HUE UNIVERSITY

UNIVERSITY OF MEDICINE AND PHARMACY

NGUYEN MINH THAO

EVALUATION OF LAPAROSCOPIC COMPLETE MESOCOLIC EXCISION IN COLON CANCER

Specialty: Surgery

Major code: 9 72 01 04

SUMMARY OF THE DOCTORAL THESIS IN MEDICINE

HUE - 2025

This research work was completed at:
UNIVERSITY OF MEDICINE AND PHARMACY, HUE UNIVERSITY

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STRUCTURE OF THE THESIS

The thesis is presented in 135 pages (excluding references and appendices).

It includes: 2 pages of Introduction, 45 pages of Literature Review, 19 pages of Subjects and Methods, 30 pages of Results, 36 pages of Discussion, 2 pages of Conclusion, and 1 page of Recommendation.

The thesis contains 55 tables, 9 charts, 27 figures, and 182 references, of which 13 are in Vietnamese and 169 are in English.

The appendices include published research works, references, research forms, and patient lists.

INTRODUCTION

1. Rationale

Colorectal cancer is one of the most common malignancies, ranking third worldwide and fifth in Vietnam. Surgery remains the standard and most important treatment.

Currently, colectomy with complete mesocolic excision (CME) has been widely adopted due to its ability to achieve radical lymph node dissection, providing superior outcomes compared to conventional surgery. This technique has been shown to reduce local recurrence and significantly improve survival after surgery. Moreover, CME increases the number of harvested lymph nodes, enabling more accurate disease staging.

Adjuvant chemotherapy is recommended for stage III and certain high-risk stage II colon cancer patients. Among these risk factors, analyzing fewer than 12 lymph nodes indicates a high risk and affects staging accuracy. Therefore, harvesting at least 12 lymph nodes has become a standard practice. However, a considerable proportion of patients still do not meet this requirement postoperatively.

One major challenge in clinical practice is the dissection of lymph nodes from surgical specimens. Although CME specimens typically contain sufficient lymph nodes, manual palpation and visual inspection are often limited, especially in early-stage cancers or when lymph nodes are small. Consequently, many patients have insufficient lymph nodes for staging, which directly affects the accuracy of pTNM classification and subsequent treatment decisions.

To overcome this limitation, various solutions have been investigated to highlight lymph nodes in surgical specimens, thereby facilitating easier and more effective dissection. Among these, the GEWF solution (Glacial acetic acid – Ethanol – Water – Formalin) has been highly valued for its safety, effectiveness, simplicity, short processing time, and low cost.

In Vietnam, while CME has been introduced in some centers, lymph node dissection after surgery at many hospitals still mainly relies on manual palpation and inspection, with limited application of supportive solutions such as GEWF. This suggests substantial potential for improving treatment quality and staging accuracy.

Based on this context, we conducted the study: **"Evaluation of laparoscopic complete mesocolic excision in colon cancer"** with two objectives:

1. To investigate clinical and paraclinical characteristics, and to evaluate the results of lymph node harvesting using GEWF solution.

2. To evaluate the outcomes of laparoscopic CME in the treatment of colon cancer.

2. Scientific and Practical Significance of the Thesis

CME plays a crucial role in both the scientific and practical aspects of colon cancer management.

From a scientific perspective:

CME is based on the principle of sharp dissection along the anatomical planes of the mesocolon and high ligation at the origin of tumor-feeding vessels, ensuring en bloc removal of the mesocolon with its associated lymphatic system. This ensures oncologically radical surgery, taking into account the biological behavior of cancer spread, and contributes to standardizing surgical techniques.

Many studies have shown that CME increases the number of harvested lymph nodes, improves staging accuracy, and provides a strong scientific basis for adjuvant treatment decisions.

From a practical perspective:

CME reduces local recurrence and significantly improves survival after surgery, establishing a new surgical standard that can be widely applied in surgical centers.

This study further clarifies the role of lymph node dissection in CME and demonstrates the effectiveness of GEWF in highlighting lymph nodes, thereby increasing lymph node yield and improving

staging accuracy. This provides theoretical grounds for standardizing specimen processing.

Practically, the use of GEWF enhances the detection rate of 12 or more lymph nodes, overcomes the limitations of manual methods, and can be widely implemented due to its safety and low cost. This enhances diagnostic accuracy, informs adjuvant therapy decisions, and improves prognosis for patients.

CHAPTER 1. LITERATURE REVIEW

1.1. Anatomy of the colon

The colon is about 150 cm long, surrounding the small intestine in a U-shaped frame. It consists of the cecum, appendix, ascending, transverse, descending, and sigmoid colon. Unlike the small intestine, the colon is larger in diameter, less mobile, and characterized by taeniae coli, haustra, semilunar folds, and epiploic appendages. Its diameter ranges from 2.5 cm at the sigmoid to 7.5 cm at the cecum.

The colon is supplied by branches of the superior and inferior mesenteric arteries, which form extensive anastomotic arcades.

Its wall consists of five layers, closely related to a rich lymphatic system, which plays a crucial role in cancer pathology.

1.2. Pathology of colon cancer

1.2.1. Gross, microscopic features, and classification

Colorectal cancer presents with various gross patterns: exophytic masses that grow into the lumen, ulceroinfiltrative types that extend into the bowel wall, diffuse infiltrative types that are difficult to detect, and annular constrictive types that cause obstruction. These patterns may coexist. Right-sided tumors are often exophytic, while transverse colon tumors are frequently ulcerative or annular.

Histologically, over 90% are adenocarcinomas with varying degrees of differentiation; poorly differentiated tumors generally carry a worse prognosis.

The AJCC TNM staging system and WHO classification provide critical information for staging, prognosis, and treatment selection.

1.2.2. Lymph node revealing solutions

Adequate lymph node harvest is essential for accurate staging and treatment planning in colon cancer. However, conventional manual

dissection often misses small nodes (<5 mm) and is operator-dependent.

