



Enhanced recovery after abdominal wall reconstruction: a systematic review and meta-analysis

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Abstract

Background Enhanced recovery after surgery (ERAS) are evidence-based protocols associated with improved patient outcomes. The use of ERAS pathways is well documented in various surgical specialties. The aim of this systematic review and meta-analysis was to examine the efficacy of ERAS protocols in patients undergoing abdominal wall reconstruction (AWR).

Methods This systematic review and meta-analysis were reported according to PRISMA and MOOSE guidelines. The databases PubMed, EMBASE, CINAHL, Web of Science and Cochrane Library were searched for original studies comparing ERAS with standard care in patients undergoing AWR. The primary outcome was length of stay (LOS) and secondary outcomes were readmission and surgical site infection (SSI) and/or surgical site occurrences (SSO).

Results Five studies were included in the meta-analysis. All were retrospective cohort studies including 453 patients treated according to ERAS protocols, and 494 patients treated according to standard care. The meta-analysis demonstrated that patients undergoing AWR managed with ERAS had a mean 0.89 days reduction in LOS compared with patients treated with standard care (95% CI -1.70 to -0.07 days, $p=0.03$). There was no statistically significant difference in readmission rate (OR 1.00, 95% CI 0.53 to 1.87, $p=1.00$) or SSI/SSO (OR 1.19, 95% CI 0.67 to 2.11, $p=0.56$) between groups.

Conclusions The use of ERAS in patients undergoing AWR was found to significantly reduce LOS without increasing the readmission rate or SSI/SSO. Based on the existing literature, ERAS protocols should be implemented for patients undergoing AWR.

Keywords ERAS · Ventral hernia repair · Postoperative complications · Recovery · Length of stay

Enhanced recovery after surgery (ERAS) represents multimodal protocols to improve surgical outcomes and enhance the value of care [1]. The concept of fast-track surgery pathways was introduced in the mid-1990s as a care-bundle of evidence-based interventions to improve postoperative outcomes after surgery [2, 3]. In addition to enhanced patient outcomes, ERAS pathways are intended to provide a more economical and efficient utilization of the health care system [4]. ERAS include evidence-based protocols for preoperative, perioperative and postoperative measures with the goal of minimizing surgical stress and thus improve recovery and decrease the risk of organ dysfunction and postoperative

complications [1]. The approach is well documented in several surgical specialties and especially in colorectal surgery, where the implementation of ERAS has shown a reduction in overall postoperative complications and a significant reduction in length of stay (LOS) [5].

Abdominal wall reconstruction (AWR) for the repair of large ventral hernias is often requiring the use of component separation techniques and placement of large mesh materials. Patients undergoing AWR often have significant comorbidities and a high risk of postoperative complications, and therefore may benefit greatly from enrollment in an ERAS protocol [6].

The aim of this systematic review and meta-analysis was to examine the efficacy of ERAS protocols in patients undergoing AWR. The primary outcome was LOS and secondary outcomes were readmission and surgical site infection (SSI) and/or surgical site occurrences (SSO) requiring intervention.

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Materials and methods

The study is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines [7, 8]. The institutional review board (IRB) approval and written consent were not required for this systematic review. The protocol was not registered online before starting on this systematic review and meta-analysis.

Literature search strategy

A literature search was performed in the databases PubMed, EMBASE, CINAHL, Web of Science and Cochrane Library from initiation of the databases until 22 November 2019. The following search string was used in PubMed without language restrictions: ((incisional hernia repair) OR (ventral hernia repair) OR (abdominal wall reconstruction) OR (AWR)) AND ((fast-track) OR (enhanced recovery) OR (ERAS)). A translated search string was subsequently used in the other databases. Furthermore, the references of the included studies and the 100 first hits in Google Scholar were scrutinized for any additional eligible studies.

