Archives of Surgical Research | Meta-Analysis

Enhanced Recovery After Surgery (ERAS) versus Traditional Care in Patients Hospitalized for Colorectal Surgery: A Meta-Analysis

Hamza Azhar, Muhammad Hassan Hafeez, Safia Zahir Ahmed

IMPORTANCE Enhanced Recovery after Surgery (ERAS) is a program designed to minimize surgery-related stress and total length of stay at the hospital in patients undergoing major surgical intervention. It has proven to enable patients to recover quickly with lesser readmissions and risk of morbidity and mortality. This study aims to compare the outcomes of ERAS protocols with those of traditional care in colorectal surgery.

METHODS A PRISMA-compliant literature search was performed on the PubMed and Cochrane library and 29 eligible RCTs were extracted in which ERAS protocol was compared with conventional care in colorectal surgery.

RESULTS Twenty-nine RCTs included 4349 patients; 2164 in the ERAS care group and 2185 in the traditional care group. ERAS group had reduced time to flatus resumption (Weighted mean difference (WMD): —0.78 days, 95% CI —1.05 to —0.52, $p < 0.00001$), a shorter total length of stay (WMD: -3.13 days, 95% CI —4.16 to —2.10, $p < 0.00001$) and postoperative hospital stay (Weighted Mean Difference: —2.21 days, 95% CI —2.87 to —1.55, $p < 0.00001$), shorter time to mobilization (WMD: —16.28 hours, 95% CI —22.04 to —10.53, $p < 0.00001$), shorter time to first fluid intake (WMD: —89.96 hours, 95% CI —119.89 to —60.03, $p < 0.00001$) and solid food tolerance (WMD: —1.91, 95% CI –2.34 to —1.48, $p < 0.00001$) as compared to a traditional care group. The number of readmissions was lesser in the traditional care group as compared to the ERAS group (OR: 1.09, 95% CI 0.78 to 1.51, $p = 0.74$). The number of total complications was lower in the ERAS care group as compared to the traditional care group (OR: 0.49, 95% CI 0.36 to 0.66, $p = 0.0003$).

CONCLUSIONS Our results prove that ERAS is comparatively a better choice of surgical care protocol than conventional care, for patients who undergo colorectal surgery.

KEYWORDS Enhanced Recovery after Surgery, ERAS, Fast-track surgery, FTS, Enhanced recovery protocol, colorectal surgery

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Meta-Analysis

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Enhanced Recovery after Surgery (ERAS) or enhanced recovery protocol or fast-track surgery program, represents multimodal, evidence-based perioperative care pathways, intended to achieve rapid postoperative recovery, reduce surgical stress response and optimize bodily functions in patients experiencing major surgical procedures[1]. In the 1990s, Dr. Henrik Kehlet, a Danish surgeon and professor, initially put forward a multimodal protocol to provide patients with a fast recovery period after colonic surgery[2]. In 2001, a group of international surgeons and anesthesiologists, including Kehlet, formed an ERAS study group in London, to provide a consensus protocol of around 20 items for perioperative care of patients undergoing colonic resection surgery[3]. After the inception of the ERAS society in 2010, a series of perioperative care guidelines have been published and being practiced in colorectal surgical care settings globally. The latest ERAS guidelines for colorectal surgery highlight preoperative counseling, prehabilitation, perioperative fluid and electrolyte therapy, bowel preparation, anesthesia and analgesia protocol, perioperative nutritional care, and perioperative prevention of complications [4, 5]. Many studies and trials, as of now, have concluded that the principles of ERAS protocol, in contrast to traditional care, yields a reduced length of hospital stay, a more rapid return of gut function and mobilization, and a lesser incidence of postoperative complications and readmissions. Some studies have shown ERAS and traditional care to give the same results. Several meta-analyses have been conducted but they have used either a small number of trials or those of poor caliber. Some meta-analyses have reported outcomes of ERAS and traditional care in only laparoscopic colorectal surgery patients. Our meta-analysis attempts to compare and analyze the outcomes and efficacy of ERAS and traditional care, entailing a larger number of high-quality studies in patients undergoing colorectal surgery using any surgical approach.

METHODS

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed to carry out this meta-analysis

Literature Search

A systematic literature search of randomized controlled trials (RCTs) was conducted on the databases of PubMed and Cochrane library on 2/4/2021 according to PRISMA guidelines, using the following search terms: (enhanced recovery after surgery OR ERAS OR fast track surgery OR FTS) AND (colorectal surgery OR rectal OR colorectal cancer OR colorectal OR rectal cancer OR colon cancer). The literature search was performed on the PubMed and Cochrane library databases. All RCTs published between 1/7/2017 and 2/4/2021 were filtered out. Additionally, relevant articles were explored by manually searching the references.

Inclusion of Articles

After the PRISMA compliant literature search, 100 articles were identified through PubMed and 298 articles were identified through the Cochrane library. After the removal of 15 duplicate articles, 407 articles were screened. Of these papers, 80 articles were picked based on their titles and abstracts. Full texts of these articles were obtained and 29 articles were finally included for quantitative analysis. Only full-text English language papers were selected. All RCTs which compared ERAS care programs with traditional care in patients hospitalized for colorectal surgery were selected. All those studies which did not include a comparison of interest were excluded. Studies other than RCTs were also excluded. This has been illustrated in Figure 1.

Data Extraction and Quality Assessment

Using structured forms, the authors extracted the data on study and patient characteristics and patient outcomes from each study that met the inclusion criteria. If data were reported in medians, they were converted into values of means and standard deviations. The quality assessment of selected RCTs was done using the Cochrane collaboration risk of the bias assessment tool, as shown in Figures 2 and 3. The performance bias, selection bias, reporting bias, detection bias, attrition bias, and other biases were estimated for each study. We graded the risk of bias of each study as low, high, or unclear. In a large number of the included RCTs, the probability of performance bias was high as blinding of the surgeons, investigators, and patients were not feasible. Most of the studies showed a low risk of selection, attrition, and reporting bias.

