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ORIGINAL SCIENTIFIC REPORT

Enhanced Recovery After Surgery Programs Improve Patient Outcomes and Recovery: A Meta-analysis

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Abstract

Introduction Enhanced recovery after surgery (ERAS) programs have been developed to improve patient outcomes, accelerate recovery after surgery, and reduce healthcare costs. ERAS programs are a multimodal approach, with interventions during all stages of care. This meta-analysis examines the impact of ERAS programs on patient outcomes and recovery.

Methods A comprehensive search of all published randomized control trials (RCTs) assessing the use of ERAS programs in surgical patients was conducted. Outcomes analyzed were length of stay (LOS), overall mortality, 30-day readmission rates, total costs, total complications, time to first flatus, and time to first bowel movement.

Results Forty-two RCTs involving 5241 patients were analyzed. ERAS programs significantly reduced LOS, total complications, and total costs across all types of surgeries ($p < 0.001$). Return of gastrointestinal (GI) function was also significantly improved, as measured by earlier time to first flatus and time to first bowel movement, $p < 0.001$. There was no overall difference in mortality or 30-day readmission rates; however, 30-day readmission rates after upper GI surgeries nearly doubled with the use of ERAS programs (RR = 1.922; $p = 0.019$).

Conclusions ERAS programs are associated with a significant reduction in LOS, total complications, total costs, as well as earlier return of GI function. Overall mortality and readmission rates remained similar, but there was a significant increase in 30-day readmission rates after upper GI surgeries. ERAS programs are effective and a valuable part in improving patient outcomes and accelerating recovery after surgery.

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Introduction

Approximately 321 million surgical procedures are performed annually worldwide, and the number is expected to rise with advances in technology and improvements in healthcare [1]. Persistent pain, gut dysfunction, and immobility often impede postoperative recovery and prolong hospitalization. Actions to support return to baseline function, however, can be taken without compromising patient safety and often even reduce complications. A compilation of these elements have been shown to be more beneficial than any single element alone [2]. These "enhanced recovery after surgery" (ERAS) programs have been developed and increasingly studied over the last few

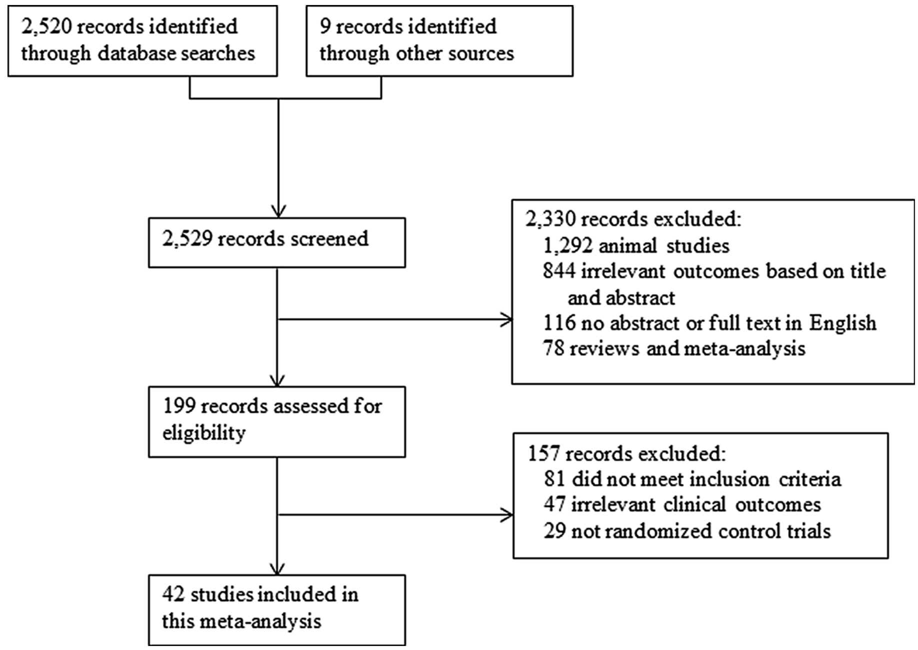

Fig. 1 CONSORT diagram of the study selection process

decades in an effort to improve patient outcomes and accelerate surgical recovery [3, 4].

ERAS programs consist of multidisciplinary and multifaceted approaches with interventions in all three phases of surgical patient care: preoperative, intraoperative, and postoperative [4]. Insulin resistance, prevention of postoperative infectious and respiratory complications, pain management, return of gastrointestinal (GI) function, and return to normal daily routine for the patient are all examples of outcomes that are targeted and assessed. Preoperative ERAS components aim to optimize the patient prior to surgery and include preadmission counseling, avoiding prolonged fasting, carbohydrate loading, selective use of bowel preparation, and antibiotic prophylaxis and thromboprophylaxis when necessary. Intraoperative ERAS components involving operative and anesthesia techniques include regional and local anesthetic blocks, avoidance of fluid overload, selective use of drains, and maintenance of normothermia, which minimizes disruption to the normal physiology. Postoperative ERAS components aim to enhance patient rehabilitation and recovery and include the avoidance of nasogastric tubes, early removal of catheters, drains, and chest tubes, prevention of postoperative nausea and vomiting, early oral nutrition, use of non-opioid oral analgesia, and early mobilization [4].

The first meta-analysis was published by Varadhan et al. in 2010 and included only six studies. This report demonstrated a significant reduction in length of stay (LOS) with the use of ERAS programs in elective open colorectal surgeries, but no difference in readmission or mortality rates [5]. More recently, Nicholson et al. [6] conducted a meta-analysis including 38 studies and demonstrated a significant overall reduction in LOS [standardized difference of means (SMD) = −1.15; 95% confidence interval (CI) −1.45 to −0.85; $p < 0.05$] and total complications [relative risk (RR) = 0.71; $p < 0.05$], with no significant difference in 30-day readmission or overall mortality with the use of ERAS programs. Limited subgroup analyses were conducted, and outcomes such as total hospital costs and return of GI function were not analyzed. Given that most studies involve colorectal surgeries, generalizations to other types of surgeries are difficult to make, and data into whether or not there are significant differences in the effectiveness of ERAS programs between different types of surgeries are lacking.

This current meta-analysis provides an updated comprehensive perspective on the impact of ERAS programs on various measures of patient outcome. Furthermore, this study aims to highlight the disparities within the published data and identify differences in the efficacy of these programs between different types of surgeries to guide future research.

