Techniques in Coloproctology (2019) 23:1023–1035
https://doi.org/10.1007/s10151-019-02079-7

REVIEW

Intracorporeal versus extracorporeal anastomosis in minimally invasive right colectomy: an updated systematic review and meta-analysis

S. H. Emile[1] · H. Elfeki[1,2] · M. Shalaby[1] · A. Sakr[1,3] · M. Bassuni[1,4] · P. Christensen[2] · S. D. Wexner[5]

Received: 22 April 2019 / Accepted: 5 September 2019 / Published online: 23 October 2019

Abstract

Background Minimally invasive colectomy has become the standard for treatment of colonic disease in many centers. Restoration of bowel continuity following resection can be achieved by intracorporeal (IC) or extracorporeal (EC) anastomosis. The aim of this systematic review was to assess the outcomes of IC compared to EC anastomosis in minimally invasive right colectomy.

Methods A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-compliant systematic literature search for studies assessing the outcome of IC and EC anastomosis in laparoscopic and robot-assisted right colectomy was conducted. The primary outcome of this review was postoperative complications. Secondary outcomes included operative time, blood loss, length of stay, conversion to open surgery, and bowel recovery.

Results Twenty-five studies including 4450 patients were evaluated. 47.7% of patients had IC anastomosis and 52.3% had EC anastomosis. The weighted mean length of extraction site incision in the IC group was shorter than the EC group. The EC group had significantly higher odds of conversion to open surgery (OR 1.87, 95% CI 1–3.45, $p=0.046$), total complications (OR 1.54, 95% CI 1.05–2.11, $p=0.007$), anastomotic leakage (AL) (OR 1.95, 95% CI 1.4–2.7, $p=0.003$), surgical site infection (SSI) (OR 1.69, 95% CI 1.4–2.6, $p=0.002$), and incisional hernia (OR 3.14, 95% CI 1.85–5.33, $p<0.001$) compared to the IC group. Both groups had similar rates of ileus, small bowel obstruction, bleeding, and intra-abdominal infection.

Conclusion IC anastomosis was associated with significantly shorter extraction site incisions, earlier bowel recovery, fewer complications, and lower rates of conversion, AL, SSI, and incisional hernia than has the EC anastomosis.

Keywords Intracorporeal · Extracorporeal · Anastomosis · Colectomy · Outcome · Meta-analysis

✉ S. H. Emile
sameh200@hotmail.com

H. Elfeki
hossamelfeki@gmail.com

M. Shalaby
mostafashalaby@mans.edu.eg

A. Sakr
ahmadsakr1987@gmail.com

M. Bassuni
bassuini@aol.com

P. Christensen
petchris@rm.dk

S. D. Wexner
wexners@ccf.org

[1] Colorectal Surgery Unit, Department of General Surgery, Mansoura Faculty of Medicine, Mansoura University Hospitals, Mansoura University, 60 Elgomhuoria Street, PO: 35516, Mansoura, Egypt

[2] Department of Surgery, Aarhus University Hospital, Aarhus, Denmark

[3] Colorectal Surgery Department, Yonsei University College of Medicine, Seoul, South Korea

[4] Department of Surgery, King's College London, London, UK

[5] Department of Colorectal Surgery, Cleveland Clinic Florida, Weston, FL, USA

Introduction

Minimally invasive colectomy has been increasingly used to treat colon cancer and other colonic diseases. Minimally invasive approaches, including laparoscopic and robot-assisted platforms, are associated with a more rapid recovery, less pain, shorter hospitalization, reduced ileus, fewer adhesions, and less postoperative morbidity and mortality, as compared to laparotomy [1–3].

The restoration of bowel continuity after minimally invasive colectomy can be performed in either an intracorporeal (IC) or extracorporeal (EC) manner. There are no clear guidelines on the indications for performing each type of anastomosis, and the selection of IC versus EC anastomosis remains at the discretion of the operating surgeons, depending on their expertise and personal preference.

To perform EC anastomosis, after sufficient mobilization of the colon inside the body, the segment to be resected is delivered outside the body through midline vertical periumbilical incision followed by control of the vascular pedicle, transection, and bowel anastomosis outside the body [4]. On the other hand, in IC anastomosis, the mobilization of the colon, vascular control of the pedicle, resection, and bowel anastomosis are performed inside the body. Afterwards, the resected segment of the colon can be delivered through a midline vertical incision or a Pfannenstiel incision which has been reported to be associated with a lower risk of incisional hernia [5].

A recent systematic review [6] of the outcome of IC and EC anastomosis in laparoscopic right hemicolectomy reported lower short-term complications particularly surgical site infection (SSI), shorter hospital stay, and earlier return of bowel function in favor of IC anastomosis. Both groups were comparable in regard to the incidence of anastomotic leakage (AL), ileus, and operation-related mortality.

The aim of this systematic review was to present an updated analysis of the outcomes of IC and EC anastomosis in minimally invasive right colectomy, including both laparoscopic and robot-assisted approaches. The main outcomes of this review were the incidence of complications, including AL, incisional hernia and SSI, operation time, length of hospital stay, and bowel recovery.

Materials and methods

Registration

The registration number of this systematic review in the PROSPERO register is CRD42019117741. For this type of study, Institutional Review Board (IRB) approval and informed consent from patients were deemed unnecessary.

Search strategy

A systematic literature search for studies that assessed the outcome of IC versus EC colonic anastomosis was performed in line with the screening guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Fig. 1) [7].

We searched electronic databases including PubMed/Medline, Scopus, Embase, and Cochrane library for published and ahead-of-publication studies from January 2000 through October 2018. The PubMed function "related articles" was utilized to extend the search process.

Keywords used in the search process included: *"intracorporeal," "extracorporeal," "laparoscopic," "totally laparoscopic," "laparoscopic-assisted," "right colectomy," "right hemicolectomy," "robotic," "robot-assisted," "anastomosis," "colorectal," "minimally invasive," and "outcome"*. In addition, medical subject headings (MeSH) terms: (colorectal), (anastomosis), (laparoscopic), (robotic), (minimally invasive), and (colectomy) were used.

The bibliography section of each study was searched for other relevant articles. Duplicate publications and conference abstracts with no full-text version were excluded, and the remaining articles were screened by title and abstract, and then subsequently full-text screening followed. The full text of each article was independently reviewed by one of four authors (S.E, H.E, M.S, and A.S) under the guidance and supervision of the senior author (S.D.W.) to verify eligibility for inclusion.

Eligibility criteria

Studies that were considered eligible for inclusion in this review fulfilled three criteria: (1) original articles comparing IC and EC anastomosis in minimally invasive (laparoscopic or robotic) right colectomy; (2) included a minimum of 15 patients in each group; (3) clearly reported the outcomes assessed in this review which include operative time, incidence of AL and other complications, and patients' recovery. Only English-language articles were included.

We excluded irrelevant articles, case series, single-arm cohort studies, editorials, case reports, reviews, meta-analyses, and animal and ex vivo studies that did not meet these criteria. In the case of studies found overlapping with previous studies conducted at the same institution and within the same time frame, only the recent study was selected to be included.