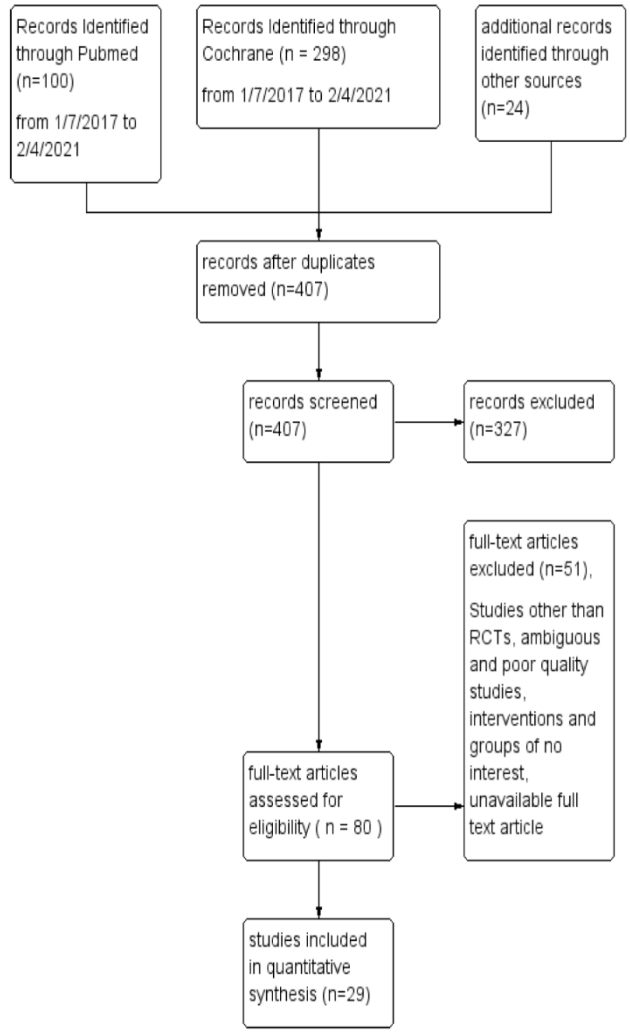

Figure 1: Showing PRISMA flow diagram

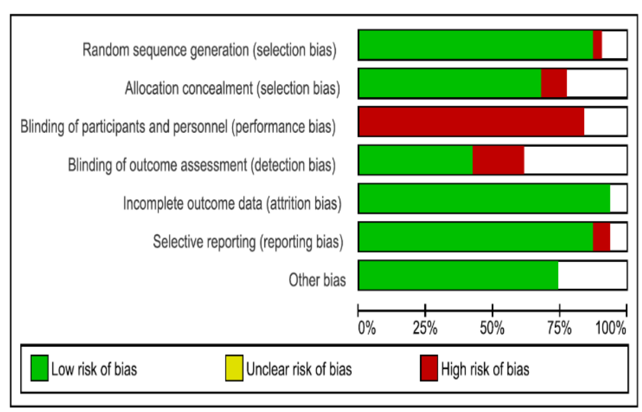

Figure 2: Risk of Bias Graphs of the Included Studies

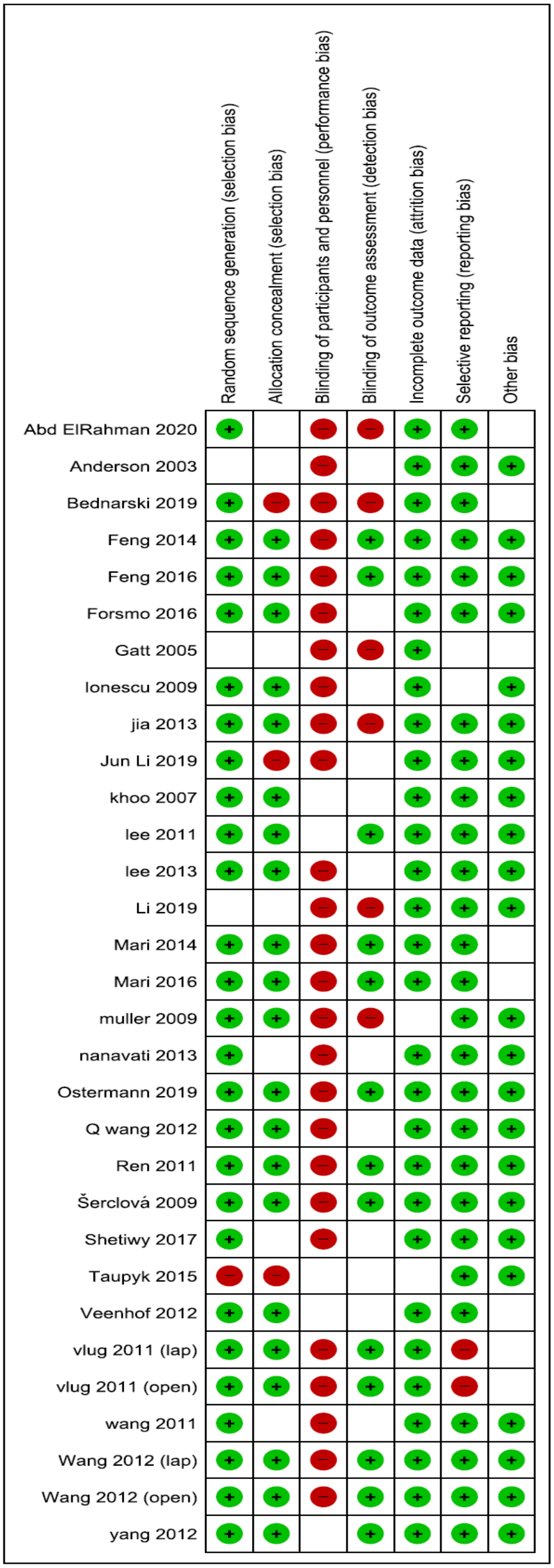

Figure 3: Risk of Bias Summary of the Included Studies

Study outcomes and Statistical Data Analysis:

We studied the outcomes of time to flatus resumption after surgery, a total length of stay and postoperative hospital stay (PHS), time to the first mobilization, time to first fluid and solid intake after surgery, readmissions, and the total number of complications. The continuous and dichotomous variables, where appropriate, were used to assess outcomes of the RCTs that compared ERAS with conventional care in colorectal surgery. Mean difference with inverse variance was used to calculate continuous variables and Odd's Ratio (OR) with the Mantel-Haenszel method with 95% Confidence Interval (CI) was used to calculate dichotomous variables. The random effect was used in the population with the heterogeneity of more than 50% and the fixed effect was used in the population with the heterogeneity of less than 50%. The Review Manager 5.4 was availed to perform the meta-analysis using the 2 x 2 Chi-square test.

RESULTS

Following the PRISMA guidelines, a literature search was done in PubMed and Cochrane library, from which 29 articles[6-34] fell under our eligibility criteria and were included in the quantitative analysis. All the included studies were randomized controlled trials. The characteristics of the studies including the number of participants, study design, type of intervention, mean age, and male to female ratio have been given in Table 1. Each study compared the ERAS care protocol with traditional care in different colonic/colorectal surgeries.

A total of 4349 patients admitted for colorectal surgery were added to the analysis with 2164 patients belonging to the ERAS care group and 2185 patients, to the traditional care group.

Time to First Flatus

Sixteen studies reported this parameter including 1363 patients in the ERAS group and 1523 patients in the traditional care group. We analyzed that the time to flatus resumption was shorter in the ERAS patients as compared to the traditional care patients (Weighted Mean Difference: —0.78 days, 95% Confidence Interval (CI) —1.05 to —0.52, $p < 0.00001$). Owing to the heterogeneity being high (92%), we used a random-effects model.