Study outcomes

The primary outcome of the study was LOS, defined as number of days of hospitalization after AWR. Secondary outcomes were 30-day readmission rate and SSI and/or SSO requiring intervention. SSI was defined as an infection occurring in the incision, deep tissue or organ space at the operation site, developing up to 30 days after surgery. SSO included SSI, seroma, wound dehiscence, enterocutaneous fistula, wound cellulitis, non-healing incisional wound, fascial disruption, skin or soft tissue ischemia or necrosis, wound serous or purulent drainage, stitch abscess, hematoma and infected or exposed mesh [9].

Study selection criteria

All original studies comparing ERAS with traditional care in patients undergoing AWR were assessed for eligibility. After removal of duplicates, all identified records were screened by title and abstract. Full-text articles were assessed by all named authors. Included studies fulfilled the following criteria: the study cohort constituted patients undergoing AWR; patients enrolled in an ERAS protocol was compared to a control group assigned to standard care; and the abovementioned study outcomes were described. Authors of identified studies were contacted to retrieve any relevant unreported

data. Exclusion criteria were conference abstracts, letters/comments and reviews. Furthermore, studies were excluded if a more recent publication with an overlapping patient population was identified.

Quality assessment of the included studies

The ROBINS-I tool was used to assess the risk of bias and the methodological quality of the included studies [10]. ROBINS-I is a tool for evaluating the risk of bias in non-randomized studies of interventions. According to ROBINS-I, each study is evaluated through “signaling questions” in seven different domains which then establish the basis for an overall risk of bias judgment for the outcome being assessed. Furthermore, the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology was used to assess the quality of evidence for outcomes reported in the included studies, and GRADEpro Guideline Development Tool software was used to develop an evidence table (Table 2) [11–13]. The included studies were evaluated on domains of study limitations (risk of bias), inconsistency, indirectness, imprecision and publications bias, and downgraded in case of important limitations. Additionally, according to GRADE, studies were upgraded to a higher level of evidence based on a strong magnitude of effect, in the presence of a dose–response gradient and residual confounding that would have reduced the demonstrated effect [13]. Finally, an overall rating of the quality of evidence across all outcomes was determined.