Materials and methods

Study selection

A comprehensive search of all published RCTs evaluating the use of ERAS programs was conducted using PubMed, Cochrane Central Registry of Controlled Trials, and Google Scholar (1966–2016). The last search was conducted on February 11, 2016. Keywords used included combinations of "enhanced recovery after surgery," "enhanced recovery after

Table 1 Characteristics of all published randomized control trials evaluating the use of enhanced recovery after surgery programs in patients undergoing surgery (1966–2016)

References	Country	Number of patients (# ERAS, # control)	Surgery
Anderson et al. [23]	Denmark	25 (14, 11)	Elective right/left open hemicolectomy
Delaney et al. [24]	USA	64 (31, 33)	Laparotomy and intestinal resection
Gatt et al. [25]	UK	39 (19, 20)	Open colorectal
Recart et al. [26]	USA	25 (13, 12)	Laparoscopic nephrectomy
Peterson et al. [27]	Denmark	70 (34, 36)	Hip replacement
Gralla et al. [28]	Germany	50 (25, 25)	Laparoscopic radical prostatectomy
Khoo et al. [29]	UK	70 (35, 35)	Colorectal (assume open)
Larsen et al. [30]	Denmark	87 (45, 42)	Total knee and hip replacement
Muehling et al. [31]	Germany	58 (30, 28)	Lung resection
Borgwardt et al. [32]	Denmark	40(17, 23)	Knee replacement
Ionescu et al. [33]	Romania	96 (48, 48)	Open colorectal
Muehling et al. [34]	Germany	99 (49, 50)	Infrarenal aneurysm repair
Muller et al. [35]	Switzerland	151 (76, 75)	Open colorectal
Serclova et al. [36]	Czech Republic	103 (51, 52)	Open colorectal
Liu et al. [37]	China	63 (33, 30)	Gastric cancer surgery
Wang et al. [38]	China	92 (45, 47)	Gastric cancer surgery
Demanet et al. [39]	France	45 (22, 23)	Radical nephrectomy
Garcia-Botello et al. [40]	Spain	119 (61, 58)	Mixed laparoscopic and open colorectal
Lee et al. [41]	Korea	100 (46, 54)	Laparoscopic colon resection
Roig et al. [42]	Spain	108 (69, 39)	Mixed laparoscopic and open colorectal
Sokouti et al. [43]	Iran	60 (30, 30)	Lung resection
Vlug et al. [44]	Netherlands	400 (193, 207)	Mixed laparoscopic and open colorectal
Wang et al. [45]	China	210 (106, 104)	Colorectal surgery
Hu et al. [46]	China	82 (40, 42)	Laparoscopic and open gastric cancer surgery
Kim et al. [47]	Korea	44 (22, 22)	Surgery for gastric cancer
Ren et al. [48]	China	597 (299, 298)	Colorectal (assume open)
Wang et al. [49]	China	163 (81, 82)	Mixed laparoscopic and open colorectal
Wang et al. [50]	China	99 (49, 50)	Laparoscopic colon resection
Yang et al. [51]	China	62 (32, 30)	Open colorectal
Feng et al. [52]	China	119 (59, 60)	Gastric cancer surgery
Jones et al. [53]	UK	91 (46, 45)	Liver resection
Lemanu et al. [54]	New Zealand	78 (40, 38)	Laparoscopic sleeve gastrectomy
Ni et al. [55]	China	160 (80, 80)	Hepatectomy
Feng et al. [56]	China	116 (57, 59)	Rectal cancer surgery
Gonenc et al. [57]	Turkey	47 (21, 26)	Perforated ulcer disease surgery
Jia et al. [58]	China	233 (117, 116)	Open colorectal
Li et al. [59]	China	445 (208, 237)	Colorectal
Lu et al. [60]	China	297 (135, 162)	Hepatectomy
Mari et al. [61]	Italy	50 (25, 25)	High anterior resection
Nanavati et al. [62]	India	60 (30, 30)	Any gastrointestinal
Zhao et al. [63]	China	68 (34, 34)	Esophagectomy
Bu et al. [13]	China	256 (128, 128)	Gastric cancer surgery

thoracic surgery," "enhanced recovery program," "fast track," "ERAS," and "ERATS." RCTs comparing the use of an ERAS program with conventional standard of care, with $\geq$4 components of the ERAS program, were included.

Data extraction

Articles retrieved were assessed for eligibility (Fig. 1). Primary clinical outcomes included hospital LOS, 30-day

Table 2 Components of the enhanced recovery after surgery program utilized in all randomized control trials evaluating the use of enhanced recovery after surgery programs (1966–2016)

References	Preoperative							Intraoperative				
	Preadmission counseling	Fluid and carbohydrate loading	No prolonged fasting	No/selective bowel preparation	Antibiotic prophylaxis	Thrombo-prophylaxis	No premedi-cation	Short-acting anesthesia agents	Mid-thoracic epidural anesthesia/analgesia	No drains	Avoidance of salt and water overload	Maintenance of normoth-ermia
Anderson et al. [23]	x	x	x	x				x	x	x		
Delaney et al. [24]												
Gatt et al. [25]	x	x		x				x		x		
Recart et al. [26]												
Peterson et al. [27]	x								x			
Gralla et al. [28]	x	x	x		x					x	x	x
Khoo et al. [29]		x	x						x			
Larsen et al. [30]	x	x	x									
Muehling et al. [31]	x		x						x			x
Borgwardt et al. [32]	x								x	x		
Ionescu et al. [33]	x	x	x	x						x		
Muehling et al. [34]			x	x								x
Muller et al. [35]			x		x	x			x	x		
Serclova et al. [36]	x	x	x	x					x			
Liu et al. [37]	x	x	x	x						x		x
Wang et al. [38]	x		x	x			x		x	x	x	
Demanet et al. [39]												
Garcia-Botello et al. [40]	x		x	x	x	x						
Lee et al. [41]	x											
Roig et al. [42]		x	x	x					x	x		
Sokouti et al. [43]									x			
Vlug et al. [44]	x	x	x	x			x	x		x	x	
Wang et al. [45]	x	x	x	x			x		x	x	x	
Hu et al. [46]	x		x	x						x	x	
Kim et al. [47]	x	x	x	x								x
Ren et al. [48]		x		x					x	x	x	
Wang et al. [49]		x	x	x					x	x		
Wang et al. [50]		x	x	x					x		x	
Yang et al. [51]		x	x		x					x	x	x
Feng et al. [52]		x	x							x		x
Jones et al. [53]	x	x	x	x	x	x	x		x	x	x	x
Lemanu et al. [54]	x	x	x			x				x		
Ni et al. [55]	x	x	x	x			x		x	x	x	
Feng et al. [56]		x	x	x						x		x
Gonenc et al. [57]	x	x		x	x	x		x			x	x