Various supportive techniques have been studied, including dye injection, indocyanine green (ICG) fluorescence, and chemical fat-clearing solutions. Among these, GEWF (Glacial acetic acid – Ethanol – Water – Formalin), introduced by Koren et al. in 1997, has proven to be a safe and efficient method compared to toxic and time-consuming agents such as xylene and acetone.

GEWF highlights lymph nodes within adipose tissue, shortens processing time (about 6 hours), has low toxicity, is inexpensive, and can be easily implemented in most hospitals. Multiple studies have shown GEWF increases lymph node yield—particularly small nodes—thereby improving staging accuracy and reducing the rate of cases with <12 nodes. Research from Japan, Europe, and recently Vietnam has confirmed that GEWF application after colectomy may even detect additional metastatic nodes, potentially changing disease stage.

Compared to complex fat-clearing methods that require days of processing with acetone or xylene, GEWF offers clear practical advantages due to its safety, rapidity, and feasibility. Since 2021, GEWF has been introduced in several central hospitals in Vietnam, with encouraging initial results.

1.3. Clinical and paraclinical characteristics of colon cancer

1.3.1. Clinical symptoms

Colon cancer symptoms often appear early but are nonspecific.

Abdominal pain is common: in right-sided colon cancer, the pain is usually dull, later progressing to sub-obstruction; in left-sided colon cancer, pain is often colicky due to luminal narrowing.

Digestive disturbances include constipation, diarrhea, or alternating episodes, accompanied by bloating, excessive gas, and stools containing mucus or blood. Stool blood appears dark red in right-sided colon cancer and bright red in left-sided colon cancer, which can be mistaken for inflammatory bowel disease, such as colitis.

General symptoms include fatigue, anorexia, weight loss, and anemia.

Physical examination of the abdomen often reveals findings only at advanced stages, such as palpable mass, liver metastases, ascites, or intestinal obstruction.

1.3.2. Paraclinical investigations

Colonoscopy is the most common diagnostic tool, enabling the detection, assessment of tumor location and size, and biopsy for histopathological examination. However, early-stage lesions may be missed if bowel preparation is inadequate.

Imaging studies such as ultrasound, CT scan, MRI, and PET/CT play essential roles in evaluating tumor invasion, lymph node involvement, distant metastases, and complications. Among these, CT and MRI are beneficial, while PET/CT provides high sensitivity but at a higher cost.

Blood tests, especially those for carcinoembryonic antigen (CEA), are helpful for prognosis, treatment monitoring, and detecting recurrence.

1.4. Treatment of colon cancer

Current treatment of colon cancer includes a combination of local treatment, radical surgery, and systemic therapy.

1.4.1. Early colon cancer treatment

Ở giai đoạn sớm, khi bệnh được phát hiện nhờ các chương trình tầm soát, nội soi cắt polyp nguyên khối (en-bloc) là lựa chọn hiệu quả. Các kỹ thuật cắt bỏ niêm mạc (EMR) và bóc tách dưới niêm mạc (ESD) cho phép đánh giá chính xác mức độ xâm lấn và nguy cơ di căn hạch, tuy nhiên chỉ phù hợp khi khối u nhỏ, ít xâm lấn. Với polyp ác tính hoặc ung thư pT1, chỉ định điều trị phụ thuộc đặc điểm mô học và yếu tố nguy cơ, có thể chỉ cần theo dõi sau cắt nội soi hoặc phải phẫu thuật cắt đoạn đại tràng kèm nạo hạch.

1.4.2. Treatment of locally advanced colon cancer

At this stage, surgery remains the primary treatment option. International studies have shown that survival strongly depends on the ability to achieve radical resection.

Colon cancer surgery has become increasingly standardized with the adoption of complete mesocolic excision (CME), based on embryological planes and lymphadenectomy. However, the extent of lymphadenectomy (D2 vs. D3) remains controversial due to potential complications.

Laparoscopic surgery has become the standard in many countries because of its clear short-term benefits.

1.4.3. Palliative or temporary surgery

In complicated cases, such as obstruction or perforation, temporary procedures may be performed, including the creation of a diverting stoma or the placement of an endoscopic stent.

In metastatic disease, local surgery combined with multimodality therapy is increasingly applied, especially for liver, lung, and peritoneal metastases, thanks to advances in resection and ablation techniques.

1.4.4. Systemic therapy

Systemic therapy mainly consists of chemotherapy as an adjuvant treatment.

According to NCCN guidelines, chemotherapy is recommended for high-risk stage II and all stage III patients. Standard regimens include 5-FU/leucovorin, FOLFOX, or CAPEOX.

The rational combination of treatment modalities has significantly improved prognosis and survival in colon cancer.

1.4.5. Complete Mesocolic Excision (CME)

Surgery remains the most important curative treatment for colon cancer.

For decades, colectomy was performed by resecting a segment of colon with adequate margins and regional lymphadenectomy. However, significant variations in recurrence and survival rates across centers raised the question of whether surgical technique directly influences oncologic outcomes.

Based on this, the concept of complete mesocolic excision (CME) was introduced by Hohenberger et al. in 2009, inspired by the success of total mesorectal excision (TME) for rectal cancer described by Heald. CME quickly gained wide attention and is now considered a new standard in colon cancer surgery.

1.4.5.1. Embryological basis and principles of CME

CME is based on three key principles:

Dissection along embryological planes: The colon and mesocolon are enveloped by a thin fascial layer, clearly separated from retroperitoneal structures. Dissection along Toldt’s fascia ensures intact removal of the mesocolon, minimizes injury to vessels and nerves, and reduces bleeding and complications.

Central Vascular Ligation (CVL): High ligation of the main feeding vessels at their origin (superior or inferior mesenteric arteries

or their main branches) enables a radical D3 lymphadenectomy, thereby increasing lymph node yield and staging accuracy.

Adequate specimen length: A wide resection of the colon and mesocolon ensures the complete removal of the lymphatic drainage system, thereby reducing local recurrence.