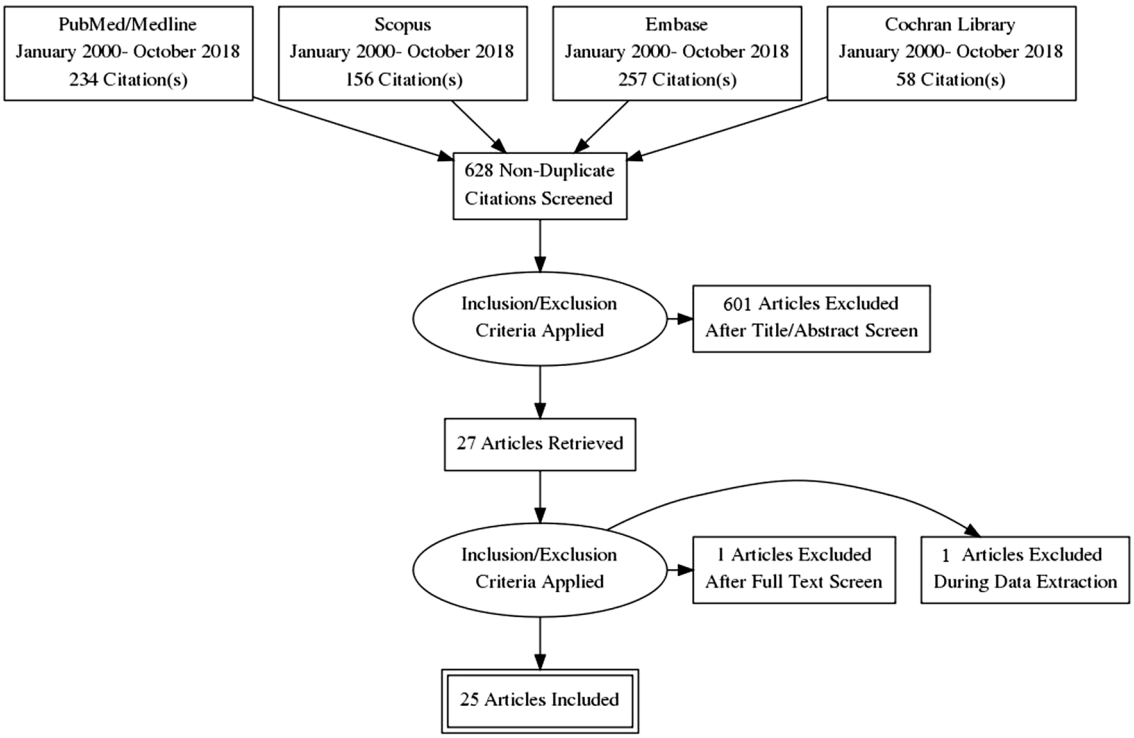

Fig. 1 PRISMA flowchart illustrating the search strategy for the systematic review

Assessment of methodological quality and bias within the included studies

Three investigators (H.E, M.S, A.S) independently assessed the methodological quality and risk of bias in each study and any discrepancies in interpretation were resolved by discussion and mutual agreement.

The revised grading system of the Scottish Intercollegiate Guidelines Network (SIGN) [8] was used to assess the risk of bias in each study: a score of less than 8 indicated poor quality; a score of 8–14 implied fair quality, and a score of more than 14 indicated good quality.

Data collection objectives

The following data were collected from each study included:

- Type, country, and duration of each study.
- Patient characteristics including number, age, gender distribution, body mass index (BMI), and indication for surgery (benign or malignant).
- Technical details of the procedure that comprise the type of minimally invasive approach, length of minilaparotomy incision, type of anastomosis (IC vs EC), method of construction of the anastomosis (hand-sewn vs stapled), operation time, conversion to open surgery, and estimated blood loss.
- Duration of postoperative hospital stay and time to first flatus.
- Number and type of postoperative complications including SSI, bowel obstruction, AL, and incisional hernia.
- Follow-up duration in months.

Outcomes of the review

The primary outcome of this review was the incidence of postoperative complications including SSI, AL, and clinically diagnosed incisional hernia in each group. Four [14, 23, 27, 32] studies defined AL as all conditions with clinical or radiologic anastomotic dehiscence, with or without the need for surgical revision, one study [13] defined it as extravasation of contrast at radiographic imaging, whereas another study [21] identified AL after radiologic confirmation (contrast radiograph or computed tomography scan) or after re-intervention revealing leakage. Secondary outcomes included operative time, estimated blood loss, length of hospital stay, conversion to open surgery, and time to first flatus.

Assessment of publication bias across the included studies

A funnel plot of the standard error of the complication rates against the complication rates of the studies included was used to assess the publication bias across the studies of this

review. In the absence of publication bias, it is assumed that studies with high precision will be plotted near the average (straight vertical line), and studies with low precision will be spread evenly on both sides of the vertical line, creating a funnel-shaped distribution. Publication bias was further assessed using Egger's regression Test.

Statistical analysis

Data were analyzed using SPSS version 23 (IBM corp, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD), or median and normal range. Categorical variables were expressed as number and percentage. A p value less than 0.05 was considered significant.

A meta-analysis of complication rates across the studies was conducted using open-source, cross-platform software for advanced meta-analysis "openMeta[Analyst]™" version 12.11.14. Data were pooled and the weighted mean rates with 95% confidence interval (CI) were calculated. Statistical heterogeneity was determined by the Cochrane Q test and the Inconsistency (I^2) statistics. I^2 is the proportion of total variation observed between the studies attributable to differences between studies rather than sampling error. Heterogeneity was considered low if $I^2 < 25\%$ and high if $I^2 > 75\%$. If no significant statistical heterogeneity was present, a fixed-effect model was used to pool data, whereas in the case of significant ($p < 0.1$) statistical heterogeneity, the binary random-effect model was utilized for pooling of data.

Results

Study and patient characteristics

After initial screening of 705 citations, 25 studies [9–33] were eligible to be included to this review. All included studies were retrospective except one prospective cohort study [28] and one randomized trial [13]. Eighteen studies were single-center studies and seven were multicenter. Nineteen studies were of fair quality and six were of good quality. The median quality score was 13 (range 9–15).

The studies included 4450 patients (male 50.1%; female 49.9%) with a median age of 68.5 (range 60.7–74) years and a median body mass index (BMI) of 26.5 (range 21.7–43.9) kg/m^2. Minimally invasive right colectomy was performed for benign indications in 1077 (24.2%) patients and for colon cancer in 3373 (75.8%) patients. A total of 3255 (73.1%) procedures were performed laparoscopically and 1195 (26.9%) were with robot-assisted approach. The median follow-up duration was 16 (range 1–48) months. The characteristics of the studies reviewed are shown in Table 1.

Demographics of patients in the IC and EC anastomosis groups

A total of 2123 (47.7%) patients had IC anastomosis and 2327 (52.3%) had EC anastomosis. The male-to-female ratio in both groups was 1:1. The median age of patients in both groups was similar (68 years in the IC anastomosis group vs 69 years in the EC anastomosis group). Both groups had similar median BMI (26.2 vs 26.6 kg/m^2).

Four studies [14, 16, 20, 32] reported the number of patients with diabetes mellitus with no difference between the two groups (Akram et al. [14] 23.6% vs 23.6%), (Lujan et al. [16] 19.1% vs 16.3%), (Shaprio et al. [20] 27% vs 28%), and (Scatizzi et al. [32] 7.5% vs 7.5%). There were no data on the smoking status of patients in any of the studies. Malignancy was the indication for right colectomy in 78.4% of patients in the IC anastomosis group and 73.4% of patients in the EC group (Table 2).

Technical details of the IC and EC anastomosis groups

All IC anastomoses and 56% of EC anastomoses were stapled anastomoses. The weighted mean length of the extraction site incision was shorter in the IC group than the EC group (4.9; 95% CI 4.45–5.35 cm vs 7.15; 95% CI 5.9–8.4 cm). The weighted mean difference of 2.24 cm in extraction incision length between the two groups was statistically significant (95% CI 1.23–3.25, $p < 0.001$).

The weighted mean operative time in the IC group was similar to the EC group (159.6; 95% CI 112–207.1 min vs 158.9; 95% CI 138.9–178.9 min). The weighted mean difference in operative times between the two groups was no statistically significant (4.1; 95% CI − 18.6 to 26.9, $p = 0.72$).

The weighted mean estimated blood loss in the IC group was less than in the EC group (66.5; 95% CI 48.5–84.4 ml vs 80.3; 95% CI 66.6–94.1 ml) (Table 3). The weighted mean difference in estimated blood loss between the two groups was statistically significant (12.5; 95% CI 5.6–19.4, $p < 0.001$). The median number of lymph nodes harvested in IC group was 19.1 (range 14–26) compared to 19 (range 11.9–30) in the EC group.