Table 2 continued

References	Preoperative Preadmission counseling	Fluid and carbohydrate loading	No prolonged fasting	No/selective bowel preparation	Antibiotic prophylaxis	Thrombo-prophylaxis	No premedi-cation	Intraoperative Short-acting anesthesia agents	Mid-thoracic epidural anesthesia/ analgesia	No drains	Avoidance of salt and water overload	Maintenance of normoth-ermia
Jia et al. [58]		x	x	x					x	x		
Li et al. [59]	x		x	x	x				x	x		x
Lu et al. [60]	x	x	x	x	x					x		
Mari et al. [61]		x	x								x	
Nanavati et al. [62]		x	x	x	x					x		
Zhao et al. [63]	x	x	x				x		x	x		x
Bu et al. [13]	x	x	x	x	x					x		x

Study	Postoperative Mid-thoracic epidural anesthesia/ analgesia	No nasogastric tubes	Prevention of nausea and vomiting	Avoidance of salt and water overload	Early removal of catheter	Early oral nutrition	Non-opioid oral analgesia/ NSAIDs	Early mobilization	Stimulation of gut motility	Audit of compliance/ outcomes
Anderson et al. [23]	x	x					x	x		
Delaney et al. [24]		x				x	x	x		
Gatt et al. [25]		x			x	x	x	x	x	
Recart et al. [26]						x	x	x	x	
Peterson et al. [27]	x					x		x		
Gralla et al. [28]		x			x	x	x	x	x	
Khoo et al. [29]	x	x			x	x	x	x		
Larsen et al. [30]						x		x		
Muehling et al. [31]						x	x	x		
Borgwardt et al. [32]							x	x		
Ionescu et al. [33]		x			x	x	x	x	x	
Muehling et al. [34]		x		x		x	x	x		
Muller et al. [35]		x			x	x		x		
Serclova et al. [36]	x	x			x	x				
Liu et al. [37]						x	x	x		
Wang et al. [38]	x				x	x		x		
Demanet et al. [39]					x	x		x	x	
Garcia-Botello et al. [40]		x	x		x	x		x		
Lee et al. [41]		x			x	x		x		
Roig et al. [42]		x				x	x	x		
Sokouti et al. [43]	x					x		x		
Vlug et al. [44]		x			x	x	x	x		
Wang et al. [45]	x	x		x	x	x		x		

Table 2 continued

Study	Postoperative									
	Mid-thoracic epidural anesthesia/ analgesia	No nasogastric tubes	Prevention of nausea and vomiting	Avoidance of salt and water overload	Early removal of catheter	Early oral nutrition	Non-opioid oral analgesia/ NSAIDs	Early mobilization	Stimulation of gut motility	Audit of compliance/ outcomes
Hu et al. [46]		x			x	x	x	x	x	
Kim et al. [47]		x			x	x		x		
Ren et al. [48]	x		x		x	x	x	x	x	
Wang et al. [49]	x				x	x		x		
Wang et al. [50]					x	x		x		
Yang et al. [51]	x	x			x	x	x	x		
Feng et al. [52]					x	x		x		
Jones et al. [53]	x	x	x	x	x	x	x	x		
Lemanu et al. [54]		x	x			x		x		
Ni et al. [55]	x				x	x		x		
Feng et al. [56]					x	x	x	x		
Gonenc et al. [57]			x		x	x	x	x	x	
Jia et al. [58]		x			x	x		x		
Li et al. [59]					x	x	x	x		
Lu et al. [60]					x	x		x		
Mari et al. [61]		x			x	x	x	x		
Nanavati et al. [62]		x			x	x	x	x		
Zhao et al. [63]	x	x			x	x		x		
Bu et al. [13]	x	x				x		x		

Components included in this table are the components that were indicated in the paper. More components may have been utilized, but not recorded