Study	Year of publication	Study Design	Type of surgery	No. of participants		Age (Mean ± SD)		Gender (M/F)	
				ERAS	TC	ERAS	TC	ERAS	TC
Abd ElRahman et al	2020	RCT	Colon cancer surgery	40	40	49.5 ± 10.4	49.7 ± 8.4	20/20	20/20
Ostermann et al	2019	RCT	Colorectal surgery	75	75	80.06 ± 4.38	78.27 ± 4.17	26/49	35/40
Li et al	2019	RCT	Colorectal cancer surgery	100	100	56.2 ± 5.5	55.3 ± 5.3	65/35	68/32
Mari et al	2014	RCT	Colorectal surgery	25	25	63.3 ± 13.7	63.3 ± 13.7	12/13	12/13
Mari et al	2016	RCT	Colorectal surgery	70	70	63.78 ± 8.65	66.43 ± 10.12	39/31	35/35
Jun Li et al	2019	RCT	Colorectal cancer surgery	172	170	59.8 ± 10.09	61.3 ± 11.21	110/62	103/67
Bednarski et al	2019	RCT	Colorectal cancer surgery	14	16	58.7 ± 12.6	59.3 ± 10.2	6/8	10/6
Forsmo et al	2016	RCT	Colorectal surgery	154	153	64.24 ± 12.46	65.15 ± 13.98	83/71	82/71
Šerclová et al	2009	RCT	Open intestinal resection	51	52	35.1 ± 11	37.6 ± 12.5	20/31	32/20
Anderson et al	2003	RCT	Colorectal surgery	14	11	62.18 ± 10.70	69.47 ± 8.48	6/8	5/6
Feng et al	2014	RCT	Rectal cancer surgery	57	59	53.95 ± 11.95	56.31 ±, 11.52	36/21	40/19
Feng et al	2016	RCT	Colorectal cancer surgery	116	114	58.12 ± 11.04	58.31 ± 10.89	66/50	63/51
Gatt et al	2005	RCT	Colorectal surgery	19	20	67.36 ± 13.61	66.64 ± 10.37	9/10	14/6
Ionescu et al	2009	RCT	Colorectal cancer surgery	48	48	60.94 ± 9.9	63.1 ± 12.19	30/18	31/17
Jia et al	2013	RCT	Colorectal cancer surgery	117	116	75.66 ± 4.18	74.78 ± 4.01	76/41	70/46
Khoo et al	2007	RCT	Colorectal cancer surgery	35	35	67.66 ± 32.00	67.66 ± 29.52	12/23	15/20
Lee et al	2011	RCT	Colon cancer surgery	46	54	61.9 ± 11.2	60.6 ± 0.0	26/20	30/24
Lee et al	2013	RCT	Rectal cancer surgery	52	46	61.2 ± 10.8	61.7 ± 10.8	34/16	28/18
Muller et al	2009	RCT	Colon cancer surgery	76	75	59.88 ± 48.36	62.52 ± 37.79	37/39	40/35
Nanavati et al	2013	RCT	Intestinal surgery	30	30	34.77 ± 14.40	33.5 ± 12.36	17/13	15/15
Yang et al	2012	RCT	Colorectal cancer surgery	32	30	57.2 ± 11.70	59.5 ± 12.10	20/12	22/8
Ren et al	2011	RCT	Colorectal cancer surgery	299	298	53.38 ± 40.22	53.63 ± 43.95	178/121	190/108
Shetiwy et al	2017	RCT	Colorectal cancer surgery	35	35	48.54 ± 12.29	53.63 ± 11.5	21/14	24/11
Taupyk et al	2015	RCT	Colorectal cancer surgery	31	39	58.5 ± 8.4	57.4 ± 10.1	22/9	20/19
Veenhof et al	2012	RCT	Colon cancer surgery	36	43	63.38 ± 10.17	66.05 ± 9.88	10/9	19/4
Vlug et al	2011	RCT	Colon cancer surgery	193	207	66 ± 9.4	67 ± 7.95	107/86	127/80
Wang et al	2011	RCT	Colorectal cancer surgery	106	104	54.53 ± 23.29	53.94 ± 20.29	65/41	60/44
Wang et al	2012	RCT	Colon cancer surgery	81	82	56.45 ± 17.7	55.75 ± 15.7	51/30	51/31
Wang et al	2012	RCT	Colorectal cancer surgery	40	38	72.41 ± 12.30	73.06 ± 13.09	22/18	20/18

Table 1: Overview and Characteristics of Included Studies

Study or Subgroup	ERAS Mean	ERAS SD	ERAS Total	TC Mean	TC SD	TC Total	Weight	Mean Difference IV, Random, 95% CI
Feng 2014	2.2	0.9	57	2.82	0.83	59	7.4%	-0.62 [-0.94, -0.30]
Feng 2016	3.71	1.14	116	4.26	1.52	114	7.2%	-0.55 [-0.90, -0.20]
Forsmo 2016	1.7	2.99	154	5.56	9.72	153	2.0%	-3.86 [-5.47, -2.25]
jia 2013	2.0208	0.39958	117	3.2358	0.299166	116	8.2%	-1.21 [-1.31, -1.12]
Jun Li 2019	56	26	25	71	27	170	0.1%	-15.00 [-25.97, -4.03]
lee 2011	2.37533	1.122	46	2.5241	1.2058	54	6.6%	-0.15 [-0.61, 0.31]
lee 2013	1.4304	0.85775	52	1.99	1.1159	46	7.0%	-0.56 [-0.96, -0.16]
Mari 2014	0.9	0.78	25	2.1	0.94	25	6.5%	-1.20 [-1.68, -0.72]
Mari 2016	1.6	0.7	70	2.1	0.8	70	7.7%	-0.50 [-0.75, -0.25]
Q wang 2012	1.3508	0.4485	40	1.686	0.6099	38	7.7%	-0.34 [-0.57, -0.10]
Ren 2011	2.237	0.712	299	2.6291	0.8333	298	8.1%	-0.39 [-0.52, -0.27]
Taupyk 2015	1.6	0.8	31	2.5	0.9	39	6.9%	-0.90 [-1.30, -0.50]
vlug 2011 (lap)	1.352	0.7522	100	2	1.5026	109	7.4%	-0.65 [-0.97, -0.33]
vlug 2011 (open)	1.7042	1.5061	93	2	1.5049	98	6.8%	-0.30 [-0.72, 0.13]
wang 2011	2.1	2	106	3.2	2.5	104	5.7%	-1.10 [-1.71, -0.49]
yang 2012	2	1	32	4	2	30	4.7%	-2.00 [-2.80, -1.20]
Total (95% CI)			**1363**			**1523**	**100.0%**	**-0.78 [-1.05, -0.52]**

Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 193.36$, df = 15 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: Z = 5.78 ($P < 0.00001$)

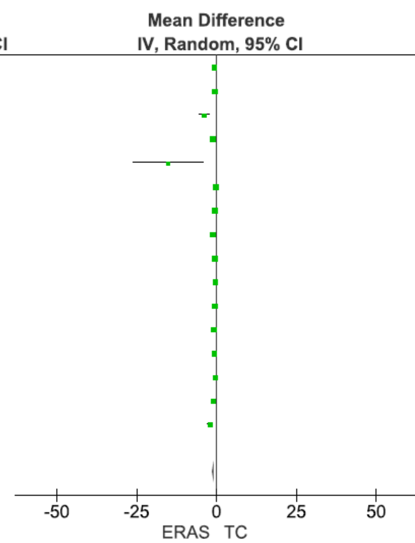

Figure 4: Forest Plot of Time to First Flatus in ERAS vs. Traditional Group with the pooled result of 0.78% (95%CI-1.05-0.52%)

The total length of Stay & Post-Operative Hospital Stay

Sixteen RCTs mentioned the total length of stay. It included 1184 patients in the ERAS group and 1190 patients in the conventional care group. The outcome showed that the total length of stay was shorter in the ERAS group (Weighted Mean Difference: —3.13 days, 95% CI —4.16 to —2.10, p < 0.00001) than in the traditional care group. High heterogeneity of 94% was observed and a random effect model was used. PHS was reported in 17 RCTs with a total of 1562 patients in the ERAS group and 1581 in the traditional care group. The Postoperative Hospital Stay (PHS) also resulted as shorter in the ERAS care group (Weighted Mean Difference: —2.21 days, 95% CI —2.87 to —1.55, p < 0.00001) as compared to the conventional care group. Due to high heterogeneity, a random-effects model was used for analysis.

