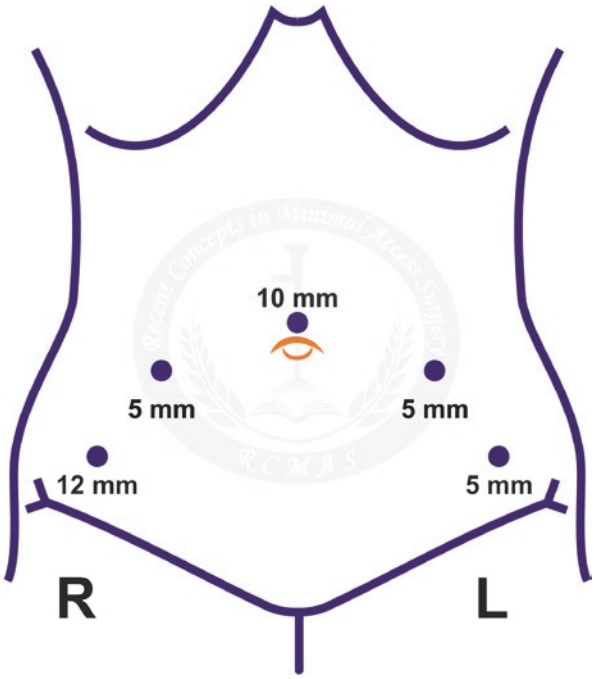

Fig. 11 Port positions for left sided colonic resections

another 12-mm port (for stapler) is placed at 2 cm above and medial to the right anterior superior iliac spine, additional 5-mm port can be inserted for bowel retraction (Fig. 11). At the commencement of operation, a diagnostic laparoscopy is performed to assess for metastatic disease. The procedure is performed with patient placed in Trendelenburg position and the table tilted to left up.

Pedicle Ligation: (Fig. 12) The omentum is displaced superiorly over the liver. A useful manoevure commonly practised for retraction of the uterus anteriorly is slinging the uterus using a percutaneous suture loop passed directly and tied above the skin over a piece of gauze. Retraction of the sigmoid colon to the left and anteriorly helps in identification of the sigmoid vessels and inferior mesenteric artery.

The peritoneum is incised caudal and to the right of the vascular trunk, at the level of sacral promontory and further dissection proceeds cranially to the origin of the vascular trunk (Fig. 13). Care should be taken to make the tunnel anterior to the ureter and hypogastric nerve plexuses which lie in close proximity. The superior rectal artery is lifted cranially and all vessels are skeletonized, and ligated separately using endoscopic clips (Fig. 14). In high ligation the inferior mesenteric artery is ligated at its origin whereas in low ligation, inferior mesenteric artery is ligated distal to its left colic branch (Fig. 12).

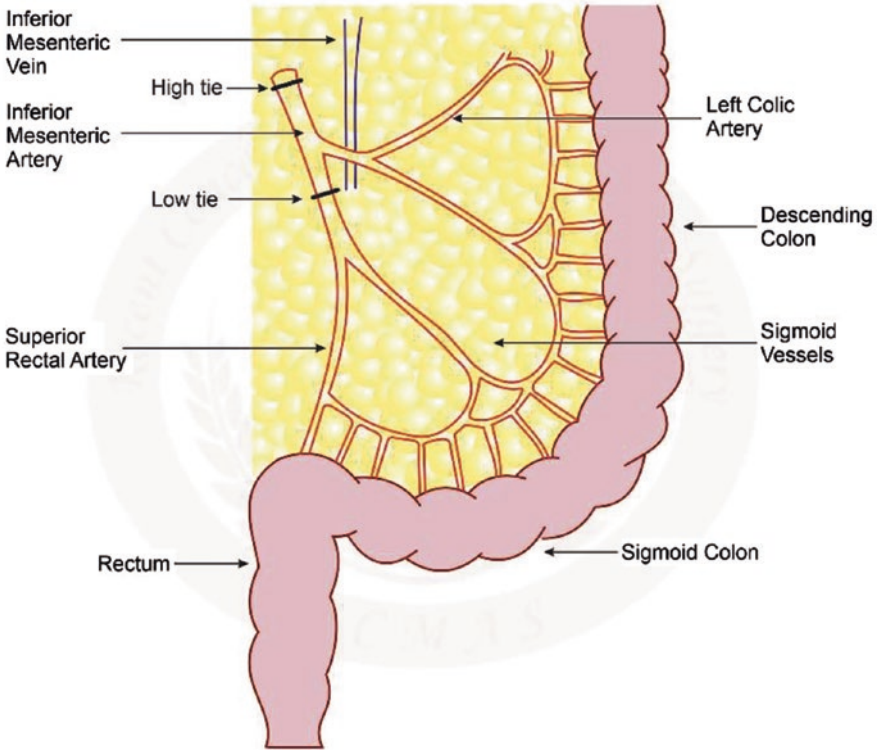

Fig. 12 Blood supply of left colon with site of doing high or low ligation of inferior mesenteric artery