NSAIDS non-steroidal anti-inflammatories

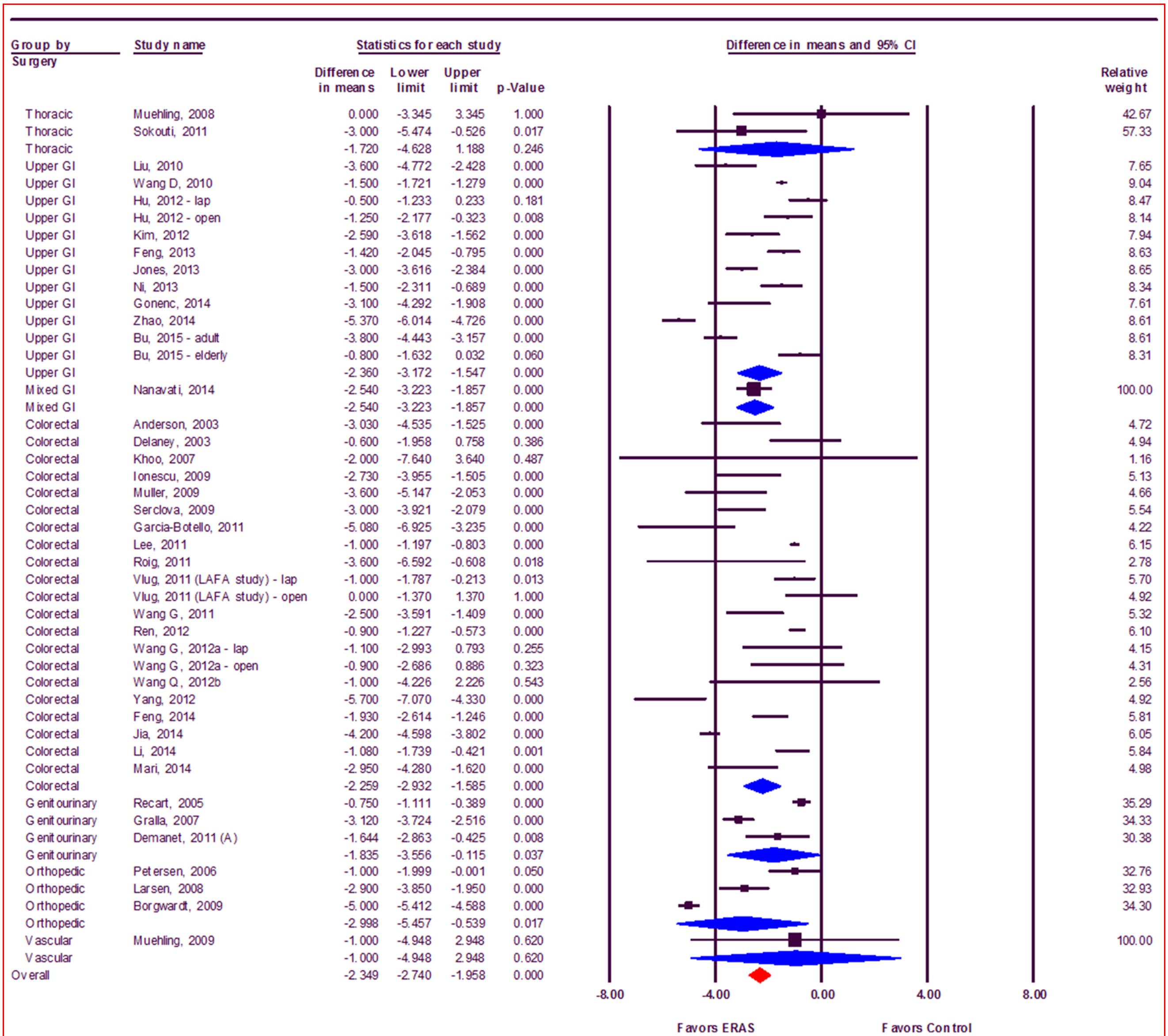

Fig. 2 Forest plot evaluating the difference in means in length of stay with the use of the enhanced recovery after surgery programs

readmission rates, overall mortality within 30 days of surgery, and total costs. Total complications, time to first flatus, and time to first bowel movement were also analyzed. Cost analysis was conducted in US dollars (USD), with currency conversion rates on July 27, 2015 (1 RMB = 0.160974 USD, 1 Euro = 1.10629 USD, and 1 NZD = 0.660284 USD).

Statistical analysis

RR and 95% CI for categorical data and difference in means (MD) and 95% CI for continuous data were calculated. Meta-analysis of the pooled data was performed using Comprehensive Meta-Analysis software Version 3 (Biostat, Englewood, NJ, USA). A continuity correction factor of 0.5 was applied to studies with zero incidence to calculate the RR and variance. Both the fixed-effect model and random-effect model were considered, depending on the heterogeneity of the included studies. Heterogeneity between studies was assessed using both Cochrane's Q statistic and I^2 statistic and considered statistically significant when $p < 0.05$ or $I^2 > 50$. If heterogeneity was observed, data were analyzed using a random-effect model, whereas a fixed-effect model was utilized in the absence of heterogeneity. Sensitivity analyses were conducted to determine the influence of each study on the overall relative risk estimates by removing each study in succession. Publication bias regarding the primary outcome (LOS) was

Group by Surgery	Study name	Risk ratio	Lower limit	Upper limit	p-Value	Relative weight
Upper GI	Liu, 2010	2.735	0.116	64.691	0.533	3.00
Upper GI	Wang D, 2010	1.044	0.067	16.200	0.975	3.99
Upper GI	Kim, 2012	3.000	0.129	69.868	0.494	3.03
Upper GI	Jones, 2013	4.894	0.241	99.182	0.301	3.32
Upper GI	Lemanu, 2013	0.950	0.397	2.276	0.908	39.33
Upper GI	Gonenc, 2014	2.476	0.501	12.228	0.266	11.77
Upper GI	Zhao, 2014	3.000	0.126	71.147	0.496	2.99
Upper GI	Bu, 2015 - adult	3.000	0.629	14.310	0.168	12.30
Upper GI	Bu, 2015 - elderly	4.000	1.185	13.505	0.026	20.27
Upper GI		1.922	1.111	3.324	0.019	
Mixed GI	Nanavati, 2014	1.000	0.066	15.260	1.000	100.00
Mixed GI		1.000	0.066	15.260	1.000	
Colorectal	Delaney, 2003	0.532	0.146	1.946	0.340	11.49
Colorectal	Gatt, 2005	0.263	0.032	2.148	0.213	4.38
Colorectal	Khoo, 2007	3.000	0.328	27.461	0.331	3.94
Colorectal	Muller, 2009	1.480	0.255	8.608	0.662	6.23
Colorectal	Garcia-Botello, 2011	1.426	0.247	8.230	0.691	6.29
Colorectal	Vlug, 2011 - lap	0.934	0.325	2.686	0.900	17.32
Colorectal	Vlug, 2011 - open	1.054	0.384	2.889	0.919	18.99
Colorectal	Wang G, 2011	0.436	0.139	1.372	0.156	14.70
Colorectal	Wang G, 2012a - lap	0.333	0.036	3.070	0.332	3.92
Colorectal	Wang G, 2012a - open	1.537	0.271	8.725	0.628	6.40
Colorectal	Wang Q, 2012b	0.680	0.119	3.896	0.665	6.34
Colorectal		0.815	0.525	1.265	0.361	
Genitourinary	Gralla, 2007	2.000	0.194	20.671	0.561	100.00
Genitourinary		2.000	0.194	20.671	0.561	
Overall		1.151	0.822	1.612	0.412	

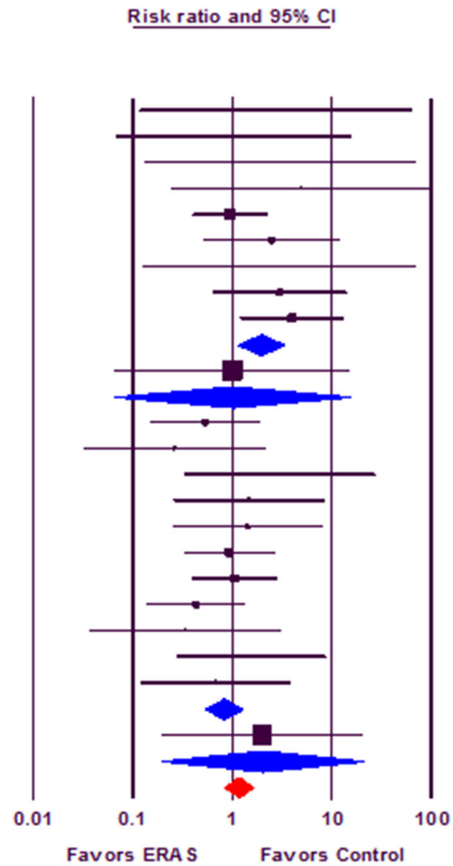

Fig. 3 Forest plot evaluating the relative risk of readmission within 30 days with the use of the enhanced recovery after surgery programs

visually evaluated by a funnel plot and quantitatively evaluated using Egger's and Begg's tests. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Forty-two RCTs were identified, involving 5241 patients (2595 ERAS and 2646 standard of care) (Tables 1 and 2, and Supplementary Material).

Effects of ERAS programs on length of stay

Meta-analysis demonstrated a significant reduction in LOS by 2.35 days with the use of the ERAS program compared to standard of care (MD = −2.349 days; 95% CI −2.740 to −1.958; $p < 0.001$; Fig. 2).