Conversion to open surgery was required in 60 (2.8%) patients in the IC anastomosis group as compared to 123 (5.3%) patients in the EC anastomosis group (Table 3) (OR 1.87, 95% CI 1–3.45, $p = 0.046$, $I^2 = 49.7\%$) (Fig. 2).

Postoperative complications in both groups

Complications developed in 507 (23.8%) patients in the IC group versus 773 (33.2%) in the EC group. Patients in the EC group had significantly higher odds of complications than did patients in the IC group (OR 1.54, 95% CI

Table 1 Characteristics of the studies included in the review

Study	Country	Duration	Type of study	No	Mean age	Male	BMI (Kg/m^2)	Mean follow-up in months	Quality score
Scotton et al. [9]	Italy	Jan 1998–June 2018	Retrospective	366	70.2	188	25.8	19	14
Reitz et al. [10]	USA	Jan 2014–May 2016	Retrospective	49	62.2	21	43.9	2	14
Krouchev et al. [11]	Canada	Jan 2015–Oct 2017	Retrospective	74	69.2	43	NA	1	13
Cleary et al. [12]	USA, multi-center	Jan 2010–July 2016	Retrospective	1029	66	514	29	1	13
Mari et al. [13]	Italy	June 2015–Dec 2016	Randomized trial	60	69	35	25.2	NA	12
Akrami et al. [14]	USA	Feb 2012–Aug 2017	Retrospective	110	66.5	60	27.6	3 m–5.5y	14
Martinek et al. [15]	USA, multi-center	Jan 2014–Dec 2016	Retrospective	390	62.2	170	28	NA	13
Lujan et al. [16]	USA	Jan 2009–March 2015	Retrospective	224	71.7	109	27.7	30	15
Vignali et al. [17]	Italy	Jan 2008–Dec 2015	Retrospective	128	69	86	31.5	48	13
Jian Cheng et al. [18]	China	Jan 2011–Oct 2015	Retrospective	85	68.5	52	20.5	NA	13
Hanna et al. [19]	USA, multi-center	March 2005–June 2014	Retrospective	195	61	87	25.5	10	9
Shapiro et al. [20]	Israel, multi-center	Aug 2006–Dec 2014	Retrospective	191	72	86	27.3	33.7	11
Vergis et al. [21]	Canada	Jan 2008–Sep 2009	Retrospective	50	67	26	28.1	32	12
Trastulli et al. [22]	Italy, multi-center	June 2005–May 2014	Retrospective	236	70.8	133	25.6	1	15
Milone et al. [23]	Italy, multi-center	Jan 2005–Dec 2012	Retrospective	512	66.6	265	25.3	1	15
Marchesi et al. [24]	Italy	Jan 2006–July 2010	Retrospective	55	66.9	24	26.1	NA	11
Magistro et al. [25]	Italy	Jan 2009–Sept 2011	Retrospective	80	71	38	24.3	1	13
Lee et al. [26]	USA, multi-center	March 2005–June 2010	Retrospective	86	69	38	25.7	24	10
Erguner et al. [28]	Turkey	NA	Prospective	30	65.2	15	26.5	28	15
Morpurgo et al. [29]	Italy	Jan 2008–May 2012	Retrospective	96	43	71	26.5	13	14
Roscio et al. [27]	Italy	Apr 2006–Apr 2011	Retrospective	72	63.6	33	26.2	27.7	15
Anania et al. [30]	Italy	Jan 2006– Dec 2010	Retrospective	72	74	44	27.2	NA	13
Fabozzi et al. [31]	Italy	Jan 2001–March 2009	Retrospective	100	60.7	38	21.7	48	14
Scatizzi et al. [32]	Italy	Oct 2006–Aug 2009	Retrospective	80	69.2	37	27.5	NA	15
Hellan et al. [33]	USA	Sept 2004–Apr 2008	Retrospective	80	68	45	27.5	NA	14

BMI body mass index

Table 2 Characteristics of patients in the IC and EC anastomosis groups

Study	Number		Mean age (years)		Males		BMI (Kg/m^2)		Benign indications		Malignant indications	
	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC
Scotton et al. [9]	206	160	70.1	70.3	108	80	26	25.6	0	0	206	160
Reitz et al. [10]	29	20	59.7	64.8	11	10	30.3	28.8	17	8	12	12
Krouchev et al. [11]	18	56	68.8	69.7	12	31	na	na	0	0	18	56
Cleary et al. [12]	379	650	66.2	65.9	180	334	29.6	28.2	192	343	187	307
Mari et al. [13]	30	30	66	72	19	16	24.3	26.1	0	0	30	30
Akrami et al. [14]	55	55	66.5	66.5	27	33	27.6	27.9	17	18	30	30
Martinek et al. [15]	195	195	61.7	62.8	83	87	28.6	27.4	56	47	139	148
Lujan et al. [16]	89	135	70.9	72.6	48	61	28.4	27.1	42	53	47	82
Vignali et al. [17]	64	64	69	69	43	43	31.4	31.6	11	9	53	55
Jian Cheng et al. [18]	56	29	68	69	32	20	20.3	20.6	0	0	56	29
Hanna et al. [19]	86	109	66	59	41	46	25.9	25.1	30	52	56	57
Shapiro et al. [20]	91	100	72	72	38	48	27.8	26.9	21	30	70	70
Vergis et al. [21]	21	29	65	69	13	13	27.6	28.6	12	5	9	24
Trastulli et al. [22]	142	94	68.8	70.8	81	52	25.6	25.4	22	6	120	88
Milone et al. [23]	286	226	67.7	65.6	145	120	25.2	25.4	0	0	286	226
Marchesi et al. [24]	28	27	66.2	67.7	13	11	26.1	26.2	11	10	17	17
Magistro et al. [25]	40	40	70.9	71.2	20	18	24.8	23.9	0	0	40	40
Lee et al. [26]	51	35	70	66	25	13	25.7	25.4	0	0	51	35
Erguner et al. [28]	15	15	67.5	63	8	7	27	26	0	0	15	15
Morpurgo et al. [29]	48	48	68	74	27	16	25	28	0	0	48	48
Roscio et al. [27]	42	30	63.5	63.7	21	12	26	26.3	0	0	42	30
Anania et al. [30]	39	33	74.5	74	24	20	26.3	28.1	14	11	25	22
Fabozzi et al. [31]	50	50	62.1	59.4	21	17	21.4	22.1	0	0	50	50
Scatizzi et al. [32]	40	40	68.5	70	18	19	27	28	0	0	40	40
Hellan et al. [33]	23	57	69	67	16	29	27	28	6	19	17	38

IC intracorporeal, *EC* extracorporeal, *BMI* body mass index

1.13–2.11, $p=0.007$, $I^2=71.2\%$) (Fig. 3). Death of one patient (0.05%) in the IC group and ten (0.43%) patients in the EC group was recorded (OR 1.48, 95% CI 0.71–3.06, $p=0.29$, $I^2=0$).

A total of 68 (2.9%) patients in the EC group and 28 (1.3%) patients in the IC group experienced AL (OR 1.95, 95% CI 1.25–3.06, $p=0.003$, $I^2=0$) (Fig. 4). SSI developed in 157 (6.7%) patients in the EC group and 86 (4%) patients in the IC group (OR 1.69, 95% CI 1.2–2.4, $p=0.002$, $I^2=18.1$). Excluding five studies with only 1 month of follow-up, 5.2% (66/1261) patients in the EC group developed incisional hernia as compared to 1.1% (14/1258) patients in the IC group (OR 3.14, 95% CI 1.85–5.33, $p<0.001$, $I^2=0$) (Fig. 5).