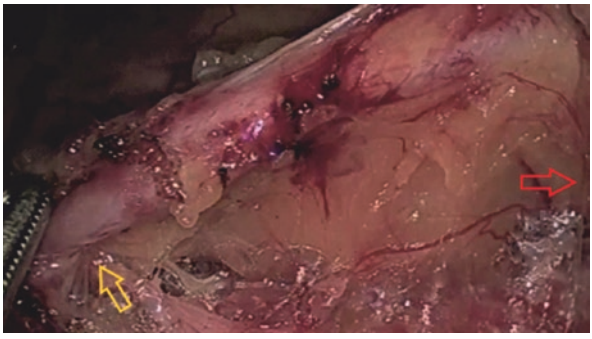

Fig. 13 Medial to lateral dissection from right side (Red arrow—Pelvis direction) showing the tented inferior mesenteric artery with its base (Yellow arrow)

Total Mesorectal Excision and Rectal Mobilization The dissection for TME is initially done posteriorly and laterally then subsequently anteriorly. The lateral peritoneal attachments of the rectum are incised down to the level of peritoneal reflection. The sigmoid colon is retracted ventrally to open the retrorectal space and

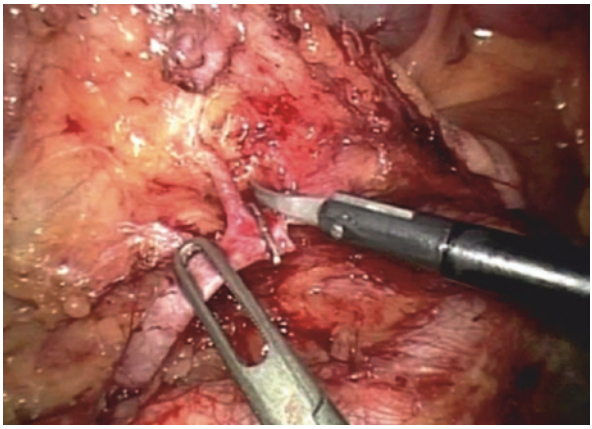

Fig. 14 Superior rectal artery being dissected and ligated. Iliac vessel is seen to its right

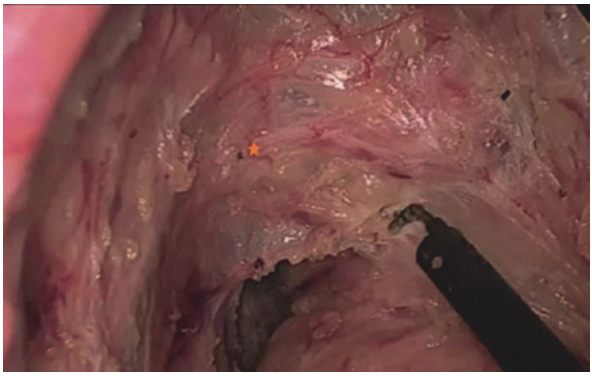

Fig. 15 Dissection showing the pelvic parasympathetic nerves* laterally

dissection is carried out in the avascular presacral plane between the parietal and visceral pelvic fascia. The hypogastric autonomic nerves which lie posteriorly, comes close to the mesorectum inferiorly and supply branches to the rectum where they should be carefully dissected by sparing the pelvic branches. Vessels entering the rectum can be addressed with harmonic or vessel sealing devices. Caudally the dissection is continued to the rectosacral fascia following which the rectum curves anteriorly to the pelvic floor (Fig. 15)

Anteriorly the peritoneum is incised to the level of rectovesical or rectovaginal pouch. Traction counter traction remains an integral part of TME. Usually, a gauze piece can be tied around rectum to pull the rectum out of the pelvis and provide traction and counter traction. Dissection proceeds anterior to the Denonvillier's fascia, posterior to the seminal vesicles in male patients and in the rectovaginal septum in females.