Subgroup analysis identified a significant reduction in LOS among GI surgeries (MD = −2.39; 95% CI −2.801 to −1.975; $p < 0.001$), with similar reductions among both upper GI (MD = −2.360; 95% CI −3.172 to −1.547; $p < 0.001$) and colorectal (MD = −2.259; 95% CI −2.932 to −1.585; $p < 0.001$) surgeries. Significant reductions were also observed among genitourinary (MD = −1.835; 95% CI −3.556 to −0.115; $p = 0.037$) and orthopedic surgeries (MD = −2.998; 95% CI −5.457 to −0.539; $p = 0.017$) but not among the two studies involving thoracic surgery or the single study involving vascular surgery. No significant between group heterogeneity was observed ($p = 0.921$).

There were significantly greater reductions in LOS among studies in European countries (RR = −3.300; $p < 0.001$) compared to Asian countries (RR = −1.704; $p < 0.001$), $p < 0.001$. Similar variations were seen among all types of surgeries.

Effects of ERAS programs on readmission within 30 days

Meta-analysis showed no significant difference in 30-day readmission rates between the ERAS and control groups (RR = 1.151; $p = 0.412$; Fig. 3). There was no significant

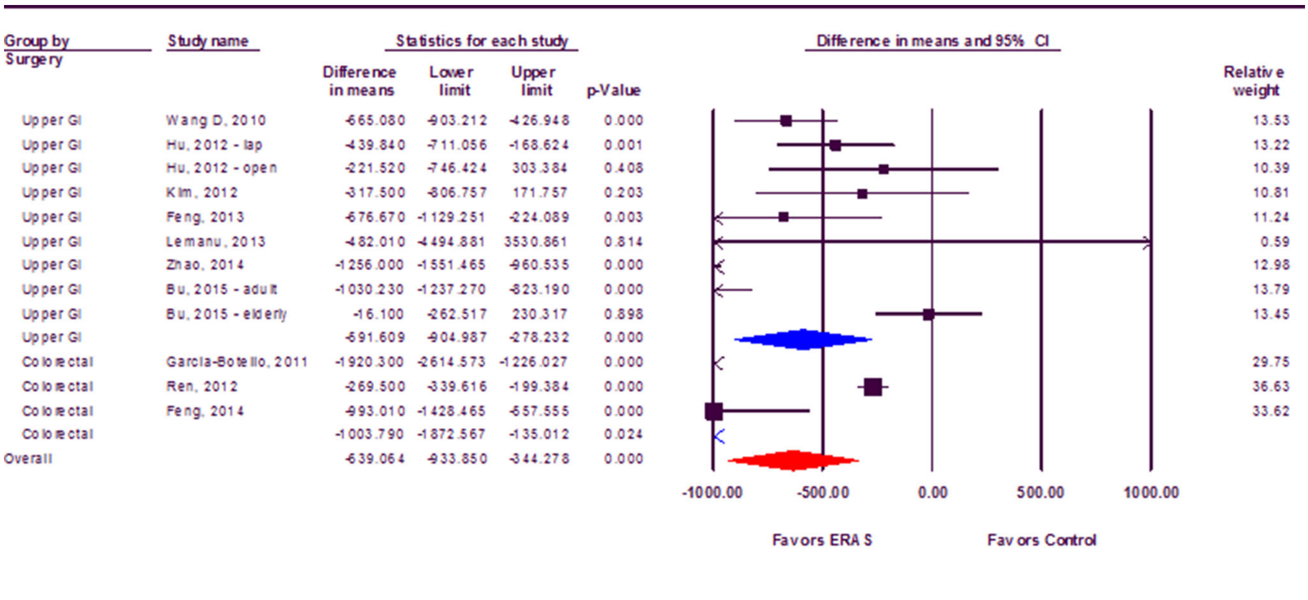

Fig. 4 Forest plot evaluating the difference in means for total cost of hospital stay with the use of the enhanced recovery after surgery programs

change in 30-day readmission rates among GI surgeries (RR = 1.138; $p = 0.457$).

There was a significant increase in 30-day readmission rates among upper GI surgery (RR = 1.922; 95% CI 1.111–3.324; $p = 0.019$), but no significant difference in 30-day readmission rates among colorectal or genitourinary surgeries. The single study involving vascular surgery reported zero readmissions in both groups.

Effects of ERAS program on total cost of hospital stay

Meta-analysis showed a significant reduction in the total cost of hospital stay between the ERAS and control groups (MD = −\$639.064; 95% CI −933.850 to −344.278; $p < 0.001$; Fig. 4).

Subgroup analysis identified a significant reduction in total costs among upper GI (MD = −\$591.609; 95% CI −\$904.987 to −\$278.232; $p < 0.001$) and colorectal surgeries (MD = −\$1003.790; 95% CI −\$1872.567 to −\$135.012; $p = 0.024$). Cost data were not reported from any of the thoracic, vascular, or orthopedic surgery studies.

Effects of ERAS programs on postoperative complications

Meta-analysis showed a significant 38.0% reduction in the risk of postoperative complications between the ERAS and control groups (RR = 0.620; 95% CI 0.545–0.704; $p < 0.001$; Fig. 5). Similarly, a 27.2% reduction was seen among GI surgeries.

Subgroup analysis identified a significant reduction in the risk of postoperative complications following upper GI (RR = 0.606; 95% CI 0.473–0.778; $p < 0.001$), colorectal (RR = 0.634; 95% CI 0.542–0.741; $p < 0.001$), and genitourinary surgeries (RR = 0.429; 95% CI 0.197–0.934; $p = 0.033$). No significant reduction in the risk of complications in the one thoracic surgery study was observed.

There were significant reductions in the risk of pulmonary complications by 57.3% (RR = 0.427; 95% CI 0.307–0.594; $p < 0.001$), cardiac complications by 52.7% (RR = 0.473; 95% CI 0.291–0.767; $p = 0.002$), and surgical site infections by 27.2% (RR = 0.728; 95% CI 0.560–0.948; $p = 0.018$) with the use of ERAS programs. No significant reduction in anastomotic leaks was observed (RR = 0.806; $p = 0.308$). Reductions in all types of complications following each type of surgery were observed.