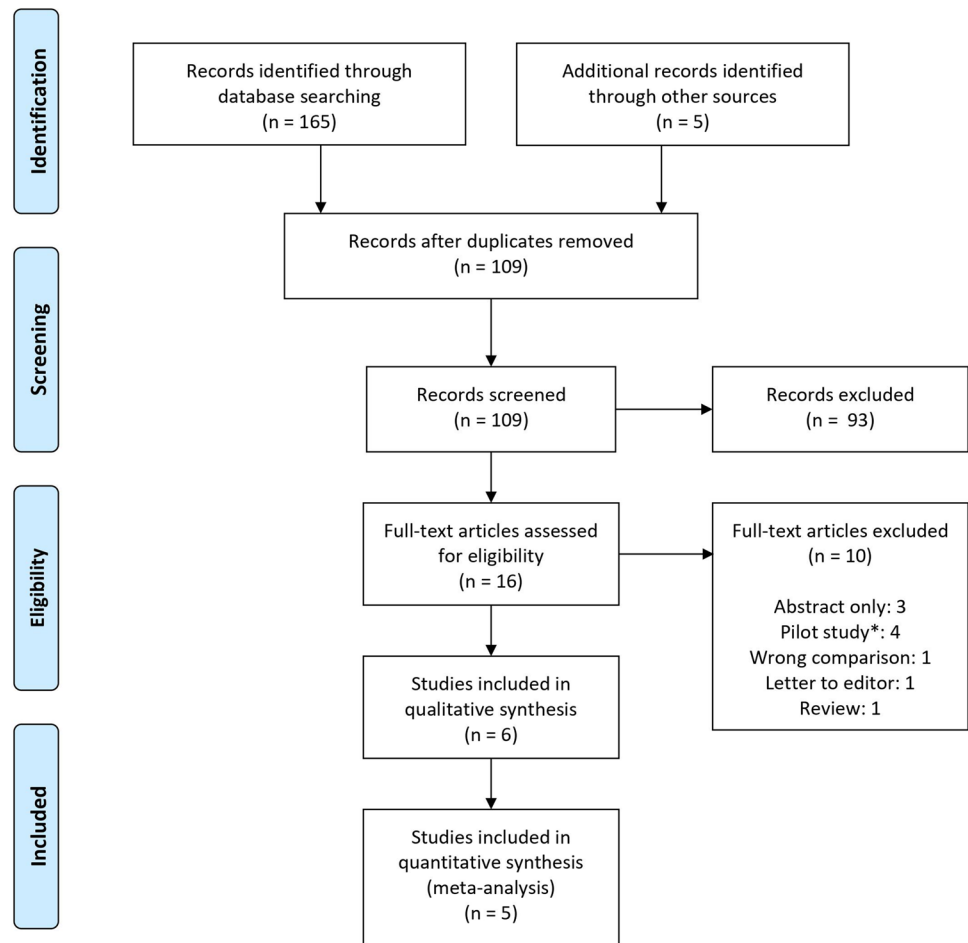
Statistics

Statistical analyses were performed with Review Manager, version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). For LOS, pooled data were analyzed with the inverse variance test using a random effects model to generate mean differences with 95% confidence intervals (CI). For dichotomous outcomes (readmission and SSI/SSO), pooled data were used to generate odds ratios (OR) with 95% CI using the Mantel–Haenszel test including a random effects model. The random effects model was used due to anticipated considerable heterogeneity among the included studies.

Results

In total, 109 unique records were screened, 16 full-text articles assessed for eligibility, and six studies were included in the review (Fig. 1). One study was excluded due to critical risk of bias [14]. The studies included a total of 947 patients undergoing AWR, 453 patients subjected to ERAS protocols compared with 493 historical controls treated according to

Fig. 1 Prisma chart of study selection for the current review



*Same data published in more recent publications with larger sample populations

standard care, considered as “non-ERAS”. All studies were retrospective cohort studies.

Assessment of the included studies

The five studies included in the meta-analyses had a moderate overall risk of bias according to the ROBINS-I tool (Table 1) [15–19]. The overall GRADE quality of evidence was evaluated to be low across all three outcomes. Detailed reasons for upgrade and downgrade are shown in Table 2 [20]. A low overall quality of evidence grade demonstrates a limited confidence in the effect estimates and that the true effect may be markedly different from the estimate of effect [11].

ERAS elements in the included studies

As illustrated in Table 3, the elements of the ERAS protocols in the included studies were heterogeneous. Only two of the included studies outlined the use of μ -opioid receptor antagonist alvimopan to accelerate intestinal recovery [15, 19].

Early oral feeding was described in three of the studies [15, 17, 18] and judicious intravenous fluid administration was reported by only two of the studies [15, 18]. However, all studies implemented postoperative multimodal pain control.

TAP block versus epidural

A transversus abdominis plane (TAP) block with use of liposomal bupivacaine was administered perioperative for all patients in two of the studies [15, 18]. Warren et al. [16] applied epidural catheters selectively for large VHR cases with expected LOS of at least 3 days. For patients not receiving an epidural, intraoperative ketamine infusion bolus was administered, followed by continuous infusion with the addition of intravenous lidocaine. Postoperative ketamine infusion was maintained at a subanesthetic dose, and epidural infusion was maintained at 8–12 ml/h of 0.125% bupivacaine. Jensen et al. [17] described placement of an epidural catheter in the thoracic vertebral interspace 8 to 10, according to the hernia location, preoperatively in all patients. The epidural anesthesia was