Thus, CME is not simply "removing more tissue," but performing precise dissection, adequate margins, and central ligation to achieve optimal oncologic outcomes.

1.4.5.2. Surgical technique of CME

CME can be performed via open, laparoscopic, or robotic surgery. The main steps include:

Dissection along Toldt's fascia, separating colon and mesocolon from retroperitoneal organs (pancreas, kidney, ureter) without breaching the mesocolic fascia.

Central vascular ligation: For right-sided cancer, ligation at the origin of the ileocolic and right colic arteries; for left-sided cancer, ligation at the root of the inferior mesenteric artery.

Colon resection of appropriate length, ensuring removal of the entire related lymphatic basin. Specimens must be removed intact without mesocolic tears to avoid tumor spread.

Some modifications, such as modified CME (m-CME) or greater omentum-preserving CME, have been proposed to reduce complications while maintaining core oncologic principles.

1.4.5.3. Comparison of CME and conventional colectomy

Compared with standard colectomy, CME offers clear differences:

Lymph node yield: on average, 10–15 more nodes, with many studies reporting more than 30 nodes compared to 15–20 in conventional surgery.

Specimen length and mesocolic area: larger, covering the entire lymphatic drainage region.

Central node metastasis detection: higher, reducing the risk of missed disease.

Oncologic outcomes: CME significantly reduces local recurrence and improves disease-free and overall survival, especially in patients with stage II–III disease. Meta-analyses show that CME minimizes the risk of local recurrence by 30–40% compared to conventional surgery.

1.4.5.4. Comparison of CME and D3 lymphadenectomy (Japanese concept)

In Japan, D3 dissection has been widely practiced, also based on high vascular ligation. Differences include:

CME emphasizes en bloc dissection along embryological planes, whereas D3 focuses more on the removal of the central node.

CME specimens are usually longer, with a larger mesocolic area and higher lymph node yield compared to D3.

Some direct comparative studies suggest CME + CVL offers superior staging and prognostic accuracy.

Overall, CME is seen as an "expanded and standardized" version of D3 based on embryological principles.

1.4.5.5. Safety and complications

Initial concerns suggested CME might increase the risks of major vessel, nerve, or ureteral injuries due to deep dissection. However, multicenter studies have shown:

CME does not increase the rates of severe complications, such as bleeding, anastomotic leak, or organ injury.

Perioperative mortality is comparable to conventional colectomy (<3%).

Hospital stay and recovery times are similar, especially with laparoscopic or robotic approaches.

The prerequisite is that surgeons must undergo specialized training, with thorough anatomical knowledge and precise dissection skills.

1.4.5.6. Scientific and practical significance

Scientific significance: CME demonstrates that surgical technique itself is crucially affected by colon cancer outcomes, not only disease stage or adjuvant therapy. CME also standardizes specimen quality, improving consistency in pTNM staging and enabling reliable comparisons between centers.

Practical significance: CME increases lymph node yield, enhances staging accuracy, guides adjuvant therapy, reduces local recurrence, and improves long-term survival. It can be applied via open, laparoscopic, or robotic surgery, aligning with modern surgical trends. CME is becoming the standard in many major centers worldwide and is recommended for stage II–III colon cancer.

1.4.5.7. Challenges and perspectives

Despite proven benefits, CME faces challenges such as the need for highly experienced surgeons, a long learning curve, standardization of training and quality control, and ongoing evaluation of technical variations (e.g., m-CME, omentum-preserving CME) through randomized trials.

In the future, combining CME with minimally invasive surgery, robotic surgery, and multimodal therapies is expected to optimize outcomes for colon cancer patients.

1.5. Studies on CME in Vietnam and Worldwide

1.5.1. Worldwide

CME was systematically described in 2009 and quickly gained international attention. It is considered a significant advance on colon cancer treatment, based on dissection along avascular embryological planes, en bloc mesocolic removal, central vascular ligation, and preservation of specimen integrity.

International studies have shown that CME provides larger specimens with wider mesocolic areas, higher lymph node yield, improved staging accuracy, and better prognosis. In Europe, numerous studies have confirmed that CME significantly reduces local recurrence and improves long-term survival compared to conventional colectomy. Large meta-analyses also confirmed CME improves specimen quality without increasing postoperative morbidity or mortality.

In Asia, results are also favorable. When CME is combined with high-level lymphadenectomy, the 5-year survival rate improves significantly. However, not all studies agree on long-term benefits—some report unclear survival differences. Moreover, CME requires advanced surgical skills, central vascular ligation, longer operative times, and may pose risks if performed by inexperienced surgeons.

Nonetheless, the majority of evidence supports CME as an oncologically superior method, increasingly recommended as routine practice in colon cancer surgery.

1.5.2. In Vietnam

In Vietnam, laparoscopic colorectal cancer surgery was introduced in the early 21st century in major centers such as Hanoi, Hue, and Ho Chi Minh City. From these early successes, the technique has become routine in many hospitals.

CME was adopted later and has only been performed in recent years at some central hospitals. Initial reports show CME is feasible under Vietnamese surgical conditions. The technique does not increase postoperative complications compared to conventional colectomy, while improving dissection quality and achieving lymph node yields that exceed international recommendations.

Although most Vietnamese studies are small case series without control groups and focus mainly on short-term outcomes, early results report acceptable complication rates, high average lymph node counts, and adequate pathological specimens. Some follow-up studies suggest CME improves local control and survival, confirming its feasibility and clinical value in Vietnam.

Overall, despite the need for larger and more comprehensive research, CME has demonstrated safety and effectiveness in the Vietnamese context, offering promising prospects for improving colon cancer treatment nationwide.

Chapter 2. SUBJECTS AND METHODS

2.1. Study subjects

Patients diagnosed with colon cancer who underwent laparoscopic colectomy with complete mesocolic excision (CME) at Hue University of Medicine and Pharmacy Hospital and Hue Central Hospital from May 2021 to October 2024.