Effects of ERAS programs on return of gastrointestinal function

Meta-analysis showed a significant reduction in time to first flatus between the ERAS and control groups (MD = −13.119 h; 95% CI −17.980 to −8.257; $p < 0.001$; Fig. 6). Subgroup analysis identified earlier time to first flatus after both upper GI (MD = −9.323; 95% CI −14.760 to −3.886;

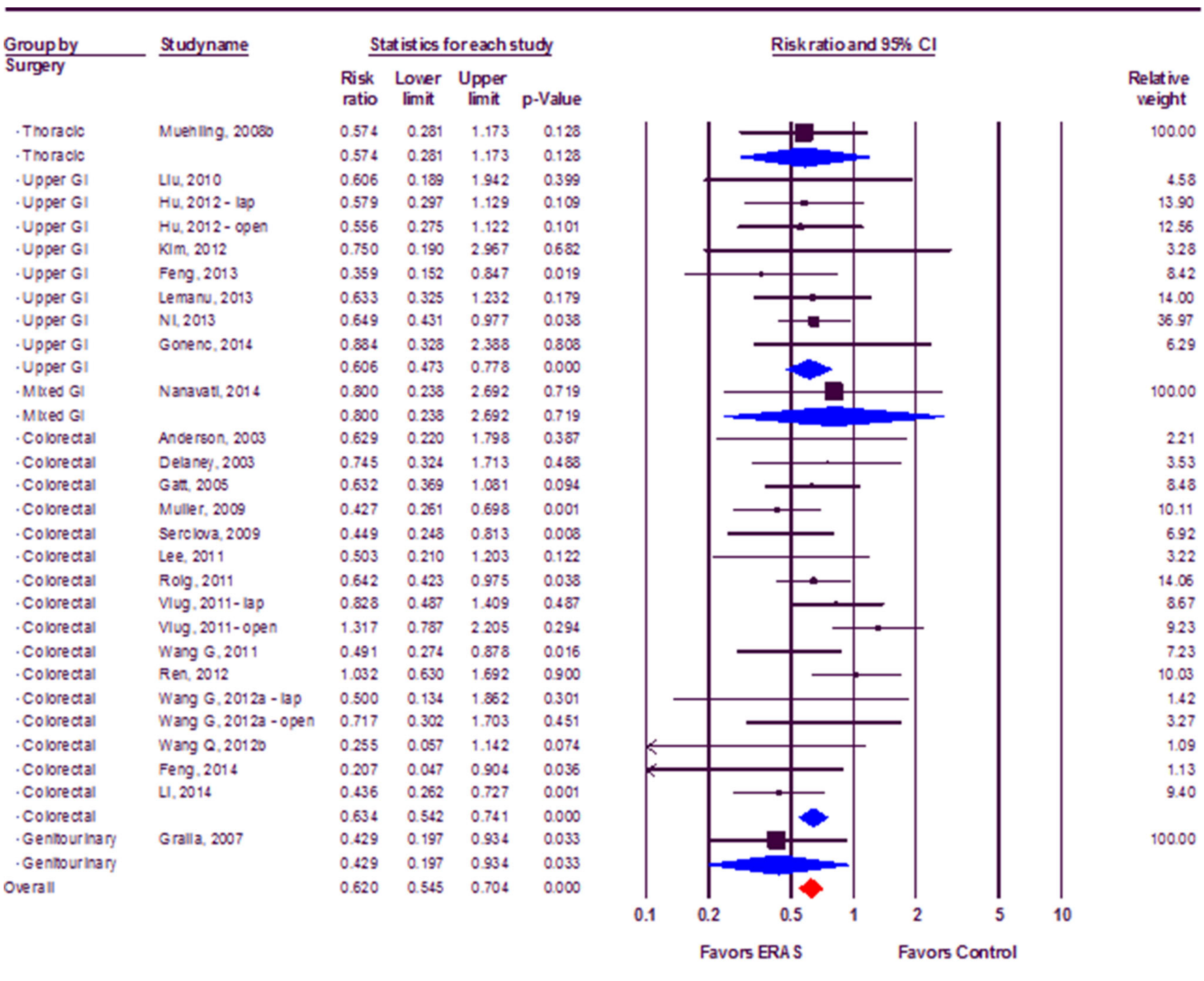

Fig. 5 Forest plot evaluating the relative risk of postoperative complications with the use of the enhanced recovery after surgery programs

$p = 0.001$) and colorectal surgeries (MD = −28.247; 95% CI −39.101 to −17.392; $p < 0.001$).

Meta-analysis showed a significant reduction in time to first bowel movement between the ERAS group and control groups (MD = −33.860 h; 95% CI −43.276 to −24.444; $p < 0.001$; Fig. 7). Subgroup analysis identified earlier time to first bowel movement after both upper GI (MD = −33.765; 95% CI −50.836 to −16.695; $p < 0.001$) and colorectal surgeries (MD = −33.901; 95% CI −45.190 to −22.612; $p < 0.001$).

Effects of ERAS programs on mortality

Meta-analysis showed no significant reduction in the risk of mortality (RR = 0.708; $p = 0.283$; Fig. 8). Similarly, there was no significant reduction in the risk of mortality among thoracic, upper GI, colorectal, or orthopedic surgeries, and no significant between group heterogeneity was observed ($p = 0.898$).

Laparoscopic versus open techniques

Although ERAS programs significantly reduced LOS in both laparoscopic (MD = −1.00; $p < 0.001$) and open (MD = −2.441; $p < 0.001$) colorectal surgeries, there was a significantly greater reduction seen among open surgeries ($p < 0.001$). No significant difference was found among readmission rates (RR = 0.680; $p = 0.665$ for laparoscopic and RR = 1.065; $p = 0.914$ for open) or overall mortality (RR = 3.060; $p = 0.490$ for laparoscopic and RR = 0.586; $p = 0.556$ for open).