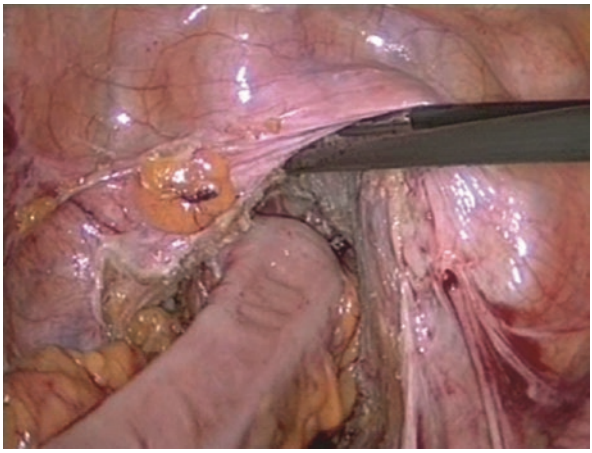

Fig. 16 Colo-anal anastomosis

Division of the Rectum

After ensuring complete circumferential mobilization to the pelvic floor, the mesorectum is dissected to the rectal wall and the rectum is divided at least 2 cm below the lesion using endostaplers.

Mobilisation of the Left Colon, Splenic Flexure and Anastomosis Proceeding in medio-lateral fashion the left and sigmoid mesocolon is dissected of the retroperitoneum and then the lateral peritoneal attachments of the colon along the white line of Toldt is released. Mobilization upto splenic flexure may be done if necessary to obtain an adequate length for anastomosing the proximal sigmoid to the distal rectum. Specimens are usually extracted through suprapubic incision and end to end colorectal anastomosis is performed using circular staplers (Fig. 16).

Advantages of Laparoscopic TME/CME

Laparoscopic resections for colorectal cancer offers the advantage of the improved visibility due to magnification and angled optics as also good illumination of the operation field and can aid in better delineation and preservation of the pelvic autonomic nerves.

Lateral Lymph Node Dissection

After completion of TME and rectal transection, the lateral pelvic nodes are addressed. They are grouped into three regions:

- common iliac region: comprising of the common iliac & external iliac nodes,
- hypogastric region: internal iliac nodes
- obturator region: obturator nodes (Fig. 4).

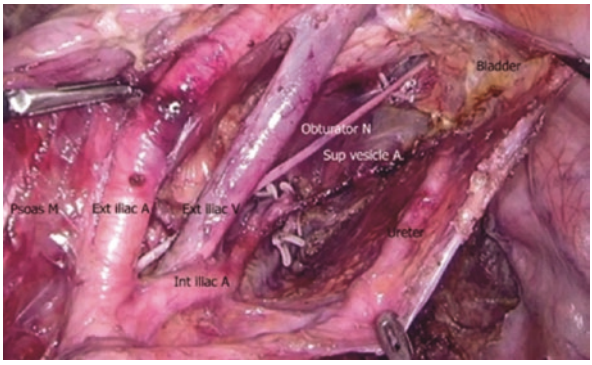

Fig. 17 Completed lateral pelvic dissection

The procedure begins by dissecting fibrofatty tissue around the aortic bifurcation at the origin of the common iliac vessels. The common iliac and external iliac nodes are dissected, thereafter, the hypogastric group is addressed by exposing the hypogastric nerve, external and internal iliac vessels, and ureter which are laid bare on the lateral pelvic wall up to the iliac bifurcation. The dissection proceeds to address the lymphatic tissues between the urinary bladder and the pelvic wall which are cleared. The lymphatic tissue along internal iliac vessels cleared upto the middle hemorrhoidal vessels. The obturator fossa is cleared of lymphoareolar tissue to lay bare the obturator nerve and vessels (Fig. 17).

Complications

Common concerns following complete mesocolic excision have been rates of

- Bleeding or vascular injury,
- Chyle leak,
- Anastomotic leakage,
- Duodenal or gastric perforations and
- Clavien Dindo grade 3 & 4 postoperative complications.

Bleeding/Vascular Injury

A recent metanalysis reported an increased risk of vascular injury with CME as compared to conventional colonic resection [45]. A higher intraoperative blood loss has also been noted in CME group as compared to non-CME [46]. Other metanalysis did not observe a higher blood loss or vascular injury with CME [47, 48]. Contrarily laparoscopic CME has been attributed to have less blood loss than open CME [19, 49].

Anastomotic Leak

Anastomotic leak rates are not found to be different following CME CVL as compared to conventional hemicolectomy, though delayed gastric emptying has been noted [50, 51, 52].

Chyle Leak

One of the chief concerns in extended lymphadenectomy is the possibility of chyle leak. Chyle leak can lead to malnutrition, electrolyte imbalance and a theoretical risk of malignant recurrences. A recent systematic review on chyle leak/chylous ascites following colonic surgery for malignancies found it to be a rare complication (5.5%). Most chyle leaks are discovered during the index admission and can be managed conservatively (diet change, total parental nutrition, drainage, somatostatin analogues) and reoperation is rarely needed [53]. Tumour location in right colon, extended lymphadenectomy and number of lymph nodes retrieved are proposed as independent associates for chyle leak after colonic resections [53, 54].