2.1.1. Inclusion criteria

Patients diagnosed with colorectal carcinoma at stages T1–T4a (cTNM), without bulky lymph nodes according to the AJCC 8th edition (based on endoscopy, contrast-enhanced chest and abdominal CT scan, and histopathology), and who had not received any prior chemotherapy.

Patients with no contraindications to laparoscopic surgery.

Patients who underwent laparoscopic colectomy with complete mesocolic excision (CME), and in whom the GEWF solution was applied for lymph node harvesting from the surgical specimens.

Patients who agreed to participate in the study.

2.1.2. Exclusion criteria

Colon cancer requiring emergency surgery due to perforation or obstruction.

Colorectal carcinoma with a depth of invasion T4b or with bulky lymph nodes detected intraoperatively.

Colon cancer is associated with familial adenomatous polyposis, Lynch syndrome, polyposis, or Peutz–Jeghers syndrome.

Synchronous primary colon cancers at multiple sites.

Pregnant or breastfeeding women.

2.2. Research methods

2.2.1. Study design

This was a prospective, descriptive, uncontrolled clinical interventional study. The design allowed longitudinal follow-up of patients, recording surgical outcomes as well as evaluating the effectiveness of the GEWF solution in lymph node retrieval.

2.2.2. Sample size, sampling method, and study sites

Sample size was calculated using the formula for a proportion study, based on the primary objective of evaluating complications and mortality related to CME surgery. With $\alpha = 0.05$, $d = 0.05$, and a reference mortality rate of 5% from international studies, the minimum required number of patients was 73. The actual study included 77 patients, ensuring representativeness.

2.2.3. Study variables

2.2.3.1. General patient characteristics

Age (<60, ≥ 60), gender, ASA classification (I–VI), weight, height, BMI according to Asian standards, and preoperative comorbidities (cardiovascular, hepatic, renal, respiratory, hypertension, etc.).

***2.2.3.2. Clinical, paraclinical features, and lymph node** distribution after GEWF*

Clinical: reason for admission, symptom duration, history of abdominal surgery, functional symptoms (abdominal pain, digestive disorders, hematochezia, etc.), physical findings (palpable mass, obstruction). Nutritional status was assessed using NRS-2002, and bowel preparation methods were recorded.

Paraclinical: blood tests (hemoglobin, anemia status, CEA), ultrasound, and CT scan to determine tumor location, morphology, and metastasis. Colonoscopy for biopsy and lesion confirmation.

Histopathology and lymph nodes: specimen length, tumor size and gross morphology, mesocolic plane quality according to CLASICC, pathological staging per AJCC 8th (pTNM), tumor differentiation. Lymph nodes retrieved after GEWF processing were categorized

according to the Japanese lymph node stations, depending on the tumor location, with assessment of metastasis.

2.2.3.3. Surgical outcomes

Intraoperative: tumor site, tumor size, invasion, surgical approach (right, left, sigmoid colectomy, etc.), vessel ligation level, intraoperative complications (vascular, nerve, or organ injury), operative time, blood loss (López-Picado formula), abdominal drainage, anesthesia, and analgesia methods.

Postoperative: pain assessment (VAS/Wong–Baker), time to first flatus, removal of drain/urinary catheter, and complications according to the Clavien–Dindo classification (grades I–V). Recorded complications included bleeding, infection, anastomotic leakage, abscess, urinary retention, ileus, and mortality. Management methods (conservative, interventional, and surgical) were noted. Other outcomes included hospital stay, follow-up, adjuvant chemotherapy, recurrence, overall survival (OS), and disease-free survival (DFS). Kaplan–Meier analysis was used to evaluate prognostic factors.

2.2.4. Study procedures

2.2.4.1. Clinical and paraclinical evaluation

All patients underwent thorough clinical examination, blood tests, imaging, and colonoscopy to confirm the diagnosis.

2.2.4.2. Enhanced Recovery After Surgery (ERAS) protocol

Pre-admission: counseling, optimization of cardiovascular status, nutrition, and anemia control.

Preoperative: light diet, no routine mechanical bowel preparation unless indicated, tumor tattooing with India ink during colonoscopy if necessary.

Intraoperative: laparoscopic surgery prioritized, minimal drain placement (only when indicated).

Postoperative: early removal of tubes, early oral intake, and early mobilization to reduce complications and enhance recovery.

2.2.4.3. Laparoscopic colectomy with CME

The type of resection depended on tumor location. Intraoperative parameters for CME quality included central vascular ligation and sharp dissection along embryological planes.

2.2.4.4. GEWF processing and lymph node distribution

Specimens were immersed in GEWF solution for 6–12 hours, then rinsed and dissected. Fatty tissue turned yellow while lymph nodes remained whitish, facilitating identification. Nodes were classified according to Japanese staging groups, measured, and placed in cassettes. Suspicious tumor invasion areas were additionally sampled for histopathology.

2.2.4.5. Follow-up

Postoperative: complications and recovery parameters recorded.

Adjuvant chemotherapy: indicated for high-risk stage II and stage III, started 3–12 weeks postoperatively.

Follow-up schedule: at 1 month, 3–6 months, 1 year, 2 years, 3 years, and annually thereafter. Evaluations included clinical examination, blood tests, CEA, imaging, and colonoscopy to detect recurrence or metastasis.

2.3. Data analysis

Data were analyzed using SPSS version 22 (IBM SPSS Statistics for Windows, Version 22.0).

Chapter 3. RESULTS

3.1. General characteristics of patients

The study included 77 patients, comprising 53.2% males and 46.8% females, with a mean age of 59.5 ± 14.5 years (range, 28–88 years). The age groups <60 and ≥60 are approximately the same. Most patients had an ASA score of 1 (68.8%) and a mean BMI of 21.1 ± 3.1 kg/m², with a predominance within the normal range (59.7%). Analysis revealed that patients aged 60 years or older had a higher ASA score, with a statistically significant difference. Comorbidities were present in 57.1% of patients, most commonly cardiovascular disease, hypertension, and genitourinary conditions, with significantly higher rates in the ≥60 years age group.