	ERAS			TC				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Abd ElRahman 2020	5.4	1.5	40	7.6	1.4	40	7.9%	-2.20 [-2.84, -1.56]
Anderson 2003	3.96	1.77	14	6.99	2.06	11	6.9%	-3.03 [-4.56, -1.50]
Bednarski 2019	3.35	5.94	14	2.24	0.74	16	4.6%	1.11 [-2.02, 4.24]
Forsmo 2016	19.75	35.92	154	19.94	34.42	153	1.4%	-0.19 [-8.06, 7.68]
jia 2013	9.01	1.75	117	13.21	1.32	116	8.0%	-4.20 [-4.60, -3.80]
Jun Li 2019	13.7	4.48	172	27	20.18	170	4.7%	-13.30 [-16.41, -10.19]
khoo 2007	15.6671	26.2813	35	25.8453	45.6058	35	0.3%	-10.18 [-27.62, 7.26]
lee 2013	6.0178	2.5732	52	6.1779	2.168	46	7.6%	-0.16 [-1.10, 0.78]
muller 2009	12.7564	21.1593	76	15.346	18.141	75	2.0%	-2.59 [-8.87, 3.69]
nanavati 2013	4.73	1.34	30	7.27	1.36	30	7.8%	-2.54 [-3.22, -1.86]
Ostermann 2019	9.84	10.43	75	13.56	7.72	75	4.9%	-3.72 [-6.66, -0.78]
Q wang 2012	5.5	0.7689	40	7	1.5408	38	7.9%	-1.50 [-2.04, -0.96]
Shetiwy 2017	4.49	0.853	35	13.31	6.89	35	5.8%	-8.82 [-11.12, -6.52]
Taupyk 2015	5.9	0.8	31	10.9	1.3	39	8.0%	-5.00 [-5.50, -4.50]
vlug 2011 (lap)	5.7039	3.0088	100	6.7036	3.7565	109	7.6%	-1.00 [-1.92, -0.08]
vlug 2011 (open)	7.7042	4.5182	93	8.7599	5.267	98	7.1%	-1.06 [-2.45, 0.33]
wang 2011	5.1	3.1	106	7.6	4.8	104	7.4%	-2.50 [-3.60, -1.40]
Total (95% CI)			**1184**			**1190**	**100.0%**	**-3.13 [-4.16, -2.10]**

Heterogeneity: Tau² = 3.40; Chi² = 269.86, df = 16 (P < 0.00001); I² = 94%
Test for overall effect: Z = 5.97 (P < 0.00001)

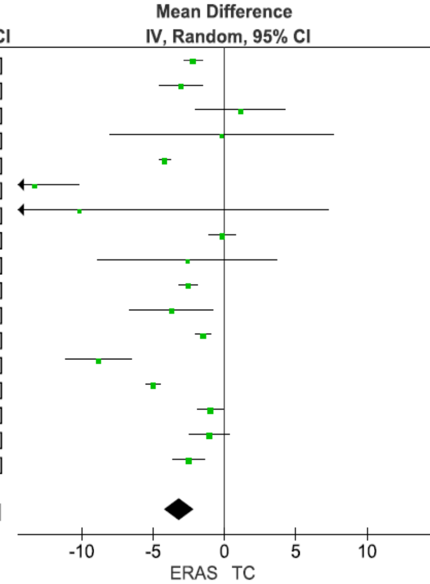

Figure 5: Forest Plot showing total length of stay in ERAS vs. Traditional Group with the pooled result of 3.13% (95%CI-4.16-2.10%)

	ERAS			TC				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Feng 2014	5.05	1.38	57	6.98	2.26	59	6.0%	-1.93 [-2.61, -1.25]
Feng 2016	7.54	2.18	116	8.62	2.83	114	6.1%	-1.08 [-1.73, -0.43]
Forsmo 2016	19.75	35.92	154	19.64	34.42	153	0.6%	0.11 [-7.76, 7.98]
Gatt 2005	5.4	1.3	19	7.6	1.07	20	6.0%	-2.20 [-2.95, -1.45]
Ionescu 2009	6.43	3.41	48	9.16	2.67	48	5.3%	-2.73 [-3.96, -1.50]
Jun Li 2019	6	1.49	172	9	2.99	170	6.2%	-3.00 [-3.50, -2.50]
lee 2011	7	1.5305	46	8	1.5233	54	6.1%	-1.00 [-1.60, -0.40]
lee 2013	8.5613	3.0498	52	8.35	2.29	46	5.5%	0.21 [-0.85, 1.27]
Mari 2016	5	2.6	70	7.2	3	70	5.7%	-2.20 [-3.13, -1.27]
Ren 2011	5.7	1.6	299	6.6	2.4	298	6.3%	-0.90 [-1.23, -0.57]
Šerclová 2009	7.4	1.3	51	10.4	3.1	52	5.7%	-3.00 [-3.92, -2.08]
Shetiwy 2017	4.49	0.85	35	13.31	6.9	35	3.6%	-8.82 [-11.12, -6.52]
Taupyk 2015	4.3	0.8	31	8	1.1	39	6.3%	-3.70 [-4.15, -3.25]
vlug 2011 (lap)	5.35	2.256	100	6.17	3.38	109	5.9%	-0.82 [-1.59, -0.05]
vlug 2011 (open)	6.88	4.14	93	7.88	3.385	98	5.5%	-1.00 [-2.08, 0.08]
wang 2011	5.1	3.1	106	7.6	4.8	104	5.5%	-2.50 [-3.60, -1.40]
Wang 2012 (lap)	6.5	4.1	41	7.4	4.2	42	4.4%	-0.90 [-2.69, 0.89]
Wang 2012 (open)	5.2	3.9	40	6.3	4.7	40	4.2%	-1.10 [-2.99, 0.79]
yang 2012	6	1	32	11.7	3.82	30	5.0%	-5.70 [-7.11, -4.29]
Total (95% CI)			**1562**			**1581**	**100.0%**	**-2.21 [-2.87, -1.55]**

Heterogeneity: Tau² = 1.76; Chi² = 231.16, df = 18 (P < 0.00001); I² = 92%
Test for overall effect: Z = 6.56 (P < 0.00001)

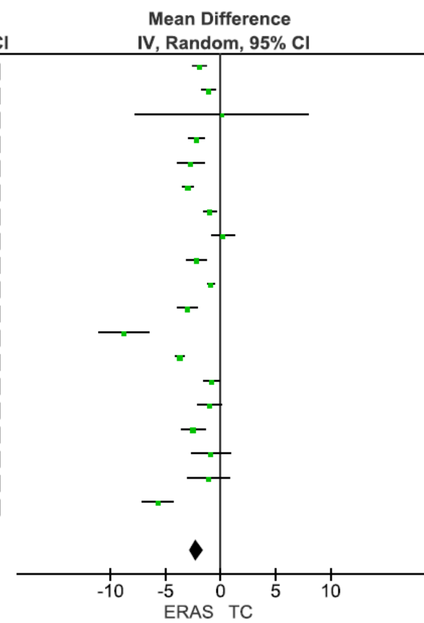

Figure 6: Forest Plot showing the postoperative length of stay in ERAS vs. Traditional Group with the pooled result of 2.21% (95%CI-2.87-1.55%)

Time to Mobilization of Patient

A total of 12 RCTs reported the time to mobilization in which 848 patients belonged to the ERAS group, while 839 patients in the traditional care group. Due to high heterogeneity, we used a random-effects model. The results showed that the time to the mobilization of patients was also shorter in ERAS patients (Weighted Mean Difference: —16.28 hours, 95% CI —22.04 to —10.53, p < 0.00001) than traditional care patients.

