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Complete mesocolic excision versus D2 lymphadenectomy in right hemicolectomy: a meta-analysis of propensity score matched studies and randomized controlled trials

Bernardo Fontel Pompeu, MD, MSc[a,b], Eric Pasqualotto[c], Patrícia Marcolin, MD[d], Lucas Monteiro Delgado[e], Beatriz D'Andrea Pigossi, MD[a], Sergio Mazzola Poli de Figueiredo, MD[f], Fernanda Bellotti Formiga, MD, MSc[a]

Introduction: The complete mesocolic excision (CME) in right-sided hemicolectomy could result in higher lymph node yield and decreased local recurrence. However, this approach could increase intraoperative and postoperative complications. Therefore, our meta-analysis aims to demonstrate the outcomes of CME versus D2 conventional lymphadenectomy in right-side colon cancer.

Methods: We searched MEDLINE, Cochrane Central Register of Clinical Trials, and Scopus for studies published until April 2024. Odds ratios (OR) with 95% confidence intervals (CIs) were pooled using a random-effects model. Heterogeneity was assessed using the Cochran Q test and I^2 statistics, with P values <0.10 and I^2 >25% considered significant. Statistical analysis was performed using R Software, version 4.1.2.

Results: Three randomized controlled trials and four observational studies comprising 2296 patients were included, of whom 1138 (49.6%) were submitted to the CME and 1158 (50.4%) to the conventional D2 lymphadenectomy. CME was associated with decreased local recurrence rates (OR 0.07; 95% CI 0.001 to 0.36; P = 0.002). There were no significant differences between groups in overall complications, severe complications, intraoperative complications, blood loss, and 30-day mortality. No difference between groups was observed in distance metastasis and 3-year disease-free survival.

Conclusion: In this meta-analysis, CME significantly decreases local recurrence rates compared with D2 conventional lymphadenectomy in patients with right-side colon cancer. No significant difference was observed between groups in rates of overall complications, severe complications, intraoperative complications, blood loss, and 30-day mortality.

Keywords: colorectal neoplasm, complete mesocolic excision, lymphadenectomy, right side colectomy

Introduction

Colorectal cancer is the third most commonly diagnosed tumor and the second leading cause of cancer-related death in the United States[1]. The main treatment for locally colon invasive tumors is segmental colectomy with regional lymphadenectomy, which is performed based on intraoperative findings[2,3]. For right-sided colon cancer with no clinical lymphadenopathy outside the field of conventional resection, the ileocolic and right branches of the middle colic vessels are divided in their origin, a procedure known as D2 conventional lymphadenectomy (D2). A minimum of 12 lymph nodes in the specimen is recommended to assign the N0 stage[2,3]. However, extended lymphadenectomy remains controversial. Complete mesocolic excision (CME) has been proposed as a technique to increase lymph node yield and improve tumor staging, but it may also increase severe intraoperative and postoperative complications[3-5]. There is ongoing debate regarding the use of CME as a routine procedure in right-sided colon cancer. While some surgeons believe CME could decrease local recurrence and improve disease-free survival[5-9], other studies fail to demonstrate the benefits of extended lymphadenectomies, with no significant difference in survival[10,11]. A previous meta-analysis comparing CME and conventional lymphadenectomy in right-sided colon cancer included one randomized controlled trial (RCT), seven observational, and three case-control studies[12]. Since then, two RCTs have been published with short-term results[13-15]. Moreover, the previous meta-analysis included observational and case-control studies, which may have introduced bias and heterogeneity in the results. To address these limitations, we have restricted the inclusion of only propensity score-matched observational studies[8-10,16]. Therefore, we aimed

[a]Department of Colorectal Surgery, Heliopolis Hospital, São Paulo, SP, Brazil, [b]USCS – University of São Caetano do Sul, São Paulo, SP, Brazil, [c]Federal University of Santa Catarina, Florianópolis, SC, Brazil, [d]Federal University of South Border, Passo Fundo, RS, Brazil, [e]Federal University of Minas Gerais, Belo Horizonte, Brazil and [f]Department of Surgery, Cleveland Clinic Foundation, Cleveland, Ohio, United States

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Corresponding author. Address: Rua Santo Antônio, 50 - Centro, São Caetano do Sul, São Paulo, SP 09521-160. Tel.: +55 11 973389944.
E-mail: bernardo.pompeu@online.uscs.edu.br (B.F. Pompeu).

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to perform an updated systematic review and meta-analysis comparing CME versus D2 in patients undergoing right-sided hemicolectomy for colon cancer, focusing exclusively on high-quality studies with a low risk of bias.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[17]. The study protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) with registration number CRD42024547934[18].

Search strategy

We systematically searched PubMed, Cochrane Central Register of Clinical Trials, and Scopus for studies published up to April 2024. The search strategy used was as follows: ("Colon Neoplasms" OR "Complete Mesocolic Excision" OR "CME" OR "D3" OR Mesocolon) AND (colectomy OR "right-sided colectomy"). We also searched for additional studies using the references of previously included studies.

Eligibility criteria

The inclusion criteria were: (1) RCTs or observational studies with propensity score match; (2) comparing CME versus D2 lymphadenectomy technique; (3) enrolling patients undergoing right hemicolectomy for right-sided colon cancer; and (4) reporting at least one outcome of interest. The exclusion criteria were: (1) overlapping populations (only the study with the highest number of patients was included); (2) left-sided colon cancer and synchronic tumors; (3) other techniques aside from right hemicolectomy. Overlapping populations were included if different outcomes were assessed.

Data extraction and endpoints

The postoperative short-term outcomes assessed were: (1) overall complications (2) intraoperative complications; (3) severe complications; (4) Clavien-Dindo ≥3 complications; (5) 30-day mortality; (6) blood loss; (7) operative conversion rates; (8) operative time; (9) length of hospital stays; (10) lymph nodes harvested. The long-term outcomes assessed were: (1) three years of disease-free survival (DFS), (2) local recurrence, and (3) distant recurrence. Two researchers (B.F.P. and E.P.) independently screened articles for inclusion criteria and extracted data from included studies. Any disagreements were resolved through consensus with a third author (F.B.F and P.M.).

Quality assessment

Two authors (B.F.P and E.P.) independently assessed the quality of included studies. For observational studies, we used the Cochrane Collaboration tool for assessing the risk of bias in non-randomized studies (ROBINS-I)[19]. In this assessment, each study was categorized as critical, serious, moderate, or low risk in the seven domains: confounding, selection, classification, deviations from intended interventions, missing data, measurement of outcomes and selection of reported results. RCTs were appraised using the Revised Cochrane risk-of-bias tool (RoB 2), in which studies are categorized as low risk, high risk, or may express some concerns in five domains: randomization, deviations from intended intervention, missing outcome data, measurement of the outcome and selection of the reported result[20]. Disagreements were resolved unanimously with the senior author (F.B.F.).