Table 1 Characteristics of the included studies

Study	Year	Study design	Number of patients	Hernia inclusion type	Hernia width, cm, mean \pm SD	BMI, kg/m ² , mean	ROBINS-I
Majumder et al.	2016	Retro cohort	100 ERAS 100 controls	Ventral hernias, primary or recurrent	ERAS 13.2 \pm 5.5 Control 14.4 \pm 5.0	ERAS 33.5 \pm 6.0 Control 33.9 \pm 7.1	Moderate overall risk of bias
Warren et al.	2017	Retro cohort	50 ERAS 73 controls	Ventral hernias, primary or recurrent	ERAS 10.1 \pm 4.6 Control 7.5 \pm 4.4	ERAS 31.8 \pm 7.1 Control 35.1 \pm 9.8	Moderate overall risk of bias
Jensen et al.	2018	Retro cohort	94 ERAS 96 controls	Complex abdominal wall defects, primary or recurrent	ERAS 14.9 \pm 5.8 Control 16.0 \pm 5.4	ERAS 28.3 \pm 4.6 Control 28.0 \pm 5.7	Moderate overall risk of bias
Colvin et al.	2019	Retro cohort	100 ERAS 100 controls	Midline, incisional or flank hernias, primary or recurrent	ERAS 15.5 \pm 6.2 Control 15.6 \pm 5.5	ERAS 31.0 \pm 5.4 Control 32.3 \pm 5.8	Moderate overall risk of bias
Ueland et al.	2019	Retro cohort	109 ERAS 125 controls	Ventral hernias, primary or recurrent	Not reported	Not reported	Moderate overall risk of bias

Retro cohort retrospective cohort study, *ERAS* enhanced recovery after surgery, *SD* standard deviation, *BMI* body mass index, *ROBINS-I* risk of bias in non-randomized studies – of interventions

discontinued on the evening of postoperative day (POD) 2, one hour after administration of oral morphine 10 mg, as analgesic bridging. The epidural catheter was then removed the morning after. In addition, the protocol by Jensen et al. utilized preoperative single-shot high dose glucocorticoid. Only one of the included studies did not report use of either epidural nor TAP block as perioperative pain control [19].

Length of stay (LOS)

All five studies reported LOS, and two of the studies demonstrated a statistically significant reduction in LOS in the ERAS group compared with standard care [15, 17]. The meta-analysis demonstrated that patients undergoing AWR managed with ERAS protocols had a mean reduction in LOS of 0.89 days compared with patients managed with standard care (95% CI – 1.70 to – 0.07 days, $p = 0.03$, Fig. 2).

Readmission rate

One study demonstrated a significant reduction in readmission rate when implementing ERAS protocols compared to standard care [15]. Readmission rates ranged from 4 to 21% for the ERAS protocol groups, and from 4 to 19% for the traditional care groups. The estimated OR (ERAS vs. standard care) for readmission was 1.00 (95% CI 0.53 to 1.87,

$p = 1.00$), indicating that readmission was equally likely to occur in both groups (Fig. 3).

Surgical site infection (SSI)/surgical site occurrence (SSO)

Four studies reported on SSI/SSO [16–19]. SSI/SSO rates ranged from 3 to 28% in the ERAS group and 3% to 40% in the standard care group. Ueland et al. [19] was the only study demonstrating a trend towards decreased SSI/SSO rates with the use of ERAS protocols. In the meta-analysis, there was no statistically significant difference in SSI/SSO (OR ERAS vs. standard care 1.19, 95% CI 0.67 to 2.11, $p = 0.56$) between groups (Fig. 4).

Other outcomes

Other outcomes relevant for evaluating the effect of ERAS were also reported. Majumder et al. [15] demonstrated that the use of ERAS resulted in significantly shorter times to liquid and regular diet (1.1 vs 2.7 and 3.0 vs 4.8 days, respectively), and significantly shorter times to flatus and bowel movement (3.1 vs 3.9 and 3.6 vs 5.2 days, respectively) compared with standard care. Warren et al. found that the use of ERAS nearly eliminated patient-controlled analgesia use and significantly reduced narcotic requirements on POD 0, 1, and 2 compared to standard care [16]. Colvin et al. showed a trend toward a decreased duration of epidurals or use of patient-controlled analgesia for ERAS compared with standard care [18].

