



Enhanced recovery after surgery protocols in adrenal surgery: a systematic review and meta-analysis

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Background: Enhanced recovery after surgery (ERAS) protocols aim to attenuate the physiological stress of surgery and accelerate postoperative recovery. While widely adopted in several surgical fields, their role in adrenal surgery remains less defined. The aim of this systematic review and meta-analysis was to evaluate the impact of ERAS protocols on perioperative outcomes in patients undergoing adrenalectomy compared with conventional care.

Methods: Eligible studies included randomized controlled trials (RCTs), prospective cohorts, and retrospective comparative analyses involving adult patients undergoing adrenalectomy managed with ERAS versus standard care. A systematic literature search was conducted in PubMed, Scopus, ScienceDirect, and the Cochrane Library, without time restrictions, with the last search performed in August 2025. Primary outcomes were postoperative length of stay (LOS), pain, and complication rates. Secondary outcomes included functional recovery, gastrointestinal recovery, and hospital costs. Risk of bias (RoB) was assessed using the RoB 2.0 tool for RCTs and the ROBINS-I tool for non-randomized studies. Quantitative synthesis was performed using a random-effects meta-analysis, with standardized mean differences (SMDs) and risk ratios used to summarize continuous and dichotomous outcomes, respectively.

Results: Six comparative studies, including a total of 429 patients, met the inclusion criteria. ERAS protocols were associated with a significant reduction in postoperative LOS, postoperative complications, and pain scores. ERAS pathways also resulted in faster functional recovery, including earlier mobilization, urinary catheter removal, and gastrointestinal recovery, without an increase in major complications. Although individual studies reported cost savings with ERAS implementation, pooled analysis did not demonstrate a statistically significant reduction in hospitalization costs.

Conclusions: ERAS protocols in adrenalectomy are associated with improved perioperative outcomes, faster recovery, and reduced postoperative morbidity without compromising safety. However, the available evidence is limited by heterogeneity and methodological quality. Further high-quality prospective studies are needed to develop and validate standardized ERAS guidelines tailored specifically to adrenal surgery.

Keywords: Adrenal; adrenalectomy; enhanced recovery after surgery (ERAS); mini-invasive

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Introduction

Over the past two decades, enhanced recovery after surgery (ERAS) programs have evolved from experimental concepts to established perioperative strategies across a broad range of surgical specialties (1). Their effectiveness has been most clearly demonstrated in colorectal and upper gastrointestinal surgery, with evidence of benefit also emerging in bariatric, hepatobiliary, thoracic, and urologic procedures (2-5). More recently, ERAS principles have been extended to complex operations such as pancreatic and abdominal wall surgery, as well as to purely demolitive procedures, including adrenalectomy (6-8). ERAS pathways are multimodal, evidence-based approaches designed to attenuate the metabolic and inflammatory stress response to surgery and to restore physiological function as quickly as possible (9). Typical components include preoperative counselling, shortened fasting with carbohydrate loading, multimodal and opioid-sparing analgesia, early oral intake and mobilization, fluid restriction, maintenance of normothermia, and the avoidance or early removal of drains and catheters. The adoption of minimally invasive techniques, which have become the gold standard for adrenalectomy, further supports the application of ERAS principles by minimizing surgical trauma and facilitating earlier recovery. Adrenalectomy, however, presents unique perioperative challenges. Many adrenal tumours are hormonally active, and conditions such as pheochromocytoma or cortisol-secreting neoplasms

predispose patients to significant hemodynamic instability and metabolic disturbances (10). Even when performed laparoscopically or retroperitoneoscopically, adrenal surgery can therefore be associated with considerable physiological stress, prolonged recovery, and postoperative discomfort (11,12). These features make adrenalectomy an ideal candidate for enhanced recovery pathways, which have the potential to improve outcomes and optimize the utilization of healthcare resources. Several groups have proposed ERAS protocols tailored to adrenalectomy, incorporating elements such as early feeding, omission of drains and urinary catheters, and standardized perioperative care. Initial findings suggest shorter hospital stay, improved pain control, and faster functional recovery without compromising safety (13-16). Nevertheless, the literature remains limited, heterogeneous, and non-standardized, and no specific guidelines from the ERAS Society exist for adrenal surgery. The present study, therefore, aims to systematically review and perform a meta-analysis of the available evidence on ERAS protocols in adrenalectomy, comparing perioperative outcomes with those of conventional management, and to identify opportunities for protocol standardization and future research. We present this article in accordance with the PRISMA reporting checklist (17) (available at <https://gs.amegroups.com/article/view/10.21037/gs-2025-aw-513/rc>).