	ERAS			TC				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Anderson 2003	49.6	4.8	14	74.16	24	11	6.2%	-24.56 [-38.96, -10.16]
Feng 2016	88.8	39.6	116	129.6	50.16	114	7.2%	-40.80 [-52.49, -29.11]
Forsmo 2016	3.35	5.23	154	1.78	3.74	153	10.2%	1.57 [0.55, 2.59]
Ionescu 2009	19.6	8.6	48	37.1	23.9	48	8.8%	-17.50 [-24.69, -10.31]
Jun Li 2019	34.42	17.94	172	56.4	17.94	170	9.8%	-21.98 [-25.78, -18.18]
khoo 2007	107.736	166.96	35	317.877	556.54	35	0.1%	-210.14 [-402.64, -17.64]
lee 2011	17.5395	5.1272	46	21	4.5699	54	10.1%	-3.46 [-5.38, -1.54]
lee 2013	18.7075	3.0498	52	19.7085	6.122	46	10.1%	-1.00 [-2.95, 0.95]
Mari 2014	31.2	19.68	25	85.2	11.52	25	8.2%	-54.00 [-62.94, -45.06]
Mari 2016	36	16.8	70	62.4	21.6	70	9.1%	-26.40 [-32.81, -19.99]
muller 2009	4	15.113	76	4	6.047	75	9.8%	0.00 [-3.66, 3.66]
Q wang 2012	12	3.0757	40	19.7103	6.1634	38	10.1%	-7.71 [-9.89, -5.53]
Total (95% CI)			**848**			**839**	**100.0%**	**-16.28 [-22.04, -10.53]**

Heterogeneity: Tau² = 84.03; Chi² = 441.68, df = 11 (P < 0.00001); I² = 98%
Test for overall effect: Z = 5.55 (P < 0.00001)

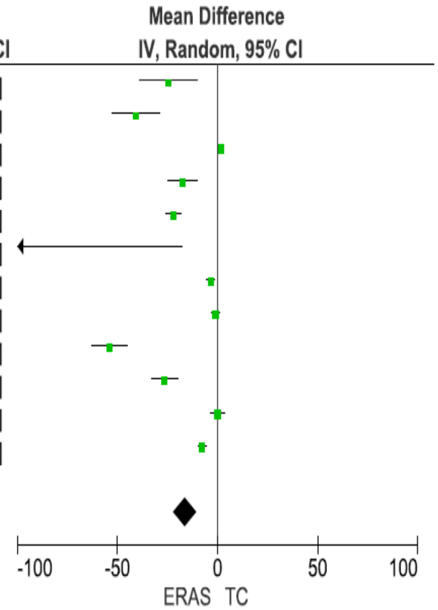

Figure 7: Forest Plot showing time to mobilization in ERAS vs. Traditional Group with the pooled result of 16.28% (95%CI-22.04-10.53%)

Time to First Fluid and Solid

Intake A total of 657 patients (ERAS) and 654 patients (traditional care) were added in 6 RCTs which mentioned the time to first fluid intake. The time was shorter in patients of the ERAS group (Weighted Mean Difference: —89.96 hours, 95% CI —119.89 to —60.03, p < 0.00001) than traditional care group. We used a random-effects model for quantitative analysis of time to fluid intake. Time for the development of tolerance to solid diet was mentioned in 14 studies with 870 patients (ERAS) and 887 in (traditional care). Using the random-effects model, results of the analysis showed that ERAS patients developed tolerance earlier (Weighted Mean Difference: —1.91, 95% CI —2.34 to —1.48, p < 0.00001) than patients receiving conventional care.

	ERAS			TC				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Ionescu 2009	10.8	7.2	48	23.52	16.8	48	19.4%	-12.72 [-17.89, -7.55]
Jun Li 2019	777.6	430.56	172	2,304	859.2	170	3.5%	-1526.40 [-1670.70, -1382.10]
lee 2011	7.2398	4.2089	46	70.116	33.1317	54	19.2%	-62.88 [-71.80, -53.96]
lee 2013	7.7688	5.3371	52	65.417	32.1407	46	19.1%	-57.65 [-67.05, -48.25]
Q wang 2012	13.0646	3.8446	40	43.8038	11.5563	38	19.4%	-30.74 [-34.60, -26.88]
Ren 2011	74.4	19.2	299	98.4	43.2	298	19.4%	-24.00 [-29.37, -18.63]
Total (95% CI)			**657**			**654**	**100.0%**	**-89.96 [-119.89, -60.03]**

Heterogeneity: Tau² = 1196.18; Chi² = 546.37, df = 5 (P < 0.00001); I² = 99%
Test for overall effect: Z = 5.89 (P < 0.00001)

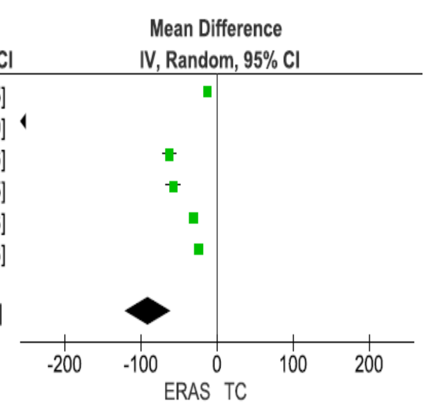

Figure 8: Forest Plot showing Time to first fluid in ERAS vs. Traditional Group with the pooled result of 89.96% (95%CI-119.89-60.03%)

Study or Subgroup	ERAS Mean	ERAS SD	ERAS Total	TC Mean	TC SD	TC Total	Weight	Mean Difference IV, Random, 95% CI
Anderson 2003	1.94	0.26	14	3.39	0.52	11	8.0%	-1.45 [-1.79, -1.11]
Feng 2016	3.27	1.27	116	5.27	1.6	114	7.9%	-2.00 [-2.37, -1.63]
Forsmo 2016	3.75	6.73	154	4.5	8.98	153	3.4%	-0.75 [-2.53, 1.03]
Gatt 2005	2.23	1	19	3.6	2.32	20	5.4%	-1.37 [-2.48, -0.26]
Ionescu 2009	1.75	0.52	48	2.67	0.96	48	8.0%	-0.92 [-1.23, -0.61]
khoo 2007	2.4223	4.637	35	5.0667	5.4109	35	2.4%	-2.64 [-5.01, -0.28]
lee 2011	1.7842	0.2391	46	4.083	0.9044	54	8.2%	-2.30 [-2.55, -2.05]
lee 2013	4.4697	4.0187	52	5.0196	2.4392	46	4.7%	-0.55 [-1.85, 0.75]
Mari 2014	1.2	0.421	25	3.81	0.98	25	7.8%	-2.61 [-3.03, -2.19]
Mari 2016	1.5	0.9	70	3	0.5	70	8.2%	-1.50 [-1.74, -1.26]
Shetiwy 2017	1.89	1.13	35	5.46	1.67	35	7.0%	-3.57 [-4.24, -2.90]
Taupyk 2015	1.1	0.3	31	3.6	0.9	39	8.1%	-2.50 [-2.80, -2.20]
vlug 2011 (lap)	1.352	0.7522	100	2	1.5026	109	8.0%	-0.65 [-0.97, -0.33]
vlug 2011 (open)	1.7042	1.5061	93	3.352	2.257	98	7.4%	-1.65 [-2.19, -1.11]
yang 2012	4	2	32	8.2	2.16	30	5.6%	-4.20 [-5.24, -3.16]
Total (95% CI)			**870**			**887**	**100.0%**	**-1.91 [-2.34, -1.48]**

Heterogeneity: Tau² = 0.57; Chi² = 196.47, df = 14 (P < 0.00001); I² = 93%
Test for overall effect: Z = 8.73 (P < 0.00001)

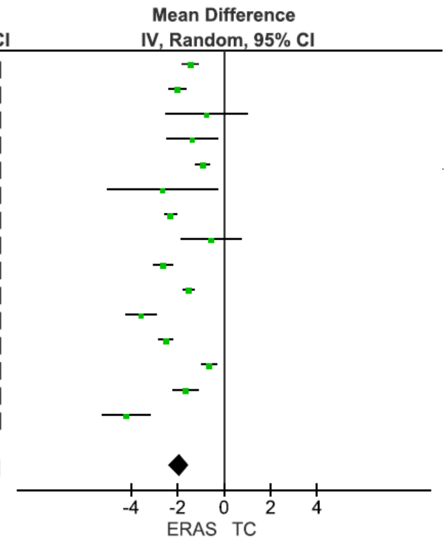

Figure 9: Forest Plot showing Time to first solid diet in ERAS vs. Traditional Group with the pooled result of 1.91% (95%CI-2.34-1.48%)