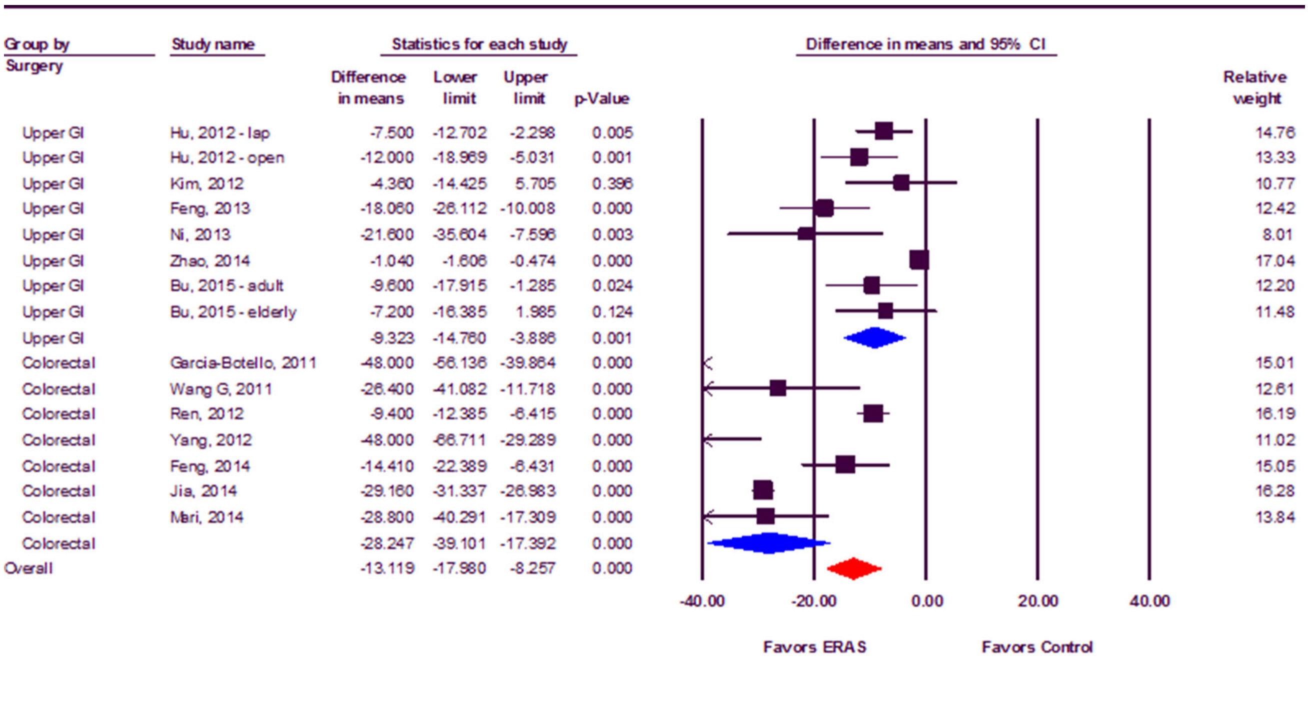

Fig. 6 Forest plot evaluating the difference in means for time to first flatus with the use of enhanced recovery after surgery programs

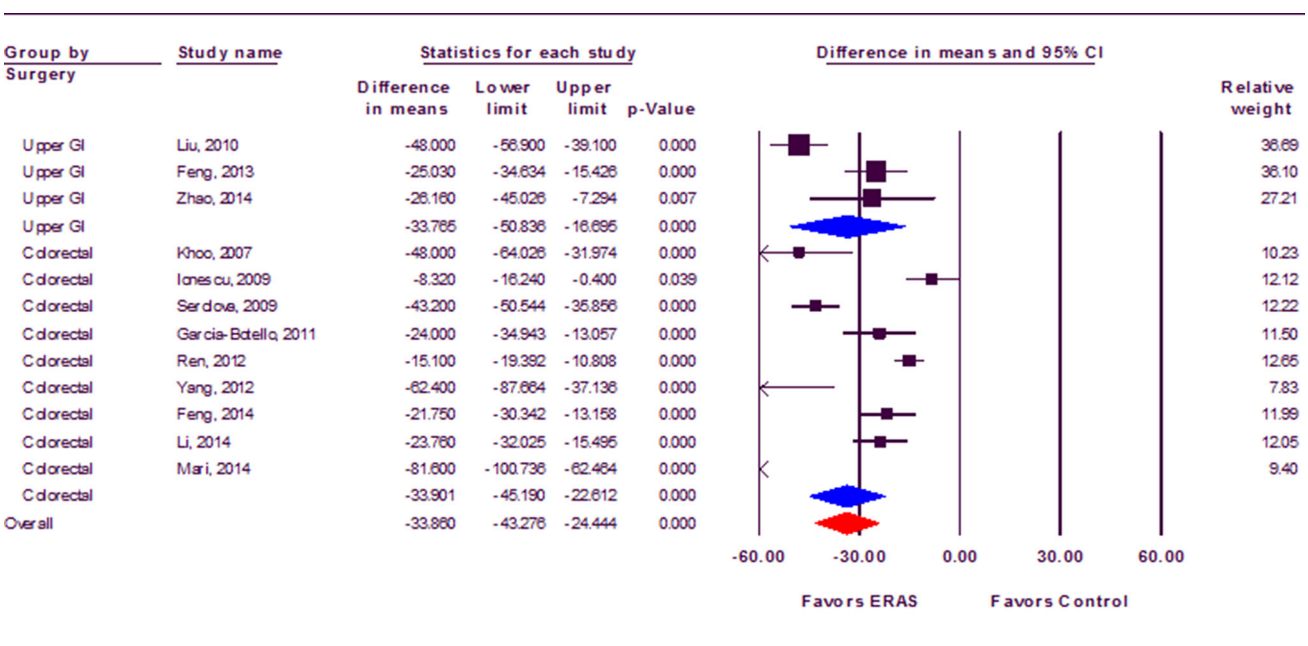

Fig. 7 Forest plot evaluating the difference in means for time to first bowel movement with the use of enhanced recovery after surgery programs

Group by Surgery	Study name	Risk ratio	Lower limit	Upper limit	p-Value	Relative weight
Thoracic	Muehling, 2008	0.933	0.061	14.219	0.960	57.40
Thoracic	Sokouti, 2011	0.333	0.014	7.870	0.496	42.60
Thoracic		0.602	0.076	4.739	0.630	
Upper GI	Jones, 2013	0.978	0.063	15.168	0.987	56.92
Upper GI	Gonenc, 2014	0.409	0.018	9.553	0.578	43.08
Upper GI		0.672	0.085	5.315	0.706	
Colorectal	Anderson, 2003	0.267	0.012	5.975	0.405	5.61
Colorectal	Gatt, 2005	4.200	0.183	96.193	0.369	5.53
Colorectal	Khoo, 2007	0.200	0.010	4.021	0.293	6.02
Colorectal	Roig, 2011	0.161	0.035	0.740	0.019	23.42
Colorectal	Vlug, 2011- lap	1.090	0.156	7.593	0.931	14.39
Colorectal	Vlug, 2011- open	2.108	0.395	11.235	0.383	19.36
Colorectal	Wang, 2011	1.962	0.181	21.312	0.580	9.53
Colorectal	Wang G, 2012a - lap	3.000	0.126	71.508	0.497	5.39
Colorectal	Wang G, 2012a - open	0.341	0.014	8.143	0.507	5.39
Colorectal	Wang Q, 2012b	3.060	0.128	73.344	0.490	5.37
Colorectal		0.790	0.378	1.649	0.529	
Orthopedic	Petersen, 2006	0.352	0.015	8.365	0.519	50.10
Orthopedic	Larsen, 2008	0.312	0.013	7.444	0.471	49.90
Orthopedic		0.331	0.035	3.118	0.334	
Overall		0.708	0.377	1.330	0.283	