Statistical analysis

We pooled odds ratio (OR) for binary outcomes and mean differences (MDs) for continuous endpoints, with 95% confidence intervals (CI). Statistical significance was defined as P <0.05. DerSimonian and Laird random-effects models were used for all endpoints. Heterogeneity was assessed using the Cochran Q test and I^2 statistics, with P values <0.10 and I^2 >25% considered significant for heterogeneity. For outcomes with significant heterogeneity, we used Baujat plots to assess each study's contribution to the overall effect and heterogeneity. Leave-out sensitivity analyses were performed by systematically removing each study from the pooled estimates to ensure the robustness of the results. Statistical analyses were performed using R Software, version 4.1.2 (R Foundation for Statistical Computing)[17,21].

Results

Study selection and characteristics

As detailed in Figure 1, the initial search identified 2309 results. Ultimately, three RCT studies and four observational studies were included in the analysis, comprising 2296 patients[8-10,13-16]. Of these, 1138 (49.6%) were submitted to the CME and 1158 (50.4%) to the conventional D2 lymphadenectomy. The mean age was 69.14 ± 5.98 years, the mean BMI was 25.8 ± 0.81 kg/m^{2,} and 1249 (54.4%) were male. Only five studies reported tumor location, and the ascending colon was the most common site (44.2%), followed by the cecum (28.7%), hepatic flexure (21.3%), and transverse colon (5.8%)[9,13-16]. Most interventions were performed by laparoscopic approach and less frequently in robotic or open procedures. Considering specimen properties, 36.9% of patients had pT3-T4 tumors in the CME group and 35.7% in the D2 conventional group. There was a high lymph node yield in both groups, with a mean of 25.54 ± 5.16 in the CME group and 20.3 ± 4.16 lymph nodes in the D2 group. Positive lymph nodes (pN+) were identified in 17.5% of the CME group and 17% of the D2 group. The conversion rates were very low, observed in 63 patients (3.4%). Four studies were able to evaluate short-term postoperative complications[13-16], while the remaining trials could report rates of disease-free survival as the primary endpoint[8-10]. Both study and surgery characteristics and specimen properties are reported in Tables 1, 2, and 3.

Pooled analyses of all studies

Surgical complications

There was no significant difference between the CME and D2 conventional technique in overall complications (OR 0.98; 95% CI 0.80 to 1.20; P = 0.861; I^2 = 0%; Fig. 2A) [8,10,13-16]. In the same way, no significant was observed in intraoperative complications (OR 1.24; 95% CI 0.72 to 2.14; P = 0.43; I^2 = 0%; Fig. 2B), severe complications (OR 1.58; 95% CI 0.99 to 2.51; P = 0.54; I^2 = 0%; Fig. 2C)[10,13-16], conversion rates (OR 1.04; 95% CI 0.64 to 1.71; P = 0.865; I^2 = 0%; Fig. 3A) [9,10,13-16]; 30 days mortality (OR 1.57; 95% CI 0.26 to 9.77; P = 0.629; I^2 = 0%; Fig. 3B) [10,13-15]. There was low heterogeneity in these outcomes. Blood loss was not different between the groups

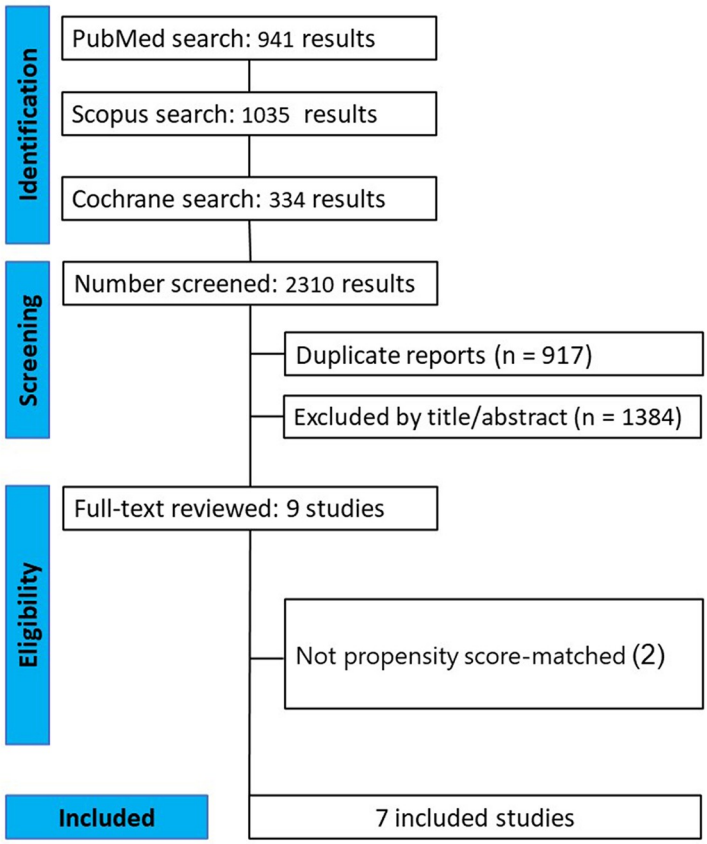


Figure 1. PRISMA flow diagram of study screening and selection.

(MD −24.8 ml; 95% CI −66.1 to 16.6; P = 0.24; I^2 = 85%; Fig. 3C)[8,9,13-15], and we observed a high heterogeneity. Clavien-Dindo ≥3 also demonstrated no difference (OR 1.01; 95% CI 0.60 to 1.69; P = 0.981; I^2 = 38 %; Fig. 3D), and we observed moderate heterogeneity[9,10,13-16].

Operative time, hospital stay, lymph nodes harvested

No difference was observed between the CME and D2 group in the length of hospital stay (MD 0.1 days; 95% CI −0.3 to 0.4; P = 0.60; I^2 = 59%; Fig. 4A) [9,10,15,16]. There was high heterogeneity. Operative time demonstrated similar results (MD −9.9 min; 95% CI −20.1 to 9.3; P = 0.31; I^2 = 38 %; Fig. 4B). There was moderate heterogeneity[8-10,13-16]. CME was associated with an increased number of harvested lymph nodes (MD 4.4 lymph nodes; 95% CI 2.6 to 6.1; P = < 0.01; I^2 = 85%; Fig. 4C) [8-10,13-16]. There was high heterogeneity.

Long-term: disease-free survival, local recurrence, and distant recurrence

No difference was observed in 3 years of disease-free survival between the CME and D2 groups (OR 0.49; 95% CI 0.14 to 1.74; P = 0.268; I^2 = 90%; Fig. 5A) [8-10]. There was high heterogeneity. The CME group significantly decreased local recurrence rates (OR 0.07; 95% CI 0.001 to 0.36; P = 0.002; I^2 = 0%; Fig. 5B)[8-10]. Finally, no difference was observed in distance recurrence between the groups (OR 0.63; 95% CI 0.31 to 1.28; P = 0.201, I^2 = 26%; Fig. 5C)[8-10]. There was a low heterogeneity.