Severe Complications and Risk Factors for Complications

Some studies have reported a higher postoperative complication rate following complete mesocolic excision [52]. The rates of Clavien-Dindo Grade 1 complications is reported to be to the tune of 40% whereas severe grade 4 complications reported is 2.7% after laparoscopic right CME. The cited independent risk factors in multivariate analysis being: age $\geq$ 65 years, body mass index (BMI) $\geq$ 28 kg/m(2) [55]. In another study on risk factors for severe complications after radical colonic surgery it was observed that anemia, elevated body mass index, and open surgery were important predictors in multinomial logistic regression [56].

Conclusion

Lymph node metastasis is an important prognostic factor in colorectal malignancies. The western concept of complete mesocolic excision with central vasculature ligation is similar to D3 lymphadenectomy practised in the east for colonic cancers. Total mesorectal excision is an established standard of care for operable rectal cancers. Laparoscopic mesocolic excision for colonic cancer and laparoscopic total mesorectal excision for rectal cancers can be performed safely with few postoperative complications and good oncological outcome. Lateral lymph node dissection is an important addition to TME for rectal cancers and has been shown to influence survival. Sentinel node biopsy with fluorescent imaging appears to be promising in early node negative colonic malignancies.

Key Clinical Points

1. In colorectal cancer, lymph node metastasis is a key factor for deciding prognosis, management, and survival of the patients. Lymphadnectomy remains the mainstay of surgical management for colorectal cancers to improve the prognosis and outcomes.
2. Laparoscopic CME with CVL is established western practice in management of colonic cancers.
3. The aim of CME with CVL technique is to dissect the embryonic fusion planes and excise in totality the tumour along with its lymphovascular contents enclosed in the mesocolon as a single entity.
4. D2 lymphadenectomy entails removal of the pericolic lymph nodes and intermediate lymph group of nodes, whereas D3 lymphadenectomy involve dissection of the main lymph nodes in addition to D2
5. Western CME-CVL is comparable to Eastern D3 lymphadenectomy.
6. Laparoscopic total mesorectal excision remains the standard of care for rectal cancers and allows better preservation of nerves and vessels ensuring complete removal of lymph nodes.
7. The size of the normal mesorectum lymph nodes in about 80% of cases is <3 mm. Most mesorectum lymph nodes are located posteriorly, and 90% of the posterior lymph nodes lie within the upper half of the upper 2/3 of the rectum. Metastasis in mesorectal node is bidirectional i.e. both superiorly and inferiorly therefore necessitating complete mesorectal excision.
8. Lateral lymph node resection is advised in mid and lower rectal cancer to improve the prognosis by reducing local recurrence but is still not the standard of care across all centres.
9. Laparoscopic sentinel lymph node biopsy can be used to detect micrometastasis and improve the staging in T1/T2 disease of colon cancer. Standardized use of sentinel lymph node removal still remains controversial as expensive instrumentation is required.
10. Flourescence imaging and molecular staging are the two new methods to enhance detection of tumor deposits in sentinel lymph nodes.

Editor's Note[1]

Anatomy

One of the crucial steps in laparoscopic total mesocolic excision is an understanding of the embryological fusion planes and vascular anatomy of the mesocolon. The vascular anatomy is particularly pertinent for right colectomy as several variations exist.

Variations in Blood Supply and Venous Drainage of Right Colon as Pertinent to Laparoscopic Right Hemicolectomy

In a study evaluating variations in colonic blood supply from superior mesenteric artery it was noted that the middle colic artery and ileocolic artery were consistently present in most patients. Whereas the right colic artery was present in 12.2% to 55.0% cases only. The right colic artery has been noted to variably originate from superior mesenteric, ileocolic, middle colic and right branch of middle colic in various studies. It is important to note that the ileocolic artery can cross the superior mesenteric vein anteriorly or posteriorly. On the other hand, the right colic artery usually crosses the superior mesenteric vein anteriorly. Similarly, variations have been noted in the venous system. The ileocolic vein consistently drains into the superior mesenteric vein and is thus considered an important anatomical marker in laparoscopic right hemicolectomy. Of particular note is the "*Trunk of Henle"* which can present as a GTH (gastrocolic Trunk of Henle). GPCT (Gastropancreaticocolic trunk) or GPT (Gastro pancreatic Trunk), the latter being rare. Right colic veins rarely drain into superior mesenteric vein in only 19% whereas the middle colic veins drain into the superior mesenteric vein in 84% cases in the rest of the cases these veins drain into the trunk of Henle. The superior right colic vein is an inconsistent vein formed from tributaries of hepatic flexure and is also known as accessory right colic vein considered to be an important source of bleeding due to avulsion [1].