53 (2.5%) patients in the IC group and 95 (4.1%) patients in the EC group experienced postoperative ileus (OR 1.33, 95% CI 0.93–1.9, $p=0.11$, $I^2=0$). 30 (1.4%) patients in the IC group and 29 (1.2%) in the EC group developed small bowel obstruction (SBO) postoperatively (OR 0.79, 95% CI 0.48–1.3, $p=0.36$, $I^2=0$). Intra-abdominal infection was recorded in 14 (0.66) patients in the IC group and 4 (0.6%) patients in the EC group (OR 1.06, 95% CI 0.57–1.95, $p=0.85$, $I^2=0$). 71 (3.3%) patients experienced postoperative hemorrhage in the IC groups versus 77 (3.3%) patients in the EC group (OR 0.96, 95% CI 0.69–1.33, $p=0.8$, $I^2=0$). A summary of the main complications recorded in each group is provided in Table 4.

Hospital stay and bowel recovery

The median length of hospital stay in the IC group was shorter than that of the EC group (5.1; range 3–11.5 days vs 6.5; range 3–12.2 days). The median time to flatus was shorter in the IC group than in the EC group (2.3 vs 2.6 days) and the median time to first bowel movement was shorter in the IC group than the EC group (3, range 1.5–3.8 days vs 3.9, range 2–4.9 days).

Publication bias assessment

The symmetry of the funnel plot (Fig. 6) with the majority of the studies present near the straight vertical line in the

Table 3 Technical and operative details of IC and EC anastomosis groups

Study	Stapled		Hand-sewn		Laparo-scopic		Robotic		Mean operation time (min)		Conversion		Lymph nodes harvested	
	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC
Scotton et al. [9]	206	0	0	160	0	160	206	0	253	209.9	5	29	23.1	20.5
Reitz et al. [10]	29	0	0	20	0	0	29	20	143.5	139.8	0	4	NA	NA
Krouchev et al. [11]	18	NA	0	NA	18	56	0	0	157.6	145	0	0	NA	NA
Cleary et al. [12]	379	0	0	650	44	397	335	253	186	150	1	19	NA	NA
Mari et al. [13]	NA	NA	NA	NA	30	30	0	0	NA	NA	0	0	NA	NA
Akrami et al. [14]	55	0	0	55	0	0	55	55	167.7	140.9	0	7	NA	NA
Martinek et al. [15]	195	195	0	0	195	195	0	0	132	140	20	7	NA	NA
Lujan et al. [16]	89	135	0	0	0	135	89	0	190.2	98.8	2	9	14.1	11.9
Vignali et al. [17]	64	64	0	0	64	64	0	0	185.1	173	4	11	21	21
Jian Cheng et al. [18]	56	29	0	0	56	29	0	0	24.7	27.4	0	0	18.5	19.2
Hanna et al. [19]	86	109	0	0	86	109	0	0	183	184.5	0	10	18	19
Shapiro et al. [20]	91	NA	0	NA	91	100	0	0	155	142	1	1	17	15
Vergis et al. [21]	21	29	0	29	21	29	0	0	170	181	0	0	19.1	17.2
Trastulli et al. [22]	NA	94	NA	94	40	94	142	0	204.3	208	10	8	19	19.5
Milone et al. [23]	286	226	0	0	286	226	0	0	166.9	157.5	9	14	18.5	17.5
Marchesi et al. [24]	28	0	0	27	28	27	0	0	205.8	196.8	0	0	20.9	17.3
Magistro et al. [25]	40	40	0	40	40	40	0	0	230	203	0	0	22	20
Lee et al. [26]	51	35	0	0	51	35	0	0	197	197	0	3	20	17
Erguner et al. [28]	15	15	0	0	15	15	0	0	100	90	0	0	22	23
Morpurgo et al. [29]	48	0	0	48	0	48	48	0	266	223	0	0	26	25
Roscio et al. [27]	42	0	0	30	42	30	0	0	176.5	186.3	0	0	25.9	22.8
Anania et al. [30]	39	33	0	0	39	33	0	0	186.8	184.1	0	0	19	14
Fabozzi et al. [31]	NA	NA	NA	NA	50	50	0	0	78	92	5	0	16.1	17.2
Scatizzi et al. [32]	40	40	0	0	40	40	0	0	150	150	2	1	26	30
Hellan et al. [33]	23	57	0	0	23	57	0	0	190	180	1	0	18	17

plot indicated no significant publication bias in the studies reviewed. According to the Egger's regression Test, the intercept was 1.15 with standard error of 0.64 and a two-tailed p value of 0.08 indicating no significant publication bias.

Discussion

Minimally invasive colectomy, whether by a laparoscopic or a robotic approach, has become the standard of treatment for benign and malignant colonic diseases in many centers around the world [34]. Viewing the current literature, a number of technical variations in minimally invasive right colectomy can be recognized. One of the important technical aspects is the technique used for restoration of bowel continuity in either an IC or EC manner.

The present systematic review included 25 studies comprising more than 4400 patients, more than double the number of patients included in a previous systematic review [6] of IC and EC anastomosis in laparoscopic right colectomy. About three-quarter of cases were performed laparoscopically and 27% by the robot-assisted approach. Colon cancer accounted for 75% of the indications for minimally invasive right colectomy.

EC anastomosis was associated with significantly higher odds of complications than IC anastomosis. To explain the higher incidence of complications in the EC group, we individually analyzed each complication, including AL, SSI, incisional hernia, SBO, ileus, bleeding, and intra-abdominal infection.

AL is one of the most dreaded complications in colorectal surgery. Although it has been suggested that inadequate perfusion of the anastomosis is the cornerstone in the development in AL, the exact mechanism behind failure of healing of the anastomosis is still not completely understood [35, 36].

In contradiction to previous reviews [6, 37, 38] that found no difference in AL between the two anastomotic techniques, we noted that EC had significantly higher odds of AL than did IC anastomosis. A potential explanation of this observation is that EC anastomosis requires exteriorization of the