Sensitivity analyses

On Baujat plot analyses, Khan *et al* contributed substantially to the heterogeneity of blood loss, Clavien-Dindo ≥III postoperative complications, and hospital stay[9]. However, the leave-one-out sensitivity analysis was performed and showed no change in the significance of the results (Supplementary Digital Content, Figures S1 and S4, available at: http://links.lww.com/MS9/A669)[9]. Lieto *et al* contributed substantially to the heterogeneity of the lymph node harvested and 3y-DFS results[8]. There was no change in the results after performing a leave-one-out analysis for the lymph node harvested. Omitting Lieto in lymph node harvested the results remain consistent. However, in the DFS, removing Lieto *et al* decreased the heterogeneity, and we observed that CME improves DFS (OR 0.25; 95% CI 0.16 to 0.38; I^2 = 0%) (Supplementary Digital Content, Figures S5-S8, available at: http://links.lww.com/MS9/A669). Magistro *et al* contributed substantially to the heterogeneity of the operative time[16]. However, the leave-one-out sensitivity analysis showed no change in the significance of the results (Supplementary Digital Content, Figures S9 and S10, available at: http://links.lww.com/MS9/A669). In addition, the funnel plot for the overall complication outcome presents an asymmetrical distribution of studies to the right side that could overestimate the effect size. Insufficient studies limit Egger test results in this meta-analysis (Supplementary Digital Content, Figure S11, available at: http://links.lww.com/MS9/A669)[21].

Table 1

Baseline characteristics of studies included in the meta-analysis

Author	Country	Patients CME/D2, n	Design	Gender (male) CME/D2, n (%)	BMI (mg/kg2) CME/D2	Age CME/D2	ASA CME/D2, n (%)	Tumor site CME/D2, n (%)
LaCoMEStaR 2021	Italy	67/65	RCT	38 (56.7)/34 (52.3)	24.9 (20.2–30.5)/26.2 (19.0–34.7)*	70.2 (44–85)/ 65.3 (26–88)*	II: 5 (7.5)/6 (9.2) III: 57 (85.0)/54 (83.1) IV: 5 (7.5)/5 (7.7)	CC: 18 (26.9)/29 (44.6) AC: 33 (49.2)/26 (40) HF: 19 (14.4)/7 (10.8) TC: 4 (5.9)/3 (4.6)
CoME-in Trial 2024	Italy	116/135	RCT	69 (51.0)/57 (49.0)	25.9 ± 4.5)/ 26.3 ± 4.5**	73 ± 15/ 74 ± 13**	I: 5 (3.8)/3 (2.6) II: 76 (57.1)/57 (50.0) III: 52 (39.1)/55 (47.4)	AC: 43 (31.9)/39 (33.6) CC: 52 (38.5)/48 (41.4) HF: 34 (25.2)/24 (20.7) TC: 6 (4.4)/5 (4.3)
RELARC 2021	China	495/500	RCT	279 (56.0)/306 (61.0)	23.6 ± 3.3/ 23.5 ± 3.1**	60 (52–66)/62 (54–67)*	I: 138 (28.0) / 129 (26.0) II: 313 (63.0)/ 334 (67.0) III: 44 (9.0)/37 (7.0)	CC: 108 (22.0)/102 (20.0) AC: 231 (47.0)/262 (5.0) HF: 122 (25.0)/113 (23.0) TC: 34 (7.0)/23 (5.0)
Giani 2022	Italy	146/146	Prospective w/ PSM	63 (43.2)/67 (45.9)	26 (23–29)/24.7 (22–28)*	75 (65–80)/75 (67–81)*	I: 21 (14.4)/17 (11.6) II: 76 (52.0)/92 (63.1) III: 49 (33.6)/37 (25.3)	NA
Khan 2021	UK	40/80	Prospective w/ PSM	19 (34)/37 (66)	26 (20–37)/28 (19–47)*	69 (34–80)/71 (37–82)*	I: 5 (12.5)/3 (3.7) II: 28 (70.0)/53 (66.3) III: 7 (17.5)/24 (30.0)	CC: 4 (10.0) ## AC: 18 (45.0) HF:12 (30.0) TC 6 (15.0)
Magistro 2022	Italy	186/186	Prospective w/ PSM	106 (56.9)/101 (54.3)	26 (24–29)/25 (23–27) *	76 (67–81)/74 (68–81)*	I:21 (11.3)/19 (10.2) II: 106 (57.0)/ 125 (67.2) III: 59 (31.7)/42 (22.6)	CC: 70 (37.6)/83 (44.6) AC: 76 (40.9)/63 (33.9) HF: 27 (14.5)/23 (12.4) TC: 13 (7.0)/17 (9.1)
Lieto 2017	Italy	88/46	Retrospective w/ PSM	42 (47.7)/31 (67.3)	26 ± 2/27 ± 2**	2.1 ± 5.0/ 2.2 ± 3.0**	NA	CC-AC: 56 (63.6)/34 (73.9) HF-TC: 32 (36.4)/12 (26.1)

**Mean ± standard deviation; * Median (range); ## tumor site percentual reported only for robotic CME procedures in Khan 2021. RCT: randomized controlled trial; NA: not available; CC: cecum; AC: ascendent colon; HF: hepatic flexure; TC: transverse colon; CME: complete mesocolic excision; D2: conventional lymphadenectomy; PSM: propensity score match.

Quality assessment

Figures 6A and 6B show individual appraisals of each study included in the meta-analysis. Three RCTs and all four observational studies were classified as having low-risk bias[8-10,13-16]. Notably, in nonrandomized control trials, confounding domains were appropriately measured and controlled through PSM.

Discussion

In this systematic review and meta-analysis of three RCTs and four observational studies with PSM, including 2296 patients, we compared the CME and D2 lymphadenectomy techniques in patients undergoing right hemicolectomy for colon cancer. We found that CME was associated with decreased local recurrence rates (OR 0.07; 95% CI 0.001 to 0.36; $P = 0.002$). Moreover, there were no significant differences between groups in overall complications, severe complications, intraoperative complications, blood loss, conversion to open surgery, 30-day mortality, distant metastasis, and 3-year disease-free survival. The rationale for performing CME in colon cancer stems from the improvement in rectal cancer patient survival after Heald introduced total mesorectal excision in 1982[6,19]. CME for right hemicolectomy aims to remove the tumor and the mesocolon in an intact envelope of peritoneum associated with central vascular ligation[3,6,9,10,14,16]. This extended lymphadenectomy reduced 5-year recurrence rates from 6.5% to 3.6%[6]. Similarly, Bertelsen *et al* reported a decrease in 5-year recurrence rates (9.7% vs. 17.9%) in patients undergoing CME compared to conventional resection[5]. In our analysis, two studies found the same results. Lieto *et al* report that the classic procedure was associated with poor prognosis, with 5-year disease-free survival rates of 49.1% versus 89.2% in the CME group[8]. The other study documented a 3-year overall survival rate ($P = 0.045$) benefit for the robotic CME group compared to laparoscopic standard procedure[9]. Conversely, the rationale for not performing CME as a routine procedure is that lymph node metastasis outside the standard field of resection compromises only 3 to 11% of colon cancer cases, and skip metastasis with central lymph node involvement occurs only in 4 % of cases[3,22,23]. A Swedish study that evaluated 2084 cases of right-sided colon cancer reported no survival benefits for extended mesocolic resection, with no difference in 3-year overall survival, disease-free survival, or local