[1] References: Main chapter references are included after the "References Editor's Note" section.

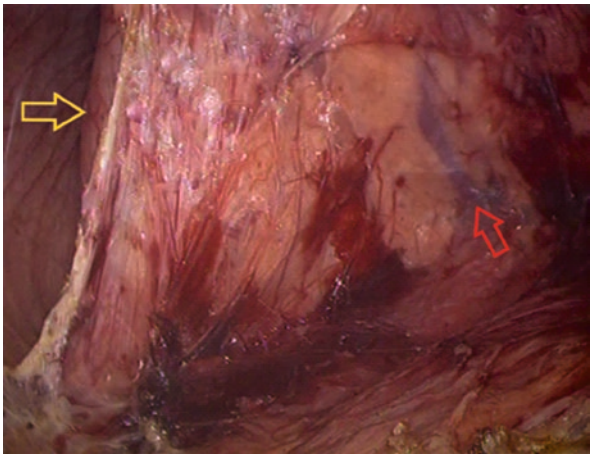

Fig. EN1 Laparoscopic right hemicolectomy image showing the dissection in Ileocolic plane (Yellow arrow: Caecum and proximal right colon, Red arrow: Ileocolic vessels)

Emryological Fusion Planes Encountered in Laparoscopic Right Hemicolectomy

Four critical view planes have been proposed in the open book model for standardization of CME in right hemicolectomy. They are essentially derived from the embryological fusion planes of colon and mesocolon and are: (a) retroperitoneal plane, (b) ileocolic plane (c) transverse mesocolic plane and (d) mesogastric plane [2].

Metaanalyses on Mesocolic Excision Versus Non Mesocolic Excision

Table EN1 tabulates the crux of the results of various meta-analysis comparing mesocolic excision versus non mesocolic excision. An advantage regarding oncological outcome parameters viz: recurrences, diseases free and overall survival has been consistently reported in latest studies. Surrogate pathological parameters of a better oncological resection such as number of lymphnodes retrieved, length of bowel excised, area of the mesocolon in specimen, distance to high tie have all been reported to be higher in the CME group [3–12].

Table EN1 Meta-analysis showing results complete mesocolic excision versus conventional excision in colectomy for colonic cancers

Study	Result
Comparing complete mesocolic excision versus conventional colectomy for colon cancer: A systematic review and meta-analysis [3]	**CME/D3 lymphadenectomy group had better oncological outcome as cited below:** • 5-year Overall survival OR = 1.29; 95% CI 1.02 to 1.64, p = 0.03 • 5-year Disease-free survival OR = 1.61; 95% CI 1.14 to 2.28; p = 0.007. **No significant differences in morbidity and mortality**
Complete mesocolic excision versus conventional hemicolectomy in patients with right colon cancer: a systematic review and meta-analysis [4].	**CME group was associated with significantly better oncological outcome as follows:** • Number of lymph nodes harvested; (MD 9.17, CI 4.67–13.68, p < 0.001). OS- 3-year; (OR 1.57, 95% CI 1.17–2.11, p = 0.003), • OS-5-year; (OR 1.41, 95% CI 1.06–1.89, p = 0.02), • DFS-5-year (OR 1.99, 95% CI 1.29–3.07, p = 0.002). **No difference in:** • complications • stage III colon cancer no significant benefit of CME on survival
Oncological reasons for performing a complete mesocolic excision: a systematic review and meta-analysis [5]	**CME group was associated with a significantly better oncological outcome as regards:** • Higher number of lymph nodes retrieved • Better pooled 5-year overall survival • Lower rates of local recurrence • Lower rates of distant recurrence **Disadvantage of CME:** • Higher incidence of vascular injury odds ratio 3, P < 0.001.
Complete mesocolic excision versus conventional surgery for colon cancer: A systematic review and meta-analysis [6]	**CME/ D3 lymphadenectomy had superior oncological outcome with respect to:** • OS -3 year RR 0.69 (95% CI 0.51–0.93, P = 0.016 • OS - 5 year RR 0.78 (95% CI 0.64–0.95, P = 0.011 • DFS - 5 year RR 0.67, 95% CI 0.52–0.86, P < 0.001 **No statistically significant differences in:** • complications • anastomotic leak

(continued)

Table EN1 (continued)