Table 2 Grading of recommendations, assessment, development and evaluation (GRADE) summary of outcomes

Certainty assessment		No of patients			Effect		Certainty		Importance		
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ERAS	Standard care	Relative (95% CI)	Absolute (95% CI)	
Length of stay (assessed with: Number of days of hospitalization after AWR)											
5	Observational studies	Not serious	Serious ^a	Serious ^b	Not serious	None	453 patients	493 patients 0.0%	Mean Difference -0.89 (-1.70 to 0.07) [Length of stay]	- per 1 000 (from - to -) - per 1 000 (from - to -)	⊕⊕○○ LOW CRITICAL
Readmission rate (follow up: 30 days)											
5	Observational studies	Not serious	Serious ^a	Serious ^b	Not serious	None	56/453 (12.4%)	0.0%	OR 1.00 (0.53 to 1.87)	0 fewer per 1 000 (from 0 to 0 fewer)	⊕⊕○○ LOW IMPORTANT
Surgical site infection/surgical site occurrence											
4	Observational studies	Not serious	Serious ^a	Serious ^b	Not serious	None	67/353 (19.0%)	71/393 (18.1%) 0.0%	OR 1.19 (0.67 to 2.11)	27 more per 1 000 (from 52 fewer to 137 more) 0 fewer per 1 000 (from 0 to 0 fewer)	⊕⊕○○ LOW IMPORTANT

Question ERAS compared to Standard care for patients undergoing AWR

AWR abdominal wall reconstruction, *CI* confidence interval, *OR* odds ratio

^aDue to significant heterogeneity across studies

^bDue to differences in population and intervention among the included studies

Table 3 Comparison of ERAS protocol elements in the studies included in meta-analyses

Study	Preoperative protocol	Perioperative (intraoperative) protocol	Postoperative protocol
Majumder 2016	Weight loss counseling Diabetic control (HbA1c < 8) Smoking cessation (≥ 4 weeks) OSA screening IMPACT nutrition shake MRSA screening	SQ Heparin 5000 \times 1 + SCDs PO Alvimopan 12 mg \times 1 PO Gabapentin 100–300 mg \times 1 1. Generation Cephalosporin + Vancomycin for positive MRSA screen Minimization of narcotics/paralytics TAP block, liposomal bupivacaine	IV Hydromorphone PCA PO Oxycodone 5–10 mg q 4 h PRN after PCA PO Acetaminophen 650 mg q 6 h PO Gabapentin 100–300 mg tid IV/PO Diazepam 5 mg q 6 h PRN PO NSAIDs 600–800 mg q 6–8 h PRN NPO except meds on POD0 only Scheduled diet advancement: POD1 limited clears POD2 clear liquids ad lib POD3 regular diet PO Alvimopan 12 mg until discharge or POD7 Fluid conservative strategy
Warren 2017	300 ml carbohydrate-rich beverage Pregabalin 75 mg Acetaminophen 1000 mg Celecoxib 400 mg Oxycodone HCl extended release 10 mg EPI selectively for large VHR cases	IV Ketamine bolus, followed by IV 0.5 mg/kg/h IV Lidocaine For patients receiving EPI: only IV Bupivacaine	IV Ketamine 8–16 mg/h IV Ketorolac IV Acetaminophen PO Oxycodone or Hydrocodone PRN EPI 8–12 ml/h of 0,125% Bupivacaine
Jensen 2018	Weight loss if BMI > 35 kg/m ² Complete smoking cessation Reduction in alcohol consumption if excessive Information about expected discharge and discharge criteria PO Paracetamol 1 g PO Ibuprofen 400 mg PO Gabapentin 600 mg High dose glucocorticoid LMWH 3500 IU EPI	IV Methylprednisolone 125 mg Abdominal binder applied at completion of surgery	PO Paracetamol 1 g \times 4 PO Ibuprofen 400 mg \times 3 Required daily assessment of discharge criteria EPI until POD2 PO Morphine 10 mg 1 h before pausing EPI PO Morphine or oxycodone PRN Early oral feeding Pulmonary physiotherapy Chewing gum until bowel function Urinary catheter removed after 24 h Enema after 48 h if no bowel function Drains removed when daily output < 60 mL Abdominal binder until 30-day follow-up
Colvin 2019		TAP block, liposomal bupivacaine Goal directed IVF Foley Subfascial drains	IV PCA with hydromorphone max. 0.2 mg q 6 min. until POD3 Toradol q 6 h PO Acetaminophen 650 mg q 6 h on POD1 PO Gabapentin 300 mg \times 3 on POD1 PO Oxycodone 5 mg q 4 h on POD2 NPO in PACU Scheduled diet advancement: POD0 Clear liquid POD1 Milk of magnesium 30 mL \times 2 and Docusate 100 mg \times 2 POD2-3 Regular diet Limited IVF 75 mL/h and decreasing rate if good UOP and tolerating PO Discontinue IVF on POD3 Foley removed on POD2 Subfascial drains removed when output < 30 mL/24 h Early ambulation and mobilization Physical therapy PRN