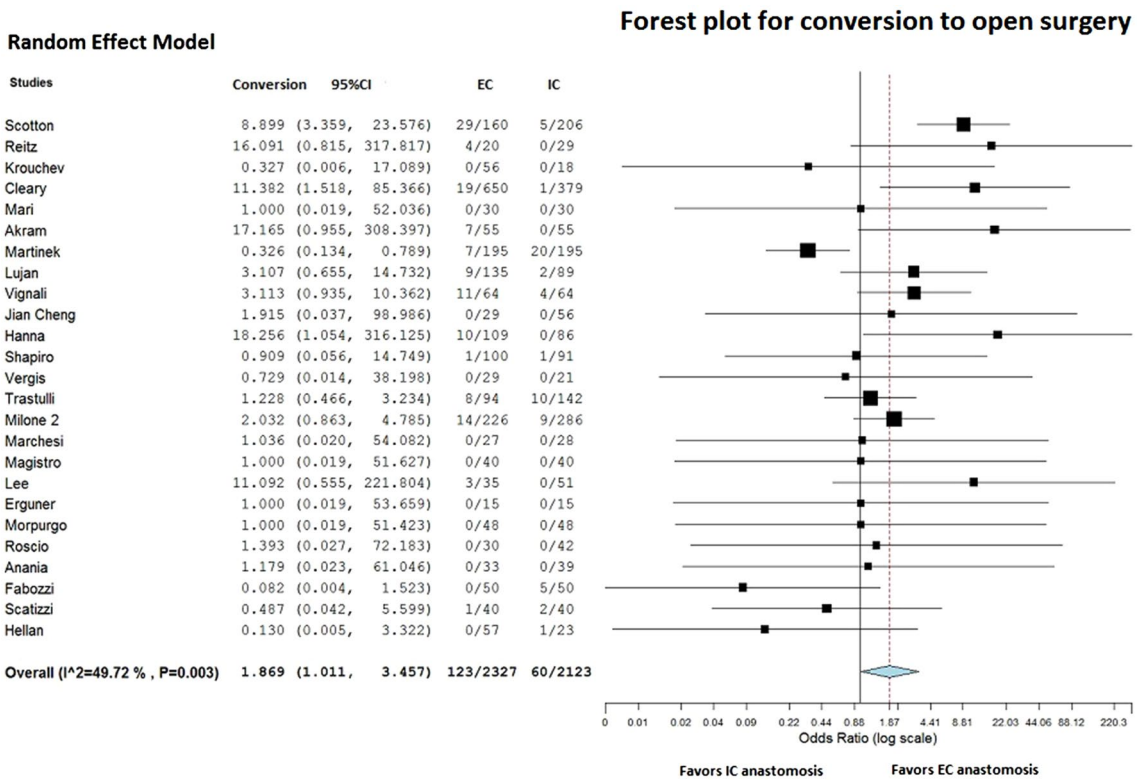

Fig. 2 Forest plot of the rate of conversion to open surgery in each group

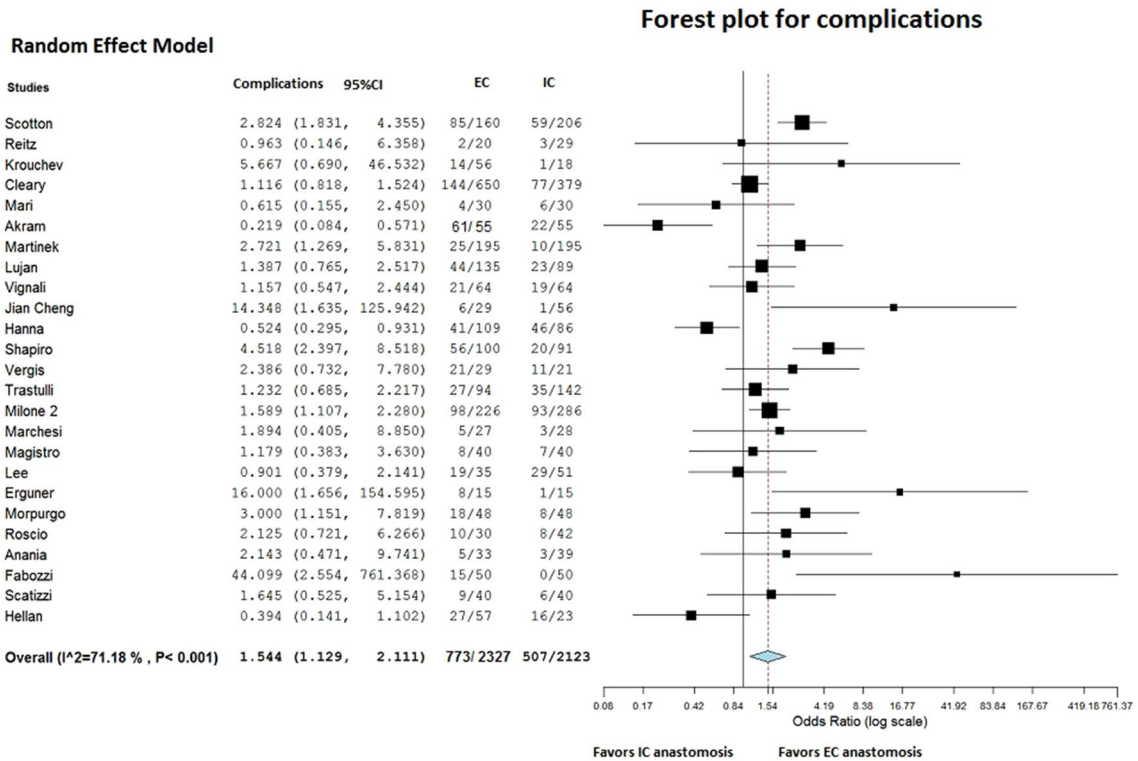

Fig. 3 Forest plot of complication rate in each group

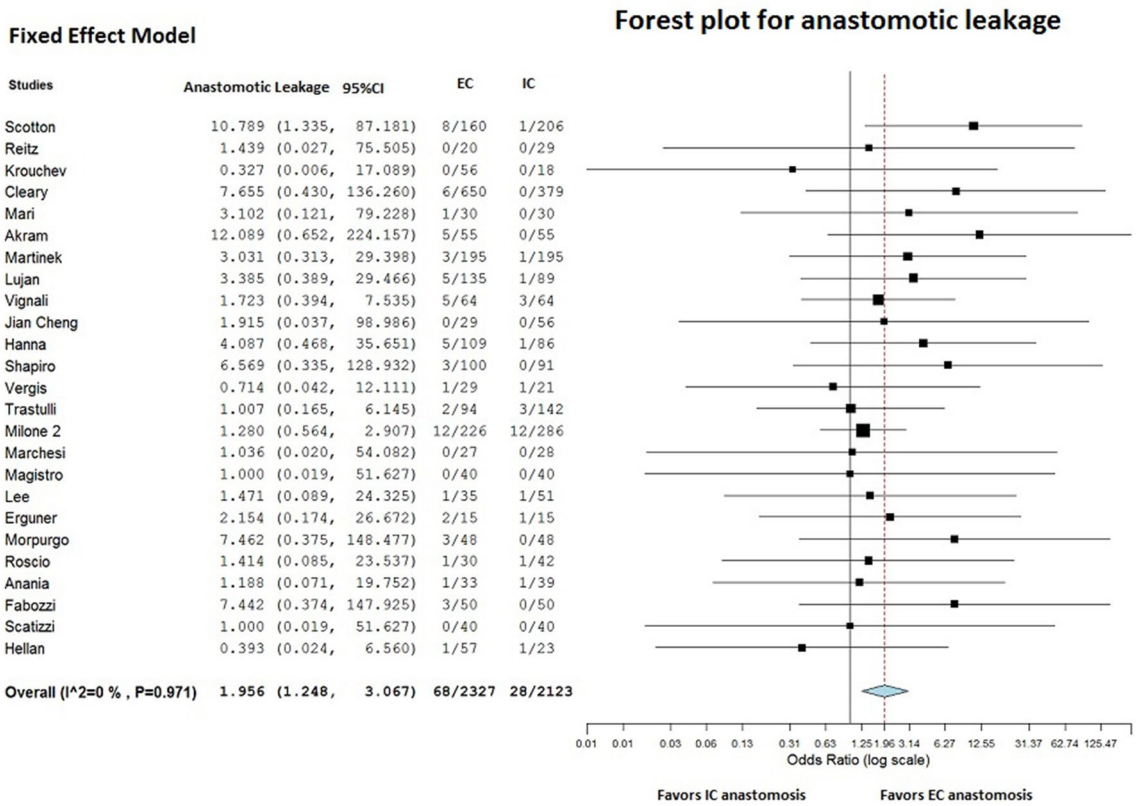

Fig. 4 Forest plot of anastomotic leakage rate in each group

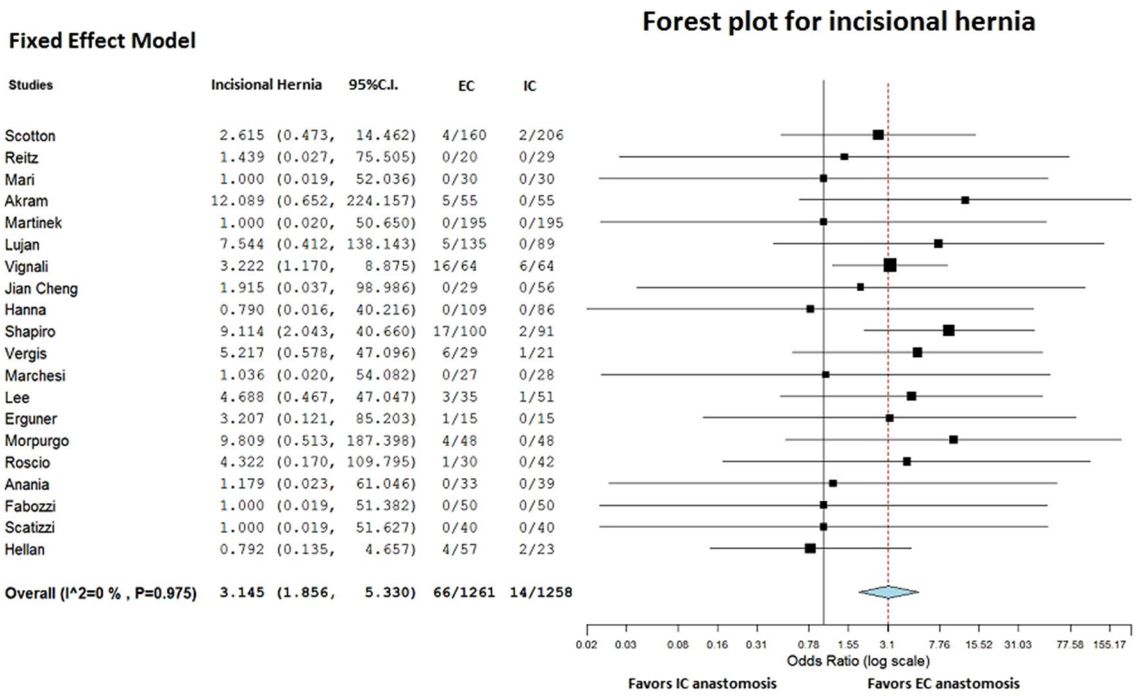

Fig. 5 Forest plot of incisional hernia rate in each group

Table 4 Complications recorded in the IC and EC anastomosis groups

Study	Total complications		Anastomotic leakage		SSI		Intra-abdominal infection		Incisional hernia		Ileus		Bowel obstruction		Bleeding	
	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC	IC	EC
Scotton et al. [9]	59	85	1	8	13	14	2	5	2	4	0	0	0	0	1	7
Reitz et al. [10]	3	2	0	0	0	0	0	1	0	0	0	1	0	0	1	0
Krouchev et al. [11]	1	14	0	0	1	2	0	0	0	0	0	12	0	0	0	0
Cleary et al. [12]	77	144	0	6	7	25	0	0	0	0	11	24	1	7	20	35
Mari et al. [13]	6	4	0	1	0	3	0	0	0	0	4	0	0	0	2	0
Akrami et al. [14]	22	61	0	5	0	4	0	0	0	5	5	12	0	0	0	0
Martinek et al. [15]	10	25	1	3	2	9	0	0	0	0	1	2	0	0	2	3
Lujan et al. [16]	23	44	1	5	3	6	0	0	0	5	4	15	1	3	1	0
Vignali et al. [17]	19	21	3	5	5	11	3	0	6	16	0	0	4	2	1	1
Jian Cheng et al. [18]	1	6	0	0	1	4	0	0	0	0	0	0	0	1	0	1
Hanna et al. [19]	46	41	1	5	9	6	3	4	0	0	0	0	19	9	0	0
Shapiro et al. [20]	20	56	0	3	4	14	1	1	2	17	6	10	0	2	3	4
Vergis et al. [21]	11	21	1	1	3	7	0	1	1	6	0	0	0	0	0	0
Trastulli et al. [22]	35	27	3	2	9	5	2	1	0	0	3	3	5	3	7	4
Milone et al. [23]	93	98	12	12	11	24	0	0	0	0	0	0	0	0	26	17
Marchesi et al. [24]	3	5	0	0	0	0	0	0	0	0	1	0	0	0	1	0
Magistro et al. [25]	7	8	0	0	0	1	0	0	0	0	1	1	0	0	3	3
Lee et al. [26]	29	19	1	1	6	3	3	1	1	3	12	6	0	0	0	0
Erguner et al. [28]	1	8	1	2	0	3	0	0	0	1	0	0	0	0	0	0
Morpurgo et al. [29]	8	18	0	3	5	7	0	0	0	4	0	0	0	0	0	0
Roscio et al. [27]	8	10	1	1	1	1	0	0	0	1	0	0	0	0	0	1
Anania et al. [30]	3	5	1	1	0	0	0	0	0	0	0	0	0	1	0	0
Fabozzi et al. [31]	0	15	0	3	0	3	0	0	0	0	0	0	0	0	0	0
Scatizzi et al. [32]	6	9	0	0	1	2	0	0	0	0	0	0	0	0	2	0
Hellan et al. [33]	16	27	1	1	5	3	0	0	2	4	5	9	0	1	1	1
Total	507	773	28	68	86	157	14	14	14	66	53	95	30	29	71	77

IC intracorporeal, *EC* extracorporeal, *SSI* surgical site infection

bowel ends which necessitates greater colonic mobilization. Traction on the bowel ends through the extraction site incision, especially in obese individuals with thick abdominal wall, may lead to mesenteric injuries, compromising the blood supply of the anastomosis [39, 40]. Conversely, IC anastomosis does not require as much mobilization, and therefore, there is less traction on the bowel ends and the mesentery.