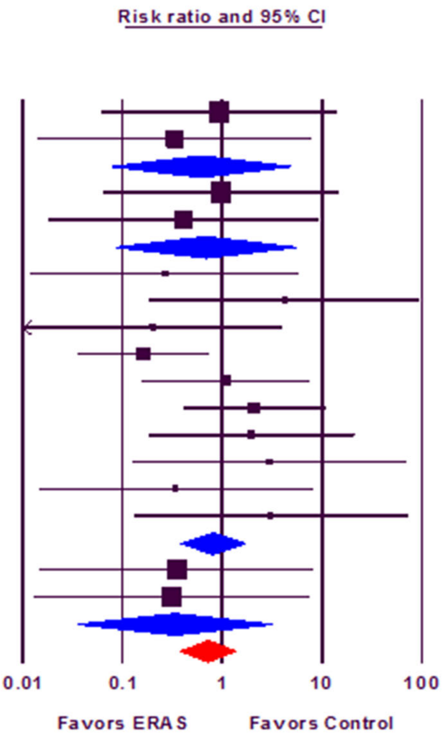

Fig. 8 Forest plot evaluating the relative risk of mortality with the use of the enhanced recovery after surgery programs

Subgroup analysis comparing laparoscopic and open techniques was not performed for non-colorectal surgeries, due to insufficient number of studies.

Sensitivity analyses

Similar overall effect estimates for length of stay, 30-day readmission rates, overall mortality, total hospital costs, postoperative complications, time to first flatus, and time to first bowel movement were observed with the removal of any single study.

Publication bias

There was no asymmetry on the funnel plot and no evidence of publication bias for the primary end point (LOS) by either the Egger's ($p = 0.109$) or Begg's test ($p = 0.722$).

Discussion

Surgery represents a major trauma to the body, triggering a cascade of physiological responses, collectively termed the stress response [7]. Surgical recovery is a complex process encompassing physical, psychological, social, and economic factors [8, 9]. ERAS programs involve evidence-based perioperative care elements aimed at addressing issues such as insulin resistance, pain management, return of GI function, and the prevention of postoperative infections and respiratory complications [7, 10]. When integrated together, ERAS programs seek to improve patient recovery and outcomes, by reducing complications and facilitating earlier hospital discharge [7, 10].

The current meta-analysis demonstrates that ERAS programs are associated with significant reductions in LOS, total hospital costs, total complications, and earlier return of GI function, with no difference in overall mortality or 30-day readmission rates, which is consistent with previous meta-analyses [6, 11]. In particular, significant reductions in SSIs, cardiac and pulmonary complications were seen. By reducing postoperative complications, ERAS programs reduce the need for hospitalization, and in turn, decrease LOS and total costs. Despite extensive available data documenting the effectiveness of ERAS, significant disparities between published studies exists. Moreover, a majority of studies have involved only colorectal surgeries, and significant differences exist between the LOS reductions observed between different types of surgeries.

Nearly all published studies involving colorectal surgery patients, and ERAS programs have shown reductions in LOS, overall complication rates, and readmission rates in both open and laparoscopic cases. A greater reduction in LOS was observed with open surgeries, possibly attributable to the longer LOS associated with open surgeries compared to laparoscopic surgeries. Similarly, a meta-analysis by Greco et al. [11] reported a significant reduction in overall morbidity by 40% and LOS by 2.28 days, without increasing readmission rates. Furthermore, there were no significant differences in readmission rates or mortality between the laparoscopic and open approach, concluding that laparoscopic surgery with the ERAS program does not compromise patients safety [12].

ERAS programs have proved beneficial in reducing postoperative complications, LOS, and total costs associated with upper GI surgeries. However, this appears to come at a cost of a significant increase in 30-day readmission rates following. It has been speculated that increased postoperative complications in the elderly may contribute to the higher readmission rates. Although there were insufficient number of studies involving elderly patients to allow for a subgroup analysis, Bu et al. [13] reported a significant increase in readmission rates with the use of ERAS programs among the elderly patients aged 75–89 years, but not adult patients age 45–74 years, which were attributed to an increase in postoperative complications including nausea and vomiting, intestinal obstruction, and anastomotic leaks with the use of ERAS programs among the elderly patients.

In addition to improved patient outcomes, ERAS programs have been reported to improve quality of life (QOL) and patient satisfaction. Wang et al. [14] studied 117 patients undergoing colorectal surgery and reported higher QOL scores within the first 21 days among patients with the ERAS program, but similar QOL scores at day 28. A pre- and post-implementation study by Wu et al. [15] reported an improvement in patient satisfaction scores from the 37th percentile pre-implementation to >97th percentile post-implementation.

Despite the documented benefits of the ERAS programs, adoption has been slow, and multiple barriers to full implementation and utilization have been recognized [16–19]. Limited hospital resources and lack of manpower and time are most often cited as the major barriers to implementation [16]. However, ERAS programs also reduce total hospital costs and have shown to be cost-effective with savings evident in the initial implementation period [20, 21]. Johns Hopkins Hospital developed a model of net financial costs involved with implementing the ERAS program among colorectal surgeries [22]. Despite the high costs ($522,783) associated with implementing the ERAS program, there was a substantial $948,500 cost savings in just the first year, resulting in a net savings of $395,717. Savings were mostly a direct result of decreased LOS, with estimated cost reductions ranging from $830 to $3100 per day [22].

Although the results of this meta-analysis are significant, there are limitations to this study due to the variation and heterogeneity of the RCTs. The patient demographics, type of surgery, and the specific ERAS components utilized differed between the studies. Standard of care practices and average LOS also varies by country. Most studies included in this meta-analysis involved GI surgery, and only a limited number of studies examined orthopedic, thoracic, and vascular surgeries. Few studies involved the elderly patient population, and additional RCTs studying the safety and efficacy of the ERAS program in the elderly is required. This study only included elective surgeries; however, published studies have also demonstrated the benefits of ERAS programs among emergency surgeries. Lastly, ERAS programs primarily target patient outcomes prior to hospital discharge, while complete surgical recovery extends past hospital discharge. Long-term recovery and return of pre-surgical function and activities are rarely studied and require further studies.

Despite these limitations, ERAS programs are an effective and valuable tool for improving patient outcomes and accelerating recovery after surgery. By significantly reducing postoperative complications, including SSIs, ERAS programs reduce LOS and total costs. Given the number of surgical procedures performed, the risk of morbidity and mortality associated with surgery, and the significant reduction in LOS and total complications, surgeons should consider implementing ERAS programs in the care of surgical patients.

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