Study	Result
Complete Mesocolic Excision and D3 Lymphadenectomy versus Conventional Colectomy for Colon Cancer: A Systematic Review and Meta-Analysis [7]	**Better oncological outcome and pathological parameters in CME group as follows:** • Higher number of retrieved lymph nodes • Greater distance to high tie • Resected length of bowel • Larger area of resected mesentry • 3-year OS (RR 1.09, 95% CI 1.04–1.15) • 5-year OS (RR 1.05, 95% CI 1.02–1.08) • 3-year DFS (RR 1.10, 95% CI 1.04–1.17, i2 = 22%), • Decreased local recurrence (RR 0.35, 95% CI 0.24–0.51, i2 = 51%) • Fewer distant recurrences (RR 0.71, 95% CI 0.60–0.85, i2 = 34%). **Disadvantage CME group:** • Higher postoperative complications (relative risk [RR] 1.13, 95% confidence interval [CI] 1.04–1.2) **No differences were observed in:** • Anastomotic leak rates • Perioperative mortality.
Right hemicolectomy with complete mesocolic excision is safe, leads to an increased lymph node yield and to increased survival: results of a systematic review and meta-analysis [8].	**Superior oncological outcome with CME in the following aspects:** • Higher number of lymph nodes retrieved (MD 7.05, 95% CI 4.06–10.04). • Improved 3-year overall survival (RR 0.42, 95% CI 0.27–0.66) • Better 5-year disease-free survival (RR 0.36, 95% CI 0.17–0.560. **No difference in:** • anastomotic leak rates • blood loss • postoperative complications • serious postoperative complications -Clavien-Dindo grade III-IV • reoperation rate **Traditional surgery better as regards to:** • less operating time (MD 16.43, 95% CI 4.27–28.60)

Table EN1 (continued)

Study	Result
Right-side colectomy with complete mesocolic excision vs conventional right-side colectomy in the treatment of colon cancer: a systematic review and meta-analysis [9].	**Better oncological outcome and pathological parameters in CME group as regards:** • 5-year DFS 1.88 (95% CI 1.02–3.45) • 5-year OS 2.77 (95% CI 1.33–5.74) • Higher number of retrieved lymph nodes (MD 7.08 lymph nodes 95% CI 4.90–9.27). **No significant difference with respect to:** • morbidity • mortality • blood loss • hospital stay **Advantage conventional surgery:** • longer duration of surgery with CME (MD 33.69 min, 95% CI 12.79–54.59)
D3-lymphadenectomy enhances oncological clearance in patients with right colon cancer. Results of a meta-analysis [10].	**Better oncological outcome and pathological parameters with CME + D3 as noted below:** • tumour to vascular tie distance greater, • greater length of colonic resection, • wider mesentery resection • greater number of retrieved lymph nodes. • decrease risk of local recurrence (HR:0.17) • better 3-year OS (HR:0.53) • better 5-year OS (HR:0.57) **No differences noted in:** • morbidity related variables
Laparoscopic Complete Mesocolic Excision Versus Noncomplete Mesocolic Excision: A Systematic Review and Meta-analysis [11].	**CME scored better as regards:** • less blood loss ($P < 0.001$, (WMD) = −12.01, 95% (CI): −13.56 to −10.45), • more harvested lymph nodes ($P < 0.001$, WMD = 6.50, 95% CI: 3.57–9.42), • longer resected colon length ($P = 0.004$, WMD = 3.57, 95% CI: 1.12–6.03), • greater distance from tumor to high tie ($P < 0.001$, WMD = 1.36, 95% CI: 0.87–1.85), • greater distance from nearest bowel wall to high tie ($P < 0.001$, WMD = 1.36, 95% CI: 0.87–1.85). **No differences were observed in terms of:** • operative time, • complications, • wound infection, • ileus, • Proximal resected margin • Distal resection margin • Disease-free survival

(continued)

Table EN1 (continued)

Study	Result
Safety, quality and effect of complete mesocolic excision vs non-complete mesocolic excision in patients with colon cancer: a systemic review and meta-analysis [12]	**Advantage of CME in oncological outcome and pathological parameters:** • longer length of resected colon (WMD 47.06, 95% CI: 10.49–83.62), • greater tumor to the high tie distance (WMD 17.51, 95% CI: 15.16–19.87), • larger area of resected mesentery (WMD 36.09, 95% CI: 18.06–54.13) • more harvested lymph nodes (WMD 6.13, 95% CI: 1.97–10.28). • better 5-year survival (HR) 0.33, 95% CI: 0.13–0.81], • improved 3-year survival (HR 0.58, 95% CI: 0.39-0.86) • better 3-year survival for Stage III disease (HR 0.69, 95% CI: 0.60–0.80) **Disadvantage CME:** • more intra-operative blood loss [weighted mean difference (WMD) 79.87, 95% CI: 65.88–93.86], • higher surgical complications (relative risk 1.23, 95% CI: 1.08–1.40)

CME complete mesocolic excision, *OR* odds ratio, *HR* hazard ratio, *WMD* weighted mean difference, *CI* confidence interval, *OS* overall survival, *DFS* disease free survival, *RR* risk ratio, *MD* mean difference

Meta Analyses on Laparoscopic and Open Mesocolic Excision

Table EN2 enlists the results of metanalysis comparing laparoscopic and open mesocolic excision. A better postoperative recovery, lower blood loss, less requirement for blood transfusion, lower overall postoperative complications, less wound infections, early recovery of gastrointestinal function and shorter hospital stay are some of the reported benefits of laparoscopic over open CME for colonic cancers [13–16].