Methods

Review question and Patient, Intervention, Comparison, Outcomes (PICO) framework

This systematic review was designed to evaluate the role of ERAS protocols in adrenalectomy, compared to standard perioperative care. The review was registered on PROSPERO (Protocol: CRD420251114409). The review question was structured using the PICO model to define the study population, intervention, comparison, outcomes, and eligible study designs. The Population of interest consisted of adult patients (≥ 18 years) undergoing elective adrenalectomy for benign or malignant lesions, with or without endocrine activity. All surgical approaches were considered, including laparoscopic, Robot-assisted, and

Highlight box

Key findings

- Standardization of enhanced recovery after surgery (ERAS) pathways in adrenal surgery.

What is known and what is new?

- ERAS protocols possibly increase perioperative outcomes.
- The application of ERAS protocols improves patients outcomes and social costs.

What is the implication, and what should change now?

- Extensive application of ERAS protocols can lead to increase in patients outcomes and satisfaction. Further trials are needed to verify the economic implications.

open. The Intervention involved the implementation of a structured ERAS protocol, which included one or more perioperative elements such as preoperative counseling, reduced fasting, carbohydrate loading, multimodal analgesia with opioid-sparing techniques, early mobilization, early oral feeding, and omission of drains or urinary catheters. The comparison group included patients managed with conventional perioperative care not based on formal ERAS principles. Primary outcomes were defined as postoperative length of stay (LOS), pain scales, and rates of postoperative complications. Secondary outcomes included time to first oral intake, gastrointestinal recovery, ambulation, and cost-related endpoints, when available. Eligible study designs included randomized controlled trials (RCTs), prospective cohort studies, and retrospective comparative studies.

Search strategy

A comprehensive search was conducted in August 2025 across four electronic databases: PubMed, Scopus, ScienceDirect, and the Cochrane Library. No time filters were applied. The search was limited to studies published in the English language. To optimize the precision of the search, both free-text terms and Medical Subject Headings (MeSH) were used. The following terms were applied in various combinations: “Adrenalectomy”, “Enhanced Recovery After Surgery”, “ERAS”, “Laparoscopy”, “Retroperitoneoscopy”, “Perioperative Care”, “Minimally Invasive Surgical Procedures”, “Adrenal Gland Neoplasms”, “Length of Stay”, “Postoperative Complications”, and “Recovery of Function”. The reference lists of all included articles were manually screened to identify any further eligible studies not captured in the initial search. Full search strings are available in [Appendix 1](#).

Study selection

Two reviewers (G.L. and M.B.S.) independently screened all retrieved records. Initial screening was based on titles and abstracts. Full-text assessment was then conducted for studies deemed potentially eligible. Disagreements were resolved through discussion or consultation with a third reviewer (G.C.). Studies were included if they met the PICO-based eligibility criteria and provided extractable data on at least one of the predefined outcomes of interest. To be included, studies had to meet the following criteria: (I) involve adult patients (≥ 18 years) undergoing elective adrenalectomy; (II) compare ERAS protocols

versus standard care; (III) report at least one clinical, functional, or economic outcome; and (IV) be designed as RCTs, prospective cohorts, or retrospective comparative studies. Exclusion criteria were: (I) studies involving pediatric populations; (II) case reports, case series without comparison groups, reviews, or editorials; (III) non-comparative studies or studies not reporting extractable clinical, functional, or economic outcomes relevant to ERAS protocols in adrenalectomy.

Data extraction

Relevant data were extracted independently by two reviewers (G.L. and M.B.S.) using a standardized data collection form. Extracted data included first author, year of publication, country, study design, sample size, patient demographics, surgical approach, ERAS components applied and reported outcomes. Any disagreements were resolved through consensus or consultation with a third reviewer (G.C.).