3.2. Clinical and Paraclinical Features

The most common reason for hospital admission was abdominal pain (70.1%), followed by bowel habit disturbances (36.4%). Other symptoms included weight loss, anemia, mucus in stool, or incidental detection at lower rates. The duration from symptom onset to hospital admission was mainly between 15–30 days (35.1%), with some cases

presenting later than 1 month, including a few with symptoms persisting for more than 3 months.

A history of abdominal surgery was noted in several patients, including McBurney's incision, Pfannenstiel incision, or laparoscopic abdominal surgery, each accounting for 3.9%.

Functional symptoms recorded included abdominal pain in 83.1%, bloody stool in 45.5%, bowel habit changes such as constipation or diarrhea in 31.2%, weight loss in 29.9%, anemia in 23.4%, mucus in stool in 16.9%, and anorexia in 11.7%.

On physical examination, 27.3% of patients had a palpable abdominal mass, 3 cases were admitted with intestinal obstruction, and 1 case presented with peripheral lymphadenopathy.

Preoperative bowel preparation was mainly performed with Fleet enema (87.0%), while 13.0% used Fortrans. Nutritional risk assessment using NRS-2002 showed 67.5% had no risk of malnutrition, while 32.5% were at risk.

Laboratory findings revealed a mean preoperative hemoglobin level of 11.8 ± 2.3 g/dl. By tumor location, the highest mean Hb was found in transverse colon tumors (13.1 g/dl), while cecal and ascending colon tumors had the lowest (11.1 g/dl).

For tumor markers, preoperatively, 59.2% of patients had CEA <5 ng/ml, which increased to 84.1% postoperatively, with 93% showing a decrease in CEA levels after surgery.

Imaging studies included chest–abdominal CT scans to exclude distant metastases. Abdominal ultrasound detected tumor location in 68.9% of cases, most commonly in the sigmoid colon (23.0%), while 31.1% were undetectable. The most frequent sonographic findings were bowel wall thickening (66.2%) and regional lymphadenopathy (16.2%).

On CT scan, the most frequent tumor location was the sigmoid colon (29.9%), followed by hepatic flexure (16.9%), and the least common at the splenic flexure (3.9%). The predominant CT findings were colonic wall thickening (89.6%) and peritoneal lymphadenopathy (54.6%).

Colonoscopy detected sigmoid colon tumors in 33.8%, followed by ascending colon tumors in 20.8%. The gross morphology on colonoscopy was mainly exophytic (84.4%); 10.4% were associated with polyps, all of which were histologically benign.

The diagnostic accuracy in tumor localization was highest for CT scans (81.8%), followed by colonoscopies (77.9%), and lowest for ultrasound (56.8%).

Histopathological results from preoperative colonoscopic biopsies revealed adenocarcinoma in 90.9% of cases; the remainder showed dysplasia or chronic inflammation. For non-adenocarcinoma cases but with obvious exophytic appearance on colonoscopy and CT scan, surgery was still indicated, and all of these cases were confirmed postoperatively as adenocarcinoma, meeting the inclusion criteria.

Postoperatively, the mean length of resected colon was 32.4 cm. The mean proximal margin was 14.7 cm, distal margin 13.6 cm, vascular ligation margin 11.2 cm, and mesenteric width 9.0 cm. Macroscopic tumor morphology was predominantly exophytic (93.5%). Complete mesocolic excision was achieved in 87% of cases.

In terms of tumor invasion, pT2 accounted for 45.5%, pT3 for 39.0%, with fewer cases of pT1 and pT4. Lymph node status showed pN0 in 61.0%, pN1 in 29.9%, and pN2 in 9.1%.

According to the AJCC 8th edition staging, stages I, II, and III accounted for 42.9%, 19.5%, and 37.7%, respectively.

Histologically, well-differentiated adenocarcinoma was the most common (59.7%).

The mean number of lymph nodes retrieved intraoperatively was 64.1, and 60.0 on histopathology. Lymph node yield varied by tumor location, decreasing from the cecum to the sigmoid. Factors associated with higher lymph node yield included age <60 years, tumor size ≥5 cm, specimen length >25 cm, and right-sided colon tumors.

A total of 4,930 lymph nodes were collected, of which 66.8% were pericolic (station 1), 20.9% intermediate (station 2), and 12.3% central (station 3). Metastatic lymph nodes totaled 117 (2.4%), mainly in pericolic nodes. Lymph node metastasis was significantly associated with depth of tumor invasion (pT), particularly in pT3–pT4 tumors.

3.3. Surgical Outcomes

3.3.1. Intraoperative Features

The mean tumor size was 4.0 ± 1.8 cm, and the mean incision length was 6.5 ± 1.5 cm. Mean operative time was 153.9 ± 40.3 minutes. The mean blood loss was 252 ± 410 ml (median, 236 ml; range, –647 to 1975 ml), with no patient requiring a blood transfusion.

Tumor location: cecum 14.3%, ascending colon 9.1%, hepatic flexure 20.8%, transverse colon 7.8%, splenic flexure 7.8%, descending colon 7.8%, and sigmoid colon 32.4%. Tumors <5 cm accounted for 66.2%. Mobile tumors accounted for 84.4%, while immobile tumors accounted for 15.6%. Depth of invasion: Tx 63.6%, T4 36.4%.

Types of laparoscopic surgery included: right hemicolectomy 33.7%, extended right hemicolectomy 15.6%, transverse colectomy 2.6%, left hemicolectomy 16.9%, and sigmoidectomy 31.2%. Central vascular ligation was performed in 97.4%, high ligation in 2.6%.

Intraoperative complications occurred in 6.5%: vascular injury 5.2%, pancreatic injury 1.3%. No intraoperative complications in 93.5%. Peritoneal drains were placed in 27.3%.

Longer operative times were statistically significant in patients with a BMI ≥23, tumors ≥5 cm, and varied according to the surgical procedure. There was no significant association between surgical method and intraoperative complications.