Table 3 (continued)

Study	Preoperative protocol	Perioperative (intraoperative) protocol	Postoperative protocol
Ueland 2019	BMI ≤ 40 kg/m ² HbA1c ≤ 8 No tobacco within the past 30 days of surgery One dose Heparin or Lovenox Gatorade or IVF's 4 h prior to surgery One dose Almivopan	< 5 cc/kg/h or < 2 L of IVF's Temperature ≥ 36°	No scheduled opioids Greater than two modes of non-opioid multimodal pain management, including: Epidural with bupivacaine, Acetaminophen, Ibuprofen, Ketorolac, Lidocaine, Gabapentin, Cyclobenzaprine, Diazepam, or Baclofen Almivopan BID until return of bowel function Scheduled Heparin or Lovenox doses Early mobilization: patient ambulation by the end of POD1

EPI epidural catheter, *HbA1c* hemoglobin A1c, *IV* intravenous, *IVF* intravenous fluids, *LMWH* low molecular weight heparin, *MIVF* maintenance intravenous fluids, *NGT* nasogastric tube, *NPO* nil per os, *OSA* obstructive sleep apnea, *PACU* post anesthesia care unit, *PCA* patient-controlled analgesia, *POD* postoperative day, *PRN* as needed, *RNF* regular nursing floor, *SCD* sequential compression device, *SQ* subcutaneous, *TAP* transversus abdominis plane, *UOP* urinary output, *VHR* ventral hernia repair

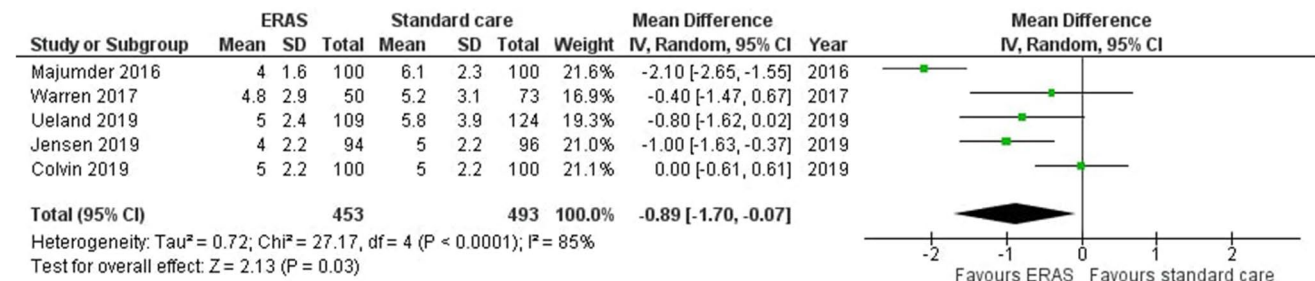


Fig. 2 Forest plot of length of stay after enhanced recovery (ERAS) and standard care after abdominal wall reconstruction for ventral hernia