Statistical analysis

For quantitative synthesis, data were pooled using Review Manager (RevMan version 5.4) from The Cochrane Collaboration. For continuous outcomes (e.g., LOS, pain scores, time to first ambulation, time to catheter or drain removal, time to first meal or flatus, hospitalization costs), effect sizes were expressed as standardized mean differences (SMDs) with 95% confidence intervals (CIs). For dichotomous outcomes (e.g., postoperative complications), risk ratios (RRs) with 95% CI were calculated. A random-effects model (DerSimonian-Laird method) was applied to account for potential heterogeneity among studies. Statistical heterogeneity was assessed using the Chi^2 test and quantified with the I^2 statistic, with values $>50\%$ considered indicative of substantial heterogeneity. When appropriate, prediction intervals were reported to indicate the expected range of effects in future studies.

Risk of bias (RoB) assessment

Two authors independently assessed the quality and RoB of included studies. For RCTs, the RoB 2.0 tool was applied, while for non-RCTs, the ROBINS-I tool was used. RoB judgments were incorporated into the overall interpretation; however, they did not serve as exclusion criteria. The overall certainty of the evidence for each primary outcome was

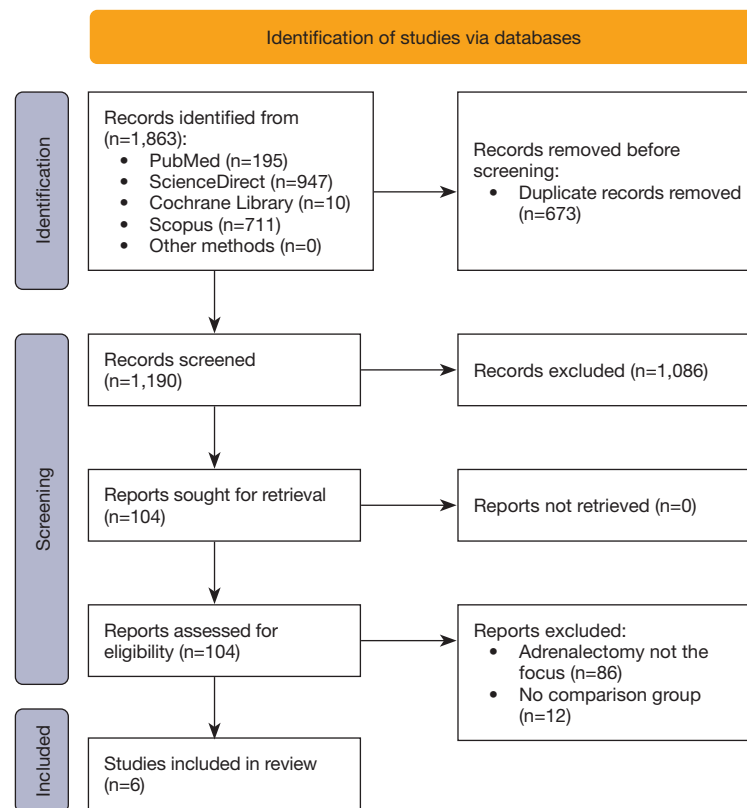


Figure 1 PRISMA 2020 flow diagram illustrating the study selection process for the systematic review. A total of 1,863 records were identified through database searches (PubMed, ScienceDirect, Cochrane Library, and Scopus). After removal of 673 duplicates, 1,190 records were screened by title and abstract. Of these, 1,086 were excluded, and 104 full-text articles were assessed for eligibility. Ninety-eight reports were excluded because adrenalectomy was not the primary focus, or no comparison group was available. Six studies met the inclusion criteria and were included in the final synthesis, both qualitative and quantitative.

planned to be assessed qualitatively following the principles of the GRADE framework. As the number of studies was limited and included both randomized and non-randomized designs, a formal quantitative GRADE assessment was not performed; however, certainty considerations were integrated into the interpretation of the results.

Results

The initial database search yielded 1,863 articles. In addition, reference list screening of the included studies did not identify any further eligible records. After removing 673 duplicates, 1,190 records were screened by title and abstract. Of these, 104 full-text articles were assessed for eligibility, and 6 studies were ultimately included in the final qualitative synthesis. The selection process is depicted in the PRISMA flow diagram (Figure 1).

