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D3 Lymphadenectomy for Right Colon Cancer: Feasibility, Safety, and Early Outcomes from a District General Hospital in London

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Rezumat

Limfadenectomia D3 în tratamentul chirurgical al cancerului de colon drept: fezabilitate, siguranță, și rezultatele clinice precoce

Introducere: Studiile retrospective raportate în literatură sugerează o eventuală tangență dintre limfadenectomia D3 şi înbunătățirea supravețuirii la distanță. Scopul studiului: Acest studiu îşi propune să raporteze rezultatele clinice precoce şi fezabilitatea tratamentului chirurgical al cancerului de colon drept prin hemicolectomie D3 şi compararea acestora cu limfadenectomia standart D2 în centru nostru.
Materiale şi Metode: Analiza retrospectivă a pacienților care au fost tratați pentru cancer de colon drept în cadrul centrului nostru în perioada ianuarie 2019 şi noiembrie 2022.
Rezultate: În acest studiu au fost incluşi 214 de pacienți care au satisfacut criteriile de selecție, 170 fiind supuşi limfadenectomiei D2 şi 44 supuşi limfadenectomiei D3. În analiza statistică a datelor colectate nu s-a depistat diferențe statistice în ceea ce priveşte durata intervenției chirurgicale, pierderea de sânge, nivelurile postoperatorii ale hemoglobinei sau necesitățile de transfuzie. Grupul pacienților cărora li s-a efectuat limfadenectomie D3 a avut o rată mai mică a complicațiilor (25%) comparativ cu grupul D2 (41,2%). La fel grupul D3 a avut, de asemenea, o rată mai mare de afectare ganglionară (45,5% față de 30,6% pentru grupul D2) şi mai mulți ganglioni limfatici excizați (19 [16, 25] vs. 23 [18, 28]). Ratele rezecții R0 nu au o diferență statistică
Concluzie: Studiul nostru demostrează fezabiliatetea limfodisecției D3 în tratamentul chirurgical al cancerului de colon drept oferind posibile beneficii pe termen lung, în special pentru pacienții tineri cu suspiciune de implicare a ganglionilor limfatici de ordin 2 şi 3.

Cuvinte cheie: CME, Limfadenectomie D3, cancer de colon drept

Abstract

Background and Objectives: Observational studies suggest a link between D3 lymphadenectomy and improved disease-free survival in some colon cancer patients. However, high-quality randomized controlled trials are needed to confirm its advantage over D2 lymphadenectomy. Concerns about potential complications with D3 have limited its use outside of Japan. This study examines short-term outcomes following D3 lymphadenectomy for right-sided colon cancer compared to the established D2 procedure.

Materials and Methods: This retrospective cohort single center study analyzed data on patients with right-sided colon cancer who underwent curative surgery within our healthcare trust between January 2019 and November 2022. Only patients treated by surgeons who routinely perform D3 lymphadenectomy were included for a homogenous study population. The decision to perform D3 was at the discretion of the operating surgeon. Data were collected from both paper charts and electronic medical records. Non-parametric statistical tests were used for data analysis.

Results: A total of 214 patients met the criteria, with 170 undergoing D2 lymphadenectomy and 44 undergoing D3 lymphadenectomy. There were no significant differences between the groups in terms of surgery duration, blood loss, postoperative hemoglobin levels, or transfusion needs. Interestingly, the D3 group had a lower complication rate (25%) compared to the D2 group (41.2%). However, the D3 group also had a higher rate of lymph node spread (45.5% vs. 30.6% for D2) and more lymph nodes removed (19 [16, 25] vs. 23 [18, 28]). Importantly, both groups achieved similar complete tumour removal rates.

Conclusions: This study suggests D3 lymphadenectomy for right-sided colon cancer might be safe with potential benefits, especially for younger patients with suspected lymph node involvement. However, the limited sample size necessitates larger, randomized trials to confirm these findings and potentially establish D3 lymphadenectomy as standard care.

Key words: complete mesocolic excison, D3 lymphadenectomy, right-sided colon cancer

Introduction

Colon cancer is the second most common gastrointestinal malignancy worldwide and is associated with a high mortality rate (1). It is estimated that 900,000 people die from colon cancer on average, representing 10% of cancer related deaths (2). Differences in embryologic development, clinical presentation, patient demographics, and tumour biology exist between right and left-sided colon cancer (2-7). Lymph node harvest is a key factor associated with improved survival from colonic malignancy and may be more important in right-sided disease. These factors may explain why the overall survival of patients with right-sided colonic cancer (RCC) remains low (8). The advent of total mesorectal excision (TME) in the treatment of rectal cancer, first proposed by Heald in 1982, has subsequently modified the views on the surgical treatment of colon cancer as well (9). TME has been credited with a decrease in local recurrence rates and consequently with improving survival rates in rectal cancer surgery. This approach is based on dissection along the embryological planes of the endopelvic fascia, which enables the dissection of a complete package of lymph nodes and enhances the oncological quality of surgery,

thereby improving survival rates. Hohenberger adapted the theory of TME to colon cancer, termed complete mesocolic excision (CME), which has demonstrated improved lymph node yield and improved survival in non-randomised trials (10).

As described by Hohenberger CME is a surgical technique characterized by three key components: (1) embryological dissection: precise dissection in the embryological planes to reme the mesentery and its associated lymphatics along natural anatomical planes, preserving the integrity of the mesocolic envelope; (2) central vascular ligation: vascular ligation of vessels supplying the bowel affected by tumour near the superior mesenteric vein to ensure complete lymph node removal; and (3) oncological resection: sufficient bowel resection to achieve clear margins and optimal anastomosis site viability.