3.3.2. Postoperative Features

Postoperative pain assessed by VAS decreased from day 1 (4.4 ± 1.2) to day 3 (2.8 ± 1.1). Intravenous paracetamol analgesia had a median duration of 4 days, and oral analgesia averaged 2.9 days.

Mean time to first flatus was 2.1 ± 0.9 days. Median time to oral feeding was 1 day. Median time to urinary catheter removal was 1 day.

Postoperative complications occurred in 15.6%: anastomotic leakage 1.3%, residual abscess 1.3%, wound infection 7.8%, subcutaneous emphysema 3.9%, and early small bowel obstruction 1.3%.

According to the Clavien–Dindo classification, the results are as follows: grade I, 13.0%; grade II, 2.6%. No cases of peritonitis, intra-abdominal hemorrhage, urinary tract infection, pneumonia, or postoperative mortality were recorded.

Mean hospital stay was 7.3 ± 2.2 days, with a maximum of 17 days.

Adjuvant chemotherapy was not indicated in 31.2%, administered in 51.9%, and indicated but not received in 16.9%.

3.3.3. Follow-up Outcomes

The follow-up duration ranged from 7 to 48 months, with 69 patients followed for 12 months or longer.

Overall survival rates were 100% at 1 year, 91.5% at 2 years, and 95.5% at 3 years.

Disease-free survival rates were 98.6% at 6 months, 95% at 1 year, 90% at 2 years, and 94.7% at 3 years.

There were 8 cases of recurrence or metastasis (10.4%), with a mean time of 12.4 months; and 5 deaths (6.5%), with a mean time of 20.8 months.

Mean overall survival was 45.5 months, and mean disease-free survival was 43.1 months. At 2 years, the overall survival rate was 92.7%, and at 3 years, it was 90.4%.

No statistically significant differences in survival were found regarding age, ASA score, tumor size, postoperative complications, or tumor differentiation.

A statistically significant difference in survival was observed with adjuvant chemotherapy: patients who received chemotherapy or had no indication achieved 100% survival at 3 years, while those indicated but untreated achieved only 59.2%.

By stage, 3-year survival was 100% in early-stage disease and 82.3% in advanced-stage disease.

Chapter 4. DISCUSSION

4.1.1. Age

The mean age of patients was 59.5 ± 14.5 years (range 28–88). This result is similar to many domestic studies but lower than those in Western countries, where the mean age is over 70.

4.1.2. Gender

Males accounted for 53.2% and females 46.8%, showing a nearly balanced ratio. Some domestic studies reported differences, with either female predominance or male predominance. International data also show similar ratios, with males generally accounting for 52–56%.

4.1.4. ASA classification and comorbidities

Most patients were ASA 1 (68.8%), followed by ASA 2 (24.7%) and ASA 3 (6.5%). This differs from some international studies where ASA 2 predominates. ASA classification was age-related: patients <60 were mainly ASA 1, while those ≥60 had higher rates of ASA 2–3, which is also associated with increased risk of postoperative complications.

A total of 57.1% of patients had comorbidities, most commonly cardiovascular diseases (28.6%), hypertension (16.9%), and genitourinary diseases (14.3%). Most comorbidities were mild and controlled preoperatively. International studies also show that comorbidities, particularly cardiovascular disease and hyperglycemia, are associated with ASA classification and postoperative complications.

4.1.5. Body mass index (BMI)

The mean BMI was 21.1 ± 3.1 kg/m²; most individuals were within the normal range (59.7%), with 22.1% classified as overweight and 18.2% as underweight. This is consistent with other Asian populations but lower than in Europe (25–26). Some studies suggest that BMI affects vascular distances and the mesenteric area, but does not alter colon length in CME surgery.

4.2. Clinical and paraclinical characteristics

4.2.1. Clinical characteristics

Abdominal pain, bowel habit disturbances, and chronic anemia were the main symptoms in our study population. These are typical clinical features of colorectal cancer, particularly when patients present at advanced stages. The low proportion of early-stage detection reflects the lack of widespread colorectal cancer screening programs in Vietnam.

In countries with established screening programs using colonoscopy and fecal occult blood testing, early detection rates are higher, thereby reducing the number of patients admitted with advanced symptoms.

Bowel preparation before surgery was not routinely performed in this study, consistent with modern treatment trends (ERAS), aiming to reduce electrolyte disorders and infection risk. However, in cases of small tumors or tumors difficult to localize, bowel preparation remains useful for tumor marking.

Another noteworthy point is that nearly one-third of patients were at nutritional risk, mainly elderly individuals. This suggests the need for preoperative nutritional assessment and support, as malnutrition has been shown in many studies to increase postoperative complications and length of hospital stay.

4.2.2. Paraclinical characteristics

Anemia was detected in about half of patients, more commonly in females and in those with right-sided colon cancer. This finding is expected because right-sided tumors often cause occult bleeding and present with iron-deficiency anemia, rather than visible hematochezia as in left-sided tumors. Compared with international studies, the anemia rate in our study was higher, likely related to patients presenting late.

CEA levels were elevated in nearly 40% of cases, a rate similar to that reported in the international literature (30–50%). Postoperatively, CEA levels declined markedly, confirming the role of this biomarker in evaluating treatment response and monitoring recurrence. However, its limited sensitivity means it must be combined with clinical, imaging, and histopathological evaluation.

Imaging findings showed CT scans had higher sensitivity than ultrasound in detecting tumors and metastatic lymph nodes, and also helped stage the disease. This aligns with current recommendations recognizing CT as an essential preoperative diagnostic tool. Nevertheless, colonoscopy remains the gold standard for definitive diagnosis and biopsy sampling.

Histopathological results showed adenocarcinoma as the predominant type, consistent with the epidemiology of colorectal cancer. The average number of harvested lymph nodes was high, due to the CME technique and the application of the GEWF solution for lymph node retrieval, which far exceeded the minimum of 12 nodes required for accurate staging. This is significant because a higher lymph node yield not only reflects surgical quality but also improves prognostic reliability.