Readmissions Eleven RCTs reported the number of readmissions having a total of 990 patients (ERAS) and 1002 patients (traditional care). Dichotomous variables were used to assess the outcome of this parameter. Due to low heterogeneity, we used a fixed-effects model. The results showed that the traditional care group had a lesser number of readmissions with a total of 75 readmissions (7.4%) and the ERAS group had more number of readmissions with a total of 80 readmissions (8.08%). The forest plot also shows this variation (OR: 1.09, 95% CI 0.78 to 1.51, p = 0.74)

Study or Subgroup	ERAS Events	ERAS Total	TC Events	TC Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bednarski 2019	2	14	0	16	0.6%	6.60 [0.29, 150.07]
Forsmo 2016	29	154	21	153	25.2%	1.46 [0.79, 2.69]
Gatt 2005	1	19	4	20	5.5%	0.22 [0.02, 2.20]
Jun Li 2019	10	172	9	170	12.6%	1.10 [0.44, 2.79]
khoo 2007	3	35	1	35	1.3%	3.19 [0.32, 32.24]
muller 2009	3	76	2	75	2.9%	1.50 [0.24, 9.24]
nanavati 2013	1	30	1	30	1.4%	1.00 [0.06, 16.76]
Ostermann 2019	6	75	5	75	6.8%	1.22 [0.35, 4.18]
Shetiwy 2017	4	35	4	35	5.2%	1.00 [0.23, 4.36]
vlug 2011 (lap)	13	193	14	207	18.6%	1.00 [0.46, 2.18]
wang 2011	4	106	9	104	12.9%	0.41 [0.12, 1.39]
Wang 2012 (lap)	4	81	5	82	7.0%	0.80 [0.21, 3.09]
Total (95% CI)		**990**		**1002**	**100.0%**	**1.09 [0.78, 1.51]**
Total events	80		75			

Heterogeneity: Chi² = 7.70, df = 11 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.50 (P = 0.62)

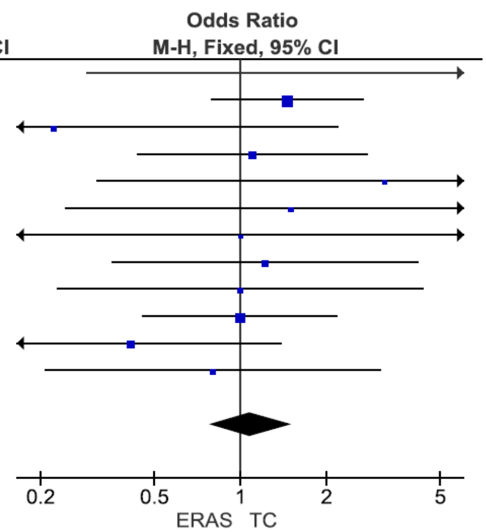

Figure 10: Forest Plot showing Readmission Rate in ERAS vs. Traditional Group with the pooled result of 1.09% (95%CI-0.78-1.51%)

Complications

Twenty-seven RCTs reported many complications, 20 RCTs mentioned anastomotic leaks, 9 RCTs mentioned intestinal obstructions, 15 articles reported the development of postoperative ileus, and 24 studies mentioned surgical site infections. Outcomes of all of these studies were assessed using dichotomous variables. There were a total of 404 complications (19.7%) in the ERAS group and 677 complications (32.7%) in the traditional care group (OR: 0.49, 95% CI 0.36 to 0.66, p = 0.0003). There was a lesser percentage of anastomotic leaks in the ERAS group (OR: 0.81, 95% CI 0.56 to 1.16, p = 0.52) than in the traditional care group. A total of 53 anastomotic leaks were observed in ERAS patients (2.94%) and 67 (3.68%) were observed in traditional care patients. A total of 17 patients (2.06%) developed an intestinal obstruction in the ERAS group while 25 patients (3.02%) suffered from intestinal obstruction in the traditional care group (OR: 0.71, 95% CI 0.39 to 1.28, p=0.25). 54 patients (5.33%) in ERAS group developed postoperative ileus while 69 patients (6.68%) in traditional care developed postoperative ileus (OR: 0.76, 95% CI 0.52 to 1.11, p = 0.52). 4.89% patients (96 patients out of 1963 patients) suffered from surgical site infection in ERAS group and 7.19% patients (142 patients out of 1973 patients) suffered from surgical site infection in traditional care group (OR: 0.67, 95% CI 0.51 to 0.87, p = 0.51).

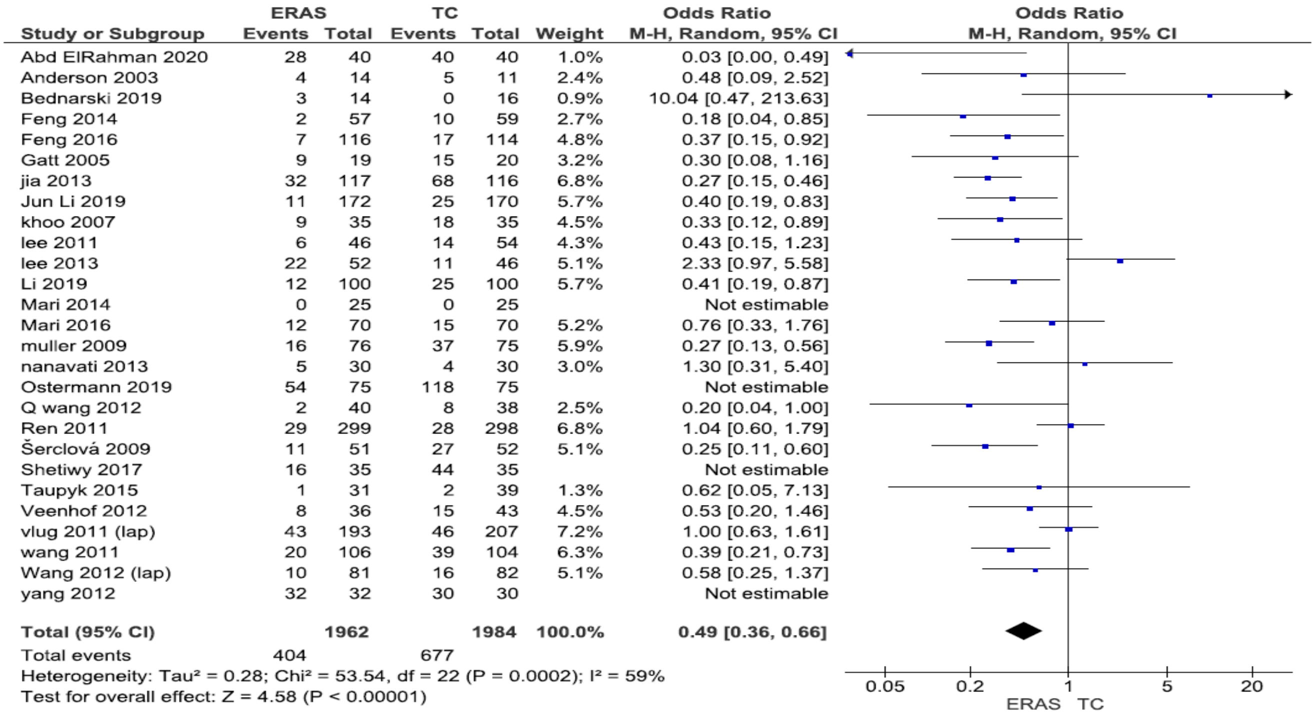

Figure 11: Forest Plot showing the total number of complications in ERAS vs. Traditional Group with the pooled result of 0.49% (95%CI-0.36-0.66%)