For decades, Japanese surgeons have employed CME in the form of D3 lymphadenectomy (LDN). Its adoption in Europe was largely spurred by West et al.'s landmark study (11), which linked quality specimens to improved long-term survival. The influence of specimen-encompassed lymph node count on oncological outcomes has sparked intense interest within the colorectal community regarding the optimal extent of lymph node dissection (12,13).

This debate stems from the lack of consensus on the precise boundaries of a "D2" or "D3" dissection.Despite reports in the literature highlighting the oncological benefits and safety of CME with D3 LDN, a substantial portion of colorectal surgeons remain wary. Their concern stems from potential increased morbidity associated with lymph node dissection in the superior mesenteric vein and artery territory, including pancreatits, erratic bowel function, gastroparesis, and intraoperative bleeding/vascular injury (14,15).

Despite evidence supporting CME with D3 for RCC, United Kingdom(UK) secondary care hospitals exhibit hesitation due to two interconnected issues: terminological ambiguity ("D2," "D3," "CME") in the western literature hindering data comparability and the absence of a standardized CME protocol, leading to inconsistent surgical approaches. This necessitates a multipronged approach: harmonization of terminology with precise definitions and illustrations, followed by the development of evidence based CME guidelines through expert consensus and prospective trials, ultimately fostering improved communication, robust data analysis, and optimized patient care. The adoption of standardization is crucial for dispelling UK skepticism and unlocking the complete potential of CMD + D3 LDN in tratment of RCC.

This study aims to evaluate the short-term outcomes and feasibility of a standardized CME with D3 LDN via the SMV-first (open book) approach for treating node positive RCC patients in a UK secondary care setting (16).

Materials and Methods

Study Design

A retrospective single center cohort audit was undertaken to determine the outcomes of patients who underwent D3 LDN using open, laparoscopic, and robotic approaches and compared with conventional D2 LDN in the treatment of RCC. This audit was approved by the Divisional Governance committee and complied with all local guidelines on information and research governance. This study has been reported in line with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria (17).

Patient selection

This study included patients who met the following inclusion criteria: age 18 years or older, provided written informed consent, had biopsy proven malignant colonic lesions or a suspicious lesion located proximally to the splenic flexure, had a local multidisciplinary team recommended right or extended right hemicolectomy intended for curative treatment, underwent an elective or semielective surgery, were operated on by a surgeon experienced in D3 LDN using open, laparoscopic, or robotic approaches, were deemed fit for

surgery, and had undergone minimal staging investigations including a CT scan of the chest, abdomen, and pelvis with intravenous contrast and a full colonoscopy. Patients were excluded if they received palliative treatment, underwent emergency surgery within the first 24 hours of admission, or required more extensive colonic resection.

Setting

Barking, Havering and Redbridge University Hospitals NHS Trust is a large acute NHS distric general Hospital in England, serving a population of around 750,000 from a wide range of social and ethnic groups across North East London. BHRUT is an established referral colorectal unit with a surgical ELECTIVE HUB being one of the first eight institutions in the country that has been accredited by Getting It Right First Time as part of the national scheme (18). We offer to our patients all possible minimally invasive approaches including laparoscopic, robotic, and transanal for rectal pathologies, HIPEC for peritoneal malignancy, and pelvic exenteration surgery for advanced pelvic malignancies. Our department of colorectal surgery includes six colorectal consultants who collectively perform over 250 colorectal resection procedures annually, on average.

Time period and data collection

In a retrospective analysis, clinical data from patients who underwent RCC surgery between January 2019 and November 2022 were acquired by local colorectal multidisciplinary team coordinators. Following the initial screening and application of inclusion /exclusion criteria, a final list of study participants was established, with subsequent data collection occurring retrospectively from both paper notes and electronic medical records.

Variables and Outcomes

Patient demographics included age, sex, BMI, American Society for Anaesthesiology (ASA) grading , World Health Organisation (WHO) performance status and tumour location. Tumour characteristics and intraoperative parameters identified included surgical procedure, total operative time (operative time from the first skin incision until suturing of the last incision), conversion (open extension of the initially planned incision), and estimated blood loss.The requirement for transfusion was used as a surrogate marker of significant blood loss, as this was inconsistently documented, or marked as negligible. Outcome measures included specimen quality (completeness of resection and lymph node yield) and 30 day postoperative complications according to the Clavien-Dindo (CD) classification (19). Anastomotic leaks were considered in cases with clinical or radiological features of anastomotic dehiscence. Prolonged ileus was defined as the inability to tolerate oral intake due to a cessation of gastrointestinal motility, in the absence of mechanical obstruction, persisting for more than four days. The length of in patient stay (LOS) measured on nights, readmission rates, and 90-day mortality were also recorded. The primary outcomes were complication rates for CD III-IV, LOS, number of harvested lymph nodes, and negative resection margin. Secondary outcomes were operative time, intraoperative estimated bloodloss, and conversion rates of minimally invasive approaches

Surgical Technique

All patients underwent a standard preoperative workup and discussion in the local colorectal cancer multidisciplinary meeting. All patients included in the study underwent surgery with curative intent, and the choice of the extent of lymph node dissection was at the discretion of the operating surgeon. The D3 LDN beeing offered to the patients with clinical node positive disease and T3/4 lesions. All procedures were preceded via urinary catheterisation. During laparoscopic procedures, the patients were placed on the operating table in the light Trendelenburg position with legs apart or in the supine position. In the robotic cases, all the patients

were supine on the operating table. In cases where a robotic platform was used, pneumoperitoneum was achieved via Veress needle insufflation or open access via intended extraction of the specimen site. In laparoscopic cases 4 trocars technique was used. The Conventional D2 LDN employes two main port placement variations (*Fig. 1 A,B*). In contrast, for laparoscopic D3 LDN (*Fig. 2A*), the patients were positioned with their legs apart, and the surgeon stood between them. Robotic D3 procedures (*Fig. 2B*) were performed using the DaVinci XI system (Intuitive Surgical, Inc., Sunnyvale CA, USA).