The current evidence on ERAS in adrenal surgery is derived from six comparative studies, encompassing a total of 429 patients. The body of literature is heterogeneous in design, including one RCT (18), one prospective observational study (19), and four retrospective comparative analyses (14,15,20,21). Across these diverse settings, ERAS pathways consistently integrated perioperative measures, including shortened fasting with carbohydrate loading, structured counseling, multimodal analgesia, normothermia, and fluid restriction. Postoperatively, early feeding and mobilization, along with the omission or accelerated removal of catheters and drains, were universal practices. Despite differences in design and protocol intensity, all studies reported shorter hospital stay, faster functional recovery, improved pain control, and reduced costs, without an increase in complication rate. A summary of the selected studies is shown in Table 1.

Table 1 Summary of the main characteristics of the studies included in the meta-analysis evaluating ERAS vs. conventional care in adrenalectomy

Study	Design	N (ERAS vs. CC)	Surgical approach	ERAS components	Main outcomes
Tang <i>et al.</i> (18)	RCT, single center	100 (50 vs. 50)	Retroperitoneoscopic LA	No bowel prep, reduced fasting (solids 6 h, liquids 2 h), carbohydrate drinks, multimodal analgesia (parecoxib), early feeding & mobilization, early catheter/drain removal	↓ Time to flatus (19 vs. 38 h), diet (19 vs. 53 h), ambulation (20 vs. 52 h); ↓ LOS (2.35 vs. 5.23 d); ↓ pain scores, CRP & IL-6; no ↑ complications
Yan <i>et al.</i> (20)	Retrospective case-control	106 (53 vs. 53)	Laparoscopic (TLA/RPA)	Counseling, reduced fasting, carbohydrate drinks, no bowel prep, multimodal analgesia, no drains, early mobilization, early oral feeding	↓ LOS (2.5 vs. 8.4 d); ↓ complications (1 vs. 7, P=0.031); faster GI recovery; cost saving (~¥18,000/patient); faster return to work, ↓ caregiver burden
He <i>et al.</i> (21)	Retrospective comparative	47 (26 vs. 21)	Laparoscopic LA for primary aldosteronism	Shortened fasting/drinking, no bowel preoperative, perioperative education, individualized nutrition, normothermia, fluid restriction (<1,000 mL POD1), no routine antibiotics, early oral intake, POD1 mobilization, early catheter removal	↓ Total LOS (11.3 vs. 14.2 d) and post-op LOS (3.3 vs. 5.4 d); ↓ costs; no ↑ complications (urinary retention, effusion, GI issues)
Lelli <i>et al.</i> (14)	Retrospective comparative	61 (32 vs. 29)	Laparoscopic transperitoneal	Structured counseling, low-calorie diet in obese, reduced fasting, TAP block, normothermia, no drains, no NG tube, fluid restriction, POD1 catheter removal, early mobilization/feeding	↓ LOS (3.5 vs. 4.6 d); ↓ pain (NRS 3.8 vs. 5.2), ↓ rescue analgesics (2.7 vs. 5.4); earlier return to daily activities (14 vs. 18 d); no ↑ complications
van de Wiel <i>et al.</i> (19)	Prospective observational	30 (15 vs. 15)	Posterior PRA for PA	AFTER protocol: pre-op educational video, day-of-surgery admission, standardized anesthesia, catheter during surgery only, oral analgesia, early feeding/mobilization, home BP monitoring	↓ LOS (32 vs. 57 h; 93% discharged POD1 vs. 53%); ↓ opioid use; ↑ satisfaction; similar recovery time (28 d), complications, and QoL
Luo <i>et al.</i> (15)	Retrospective comparative	85 (42 vs. 43)	Retroperitoneoscopic LA	4N-ERAS: no Foley, no drains, no antibiotics, “no pain” (local anesthesia + multimodal), fluid restriction, early feeding & mobilization	↓ LOS (4.5 vs. 6.6 d); ↓ pain (NRS 1.3 vs. 2.3); ↓ costs (¥20.6k vs. ¥23.2k); faster GI recovery (flatus 6 vs. 10 h; ambulation 8 vs. 13 h); no ↑ complications (6 vs. 11, NS)

↓, lower; ↑, higher. AFTER, adrenal fast-track and enhanced recovery; BP, blood pressure; CC, conventional care; CRP, C-reactive protein; ERAS, enhanced recovery after surgery; GI, gastrointestinal; IL-6, interleukin-6; LA, laparoscopic adrenalectomy; LOS, length of stay; NG, nasogastric; NRS, Numeric Rating Scale; NS, not significant; PA, primary aldosteronism; POD1, postoperative day 1; PRA, posterior retroperitoneoscopic adrenalectomy; QoL, quality of life; RCT, randomized controlled trial; RPA, retroperitoneoscopic adrenalectomy; TAP, transversus abdominis plane; TLA, transperitoneal laparoscopic adrenalectomy.