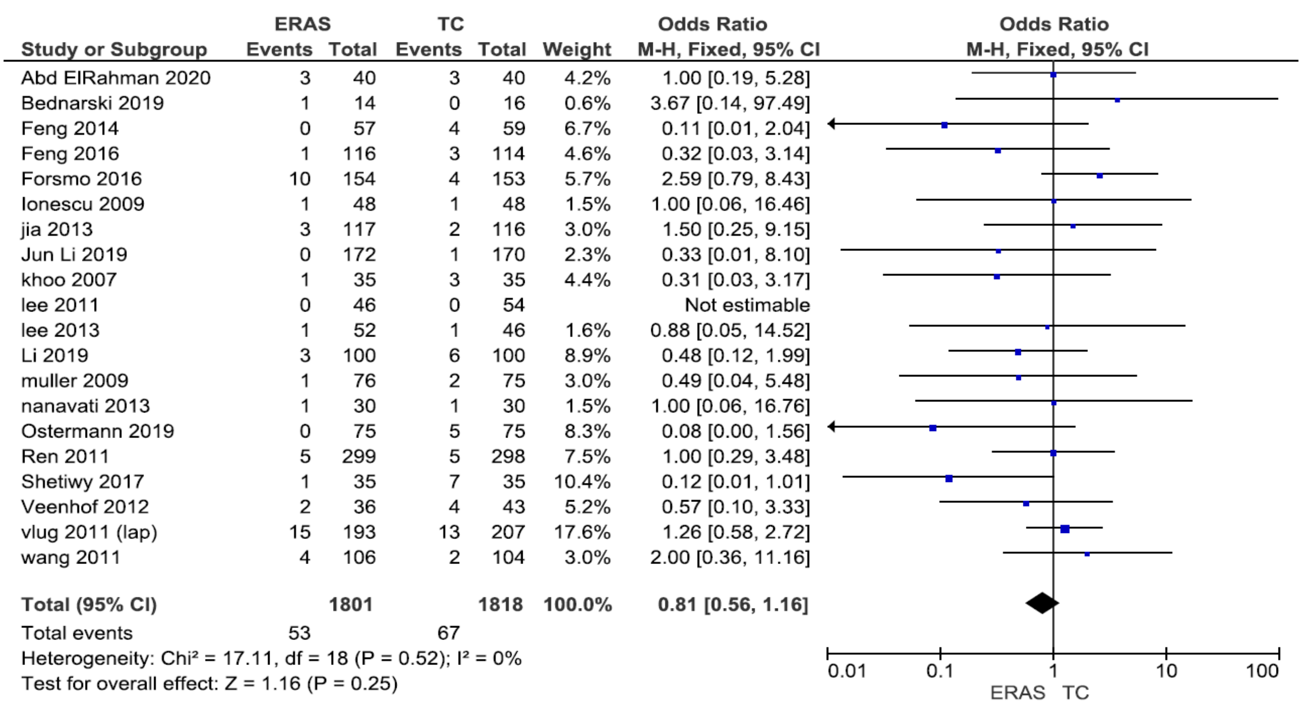

Figure 12: Forest Plot showing the total number of anastomotic leaks in ERAS vs. Traditional Group with the pooled result of 0.81% (95%CI-0.56-1.16%)

Study or Subgroup	ERAS Events	ERAS Total	TC Events	TC Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Abd ElRahman 2020	2	40	2	40	7.1%	1.00 [0.13, 7.47]
Bednarski 2019	1	14	0	16	1.6%	3.67 [0.14, 97.49]
jia 2013	4	117	6	116	21.8%	0.65 [0.18, 2.36]
Li 2019	0	100	1	100	5.6%	0.33 [0.01, 8.20]
Ostermann 2019	2	75	0	75	1.8%	5.14 [0.24, 108.81]
Q wang 2012	0	40	2	38	9.5%	0.18 [0.01, 3.88]
Ren 2011	6	299	7	298	25.8%	0.85 [0.28, 2.56]
Taupyk 2015	0	31	2	39	8.2%	0.24 [0.01, 5.14]
wang 2011	2	106	5	104	18.6%	0.38 [0.07, 2.01]
Total (95% CI)		**822**		**826**	**100.0%**	**0.71 [0.39, 1.28]**
Total events	17		25			

Heterogeneity: Chi² = 4.82, df = 8 (P = 0.78); I² = 0%
Test for overall effect: Z = 1.14 (P = 0.25)

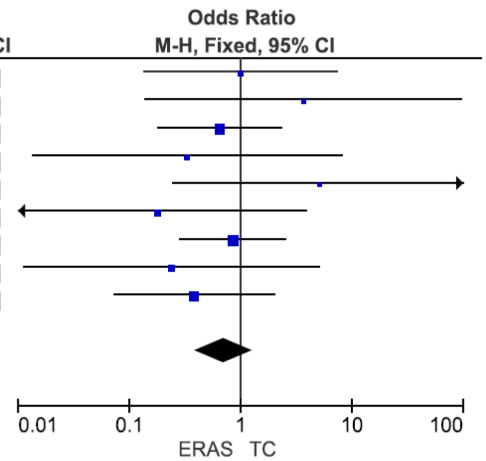

Figure 13: Forest Plot showing the total number of intestinal obstructions in ERAS vs. Traditional Group with the pooled result of 0.71% (95%CI-0.39-1.28%)

Study or Subgroup	ERAS Events	ERAS Total	TC Events	TC Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Abd ElRahman 2020	5	40	6	40	8.3%	0.81 [0.23, 2.90]
Anderson 2003	1	14	1	11	1.6%	0.77 [0.04, 13.87]
Feng 2014	0	57	1	59	2.3%	0.34 [0.01, 8.50]
Feng 2016	1	116	2	114	3.2%	0.49 [0.04, 5.45]
Forsmo 2016	4	154	8	153	12.3%	0.48 [0.14, 1.64]
Gatt 2005	3	19	3	20	3.9%	1.06 [0.19, 6.05]
lee 2011	2	46	1	54	1.4%	2.41 [0.21, 27.46]
lee 2013	15	52	6	46	7.1%	2.70 [0.95, 7.70]
Mari 2016	2	70	4	70	6.1%	0.49 [0.09, 2.74]
muller 2009	3	76	4	75	6.1%	0.73 [0.16, 3.38]
nanavati 2013	3	30	10	30	14.2%	0.22 [0.05, 0.91]
Ostermann 2019	4	75	9	75	13.4%	0.41 [0.12, 1.41]
Shetiwy 2017	2	35	5	35	7.4%	0.36 [0.07, 2.02]
Veenhof 2012	4	36	4	43	5.1%	1.22 [0.28, 5.26]
vlug 2011 (lap)	5	193	5	207	7.4%	1.07 [0.31, 3.77]
Total (95% CI)		**1013**		**1032**	**100.0%**	**0.76 [0.52, 1.11]**
Total events	54		69			

Heterogeneity: Chi² = 13.08, df = 14 (P = 0.52); I² = 0%
Test for overall effect: Z = 1.43 (P = 0.15)

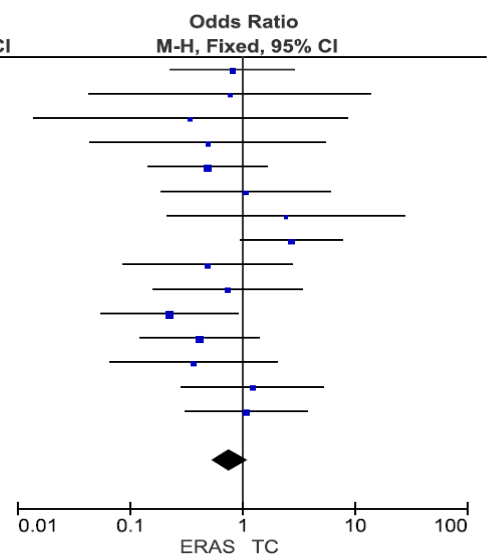

Figure 14: Forest Plot showing the total number of postoperative ileus in ERAS vs. Traditional Group with the pooled result of 0.76% (95%CI-0.52-1.11%)