Both D2 and D3 dissections for RCC employ blunt and sharp dissection along embryologic planes, including careful separation of Toldt's fascia from the retroperitoneum, while preserving the lymph node package near tumour-supplying vessels (10). The key distinction lies in dissection of the adipose tissue anterior to the superior mesenteric vein (SMV) along its course before pancreatic neck entry. Regardless of D2 or D3, complete mesocolon mobilization with vascular and lymphatic drainage is crucial for optimal oncological outcomes and anastomosis lengths. The ileum was transected 5-10 cm from the cecum. For caecal, ascending colon, or hepatic flexure tumours, the ileocolic artery and vein are ligated along with the right colic artery and vein (if present) and the right branch of the middle colic vessels. For midtransverse or distal transverse tumours, central ligation of the middle colic vessels was performed alongside the other mentioned vessels, and all anastomoses performed extra-corporally were standard Barcelona technique with PROXIMATE® TLC75 linear stapler (Ethicon) (20). Ten right-sided colectomies performed intracorporeal anatomosis on a robotic platform as isoperistaltic or antiperistaltic using a Sure Form 60 linear stapler (Intuitive Surgical, Inc., Sunnyvale, CA, USA) and

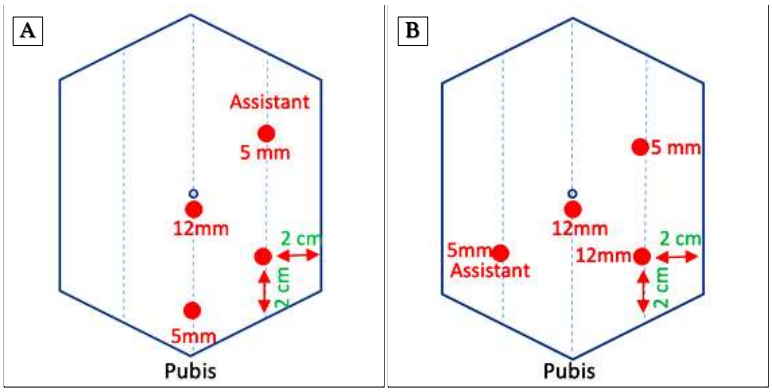

Figure 1. Laparoscopic port placement used in conventional D2 dissection: **(A)** 12 mm infra-umbilical port (Hasson technique) for initial access and CO2 insufflation, 5 mm suprapubic port for surgeons left hand, 12 mm left iliac fossa port for right-handed instrument manipulation, and 5 mm left upper quadrant assistant port. **(B)** 12 mm infra-umbilical (Hasson technique) for initial access and CO2 insufflation, 12 mm left iliac fossa and 5 mm left upper quadrant for surgeon's left- and right-handed instruments, respectively, Optional 5 mm McBurney port, solely utilized by the assistant for retraction in challenging cases with bulky tumours.

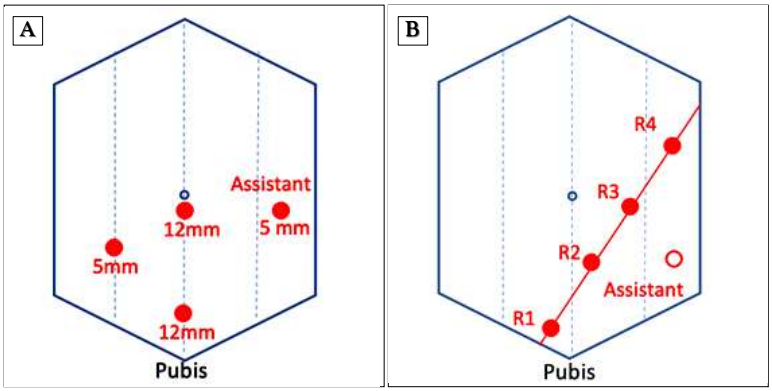

Figure 2. Laparoscopic port placement used in D3 dissection as well as robotic cases **(A)** 12 mm infra-umbilical (Hasson technique) for initial access and CO2 insufflation, 12 mm in suprapubic area for surgeons right hand dissection, 5 mm port in Mc Burney point for surgeons left hand and 5 mm assistant port in left mesogastrum in line with infraumbilical port; **(B)** Standard four-port technique (7-8 cm separation) plus an additional 5 mm or 12 mm assistant port on the opposite side (AirsealR, Applied Medical) for all resections. A two right-handed, one left-handed instrument configuration was standard. For intracorporeal anastomosis, arm R3 or R4 was upgraded to a 12 mm port to accommodate the robotic stapler.

hand-oversew enterotomy. Specimen extraction was performed via a Pfannenstiel incision or extension of the midline port.

D2 LDN

For conventional D2 lymphadenectomy standard medial to lateral dissection respecting the avascular mesocolic plane was performed in all minimally invasive resections, whereas the lateral to medial approach was preferred in open procedures. For this extent of lymph node dissection, the SMV was not exposed, and the vessels that supply the tumour were taken 1-2 cm distance from SMV leaving lymph node stations no. 203, 213, and 223, according to Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma behind (21).

D3 LDN

In addition to the dissection area described in the D2 LDN, the CME +D3 LDN procedure cleans the adipose tissue on the anterior surface of the SMV. The surgical technique used for D3 LDN was the superior mesenteric vein (SMV) first approach or " Open Book Technique" described by Benz et. al. (16). It is a very standardised approach that can be reproduced with appropriate training and support in specialised centers.