Table 2

Surgical characteristics of the included studies included in the meta-analysis

Author	Surgeon experience	Approach	Anastomotic Technique	Anastomosis approach,	Operative time	Blood Loss	Conversion	Follow up (Mean)
		n (%)	CME/D2, n (%)	CME/D2, n (%)	CME/D2, min	CME/D2, ml	CME/D2, n (%)	
LaCoMEStaR 2021	>35 laparoscopic CME	Laparoscopic (100)	Endo-stapler with the double-line suture	Extra/Intra	163 (135–195)/ 150 (125–180)*	185 (50–350)/ 200 (50–300)*	2 (3.0)/3 (4.6)	30 days
CoME-in Trial 2024	Evaluated by an expert committee via unedited videos	Open (7.2) Laparoscopic (85.0) Robotic (7.6)	Handsewn: 6 (5.2)/11 (8.1) Stapler: 110 (95)/124 (92)	Extra: 23 (20.0)/ 15 (11.0) Intra: 93 (80.0)/ 120 (89.0)	176 ± 80/ 172 ± 72[a]	50 ± 85/ 50 ± 100[a]	7 (5.3)/6 (5.4)	90 days
RELARC 2021	≥100 laparoscopic colorectal/ year, ≥20 CME/D2	Laparoscopic (100)	Stapler: 493 (100)/ 497 (99) Handsewn: 2 (<1%)/3 (1%)	Extra: 443 (90.0)/ 432 (86.0) Intra: 52 (10.0)/ 68 (14.0)	216.3 (130–300)/ 191.5 (120–310)*	185 (50–350)/ 200 (50–300)*	8 (2.0)/16 (3.0)	30 days
Giani 2022	NA	Laparoscopic (100)	NA	NA	195 (170–240)/ 235 (194–291)*	NA	NA	36 months
Khan 2021	NA	Laparoscopic D2 (66.7) Robotic CME (33.3)	NA	NA	180 (128–300)/ 130 (90–280)*	10 (0–20)/50 (10–250)*	0 (0)/4 (5)	36 months
Magistro 2022	NA	Laparoscopic (100)	Endo-stapler with double-line suture	Intra	200 (170–240)/ 230 (200–276)*	NA	7 (3.8)/10 (5.4)	90 days
Lieto 2017	NA	Laparoscopic (100)	NA	NA	160 ± 26/ 188 ± 65[a]	NA	NA	60 months

[a]Mean ± standard deviation; * Median (range); NA: not available; CME: complete mesocolic excision; D2: conventional lymphadenectomy; Extra: extracorporeal anastomosis; Intra: intracorporeal anastomosis.

recurrence[11]. While our meta-analysis demonstrates that CME significantly decreases local recurrence, we found no difference in disease-free survival and distant recurrence rates. This suggests that the potential benefits of CME in reducing local recurrence may not translate to improved long-term survival outcomes, possibly due to the low incidence of lymph node metastasis outside the standard field of resection and skip metastasis. Improvements in lymphadenectomy are crucial for accurate staging and potential survival benefits in colon cancer[3,10,16,24]. A minimum of 12 lymph nodes should be examined in the surgical specimen to properly assign the N0 stage[2,3]. A higher number of resected lymph nodes in CME has been consistently demonstrated in recent RCTs. The CoME-in trial reported a median of 25 lymph nodes in CME and 20 in the no-CME group[13]. Similarly, the RELARC trial found a median number of lymph nodes harvested was 26 versus 23[15]. Finally, the LaCoMEStaR trial documented a median of 23.8 and 16.6 lymph nodes for the CME and D2 groups, respectively[14]. Our study demonstrated a high number of lymph node yield in both groups, with a mean of 25.54 ± 5.16 in the CME group and 20.3 ± 4.16 in the D2 group These results likely reflect the quality of the lymphadenectomy performed by high-volume surgeons experienced in minimally invasive surgical oncology. Regarding short-term outcomes, our meta-analysis showed no significant differences in overall, severe, intraoperative complications, blood loss, and 30-day mortality rates between CME and D2 procedures. While some studies suggest that CME procedures could increase intraoperative and postoperative complications, the evidence remains inconsistent. Olofsson *et al* associated perioperative bleeding and the increase of operation time with higher rates of 30-day mortality ($P = 0.008$ and $P = 0.003$)[11]. In contrast, several other studies have reported no significant differences in complication rates between CME and D2 procedures. In the CoME-in trial, intraoperative complications were very low, 3% versus 3% ($P = 0.9$)[13]. For the LaCoMEStaR trial, the intraoperative complications were 3% and 1.5% for CME versus D2, respectively[14]. Finally, the RELARC trial documented rates of intraoperative complications of 5% versus 4% ($P = 0.52$)[15]. These findings suggest that, when performed by experienced surgeons, CME may not significantly increase the risk of short-term complications compared to D2 lymphadenectomy. The most feared intraoperative complication is intraoperative bleeding[4]. The need for superior mesenteric vein dissection raises concern for potential vascular damage. However, the incidence of major vascular injury appears to be low when CME is performed by experienced surgeons. In a 10-year retrospective review of 304 right colectomies for right-sided colon cancer the reported frequency of intraoperative superior mesenteric vein injury was 1.6%[4]. Similarly, the RELARC identified vascular injury rates of 1% in CME procedures and 2% in the D2 group[15] while the CoME-in trial reported only one case of intraoperative vascular injury (0.7%). Moreover, although CME with central vascular ligation takes longer[13], our analysis showed no significant difference between the groups in operative time. This suggests that, in the hands of experienced surgeons, the increased complexity of CME may not necessarily lead to higher rates of complications or longer operative time. This study has limitations. First, only three RCTs of patients undergoing elective procedures were included, which may limit the generalizability of our findings. Second, the long-term survival results from the included RCTs have not been published yet, which limits our ability to determine whether CME procedures can improve long-term outcomes compared to non-CME techniques. However, we believe that more RCTs will