Study or Subgroup	ERAS Events	ERAS Total	TC Events	TC Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Abd ElRahman 2020	3	40	4	40	2.8%	0.73 [0.15, 3.49]
Anderson 2003	1	14	0	11	0.4%	2.56 [0.09, 69.00]
Feng 2014	0	57	1	59	1.1%	0.34 [0.01, 8.50]
Feng 2016	1	116	3	114	2.2%	0.32 [0.03, 3.14]
Forsmo 2016	18	154	22	153	14.6%	0.79 [0.40, 1.54]
Gatt 2005	0	19	4	20	3.2%	0.09 [0.00, 1.88]
Ionescu 2009	4	48	5	48	3.4%	0.78 [0.20, 3.11]
jia 2013	6	117	8	116	5.7%	0.73 [0.25, 2.17]
Jun Li 2019	1	172	0	170	0.4%	2.98 [0.12, 73.73]
lee 2013	1	52	2	46	1.6%	0.43 [0.04, 4.92]
Li 2019	3	100	6	100	4.4%	0.48 [0.12, 1.99]
Mari 2016	2	70	1	70	0.7%	2.03 [0.18, 22.91]
muller 2009	4	76	7	75	5.0%	0.54 [0.15, 1.93]
nanavati 2013	0	30	1	30	1.1%	0.32 [0.01, 8.24]
Ostermann 2019	9	75	13	75	8.6%	0.65 [0.26, 1.63]
Q wang 2012	1	40	3	38	2.2%	0.30 [0.03, 3.01]
Ren 2011	5	299	5	298	3.7%	1.00 [0.29, 3.48]
Šerclová 2009	4	51	17	52	11.6%	0.18 [0.05, 0.57]
Shetiwy 2017	2	35	11	35	7.8%	0.13 [0.03, 0.65]
Taupyk 2015	1	31	0	39	0.3%	3.89 [0.15, 98.74]
Veenhof 2012	3	36	2	43	1.2%	1.86 [0.29, 11.82]
vlug 2011 (lap)	22	193	18	207	11.5%	1.35 [0.70, 2.60]
wang 2011	4	106	7	104	5.1%	0.54 [0.15, 1.91]
yang 2012	1	32	2	30	1.5%	0.45 [0.04, 5.26]
Total (95% CI)		**1963**		**1973**	**100.0%**	**0.67 [0.51, 0.87]**
Total events	96		142			

Heterogeneity: Chi² = 22.21, df = 23 (P = 0.51); I² = 0%
Test for overall effect: Z = 2.98 (P = 0.003)

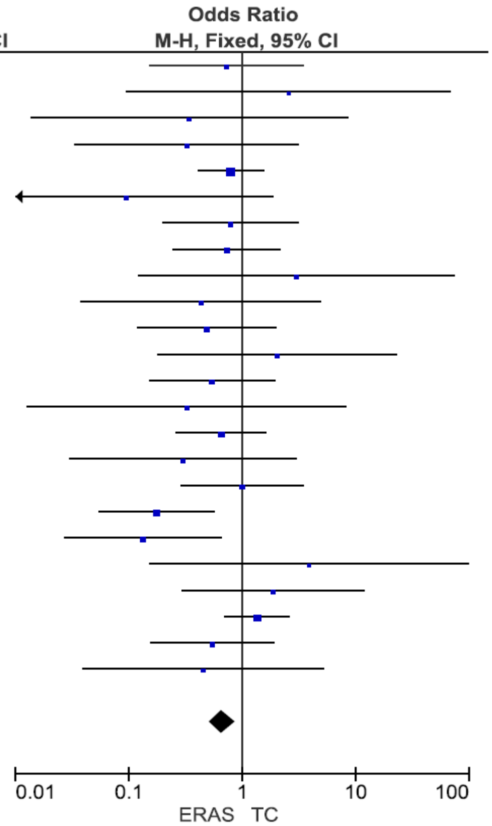

Figure 15: Forest Plot showing the total number of surgical site infections in ERAS vs. Traditional Group with the pooled result of 0.67% (95%CI-0.51-0.87%)

Sensitivity Analysis

We checked the sensitivity analysis of all the studies by excluding individually each study from the analysis of each outcome. The pooled results showed no significant difference in the exclusion of individual RCTs from the outcome analyses.

DISCUSSION

Major surgeries often pose a risk of intra- and postoperative stress in the form of prolonged hospital stay, late return of GI function, or higher rates of readmissions. The ERAS society developed its guidelines to revolutionize conventional surgical care practices in hospital settings. Unlike other surgeries, the ERAS program has been implemented vastly in the domain of colorectal surgery. Despite the growing popularity of the ERAS care program, many surgeons still exercise conventional measures in perioperative care. However, the ERAS society is earnestly working to implement this multidisciplinary evidence-based program[35].

In the past, a small number of meta-analyses have been performed to compare ERAS care versus traditional care in patients hospitalized for colorectal surgery. These included only a limited number of studies which were not sufficient to give satisfying results. More than a decade ago, Eskicioglu, Varadhan, and Lv et al conducted their meta-analyses with 4 and 6 studies, respectively[36, 37]. Later on, some meta-analyses were published with a large number of trials[38-41]. So far, our meta-analysis has included the greatest number of randomized studies (29 RCTs).

Recently, a meta-analysis included only those patients that underwent laparoscopic colorectal surgery[42], whereas our study did not disfavor any surgical approach. Some meta-analyses included both randomized and non-randomized trials[40, 42], whereas our study considered randomization essential as an inclusion criterion to screen for high-quality studies.

Other meta-analyses have studied the total length of stay and PHS as their primary outcomes along with postoperative morbidity, readmissions, and complications as their secondary outcomes[36-41, 43]. Ni et al have also included time to flatus and defecation, and inflammatory marker levels such as interleukin-6 and C-reactive protein. Their analysis included only the laparoscopically operated patients and only a small number of studies reported the outcomes of inflammatory markers[41]. Our analysis included time to first flatus, time to mobilization, time to first fluid intake, and solid diet tolerance, in addition to the length of stay, PHS, readmissions, and complications.

We included early mobilization in our study outcomes as it is an integral element of ERAS recommendations. If not addressed appropriately, prolonged bed rest can lead to thromboembolism and muscle atrophy. Postoperative oral intake is also an important factor to monitor in patients, especially after major surgeries such as colorectal surgery[5]

Although our study has given significant results in favor of ERAS protocol, there were some limitations to it. Some of the outcomes we studied were missing in most of the RCTs. Most RCTs were non-masked and did not comply with the blinding of surgeons and participants. A few RCTs reasoned that blinding was not practicable because of the comparison of different perioperative care regimens[10, 33].

Here, we would also highlight the fact that most RCTs were conducted in European and East Asian countries. Countries from other geographical regions should also practice these protocols in colorectal surgery so that the compliance of ERAS protocol could be assessed on a global level.

CONCLUSION

Our meta-analysis shows a remarkably shorter length of stay in hospital and PHS, faster restoration of normal GI function, a shorter time to regain mobilization, and a reduced incidence of total complications in the ERAS care group in comparison to the traditional care group. The rate of readmissions in both groups was non-significant. We conclude that in light of our results, ERAS protocol provides safety, expeditious recovery, and rapid return of normal physiology.

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