Ten steps of CME with D3 LDN

1. Traction is provided by an assistant on ileocaecal fat pad exposing the ileo-colic vessels.
2. Dissection was performed beneath the pedicle and carried forward to perform medial to lateral dissection. The duodenal tunnel is formed until the hepatic flexure in the retroperitoneal plane between the visceral peritoneum of the bowel mesentery and the Gerota fascia.
3. Dissection of the head of the pancreas and duodenum from the mesentery prevents eventual injury during superior dissection.
4. A swab is placed in duodenal tunnel to protect the duodenum and make the supracolic dissection easier.
5. Dissection of ileocolic vessels is followed by identification of the SMV and exposure of the anterior surface of this vessel, taking lymph node station no. 203 on the specimen site.
6. The ileocolic artery and vein were flash-ligated to their origin using Hemolock clips and divided with scissors.
7. Dissection was continued on the SMV en-bloc with specimen lymph node stations no. 213 and 223. The right colic artery and vein were clipped and divided, if present, followed by exposure of trunk of Henle and its branches.
8. The right gastroepiploic vein (RGEV), superior right colonic vein (SRCV), and right colonic vein (RCV) are clipped and divided, and the anterior superior pancreaticoduodenal(ASPDV) branch is always preserved. Middle colic vessels are identified, and right branches of the middle colic vessels are taken in cases of tumours located proximal to the mid transverse colon, for distal transverse tumours middle colic artery and vein are taken close to their origin (*Fig. 3*).
9. Bursectomy was performed, and the laser sac was entered, linking the dissection that was done from below. The right colon was mobilised laterally and, subileal dissection was performed to provide sufficient mobility of the bowel.
10. Tenth step - performing the anastomosis.

Special attention needs to be paid to the abnormal vascular anatomy of the venous colonic system especially to vascular variations in the Trunk of Henle. The venous system composed of Henle's trunk and its tributaries is the most complex, which has a direct influence on the outcome and postoperative recovery of the patients (22). Care must be taken in dissection and identification of all branches in order to prevent pancreatic branch injury, which can lead to postoperative pancreatitis, as described by other authors. Preoperative evaluation using multislice spiral CT angiography is essential for this extent of LDN in order to decrease vascular injury. Patients were managed postoperatively

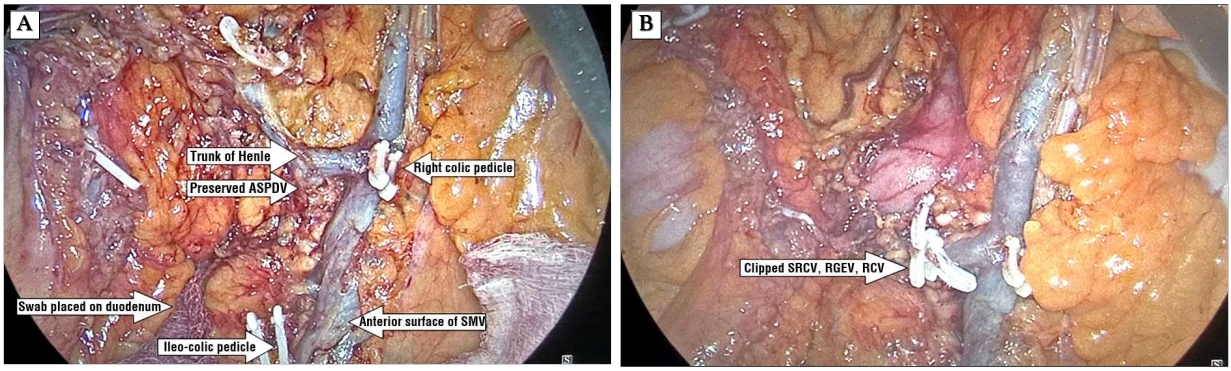

Figure 3. Laparoscopic view of CME with D3 LDN: **(A)** View of LDN over anterior circumference of SMV with clipped ileo-colic pedicle as well as right colic pedicle. We can visualise Trunk of Henle with preserved ASPDV; **(B)** Close view of Trunk of Henle with clipped SRCV, RGEV.

according to the Enhanced Recovery After Surgery (ERAS) protocol unless specific clinical factors dictated otherwise. This protocol emphasized a multimodal approach to recovery, including the removal of nasogastric tubes before anesthesia reversal. Peritoneal drains, which were infrequently used, and Foley catheters were removed on postoperative day one. Prophylactic anticoagulation to prevent venous thromboembolism was initiated six hours after surgery. Additionally, patients were encouraged to begin early ambulation and a nonrestrictive diet as early as postoperative day one. Discharge criteria were based on achieving adequate pain control with oral analgesics, independent bowel function, satisfactory mobility, and stoma independence (if applicable) (23).

Data Analysis

Data were collated into single spreadsheet (csv format). Normality of distribution was assessed using Q-Q plots. Data were treated as non-parametric and reported as median and interquartile range or number and percentage. Categorical data were analysed using Fisher's exact test, while continuous data were analysed using Wilcoxon's Rank Sum test. All variables significantly associated with the technique on univariate analysis were entered into the Cox Proportional Hazards model. The log-rank test was used to compare the statistical significance of the survival curve. Cox Proportional hazard regression models for LOS were similarly generated using the coxph function. LOS data were treated as uncensored. Statistical analysis was performed in R (version 4.2.1, The R Foundation of Statistical Computing, Vienna, Austria, www.r-project.org) using the following packages: ggpubr, survival and *Table 1*. A significance threshold of $p<0.05$ was used throughout. Significance is represented graphically as: *($p<0.05$), **($p<0.01$), ***($p<0.001$) and ****($p<0.0001$).

Results

A flowchart of patient numbers is shown in *Fig. 4*.