Table 3

Specimen characteristics in the included studies

Author	Tumor inclusion	Length of the specimen CME/D2, cm (%)	pTNM stage CME/D2, n(%)	lymph nodes Harvest CME/D2, mean (SD)	Lymph nodes + CME/D2, n (%)
LaCoMEStaR 2021	Right-sided colon cancer w/o distant metastasis	34.3 (21.5–67)/29.3 (17.5–68)*	T1: 26 (38.8)/31 (47.7) T2: 8 (12.0)/9 (13.8) T3: 29 (43.3)/21 (32.3) T4: 4 (5.9)/4 (6.1) N0: 33 (49.2)/41 (63.1) N1: 24 (35.8)/19 (29.2) N2: 10 (14.9)/5 (7.7) M0: 64 (95.5)/63 (97) M1: 3 (4.5)/2 (3.1)	26 .7 ± 11.8/23.1 ± 8.5[a]	34 (50.7)/24 (36.9)
CoME-in Trial 2024	cT2-4aN0 or cT1-4aN+	29 ± 10)/28 ± 11[a]	I: 20 (16.5)/23 (20.9) II: 64 (52.9)/54 (49.1) III: 37 (30.6)/33 (30.0) IV: 0 (0)/0 (0)	25 ± 14/20 ± 10[a]	38 (29.0)/37 (32.0)
RELARC 2021	Adenocarcinoma cT2–4aN0–2M0 or cTanyN+M0	NA	I: 48 (9.7)/47 (9.4) IIA: 218 (44.0)/226 (45.2) IIB: 47 (9.4)/43 (8.6) IIC: 2 (0.4)/3 (0.6) IIIA: 7 (1.4)/4 (0.8) IIIB: 153 (30.1)/132 (26.4) IIIC: 20 (4.0)/45 (9.0)	24.8 ± 19.6/19.7 ± 24.2[a]	180 (36)/180 (36)
Giani 2022	Right-sided colon cancer w/o distant metastasis	NA	I: 59 (40.4)/58 (39.7) II: 48 (32.9)/48 (32.9) III: 39 (26.7)/40 (27.4)	22.6 ± 9.7/20.0 ± 9.7[a]	39 (26.7)/39 (26.7)
Khan 2021	Right colon, cN1–2 disease	32.2 (30–39)/26 (20.2–3.2)*	T1/T2: 9 (22.5)/32 (40.0) T3/T4: 31 (77.5)/48 (60.0) N0: 25 (62.5)/46 (57.5) N1: 5 (12.5)/22 (27.5) N2: 10 (25.0)/12 (15.0)	36.4 ± 31.5/26.8 ± 33.9[a]	15 (38)/34 (43)
Magistro 2022	Right colon, cN1–2 disease	NA	I: 73 (39.3)/78 (41.9) II: 59 (31.7)/54 (29.0) III: 49 (26.3)/44 (23.7) IV: 5 (2.7)/10 (5.4)	22.3 ± 9.7/19.7 ± 10.4[a]	53 (29.5)/51 (24)
Lieto 2017	Right colon, cN1–2 disease	28.6 ± 3.3/30.5 ± 73[a]	I: 22 (25.0)/7 (15.3) IIA: 18 (20.5)/9 (19.5) IIB: 3 (3.4)/3 (6.5) IIIA: 6 (6.8)/1 (2.2) IIIB: 25 (28.4) /18 (39.2) IIIC: 8 (9.1)/5 (10.8) IVA: 6 (6.8)/3 (6.5)	21 ± 9/13 ± 6[a]	43 (48)/26 (56.5)

[a]Mean ± standard deviation; *Median (range); CME: complete mesocolic excision; D2: conventional. lymphadenectomy. NA: not available

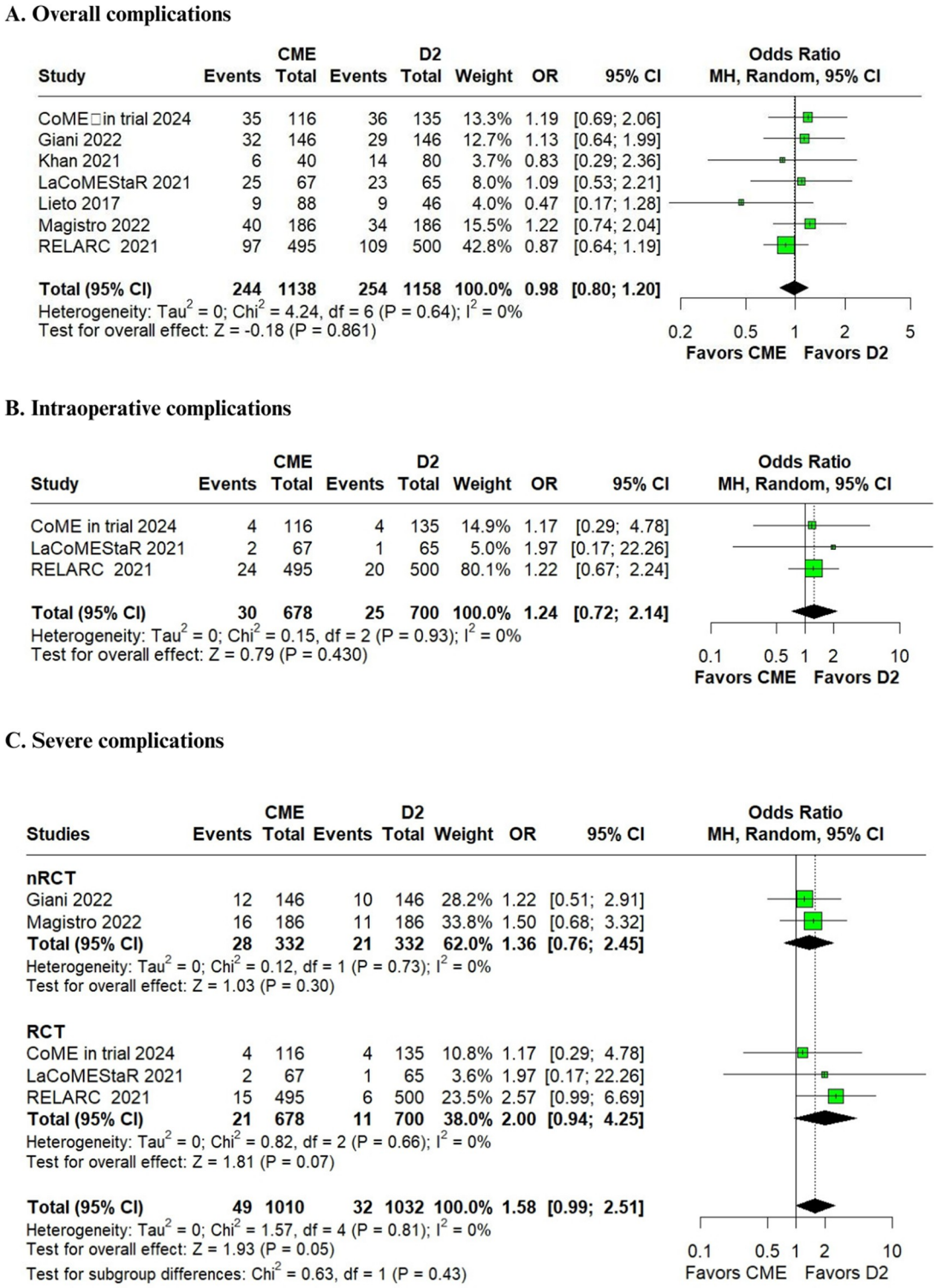
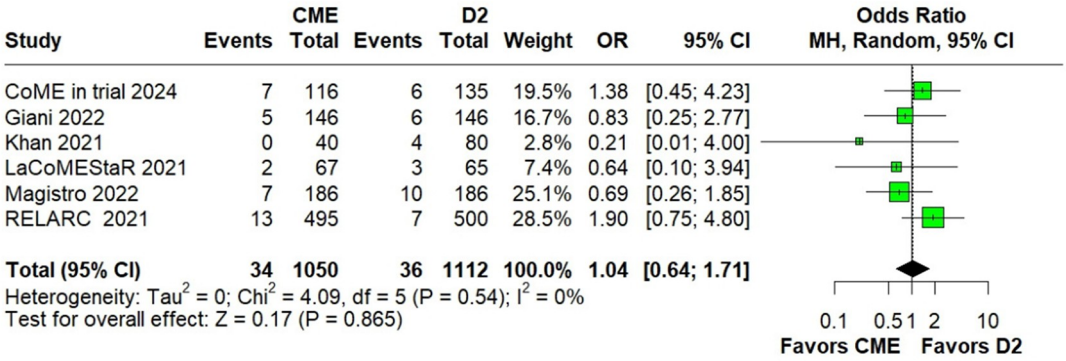