Another difference that may explain the higher incidence of AL in the EC group may be the method of performing the anastomosis in each group. While all IC anastomosis were stapled, approximately half of the EC anastomosis was hand-sewn. This finding is consistent with a Cochrane review [41] in which higher rates of AL were noted after hand-sewn as compared to stapled ileocolic anastomosis.

There were higher odds of developing SSI in the EC group as compared to with the IC group. This was in line with the findings of Ricci et al. [38] who reported reduced risk of wound infection in favor of IC anastomosis. Martinek et al. [15] also found the rate of incisional SSI significantly lower in the IC group than the EC group. In contrast, another systematic review [37] concluded that there was no significant difference in wound infection rates between the two groups. The higher incidence of infection at the extraction site incision in EC anastomosis may be due to wound contamination during exteriorization of the bowel ends and performing the anastomosis through the incision [38]. On the other hand, both groups had a similar incidence of intra-abdominal infection. Although one might hypothesize a higher likelihood of intra-abdominal contamination using the IC method with open bowel ends present within the abdomen, this was not proven given the lack of difference in the rates of intra-abdominal infection between the two groups.

In agreement with previous studies [37, 38], patients who had an EC anastomosis were more likely to develop

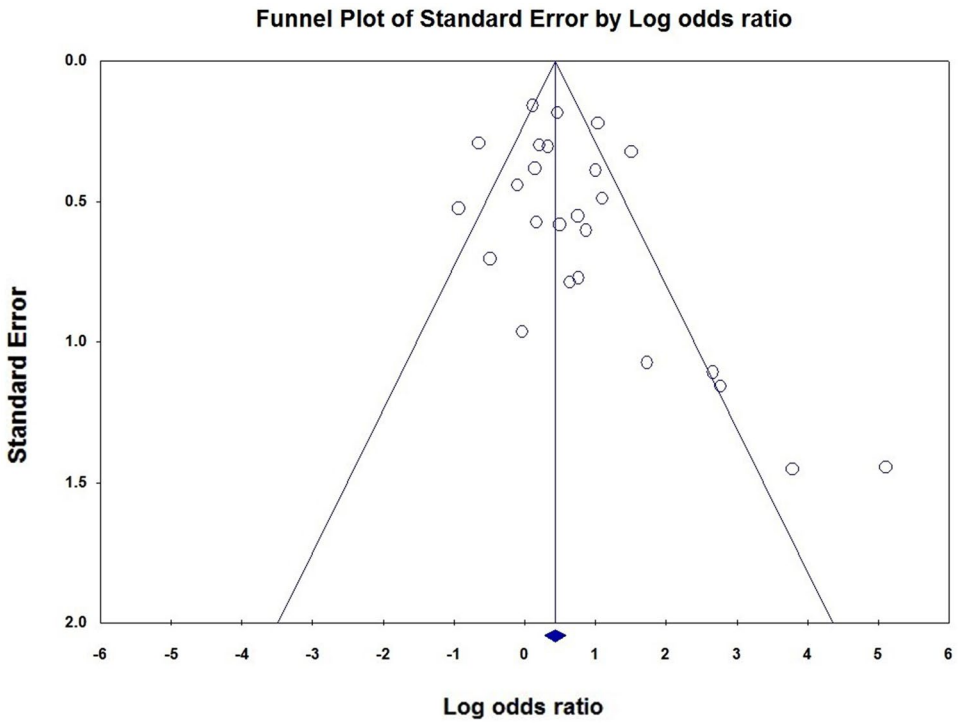

Fig. 6 Symmetrical funnel plot with the majority of the studies present near the straight vertical line in the plot indicating no significant publication bias in the studies reviewed

incisional hernia perhaps due to the longer incision required for specimen extraction and anastomosis, in the EC group. Indeed, the present systematic review found the extraction site incision to be about 2.2 cm longer in the EC group than the IC group in which the incision size was limited only by the size of the pathology [14]. In addition to its length, the location of the extraction site incision may also affect the development of incisional hernia. The extraction site incision in the EC group is usually at the midline, which is associated with the highest risk of incisional hernia, whereas extraction of the specimen in the IC group can be performed through a Pfannenstiel incision, away from the midline [4, 5]. We excluded the studies with short follow-up from the analysis to have more accurate estimates of incisional hernia rates; however, in the vast majority of the studies, the diagnosis of incisional hernia was made on a clinical basis without routine assessment by abdominal wall imaging.