Table 1 summarizes the demographic characteristics of the patients. Notably, the D3 LDN cohort was significantly younger than the D2 LDN cohort ($p=0.002$). This is likely due to the exclusion of patients over 75 years old and those with high Rockwood frailty scores during multidisciplinary team (MDT) discussions. While there were no statistically significant differences in sex, BMI, WHO performance status, tumour location, or preoperative histology, it is noteworthy that the D3 LDN group had a higher proportion of patients with comorbidity status or ASA grade 1 and 2 (68.2% vs. 48.8%). Additionally, the D3 LDN group had a higher proportion of patients with clinical stage cT3/4 tumours (88.6% vs. 67.9%). Importantly, clinical staging revealed a statistically significant

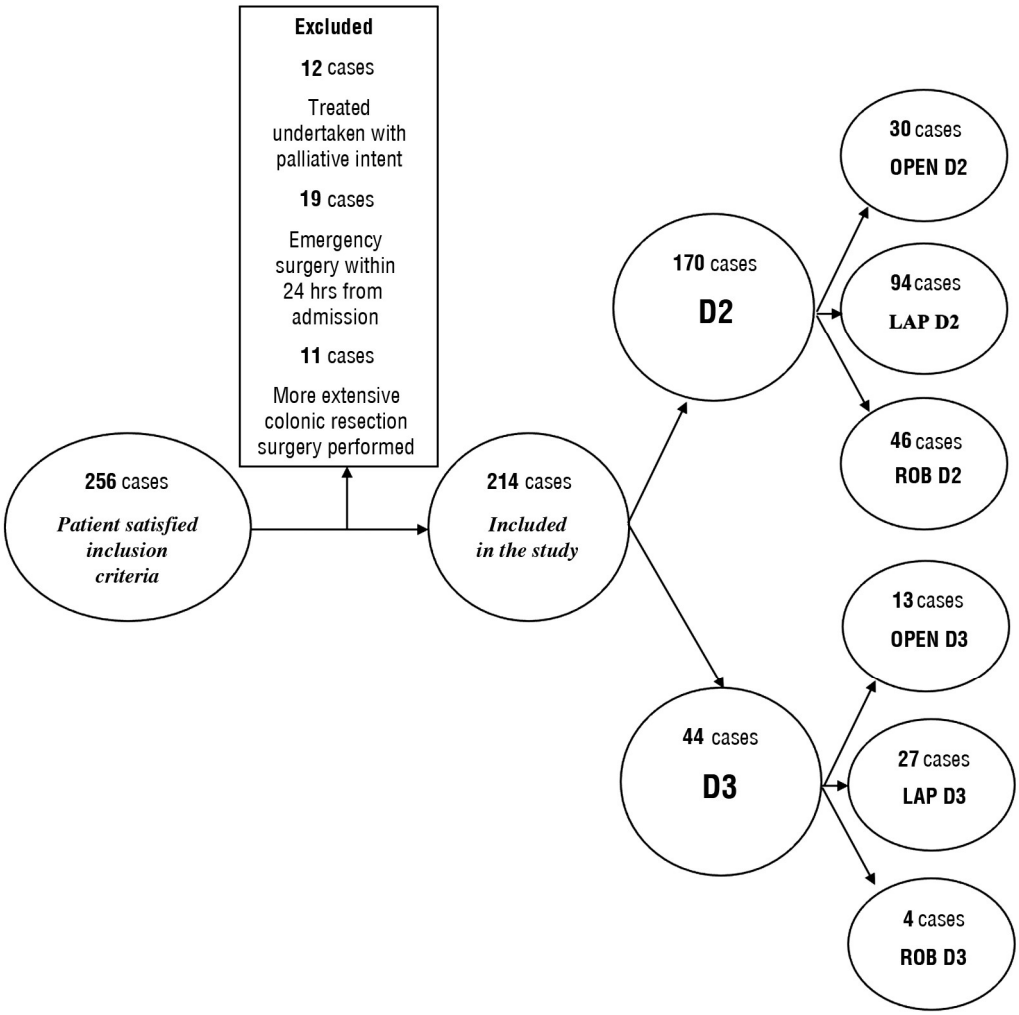

Figure 4. Patients included in this study. RCC-right colonic cancer, LAP- laparoscopic, ROB-Robotic. complication rates for CD III-IV, LOS, number of harvested lymph nodes, and negative resection margin.

difference in node-positive status, with a higher proportion of positive nodes in the D3 LDN group.

While the D3 LDN group demonstrated a numerically higher rate of open surgery compared to the D2 group (29.5% vs. 17.6%) as shown in *Table 2*, this difference did not achieve statistical significance. This is likely attributable to cases performed during the initial D3 learning curve and those with hostile abdomens initially planned for a laparotomy. However, surgical duration and estimated blood loss were comparable between the groups.

While the overall complication rate trended lower in the D3 LDN group (25%) compared to the D2 LDN group (41.2%), this difference did not reach statistical significance. Similarly, no statistically significant differences were observed in specific complications such as anastomotic leak, postoperative collection formation, surgical site infection, bleeding requiring transfusion, or return to the operating room between the two groups. Furthermore, although the D3 LDN group exhibited a lower rate of CD grade ≥II complications (25%) compared to the D2 LDN group (39.45%), this finding also lacked statistical significance. These results suggest that, within the limitations of this retrospective