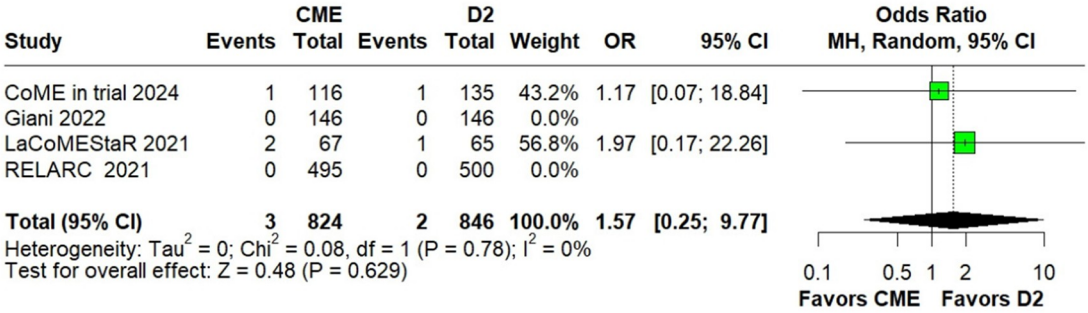
Figure 2. Forest plots of comparison between CME and D2 lymphadenectomy for right hemicolectomy. (A) Overall complications. (B) Intraoperative complications. (C) Severe complications.

be necessary for strong recommendations regarding the adoption of CME as a routine procedure for right-sided colon cancer. Finally, it is essential to highlight that the surgical procedures in the RCTs included in this meta-analysis were performed by high-volume surgeons with experience in surgical oncology techniques, which may limit the reproducibility of the results in general practice settings, where surgeon experience and volume may vary.

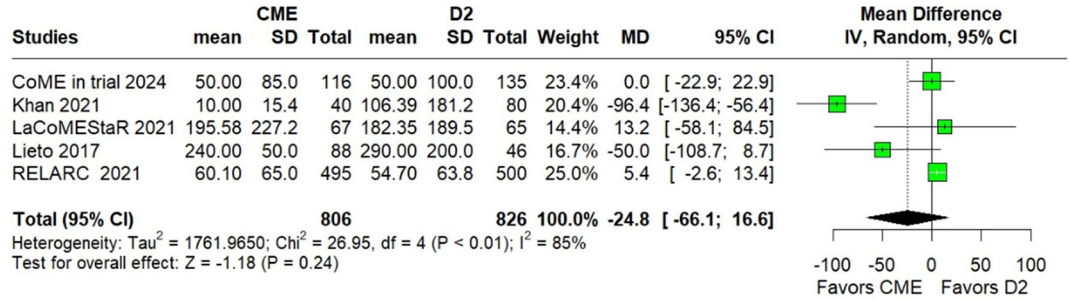
A. Conversion to open surgery



B. 30-day mortality



C. Blood loss



D. Clavien-Dindo ≥ 3

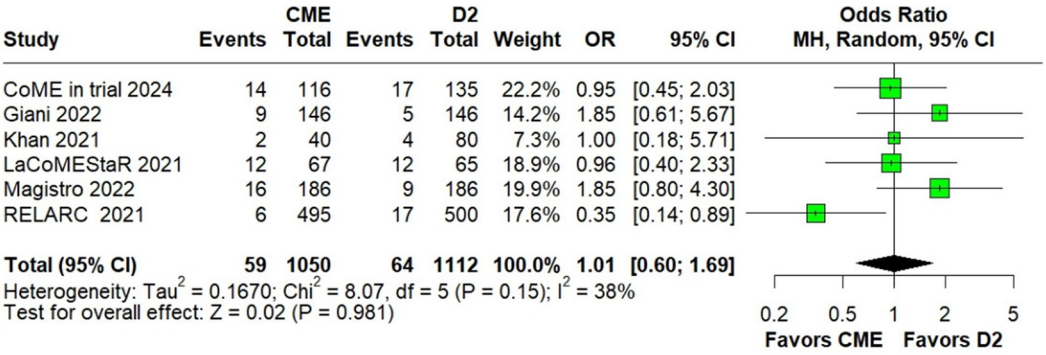


Figure 3. Forest plots of comparison between CME and D2 lymphadenectomy for right hemicolectomy. (A) Conversion to open surgery. (B) 30-day mortality. (C) Blood loss. (D) Clavien-Dindo ≥III.