Both groups had comparable odds of developing paralytic ileus and small bowel obstruction. In agreement with other authors [37, 38], the mean hospital stay was shorter in the IC group, probably because of the smaller extraction site incision that was associated with less postoperative pain and quicker recovery. Recovery of gastrointestinal function, as demonstrated by time to first flatus and time to bowel movement, was quicker in the IC anastomosis group than the EC group which goes against the findings of Ricci and colleagues [38]. Earlier recovery in the IC groups may be explained by the technical challenges of EC anastomosis in which traction on the bowel ends and the mesentery is applied with complete mobilization of the transverse colon to reach the incision. Perhaps, performing these maneuvers delays recovery of gastrointestinal function [14, 22].

A recent randomized trial [13] confirmed this hypothesis by noting that IC anastomosis is associated with significantly less surgical stress response and earlier gastrointestinal recovery as compared to EC anastomosis. The surgical stress response was assessed by measuring several markers including interleukin-6, C-reactive protein, procalcitonin, white blood cell count, and cortisol within the first 5 days after surgery. The IC group had significantly lower interleukin-6 and C-reactive protein levels did than the EC group.

The mean operative time in the IC anastomosis group was comparable to the EC group in agreement with previous reviews [37, 38]. However, Akram et al. [14] assumed that IC anastomosis may be associated with longer operative time because of the time required to release the terminal ileum, right colon, and associated mesentery from retroperitoneal and side wall attachments completely to allow performing the anastomosis and retrieval of the specimen.

Although three systematic reviews [6, 37, 38] on the same subject as our review have been published, the previous reviews focused only on laparoscopic right colectomy, whereas our review expanded the scope by including robot-assisted right colectomy, hence covering the spectrum of minimally invasive right colectomy. The number of studies in our review and the number of patients analyzed are larger than the previous reviews (25 studies versus 12, 14, and 15 studies). Previous reviews concluded that IC and

EC anastomoses yield similar rates of complications, particularly AL, whereas our review concluded that there were significantly higher rates of AL, SSI, and incisional hernia in the EC anastomosis group which is an original finding. Finally, our review included one randomized trial [13].

Limitations of the present systematic review include the fair quality of the majority of the studies with only one randomized trial included. The short-term follow-up in most of the studies did not allow us to conduct further analysis of the oncologic outcome of both groups. The definition of "conversion" was not universally reported, and therefore, the differences noted between the IC and EC groups may not be meaningful. The majority of the studies did not include a clear definition of AL, whereas the remaining studies included different definitions; therefore, the interpretation of data on AL in the IC and EC groups should be made with caution. Finally, although EC anastomosis appeared to have significantly higher odds of complications, including AL, SSI and incisional hernia, than IC anastomosis, this statistical significance may not necessarily translate to clinical significance in light of the limitations cited above. Given the limitations of the present review, a well-designed multicenter randomized trial comparing both anastomotic techniques with long follow-up is needed to corroborate our initial conclusions.

Conclusions

On the basis of the available heterogenous literature with variable or absent definitions of "conversion" and of anastomotic leak, IC anastomosis was associated with shorter extraction site incision, fewer complications, and lower rates of conversion to open surgery, AL, SSI, and incisional hernia than the EC anastomosis. Both groups had comparable rates of SBO, ileus, bleeding, and intra-abdominal infection.

Author contributions SHE designed the study. SHE, HE, MS, and AS participated in data collection and analysis, writing and drafting of the manuscript. MB and PC participated in data interpretation, drafting, and critical revision of the manuscript. SDW reviewed the collected results on regular basis and participated in drafting and critical revision of the manuscript.

Funding The authors have no relevant sources of funding to disclose.

Compliance with ethical standards

Conflict of interest The authors have no relevant conflict of interest to disclose.

Ethical approval Ethical approval for this kind of studies (systematic review) was not required.

Informed consent Informed consent is not required for this kind of studies (systematic review).

References

1. Papageorge CM, Zhao Q, Foley EF, Harms BA, Heise CP, Carchman EH, Kennedy GD (2016) Short-term outcomes of minimally invasive versus open colectomy for colon cancer. J Surg Res 204(1):83–93. https://doi.org/10.1016/j.jss.2016.04.020
2. Ma S, Chen Y, Chen Y et al (2018) Short-term outcomes of robotic-assisted right colectomy compared with laparoscopic surgery: a systematic review and meta-analysis. Asian J Surg. https://doi.org/10.1016/j.asjsur.2018.11.002
3. Park JS, Kang H, Park SY, Kim HJ, Woo IT, Park IK, Choi GS (2018) Long-term oncologic after robotic versus laparoscopic right colectomy: a prospective randomized study. Surg Endosc. https://doi.org/10.1007/s00464-018-6563-8 **(Epub ahead of print)**
4. Samia H, Lawrence J, Nobel T, Stein S, Champagne BJ, Delaney CP (2013) Extraction site location and incisional hernias after laparoscopic colorectal surgery: should we be avoiding the midline? Am J Surg 205:264–267
5. Brady MT (2019) The advantage of intracorporeal techniques. Ann Laparosc Endosc Surg 4:12
6. van Oostendorp S, Elfrink A, Borstlap W et al (2016) Intracorporeal versus extracorporeal anastomosis in right hemicolectomy: a systematic review and meta-analysis. Surg Endosc 31(1):64–77
7. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 6(6):e1000097. https://doi.org/10.1371/journal.pmed1000097
8. Scottish Intercollegiate Guidelines Network (SIGN) guidelines, methodology checklist 3. [http://www.sign.ac.uk/methodology/checklists.html]. Accessed 10 Jan 2019
9. Scotton G, Contardo T, Zerbinati A, Tosato SM, Orsini C, Morpurgo E (2018) From laparoscopic right colectomy with extracorporeal anastomosis to robot-assisted intracorporeal anastomosis to totally robotic right colectomy for cancer: the evolution of robotic multiquadrant abdominal surgery. J Laparoendosc Adv Surg Tech A 28(10):1216–1222. https://doi.org/10.1089/lap.2017.0693
10. Reitz ACW, Lin E, Rosen SA (2018) A single surgeon's experience transitioning to robotic-assisted right colectomy with intracorporeal anastomosis. Surg Endosc 32(8):3525–3532. https://doi.org/10.1007/s00464-018-6074-7
11. Krouchev R, Tamana S, Nguyen N, Yorke E, Harris D, Sampath S (2018) Total intracorporeal anastomosis for right hemicolectomy: experience from a canadiancenter. Am J Surg 215(5):905–908. https://doi.org/10.1016/j.amjsurg.2018.02.01
12. Cleary RK, Kassir A, Johnson CS et al (2018) Intracorporeal versus extracorporeal anastomosis for minimally invasive right colectomy: a multi-center propensity score-matched comparison of outcomes. PLoS One 13(10):e0206277. https://doi.org/10.1371/journal.pone.0206277
13. Mari GM, Crippa J, Costanzi ATM et al (2018) Intracorporeal anastomosis reduces surgical stress response in laparoscopic right hemicolectomy: a prospective randomized trial. Surg Laparosc Endosc Percutan Tech 28(2):77–81. https://doi.org/10.1097/SLE.0000000000000506
14. Akram WM, Al-Natour RH, Albright J, Wu J, Ferraro J, Shanker BA, McClure AM, Cleary RK (2018) A propensity score-matched comparison of intracorporeal and extracorporeal techniques for robotic-assisted right colectomy in an enhanced recovery pathway. Am J Surg. https://doi.org/10.1016/j.amjsurg.2018.06.010