Table 1. Demographic data

	D2 LDN (n=170)	D3 LDN (n=44)	P-value
Age	73 (65.2, 81.0)	66 (59.0, 74.0)	0.002
Sex			0.185
Female	83 (48.8%)	27 (61.4 %)	
Male	87 (51.2 %)	17(38.6 %)	
BMI	27 (24, 31)	26 (23, 31)	0.405
ASA			0.027
1 - 2	83 (48.8 %)	30 (68.2 %)	
3 - 4	87 (51.2 %)	14(31.8 %)	
WHO			0.694
0	95 (55.9 %)	27 (61.4 %)	
1	51 (30.0 %)	13 (29.5 %)	
2	24 (14.1 %)	4 (9.1 %)	
Localisation			0.045
Terminal ileum	1 (0.6 %)	0 (0 %)	
Appendix	4 (2.4 %)	0 (0 %)	
Caecum	70 (41.2 %)	13 (29.5 %)	
Ascending colon	51 (30.0 %)	25 (56.8 %)	
Proximal transverse colon	25 (14.7 %)	4 (9.1 %)	
Distal transverse colon	19 (11.2 %)	2 (4.5 %)	
Pre-operative histology			0.575
Adenocarcinoma	141 (82.9 %)	38 (86.4 %)	
Crohn's disease	1 (0.6 %)	0 (0 %)	
Goblet cell	2 (1.2 %)	0 (0 %)	
Mucinous Adenocarcinoma	4 (2.4 %)	2 (4.5 %)	
Neuro-endocrine tumour	1 (0.6 %)	0 (0 %)	
Signet ring cell	1 (0.6 %)	0 (0 %)	
Tubulovillous adenoma with low or high grade dysplasia	12 (7.1%)	0 (0 %)	
Highly suspicious lesion	8 (4.7 %)	4 (9.1 %)	
cT			0.049
1	8 (4.7 %)	0 (0 %)	
2	47 (27.6 %)	5 (11.4 %)	
3	76 (44.7 %)	26 (59.1 %)	
4	39 (22.9 %)	13 (29.5 %)	
cN			<0.001
0	80 (47.1 %)	8 (18.2 %)	
1	63 (37.1 %)	22 (50.0 %)	
2	27 (15,9 %)	14 (31.8 %)	
cM			1
0	161 (94.7 %)	42 (95.5 %)	
1	9 (5.3 %)	2 (4.5 %)	

Table 2. Characteristics of surgery

	D2 LDN (n=170)	D3 LDN (n=44)	P-value
Operative approach			0.014
Open	30 (17.6 %)	13 (29.5 %)	
Laparoscopic	94 (55.3 %)	27 (61.4 %)	
Robotic	46 (27.1 %)	4 (9.1%)	
Procedure			0.074
Right hemicolectomy	137 (80.6 %)	41 (93.2 %)	
Extended right hemicolectomy	33 (19.4 %)	3 (6.8 %)	
Surgery duration (min)	184 (139, 231)	180 (161, 201)	0.738
Estimated blood loss (ml)	50 (50.0, 50.0)	50 (50.0, 100.0)	0.112

Table 3. Clinical outcomes

	D2 LDN (n=170)	D3 LDN (n=44)	P-value
Overall complications	70 (41.2 %)	11 (25.0 %)	0.06
Anastomotic leak	3 (1.8 %)	2 (4.5 %)	0.271
Collection	9 (5.3 %)	1 (2.3 %)	0.674
Surgical site infection	16 (9.4 %)	3 (6.8 %)	0.776
Ileus	19 (11.2 %)	6 (13.6 %)	0.61
Post operative bleeding	11 (6.5 %)	1 (2.3 %)	0.116
Pre-operative haemoglobin level (g/L)	120 (104, 135)	115 (100,125)	0.12
Post-operative day 1 haemoglobin level (g/L)	107 (94, 117)	102 (95, 114)	0.319
Post operative transfusion requirements	25 (14.7 %)	7 (15.9 %)	0.822
Post operative red blood cells transfusions (units)	0 (0, 0)	0 (0, 0)	0.867
Return to theathre	6 (3.5 %)	1 (2.3 %)	1
Clavien- Dindo			0.273
0	102 (60.0 %)	32 (72.7 %)	
1	1 (0.6 %)	1 (2.3 %)	
2	50 (29.4 %)	9 (20.4 %)	
3	13 (7.6 %)	1 (2.3 %)	
4	4 (2.4 %)	1 (2.3 %)	
Clavien- Dindo			0.0819
0-1	103 (60.6 %)	33 (75.0 %)	
2+	67 (39.4 %)	11 (25.0 %)	
Length of stay	6 (4.0, 9.8)	5.5 (4.0, 9.2)	0.56
Overall survival	146 (85.9 %)	42 (95.5 %)	0.116

study, D3 LDN is not associated with a increased risk of postoperative complications compared to D2 LDN.

Fig. 5 depicts a forest plot analyzing the associations between various factors and the LOS for patients. The results indicate that no statistically significant associations were observed between sex, body mass index (BMI), extent of LDN, postoperative hemoglobin level, and positive resection margin with the duration of hospitalization.

Fig 6 presents a plot summarizing the results of a Cox proportional hazards regression analysis exploring factors associated with CD grade ≥II following surgery. While patient age did not exhibit a statistically significant association with CD ≥II complications, higher ASA (3 and 4) were linked to an increased risk compared to ASA 1 (ASA 3: HR=1.60, 95% CI: 0.63-4.08; ASA 4: HR=2.74, 95% CI: 0.38-2.74). Additionally, surgery on the ascending colon (HR=1.23, 95% CI: 0.88-1.71) and transverse colon (HR=1.68, 95% CI: 0.23-12.33) demonstrated a higher risk of CD II+ complications compared to caecal resections. Notably,