4.3. Surgical outcomes

4.3.1. Intraoperative characteristics

4.3.1.1. Tumor location

Tumor location is crucial for determining the surgical approach and prognosis. Left-sided tumors tend to present with more obvious symptoms and are easier to detect, while right-sided tumors are often silent and diagnosed later. In our study, the distribution of tumor locations between left and right colon was relatively balanced, consistent with the idea that epidemiological and risk factors influence tumor distribution. From a surgical standpoint, tumor location dictates

the type of resection (right, left, sigmoid, or transverse colectomy) and is associated with anatomical complexity in mesocolic dissection and central vascular ligation.

4.3.1.2. Tumor size

Tumor size reflects disease stage and influences surgical difficulty. Smaller tumors suggest early-stage disease, are more mobile, and facilitate radical resection. Larger tumors carry higher risks of invasion, adhesions, and complications during dissection. Prognostically, tumors ≥5 cm are more likely to have lymph node metastasis and poorer survival. Practically, tumor size also affects the required incision length for specimen extraction, with implications for preventing tumor rupture.

4.3.1.3. Tumor mobility

Mobility reflects the tumor's relationship with surrounding tissues. Mobile tumors are easier to dissect and usually at earlier stages, whereas immobile tumors may indicate invasion into adjacent organs. However, mobility assessment can also be influenced by peritumoral inflammation or a large tumor size, and should be interpreted with caution. Intraoperatively, mobility helps guide surgical strategy, with immobile tumors requiring preparation for extended resections.

4.3.1.4. Intraoperative TNM assessment

While intraoperative staging is only approximate, it remains useful for making immediate decisions, particularly in suspected T4 cases. Although definitive staging requires pathology, direct observation assists the surgeon in selecting resection margins and planning combined organ resections, if necessary, thereby improving the radicality of the procedure.

4.3.1.5. Laparoscopic surgical approach

Laparoscopic colectomy has become the standard of care due to its advantages in pain reduction, faster recovery, and improved cosmetic outcomes. The high proportion of laparoscopic procedures in this study reflects this trend. However, laparoscopy requires advanced technical skills, especially when applying CME, as it involves precise dissection of the mesocolic plane and central vascular ligation. The type of colectomy depended on the tumor location, with sigmoid and right colectomies being the most common, consistent with the tumor distribution.

4.3.1.6. Vascular ligation and CME technique

In CME, central vascular ligation (CVL) is essential to ensure complete lymphatic clearance. The Japanese D1–D3 classification and the European CVL concept both emphasize the high level of lymphadenectomy. CME is not only about bowel resection length but also about maintaining intact mesocolic fascia and removing the entire lymphovascular package. This distinguishes CME from conventional surgery and improves prognosis. However, CME requires thorough knowledge of anatomical variations and surgical expertise to minimize intraoperative complications.

4.3.1.7. Intraoperative complications

The main complications were bleeding and injury to adjacent organs. Pancreatic injury during left mesocolon dissection and mesenteric vascular damage are often mentioned risks. Although most can be managed intraoperatively, they highlight the technical complexity of CME. Careful identification of surgical planes and meticulous laparoscopic techniques help reduce risks.

4.3.1.8. Peritoneal drainage

Postoperative drains were selectively placed, mainly for early detection of leakage or bleeding. Current practice discourages routine drainage, as it increases the risks of retrograde infection or bowel obstruction. Drain placement should be individualized based on the surgical difficulty and risk of complications.

4.3.1.9. Incision length

In laparoscopic colectomy, the incision length is primarily used for specimen retrieval and extracorporeal anastomosis. Incisions are generally small for cosmetic purposes but must be large enough to prevent tumor rupture. This illustrates the aesthetic advantage of laparoscopy over open surgery.

4.3.1.10. Blood loss

Estimating blood loss is always challenging. In practice, estimates are used mainly to guide transfusion decisions rather than as absolute values. CME, with central vascular dissection, carries higher bleeding risks, but with surgical expertise, blood loss can be kept within acceptable limits.

4.3.1.11. Operative time

Operating time depends on tumor location, BMI, tumor size, and CME complexity. Laparoscopy generally takes longer than open

surgery, but its postoperative benefits outweigh this. CME requires longer dissection, which is reasonable, but does not significantly increase complications when protocols are standardized.

4.3.2. Postoperative characteristics

4.3.2.1. Postoperative pain management

Postoperative pain was minimized by laparoscopy and multimodal analgesia as part of ERAS. This facilitated early mobilization, improved respiratory, circulatory, and digestive function, and shortened recovery time. Reduced opioid use also helped prevent postoperative ileus.

4.3.2.2. Time to flatus and oral feeding

Early feeding has been proven safe and promotes gastrointestinal recovery. Early removal of the nasogastric tube and initiation of oral intake within 24 hours provided numerous benefits, consistent with ERAS guidelines. Time to first flatus was generally short, reflecting effective recovery protocols. Additional measures, such as chewing gum, may further stimulate bowel motility.

4.3.2.3. Postoperative complications

The most common complication was surgical site infection, with a modest rate. Severe complications such as anastomotic leakage, residual abscesses, or early bowel obstruction from drains were rare and mostly managed conservatively. This confirms the safety of CME when performed by experienced teams. The Clavien–Dindo classification helped standardize complication reporting.

4.3.3. Survival outcomes

Survival after surgery is the most important criterion for evaluating colorectal cancer treatment. International studies have shown that CME, by removing the intact mesocolon and central lymphatic system, significantly improves both overall survival and disease-free survival. Reported 5-year survival rates after CME range from 70–80%, higher than with conventional surgery. This is especially relevant for stage II–III patients, who are at higher risk of nodal metastasis and local recurrence.

In our study, short-term survival outcomes were favorable and consistent with international trends. Adherence to CME principles and multimodal treatment, including adjuvant chemotherapy, contributed to these results. It is essential to note that survival is also significantly influenced by the TNM stage. Thus, CME is not merely a surgical

technique, but a cornerstone in comprehensive colorectal cancer management, optimizing survival.