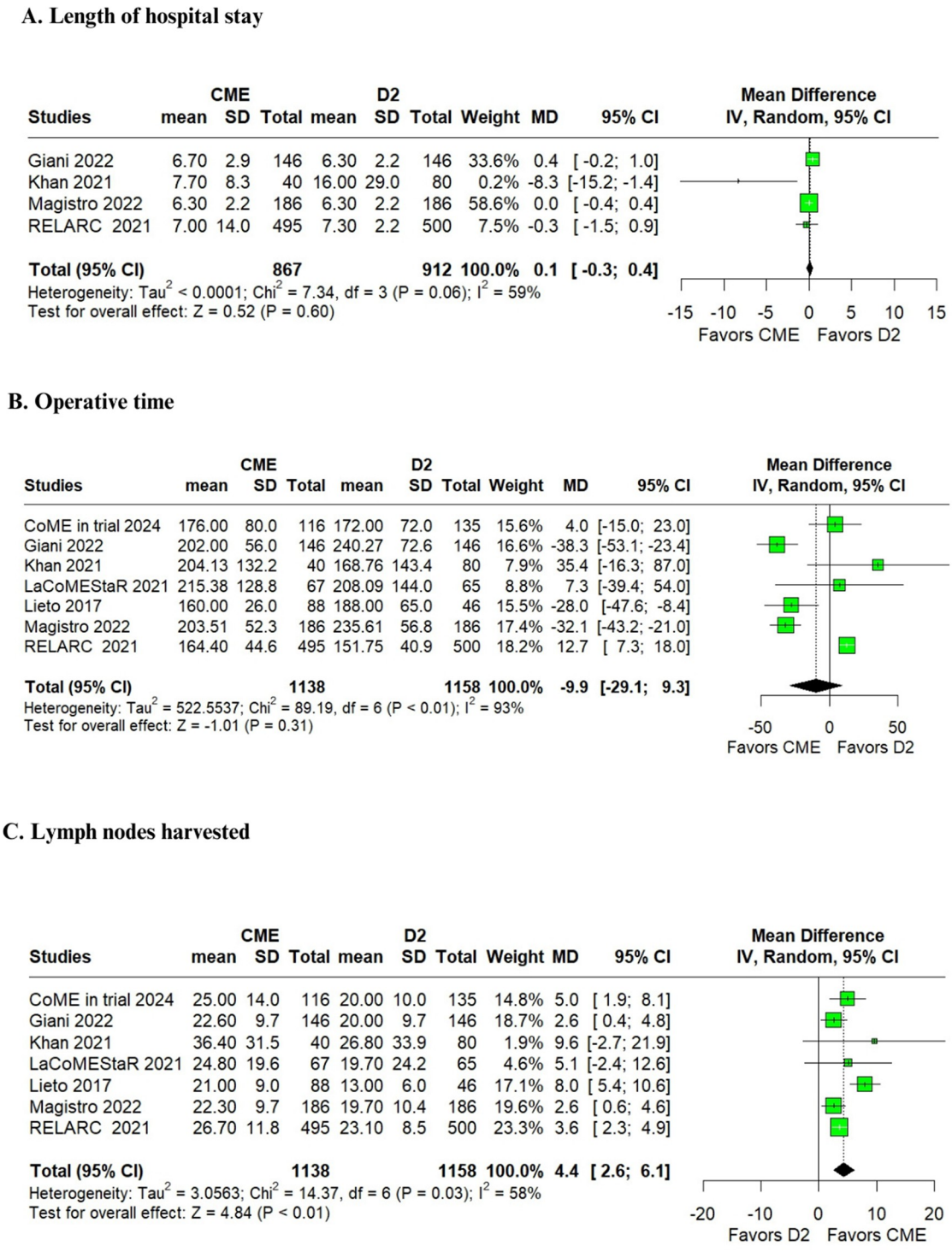


Figure 4. Forest plots of comparison between CME and D2 lymphadenectomy for right hemicolectomy. (A) Length of hospital stay. (B) Operative time. (C) Lymph nodes harvested.

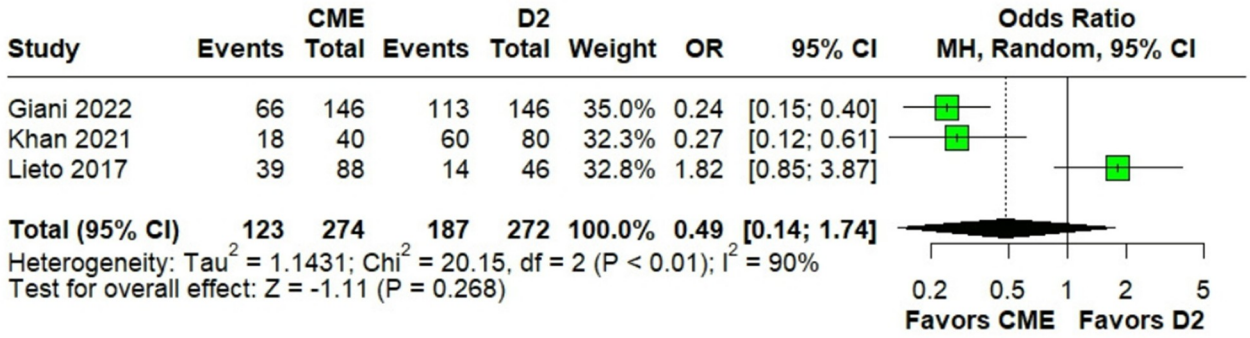
Conclusion

In this meta-analysis of three RCTs, four propensity score-matched studies and 2296 patients undergoing right hemicolectomy for colon cancer, we found that CME was associated with a reduction in local recurrence rates compared with conventional D2 lymphadenectomy. No differences were seen in operative complications, distance metastasis, or survival.

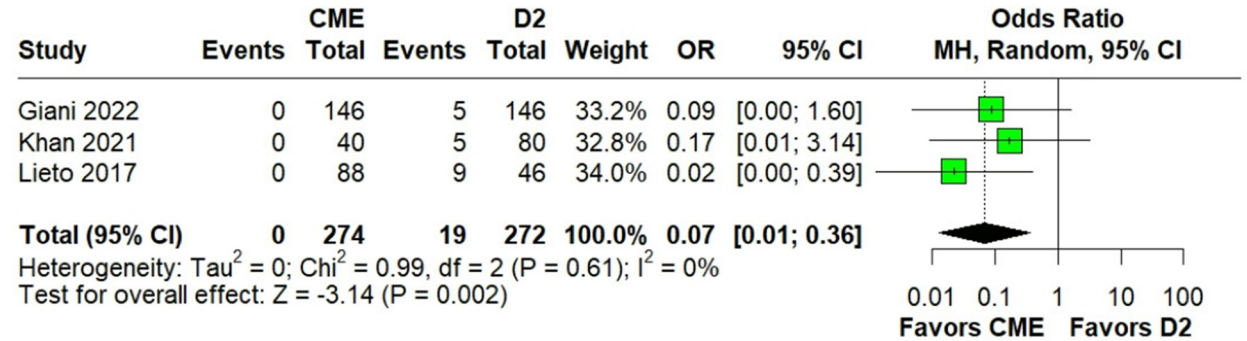
Ethical approval

Ethical approval was not required for this systematic review.