Table 4. Specimen characteristic

	D2 LDN (n=170)	D3 LDN (n=44)	P-value
pT			0.699
1	19 (11.2 %)	3 (6.8 %)	
2	31 (18.2 %)	6 (13.6 %)	
3	89 (52.4 %)	27 (61.4 %)	
4	31 (18.2 %)	8 (18.2 %)	
pN			0.036
0	117 (68.8 %)	23 (52.3 %)	
1	41 (24.1 %)	13 (29.5 %)	
2	12 (7.1 %)	8 (18.2 %)	
Total number of lymph nodes yield	19 (16, 25)	23 (18, 28)	0.014
Positive lymph nodes	0 (0, 1)	0 (0, 2)	0.038
Specimens with positive lymph nodes	52 (30.6 %)	20 (45.5 %)	0.074
Nodal status upstaging	17 (10.0 %)	6 (13.6 %)	0.584
Extramural vascular invasion positiv-ity	38 (22.4 %)	11 (25.0 %)	0.678
Perineural invasion positivity	20 (11.8 %)	2 (4.5 %)	0.256
R1 resection margin	8 (4,7 %)	2 (4.5 %)	1

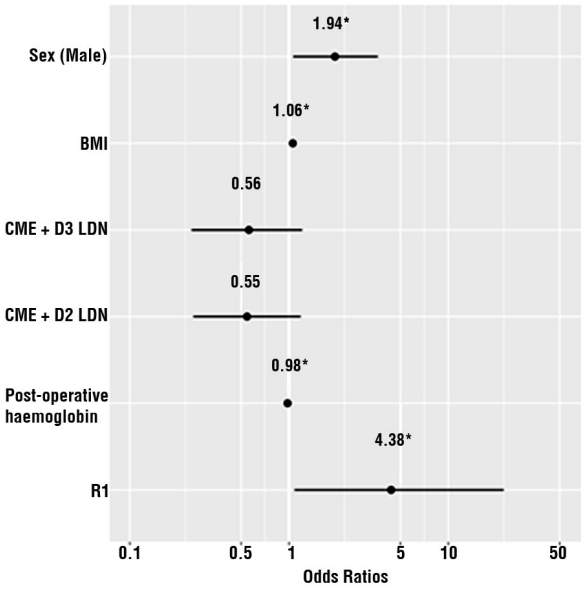

Figure 5. Factors associated with increased length of stay

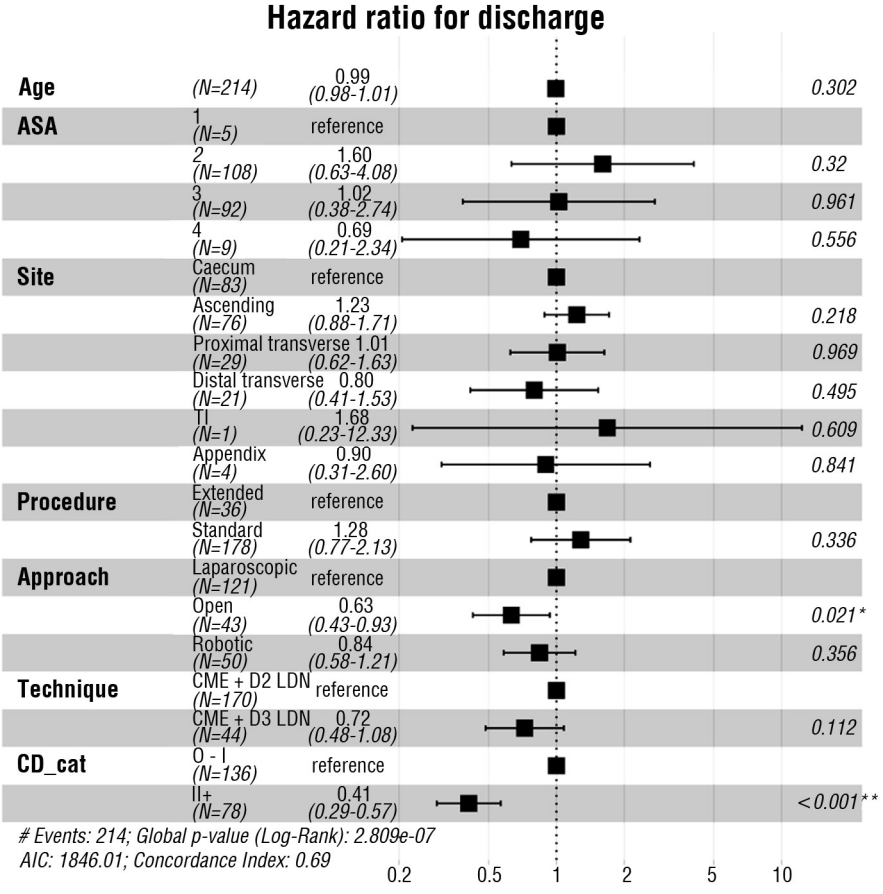

Figure 6. Factors associated with Clavien-Dindo 2+ complications

extended lymph node dissection (D3) did not differ statistically from standard dissection (D2) regarding CD II+ complications (HR = 0.72, 95% CI: 0.48-1.08).

Discussion

The adoption of CME with D3 LDN as the standard surgical approach for RCC remains a topic of ongoing debate in colorectal surgery. Although long-term survival benefits are not definitively established, accumulating evidence suggests a potential improvement (14,24). Nonetheless, most studies have reported that a standardized CME with the D3 LDN technique, implemented with appropriate training, offers a safe alternative. Morbidity, mortality, and hospital length of stay were comparable to those observed with conventional right colectomies (25-27).

Our retrospective study aimed to compare short - term ourtcomes of CME + D3 with conventional D2 resection for right colon cancer. We demonstrated that the success of this surgery hinges on meticulous preoperative vascular assessment and utilization of the SMV as a key anatomical landmark. By meticulously dissecting only the anterior fatty tissue of the SMV, we strived to preserve the delicate arterial nerve plexus surrounding the superior mesenteric artery, thereby mitigating associated complications. The consistent application of a standardized 10-step approach, as described by Benz and successfully replicated by our team, contributes to the safety and reproducibility of this procedure (16,28). Breakdown into individual steps facilitates training and ensures a consistent execution.