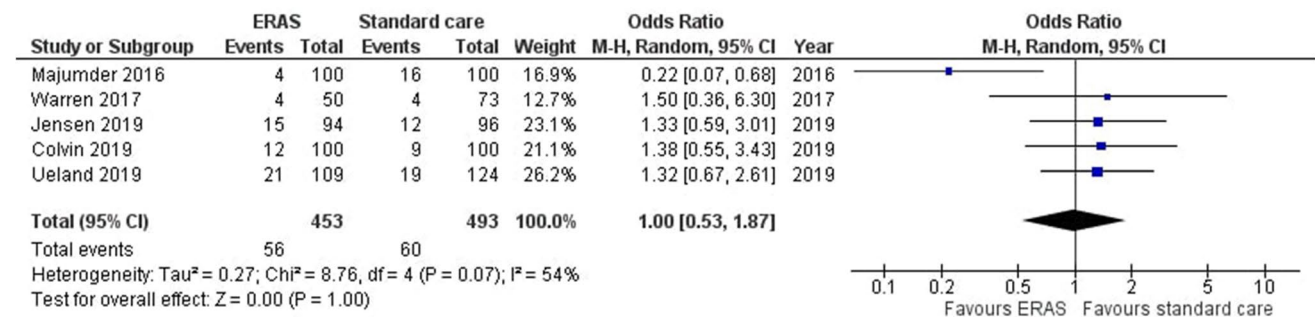


Fig. 3 Forest plot of readmission rates after enhanced recovery (ERAS) and standard care after abdominal wall reconstruction for ventral hernia

Discussion

This systematic review and meta-analysis presented the current research on ERAS protocols in relation to AWR, focusing on LOS, readmission rate and SSI/SSO. The results demonstrated a significant association between the

use of ERAS pathways and a reduction in LOS in patients undergoing AWR. There were no significant differences between the use of ERAS pathways and readmission rate or SSI/SSO in patients undergoing AWR.

This meta-analysis found a slight, yet significant reduction in LOS with the use of ERAS protocols for AWR compared with standard care. A small pilot study on ERAS,

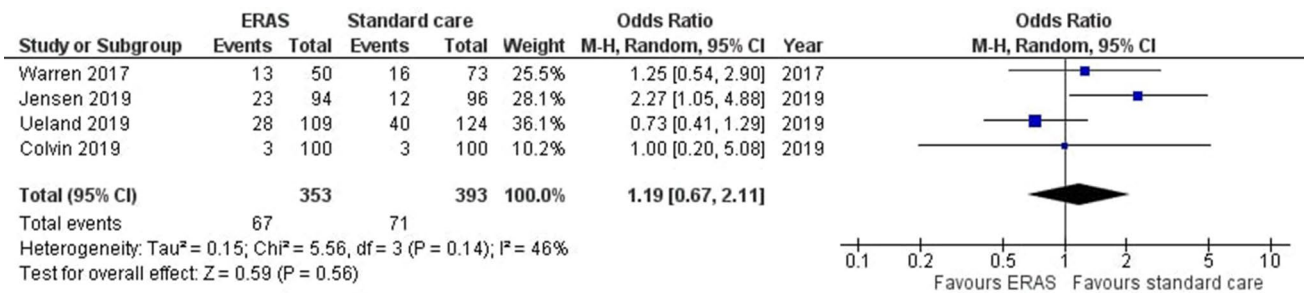


Fig. 4 Forest plot of surgical site infection/surgical site occurrence after enhanced recovery (ERAS) and standard care after abdominal wall reconstruction for ventral hernia

excluded from this review due to overlapping patient populations, also showed a significant reduction in LOS after the implementation of ERAS [21]. Even though the mean reduction in LOS was less than 1 day, these results strengthen the perception that ERAS pathways do have clinical implications to shorten LOS. However, the heterogeneity in our meta-analysis was rather high, indicating that the results from the included studies regarding LOS might not be comparable due to methodological variations in the included studies.