CONCLUSION

Through the study of 77 cases of colorectal adenocarcinoma undergoing laparoscopic colectomy with complete mesocolic excision (CME) at Hue University of Medicine and Pharmacy Hospital and Hue Central Hospital from May 2021 to October 2024, we drew the following conclusions:

1. Clinical, paraclinical features, and lymph node retrieval with GEWF

Abdominal pain was the most common symptom (83.1%), followed by palpable mass in 27.3%. Nutritional assessment showed 67.5% had no risk (NRS-2002). Postoperatively, CEA decreased in 93% of patients. CT scan had the highest accuracy in tumor detection (81.8%). Specimen characteristics: average length 32.4 ± 8.1 cm, average mesocolic width 9.0 ± 1.4 cm. Grossly, exophytic tumors accounted for 93.5%; histology showed 59.7% well-differentiated adenocarcinoma. Stage distribution: stage I (42.9%), stage III (37.7%). In surgery, 87% achieved complete mesocolic plane dissection. The average number of harvested lymph nodes was 60.0 ± 23.6. The total number of lymph nodes at levels 1, 2, and 3 was 3289, 1032, and 609, respectively, with metastases present in 101 (3.1%), 11 (1.1%), and 5 (0.8%) cases. The overall nodal metastasis rate was 2.4%. The number of patients with stage 3 lymph node metastasis was 5/77 (6.5%).

2. Surgical outcomes of laparoscopic colectomy with CME

The most common tumor site was sigmoid colon (32.4%), followed by hepatic flexure (20.8%), cecum (14.3%), and ascending colon (9.1%). Less common sites were the transverse, splenic flexure, and descending colon (each 7.8%).

Technically, 97.4% underwent CME with central vascular ligation, and 72.7% had no peritoneal drainage. Mean tumor size was 4.0 ± 1.8 cm; mean incision length was 6.5 ± 1.5 cm. Mean operative time was 153.9 ± 40.3 minutes. Blood loss by the López–Picado formula was 252 ± 410 ml (median 236 ml, range –647 to 1975 ml). Postoperative pain scores (VAS) decreased progressively: day 1 (4.4 ± 1.2), day 2

(3.6 ± 1.1), day 3 (2.8 ± 1.1). The mean time to first flatus was 2.1 ± 0.9 days (maximum, 5 days). Median time to oral feeding was 1 day (maximum 7 days). Postoperative complications (Clavien–Dindo): grade I (13.0%), grade II (2.6%). Mean postoperative hospital stay was 7.3 ± 2.2 days. Follow-up showed distant metastases in 8 patients (10.4%) and 5 deaths (6.5%). Cumulative 4-year overall survival was 90.4%, while disease-free survival was 86.1%.

RECOMMENDATIONS

Implementation of laparoscopic CME colectomy in colorectal cancer

Laparoscopic CME colectomy has proven safe and effective, with acceptable complication rates, while ensuring oncological radicality. Therefore, CME should be applied in centers equipped with adequate equipment and staffed with trained surgical teams.

Consider using GEWF solution in pathology practice

The application of the GEWF solution significantly increases lymph node yield beyond the minimum 12 nodes recommended for accurate staging. The Ministry of Health guideline currently recommends formalin fixation; however, in many centers, manual node dissection still yields limited results. Using GEWF facilitates lymph node harvest, allows for accurate staging, and informs adjuvant therapy decisions, thereby improving survival and reducing the risk of recurrence or metastasis.

LIST OF RELATED PUBLICATIONS

1. **Nguyen Minh Thao**, Pham Anh Vu, Nguyen Doan Van Phu, Dang Nhu Thanh, Ho Quoc Khanh, Nguyen Tran Bao Song, Dang Cong Thuan (2021). "Application of Glacial acetic acid, Ethanol, Water and Formalin (GEWF) solution in lymph node harvest after laparoscopic gastrectomy and colectomy for cancer." *Journal of Medicine and Pharmacy*, 11(4), pp. 110–114.
2. **Nguyen Minh Thao**, Dao Thi Minh Ha, Giap Bach Kim Tuyen, Pham Anh Vu (2022). "Preliminary results of laparoscopic colectomy with complete mesocolic excision in colorectal cancer treatment." *Journal of Medical Research*, 163(2), pp. 89–99.
3. **Nguyen Minh Thao**, Pham Minh Duc, Nguyen Huu Tri, Phan Dinh Tuan Dung, Dao Thi Minh Ha, Phan Thi Kim Xuan, Pham Anh Vu (2024). "Screening, nutritional status assessment and associated factors in patients undergoing laparoscopic colectomy for colorectal cancer." *Hue Journal of Medicine and Pharmacy*, 14(3), pp. 160–166.
5. **Thao M. Nguyen**, Thuan C. Dang, Song T.B. Nguyen, Cuong N. Pham, Duong D. Le, Duc M. Pham, Tri H. Nguyen, Dung D.T. Phan, Phu D.V. Nguyen, Phuc T. Nguyen, Vung P. Doan, Son D. Nguyen, Vu A. Pham (2024). Laparoscopic complete mesocolic excision in colon cancer: a prospective cohort study. International Journal of Surgery Protocols. http://dx.doi.org/10.1097/SP9.0000000000000026.
6. **Minh Thao Nguyen**, Cong Thuan Dang, Tran Bao Song Nguyen, Nguyen Cuong Pham, Dinh Duong Le, Minh Duc Pham, Huu Tri Nguyen, Dinh Tuan Dung Phan, Doan Van Phu Nguyen, Thanh Phuc Nguyen, Phuoc Vung Doan, Dinh Son Nguyen, Anh Vu Pham (2024). Lymph node harvesting after laparoscopic complete mesocolic excision colectomy in colon cancer with practical application of glacial acid, absolute ethanol, water, and formaldehyde solution: A prospective cohort study. SAGE Open Medicine. Volume 12: 1–10. https://doi.org/10.1177/20503121241233238