Our outcomes demonstrated that CME with D3 LDN is associated with a complication profile comparable to that of conventional D2 LDN surgery. These findings suggest that CME with D3 LDN is safe and feasible tehnique. Furthermore, the higher lymph node yield achieved with D3 LDN may translate into improved oncological outcomes, which has been reinforced by multiple studies (15,29-33)

Kotake et al published a review of 10,098 patients who had pT3 and pT4 colorectal adenocarcinoma between 1985 to 1994. Evaluation of this cohort for overall survival between the D3 LDN and D2 LDN groups revealed a highly significant difference ($p < 0.00003$) (12). They concluded that D3 resection should be considered for all T3 and T4 colon cancers.

In addition, the Danish series provided robust evidence of improved survival rates for stage 1 to stage 3 colonic cancer withD3 LDN. They demonstrated a significant improvement in disease-free survival for patients who underwent D3 LDN compared to the non—D3 LDN group. In stage I patients the 4-year DFS in the D3 LDN group was 100% versus 89.8% in the non-CME group, with a significant difference of over 10% (34). This difference increased to 14% in stage two patients but decreased to 6% in stage three patients. A short follow-up period led to an inability to derive information on overall survival. The difference was calculated to be significant in stages I and II, not in stage III.

Based on literature the number of lymph-node metastases is the most robust determinant of survival in patients with known metastatic rectal cancer; also number of retrieved lymph-nodes is closely related to the prognosis of colonic cancer. This may be partly due to the Will Rogers phenomenon of stage migration, as well as due to the decreased risk of recurrence by resection of metastatic lymph nodes. There is an inherent bias in this conclusion because CME with D3 LDN would be performed in high-volume centres with highly skilled colorectal surgeons.

Although the vast body of evidence for CME with D3 LDN is largely retrospective , three recent randomized controlled trials have shed light on the short-term outcomes of patients who underwent extended LDN compared to conventional procedures. The RELARC trial in China identified an increased risk of intraoperative vascular injuries during D3 dissection. However, the overall postoperative complication rate did not differ between the groups, and the D3 LDN group experienced fewer CD grade III-IV

complications (35). An Italian trial by DiBuono et al. observed no significant differences in postoperative complications. However, D3 LDN procedures were associated with significantly longer operative times, higher lymph node yield, and superior quality specimens (36). Similarly, the Russian COLD trial reported no discrepancies in short-term outcomes such as postoperative morbidity, hospital stay, or readmission rates. However, the D3 group achieved better specimen quality and higher lymph node count (37).

A potential limitation of this study was the marked disparity in sample sizes between the D3 LDN (n=44) and D2 LDN (n=170) groups. This imbalance arised because the choice of surgical procedure was left to the discretion of the treating surgeon. Although the D3 LDN was offered to the patients with clinical node positive disease status and T3/4 size lesions this approach may have introduced unintentional selection bias, as some surgeons may have exhibited a preference for the conventional D2 LDN procedure over the less-established D3 LDN technique.

Conclusions

This retrospective cohort study demonstrated the feasibility and safety of D3 LDN for RCC cancer within a high-volume colorectal unit, employing meticulous patient selection and thorough preoperative vascular assessment. The operation resulted in a substantial number of lymph nodes being removed without an increase in the incidence of post-surgical complications.These findings suggest potential oncological advantages, particularly in well-defined patient groups such as younger individuals with a higher likelihood of nodal involvement. However, the study's limited sample size precludes the detection of nodal upstaging, which has been reported to be 5% in published literature. To definitively establish D3 LDN as a standard surgical approach, multicenter randomized controlled trials with larger patient populations and extended follow-up periods are required.

Author's Contributions

Conceptualization, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Richard Boulton and Sandeep Kaul; methodology, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Maitreyi Patel, Victor Victor Kung, Saswata Banerjee, Nirooshun Rajendran, Joseph Huang, Richard Boulton and Sandeep Kaul; software, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Richard Boulton and Sandeep Kaul; validation, Valentin Butnari , Timothy Jones, Ahmer Mansuri, Maitreyi Patel, Victor Kung, Saswata Banerjee, Nirooshun Rajendran, Joseph Huang, Richard Boulton and Sandeep Kaul; formal analysis, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Richard Boulton and Sandeep Kaul; investigation, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Richard Boulton and Sandeep Kaul; resources, Valentin Butnari, Timothy Jones, Ahmer Mansuri , Maitreyi Patel, Victor Victor Kung, Saswata Banerjee, Nirooshun Rajendran, Joseph Huang, Richard Boulton and Sandeep Kaul; data curation, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Maitreyi Patel, Victor Victor Kung, Saswata Banerjee, Nirooshun Rajendran, Joseph Huang, Richard Boulton and Sandeep Kaul; writing - original draft preparation, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Richard Boulton and Sandeep Kaul; writing - review and editing, Valentin Butnari, Timothy Jones, Ahmer Mansuri , Maitreyi Patel, Victor Victor Kung, Saswata Banerjee, Nirooshun Rajendran, Joseph Huang, Richard Boulton and Sandeep Kaul; visualization, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Maitreyi Patel, Richard Boulton and Sandeep Kaul; supervision, Victor Victor Kung, Saswata Banerjee, Nirooshun Rajendran, Joseph Huang, Richard Boulton and Sandeep Kaul; project administration, Valentin Butnari, Timothy Jones, Ahmer Mansuri, Richard Boulton and Sandeep Kaul. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study is registered with trust audit department with the unique identifying number L-227-22 with an exemption from obtaining written informed consent due to its observational and retrospective nature. This study was not considered Research by NHS Health Research Authority. The study adhered to the principles of the Declaration of Helsinki (as revised in 2013).

Data Sharing Statement

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

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