In colorectal surgery, extensive research has demonstrated a reduction in LOS with the use of ERAS protocols [5], and in 2018, Visioni et al. [22] reported that ERAS protocols reduced LOS without increasing complications or readmission rates in non-colorectal abdominal surgery.

There was a wide range in readmission rates among the included studies, and only one of the included studies demonstrated a significant reduction in readmission rate with the use of ERAS protocols compared with standard care [15]. These results are similar to those obtained from studies of ERAS in other surgical specialties [23, 24]. Importantly, the readmission rates were not increased despite an earlier discharge from the hospital in the ERAS patients compared with standard care.

Similarly, the results regarding SSI/SSO showed a great variety within the included studies. This variation in complication rates may reflect inter-study differences in patient populations and surgical techniques applied [25]. Reasons for reduced complication rates after ERAS implementation have been proposed to include reduced catabolism, reduced loss of muscle mass as well as muscle function, all due to the fast removal of drains, early oral feeding and mobilization [26]. However, in this study, we found no difference in rates of SSI/SSO comparing ERAS and standard care after AWR.

Patients undergoing AWR are heterogenous and often have several comorbidities that might affect the outcomes regarding postoperative complications and readmission rates. Lovecchio et al. [27] showed that patients undergoing ventral hernia repair had a 4.9% 30-day readmission rate. Although complications were the main reason for

readmission, the authors underlined that surgeons must be aware of comorbidities that may increase the risk of readmission, even in the absence of complications. The most common postoperative complications in patients undergoing AWR are wound-related, such as SSI [28]. SSIs can lead to increased LOS, readmissions, reoperations as well as increase the risk of hernia recurrence [29].

In 2014, Fayeziadeh et al. [4], suggested a standard for ERAS pathways for patients undergoing AWR using evidence-based interventions. The studies included in this review represent various ERAS pathways in both the preoperative and postoperative care of the patients. This presumably reflects the patient population, which may differ significantly between institutions. Therefore, it has been suggested that the ERAS protocols for patients undergoing AWR should be individualized and flexible to improve patient outcomes [1].

The postoperative analgesic treatment of patients undergoing AWR remains subject to debate. Traditionally, epidural catheters have been used in accordance with the standard of care for patients undergoing traditional open surgery and has also been described as an important element of ERAS pathways to minimize the use of opioids [26]. Recently, however, the use of TAP blocks has gained support, as hypotensive episodes and risk of epidural headaches are avoided [30, 31]. The introduction of long-lasting liposomal bupivacaine (Exparel®) may further improve the outcomes of TAP blocks for patients undergoing AWR, however, no conclusions can be made based on the current literature [32].

ERAS protocols are, among other things, developed to provide a more efficient utilization of health care resources, with the goal of enhancing patient outcome and reducing costs [1, 33]. A recent study evaluating the clinical and financial impacts of ERAS protocols for patients undergoing AWR demonstrated that implementation of ERAS improved clinical outcomes without affecting total costs [33]. However, the study did not demonstrate a reduction in LOS, possibly due to the use of epidural analgesia. Nevertheless, a reduction in costs due to decreased LOS in

non-colorectal abdominal surgical procedures has previously been described [22].

This is the first systematic review and meta-analysis on ERAS in patients undergoing AWR. The study is limited by the fact that the included studies are retrospective cohort studies, with historical control groups, and not randomized controlled trials. This imposes a risk of selection bias. Further, the heterogeneity of the studies might have biased the meta-analyses. Nevertheless, it seems likely that ERAS pathways have a place in complex AWR, as in other major abdominal surgery.

In conclusion, ERAS after AWR was found to significantly reduce the postoperative LOS by no more than one day, but without increasing the rate of postoperative complications or readmissions. However, due to heterogeneity the results should be treated with precautions and a more uniform approach is required. Based on the current literature ERAS should be implemented for patients undergoing AWR.

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Compliance with ethical standards

Disclosures Lise Lode, Erling Oma, Nadia A. Henriksen and Kristian K. Jensen have no conflicts of interest or financial ties to disclose.

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