A. 3-years of disease-free survival



B. Local recurrence



C. Distant recurrence

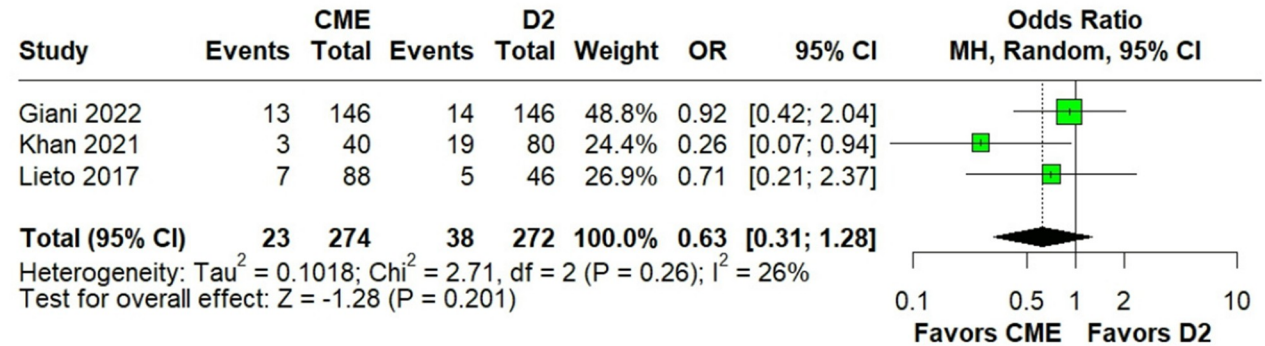
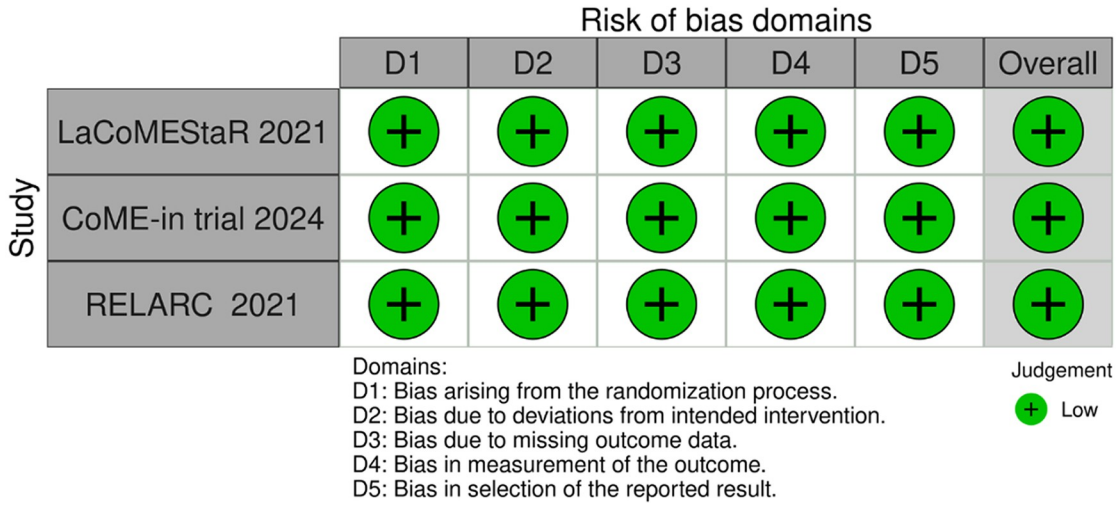


Figure 5. Forest plots of comparison between CME and D2 lymphadenectomy for right hemicolectomy. (A) 3 years disease-free survival. (B) Local recurrence. (C) Distant recurrence.

A. RoB 2



B. ROBINS-I

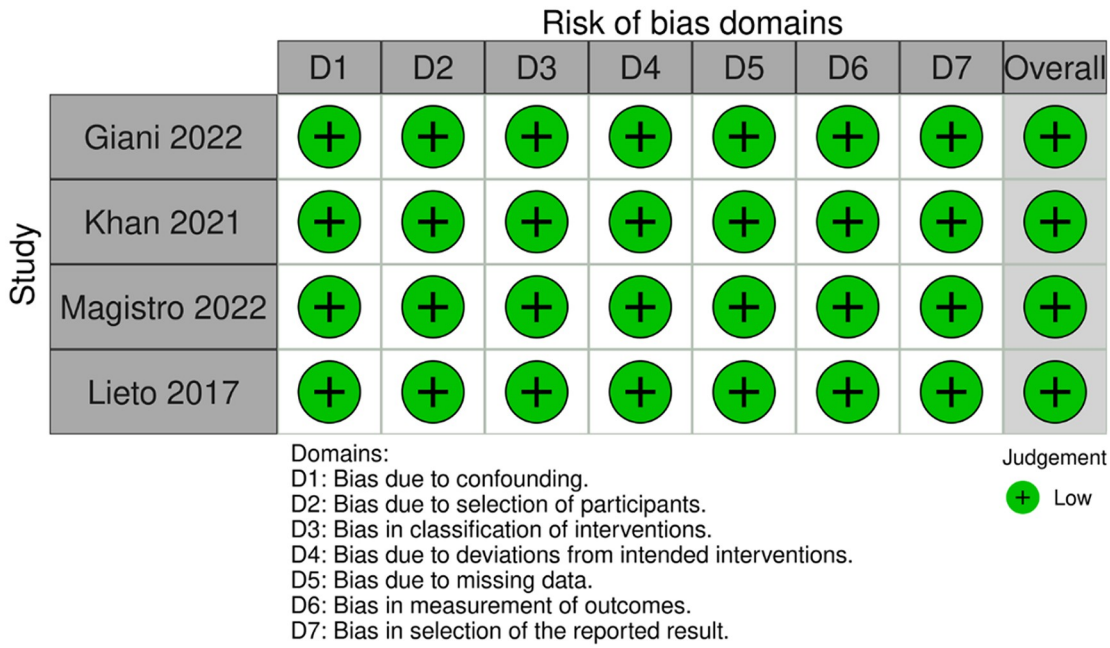


Figure 6. Critical appraisal of nonrandomized and randomized controlled trials according to the Cochrane Collaboration's tool for assessing risk of bias. (A) RoB 2. (B) ROBINS-I.

Consent

All participants provided informed consent prior to study participation. Informed consent was not required for this systematic review.

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None.

Author's contribution

Conceptualization: B.F.P., P.M., F.B.F.; methodology: B.F.P., E. P., P.M., B.D.P., S.M.P.F., F.B.F.; formal analysis and investigation: B.F.P., E.P., L.D.; writing – original draft preparation: B.F. P., E.P., P.M., S.M.P.F.; writing – review and editing: S.M.P.F., B. F.P., P.M., F.B.F. Art: B.D.P.; supervision: B.F.P., S.M.P.F., F.B.F.

Conflicts of interest disclosure

All authors report no relationships that could be construed as a conflict of interest. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. Fernanda Belloti Formiga, MD, is a spokesperson for Janssen Brazil.

Research registration unique identifying number (UIN)

PROSPERO (CRD42024547934).

Guarantor

Bernardo Fontel Pompeu.

Provenance and peer review

Not invited.

Data availability statement

Datasets generated analysing the included studies. All the studies are public available.

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