Meta Analyses on Lateral Lymph Node Dissection in Rectal Cancers

The results of metanalyses pertaining to lateral lymph node dissection is shown in Table EN3. Most metaanalyses project a higher incidence of urinary dysfunction and male sexual dysfunction associated with lateral lymphnode dissection. Though there is no major survival benefit overall it may be helpful in patients with clinically positive lateral lymph node that persist after preoperative chemoradiotherapy or those who do not receive neoadjuvant chemoradiotherapy [17–21].

Table EN2 Metaanalyses comparing laparoscopic and open mesocolic excision

Study	Result
Laparoscopic versus open complete mesocolic excision: a systematic review by updated meta-analysis [13]	**OCME vs LCME** shorter operative time in the OCME. **LCME advantageous with respect to:** • less blood loss, • lower wound infections, • earlier time to flatus, • shorter time to oral feeding, • decreased length of hospital stay **LCME had better oncological outcome and survival benefits:** • 1-year OS (HR = 0.37 (0.22, 0.65); p = 0.004), • 3-year OS (HR = 0.48 (0.31, 0.74); p = 0.008), • 5-year OS (HR = 0.64 (0.45, 0.93); p = 0.02), • 3 year DFS (HR = 0.63 (0.42, 0.97), p = 0.03) • 5-year DFS (HR = 0.68 (0.56, 0.83), p = 0.001)
Laparoscopic vs open complete mesocolic excision with central vascular ligation for colon cancer: A systematic review and meta-analysis [14]	**LCME vs OCME** **LCME better regarding following parameters** • 3 year overall survival (OR = 2.02, 95%CI: 1.31 to 3.12, P = 0.001), • 3 year disease-free survival (OR = 1.45, 95% CI: 1.00 to 2.10, P = 0.05) • area of the resected mesocolon (MD = 11.75 cm2, 95%ci: 9.50 to 13.99, p < 0.001). • decreased blood transfusion rate (or = 0.45, 95%ci: 0.27 to 0.75, p = 0.002), • earlier recovery of gastrointestinal function, • less complication rate. **No differences regarding:** • harvested lymphnodes • distance from tumor to high tie
Open compared with laparoscopic complete mesocolic excision with central lymphadenectomy for colon cancer: a systematic review and meta-analysis [15]	**LCME advantageous compared to OCME as regards:** • shorter hospital stay [WMD = 2.29 (95% CI: −0.39 to 4.98); P = 0.09] • lower rate of wound-infection [OR = 2.87 (95% CI: 1.38–5.98); P = 0.005] **LCME disadvantage:** • longer operative time [weighted mean difference (WMD) = –30.88 (95% CI: –62.38 to 0.61); P = 0.05] **No statistically significant difference was found in:** • short-term mortality • anastomotic leakage, • ileus • deep-seated infection/abscess • overall survival • disease-free survival, • local recurrence • distant metastases

(continued)

Table EN2 (continued)

Study	Result
Comparing the safety, efficacy, and oncological outcomes of laparoscopic and open colectomy in transverse colon cancer: a meta-analysis [16]	**LC had was superior to OC in terms of:** • less postoperative complications (OR 0.64, p = 0.0003), • reduced blood loss (WMD –86.84, p < 0.00001), • earlier time to first flatus passage (WMD –0.94, p < 0.00001) • early onset of oral diet (WMD – 1.25, p < 0.00001), • length of stay (WMD – 2.39, p < 0.00001). • lower recurrence rate **OC was advantageous in the following aspect:** • lower operation time (p < 0.00001). • higher rate of complete mesocolic excision (p = 0.001). **LC vs OC equivalent in terms of postoperative survival outcomes.**

LCME laparoscopic complete mesocolic excision, *OCME* open complete mesocolic excision, *OR* odds ratio, *HR* hazard ratio, *WMD* weighted mean difference, *CI* confidence interval, *OS* overall survival, *DFS* disease free survival, *RR* risk ratio, *MD* mean difference, *LC* laparoscopic colectomy, *OC* open colectomy