15. Martinek L, You K, Giuratrabocchetta S, Gachabayov M, Lee K, Bergamaschi R (2018) Does laparoscopic intracorporeal ileocolic anastomosis decreases surgical site infection rate? A propensity score-matched cohort study. Int J Colorectal Dis 33(3):291–298. https://doi.org/10.1007/s00384-017-2957-7
16. Lujan HJ, Plasencia G, Rivera BX, Molano A, Fagenson A, Jane LA, Holguin D (2018) Advantages of robotic right colectomy with intracorporeal anastomosis. Surg Laparosc Endosc Percutan Tech 28(1):36–41. https://doi.org/10.1097/sle.0000000000000384
17. Vignali A, Elmore U, Lemma M, Guarnieri G, Radaelli G, Rosati R (2018) Intracorporeal versus extracorporeal anastomoses following laparoscopic right colectomy in obese patients: a case-matched study. Dig Surg 35(3):236–242. https://doi.org/10.1159/000479241
18. Jian-Cheng T, Shu-Sheng W, Bo Z, Jian F, Liang Z (2016) Total laparoscopic right hemicolectomy with 3-step stapled intracorporeal isoperistaltic ileocolic anastomosis for colon cancer: an evaluation of short-term outcomes. Medicine (Baltimore) 95(48):e5538. https://doi.org/10.1097/MD.0000000000005538
19. Hanna MH, Hwang GS, Phelan MJ et al (2016) Laparoscopic right hemicolectomy: short- and long-term outcomes of intracorporeal versus extracorporeal anastomosis. Surg Endosc 30(9):3933–3942. https://doi.org/10.1007/s00464-015-4704-x **(Epub 2015 Dec 29)**
20. Shapiro R, Keler U, Segev L et al (2016) Laparoscopic right hemicolectomy with intracorporeal anastomosis: short- and longterm benefits in comparison with extracorporeal anastomosis. Surg Endosc 30(9):3823–3829
21. Vergis AS, Steigerwald SN, Bhojani FD et al (2015) Laparoscopic right hemicolectomy with intracorporeal versus extracorporeal anastamosis: a comparison of short-term outcomes. Can J Surg 58:63–68
22. Trastulli S, Coratti A, Guarino S et al (2015) Robotic right colectomy with intracorporeal anastomosis compared with laparoscopic right colectomy with extracorporeal and intracorporeal anastomosis: a retrospective multicentre study. Surg Endosc 29(6):1512–1521. https://doi.org/10.1007/s00464-014-3835-9
23. Milone M, Elmore U, Di Salvo E et al (2015) Intracorporeal versus extracorporeal anastomosis. Results from a multicentre comparative study on 512 right-sided colorectal cancers. Surg Endosc 29(8):2314–2320. https://doi.org/10.1007/s00464-014-3950-7
24. Marchesi F, Pinna F, Percalli L et al (2013) Totally laparoscopic right colectomy: theoretical and practical advantages over the laparo-assisted approach. J Laparoendosc Adv Surg Tech 23(5):418–424. https://doi.org/10.1089/lap.2012.0420
25. Magistro C, Di Lernia S, Ferrari G et al (2013) Totally laparoscopic versus laparoscopic-assisted right colectomy for colon cancer: is there any advantage in short-term outcomes? A prospective comparative assessment in our center. Surg Endosc 27(7):2613–2618. https://doi.org/10.1007/s00464-013-2799-5
26. Lee KH, Ho J, Akmal Y et al (2013) Short- and long-term outcomes of intracorporeal versus extracorporeal ileocolic anastomosis in laparoscopic right hemicolectomy for colon cancer. Surg Endosc 27(6):1986–1990. https://doi.org/10.1007/s00464-012-2698-1
27. Roscio F, Bertoglio C, De Luca A et al (2012) Totally laparoscopic versus laparoscopic assisted right colectomy for cancer. Int J Surg 10(6):290–295. https://doi.org/10.1016/j.ijsu.2012.04.020
28. Erguner I, Aytac E, Baca B et al (2013) Total laparoscopic approach for the treatment of right colon cancer: a technical critique. Asian J Surg 36(2):58–63. https://doi.org/10.1016/j.asjsur.2012.09.00
29. Morpurgo E, Contardo T, Molaro R, Zerbinati A, Orsini C, D'Annibale A (2013) Robotic-assisted intracorporeal anastomosis versus extracorporeal anastomosis in laparoscopic right hemicolectomy for cancer: a case control study. J Laparoendosc Adv Surg Tech A 23(5):414–417. https://doi.org/10.1089/lap.2012.0404
30. Anania G, Santini M, Scagliarini L et al (2012) A totally mini-invasive approach for colorectal laparoscopic surgery. World J Gastroenterol 18(29):3869–3874
31. Fabozzi M, Allieta R, Contul RB et al (2010) Comparison of short and medium-term results between laparoscopically assisted and totally laparoscopic right hemicolectomy: a case–control study. Surg Endosc Interv Tech 24:2085–2091
32. Scatizzi M, Kröning KC, Borrelli A, Andan G, Lenzi E, Feroci F (2010) Extracorporeal versus intracorporeal anastomosis after laparoscopic right colectomy for cancer: a case-control study. World J Surg 34(12):2902–2908. https://doi.org/10.1007/s00268-010-0743-6
33. Hellan M, Anderson C, Pigazzi A (2009) Extracorporeal versus intracorporeal anastomosis for laparoscopic right hemicolectomy. JSLS 13(3):312–317
34. Juo YY, Hyder O, Haider AH, Camp M, Lidor A, Ahuja N (2014) Is minimally invasive colon resection better than traditional approaches?: first comprehensive national examination with propensity score matching. JAMA Surg 149(2):177–184
35. Vallance A, Wexner S, Berho M et al (2017) A collaborative review of the current concepts and challenges of anastomotic leaks in colorectal surgery. Colorectal Dis 19:O1–O12
36. Chadi SA, Fingerhut A, Berho M et al (2016) Emerging trends in the etiology, prevention, and treatment of gastrointestinal anastomotic leakage. J Gastrointest Surg 20:2035–2051
37. Wu Q, Jin C, Hu T, Wei M, Wang Z (2017) Intracorporeal versus extracorporeal anastomosis in laparoscopic right colectomy: a systematic review and meta-analysis. J Laparoendosc Adv Surg Tech A 27(4):348–357. https://doi.org/10.1089/lap.2016.0485
38. Ricci C, Casadei R, Alagna V et al (2017) A critical and comprehensive systematic review and meta-analysis of studies comparing intracorporeal and extracorporeal anastomosis in laparoscopic right hemicolectomy. Langenbecks Arch Surg 402(3):417–427. https://doi.org/10.1007/s00423-016-1509-x
39. Raftopoulos I, Courcoulas AP, Blumberg D (2006) Should completely intracorporeal anastomosis be considered in obese patients who undergo laparoscopic colectomy for benign or malignant disease of the colon? Surgery 140:675–682
40. Blumberg D (2009) Laparoscopic colectomy performed using a completely intracorporeal technique is associated with similar outcome in obese and thin patients. Surg Laparosc Endosc Percutan Tech 19:57–61
41. Choy PY, Bissett IP, Docherty JG, Parry BR, Merrie A, Fitzgerald A (2011) Stapled versus handsewn methods for ileocolic anastomoses. Cochrane Database Syst Rev 7(9):CD004320