Baseline patient characteristics, surgical indications, perioperative preparation, and postoperative complications of the included studies are summarized in *Table 2*. Reporting of baseline variables was heterogeneous, and not all studies provided data for all parameters (14,15,18-21). Across individual studies, ERAS and non-ERAS cohorts were generally comparable with respect to the variables reported, including age, sex distribution, body mass index (BMI),

and tumor size (14,15,18-21). However, BMI was not consistently reported; it was reported only as a comorbidity in one study (14). American Society of Anesthesiologists (ASA) score classification was inconsistently reported and was available in three studies only (18-20). Where reported, ASA distributions were similar between ERAS and non-ERAS groups, suggesting comparable baseline perioperative risk within those cohorts. In the remaining studies, ASA

Table 2 Baseline patient characteristics, surgical indications, perioperative preparation, and postoperative complications of the included studies

Study	Group	Age (years)	Sex (M/F)	BMI (kg/m ²)	ASA score	Indication for adrenalectomy	Preoperative medications/preparation	Postoperative complications	Tumor size
Tang et al. (18)	ERAS	49.34±10.18	26/24 (M/F)	21.73±4.13	I 37; II 11; III 2	Aldosteronism [9]; Cushing [3]; pheochromocytoma [4]; incidentaloma [34]	Phenoxybenzamine for pheochromocytoma; potassium-sparing diuretics and K ⁺ supplementation for aldosteronism; correction of metabolic abnormalities for Cushing	Clavien-Dindo not used. Events: peritoneal injury 3; abdominal distension 3; vomiting 1	2.42±1.21 cm
	Non-ERAS	47.70±10.95	25/25 (M/F)	22.77±4.00	I 35; II 14; III 1	Aldosteronism [7]; Cushing [4]; pheochromocytoma [7]; incidentaloma [32]	Same as ERAS	Clavien-Dindo not used. Events: peritoneal injury 2; abdominal distension 6; vomiting 3	2.39±1.02 cm
Yan et al. (20)	ERAS	48.75±12.24	25/28 (M/F)	24.53±2.97	I-II 84.9%; III 3.8%; missing 11.3%	Functional and non-functional adrenal tumors [†] . Not explicitly reported	Pheochromocytoma and Cushing syndrome excluded; no endocrine-specific preoperative drug protocol reported	Clavien-Dindo grading stated but grade distribution not reported. Number of patients with complications: 1; no severe complications or morbidity	2.74±1.10 cm
	Non-ERAS	51.13±10.57	22/31 (M/F)	24.88±2.88	I-II 86.8%; III 5.7%; missing 7.5%	Functional and non-functional adrenal tumors [†] . Not explicitly reported	Same as ERAS	Clavien-Dindo grading stated but grade distribution not reported. Number of patients with complications: 7; no severe complications or morbidity	2.70±1.07 cm
van de Wiel et al. (19)	ERAS	51.93±6.5	7/8 (M/F)	27.53±3.00	I-II 80%; III 20%	Primary aldosteronism only	NR	Clavien-Dindo used: CD II =2; CD ≥ III =0	1.52±0.82 cm
	Non-ERAS	51.80±11.2	5/10 (M/F)	27.47±4.80	I-II 80%; III 20%	Primary aldosteronism only	NR	Clavien-Dindo used: CD II =2; CD ≥ III =0	1.54±0.69 cm
Lelli et al. (14)	ERAS	44.2±10.4	17/15 (M/F)	NR	NR	Non-functioning [9]; APA [14]; pheochromocytoma [8]; metastasis [1]	Alpha ± beta-blockade for pheochromocytoma	Clavien-Dindo used: CD I =5; CD II =2; CD IIIA = 1; CD IIIB-V =0	41.7±17.8 mm
	Non-ERAS	45.8±11.1	13/16 (M/F)	NR	NR	Non-functioning [7]; APA [17]; pheochromocytoma [3]; metastasis [2]	Same as ERAS	Clavien-Dindo used: CD I =8; CD II =4; CD ≥ III =0	43.1±19.8 mm