Table EN3 Metaanalyses on lateral lymph node dissection in rectal cancers

Study	Result
Lateral lymph node dissection reduces local recurrence of locally advanced lower rectal cancer in the absence of preoperative neoadjuvant chemoradiotherapy: a systematic review and meta-analysis [17]	**TME with LLND was associated with:** • longer operation time (WMD 90.73 min, P < 0.001). • greater intraoperative blood loss (WMD 303.20 ml, P < 0.001). • higher postoperative complications (RR = 1.35, P = 0.02). **No difference in:** • Urinary dysfunction • Sexual dysfunction • Postoperative mortality • DFS • Total recurrence • Lateral recurrence • Distal recurrence **TME with LLND had benefits regarding:** reduced local recurrence in patients who did not receive nCRT (RR 0.71, P = 0.004) not significant when combined with nCRT.

Table EN3 (continued)

Study	Result
Meta-analysis of survival and functional outcomes after total mesorectal excision with or without lateral pelvic lymph node dissection in rectal cancer surgery [18]	**No difference between groups in the following aspects:** • overall survival • 5-year overall survival • disease-free survival • 5-year disease-free survival • local recurrence • distant recurrence • total recurrence **Total mesorectal excision with lateral pelvic lymph node dissection resulted in** • longer operative time (MD: 116.02, 95% CI 89.20–142.83, P < 0.00001, I2 = 68%) • higher complications (odds ratio: 1.59, 95% CI 1.14–2.24, P = 0.007, I2 = 0%) • urinary dysfunction (odds ratio: 6.66, 95% CI 3.31–13.39, P < 0.00001, I2 = 23%) • sexual dysfunction (odds ratio: 9.67, 95% CI 2.38–39.26, P = 0.002; I2 = 51%)
Total mesorectal excision plus lateral lymph node dissection vs TME on rectal cancer patients: a meta-analysis [19]	**TME + LLND group fared worse as regards:** • more complications (OR = 1.48, 95% CI [1.07, 2.03], P = 0.02) **No significant difference was observed in** • overall survival • disease-free survival • local recurrence • urinary dysfunction
What is the role of lateral lymph node dissection in rectal cancer patients with clinically suspected lateral lymph node metastasis after preoperative chemoradiotherapy? A meta-analysis and systematic review [20].	**LLND after nCRT associated with:** • lower LLR (P = 0.02). **LLND disadvantageous due to:** • longer operative time (P < 0.01) • increased risk of urinary dysfunction (P < 0.01).
The efficacy and safety of lateral lymph node dissection for patients with rectal cancer: A systematic review and meta-analysis [21]	**No difference in** • 5-year disease-free survival rate • local recurrences **LLND associated with more:** • urinary dysfunction (OR = 2.14, 95%CI = 1.21–3.79, P = 0.009) • male sexual dysfunction (OR = 4.19, 95%CI = 1.55–11.33, P = 0.005)

TME total mesorectal excision, *LLND* lateral lymphnode dissection, *nCRT* neoadjuvant chemoradiotherapy, *LLNM* lateral lymph node metastasis, *LLR* lateral lymphnode recurrence, *OR* odds ratio, *HR* hazard ratio, *WMD* weighted mean difference, *CI* confidence interval, *OS* overall survival, *DFS* disease free survival, *RR* risk ratio, *MD* mean difference

Metaanalyses on Sentinel Lymph Node Biopsy in Colorectal Cancers

Table EN4 depicts the results of recent metaanalyses on sentinel node biopsy in colorectal cancers. A high identification rate sensitivity and diagnostic accuracy has been observed especially for early stage lesions. Colonic cancers, use of laparoscopic procedures and indocyanine green for performance of sentinel node biopsy has been noted to have a better yield [22–24].

Table EN4 Results of sentinel lymph node biopsy in colorectal cancers

Study	Result
In vivo sentinel lymph node identification using fluorescent tracer imaging in colon cancer: A systematic review and meta-analysis [22].	T3-T4 vs T1-T2 tumours • Detection rate of 90% vs 91%, • Accuracy rate of 77% vs 98%, • Sensitivity of 30% vs 80%.
Sentinel lymph node mapping for metastasis detection in colorectal cancer: a systematic review and meta-analysis [23].	• Pooled SLN detection rate 93% (95% CI, 0.91–0.94), • Overall sensitivity 0.72 (95% CI, 0.67–0.77)
Performance of Indocyanine green for sentinel lymph node mapping and lymph node metastasis in colorectal cancer: a diagnostic test accuracy meta-analysis [24]	Pooled detection rate 91% (80%–98%).

SLN sentinel lymph node, *CI* confidence interval

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