Table 2 (continued)

Table 2 (continued)

Study	Group	Age (years)	Sex (M/F)	BMI (kg/m ²)	ASA score	Indication for adrenalectomy	Preoperative medications/preparation	Postoperative complications	Tumor size
Luo <i>et al.</i> (15)	ERAS	49.35±12.01	15/27	24.63±3.35	NR	PA [7]; pheochromocytoma [3]; Cushing [7]; other [15]	Terazosin/metoprolol + volume expansion for pheochromocytoma; K ⁺ spironolactone for PA; glucocorticoids for Cushing	Clavien-Dindo not used. Total complications =6 (fever, wound infection, pulmonary infection, DVT, others)	2.63±1.15 cm
	Non-ERAS	47.09±13.83	22/21	23.60±1.99	NR	PA [18]; pheochromocytoma [7]; Cushing [2]; other [16]	Same as ERAS	Clavien-Dindo not used. Total complications =11	2.51±1.12 cm
He <i>et al.</i> (21)	ERAS	51.2±11.0	13/13	25.73±3.90	NR	Primary aldosteronism only	NR	Clavien-Dindo not used. GI discomfort 2; infections 2; hypotension 1	1.80±0.89 cm
	Non-ERAS	54.4±10.8	14/7	23.79±2.81	NR	Primary aldosteronism only	NR	Clavien-Dindo not used. GI discomfort 1; infections 4; hypotension 1	2.03±1.09 cm

Data are presented as mean ± standard deviation or n.[†], Yan *et al.* (20) excluded pheochromocytoma and Cushing syndrome, and did not provide a granular diagnostic breakdown. The Clavien-Dindo classification was applied only in Yan *et al.* (20), van de Wiel *et al.* (19), and Lelli *et al.* (14); only studies reporting explicit grade distributions are presented accordingly. APA, aldosterone-producing adenoma; ASA, American Society of Anesthesiologists; BMI, body mass index; CD, Clavien-Dindo; DVT, deep vein thrombosis; ERAS, enhanced recovery after surgery; F, female; GI, gastrointestinal; M, male; NR, not reported; PA, primary aldosteronism.

status was not reported, precluding a comprehensive assessment across all included populations. The indication for adrenalectomy varied substantially across studies (14,15,18-21). Two studies exclusively included patients with primary aldosteronism, resulting in homogeneous endocrine cohorts (19,21). Other studies enrolled mixed populations of functioning and non-functioning adrenal tumors, including aldosterone-producing adenomas, pheochromocytomas, Cushing syndrome, non-functioning incidentalomas, and, in selected cases, adrenal metastases (14,15,18). One study excluded patients with pheochromocytoma and Cushing syndrome and reported indications only as functional versus non-functional adrenal tumors, preventing further diagnostic stratification (20). Preoperative endocrine-specific medical preparation was explicitly described only in studies including hormonally active tumors (14,15,18). These measures included alpha-adrenergic blockade with or without beta-blockade and volume expansion for pheochromocytoma, potassium supplementation and mineralocorticoid antagonists for primary aldosteronism, and glucocorticoid management for hypercortisolism (14,15,18). Other studies did not report preoperative pharmacological preparation, limiting direct comparison of perioperative optimization strategies across all cohorts (19-21). Postoperative complications were reported in all studies, although the method and granularity of reporting varied considerably (14,15,18-21). The Clavien-Dindo classification was explicitly applied in three studies (14,19,20), which predominantly reported minor complications (grades I–II). Only one grade IIIA complication was observed in an ERAS cohort (14). No grade IIIB–V complications were reported. In the remaining studies, complications were reported as counts or categories without standardized grading and primarily comprised minor gastrointestinal, infectious, or transient cardiovascular events (15,18,21). Overall, clinically relevant major postoperative complications were uncommon, although heterogeneity in reporting limits direct quantitative comparison across studies.

The RoB evaluation highlighted differences in methodological quality across the studies. The five non-RCTs were assessed using the ROBINS-I tool (14,15,19-21). Two were deemed to be at serious RoB due to confounding and participant selection (14,21). Three studies were rated as having a moderate risk due to residual confounding and some concerns regarding reporting or missing data (15,19,20). The single RCT (18), assessed using the RoB 2.0 tool, was rated as having some concerns due to potential

deviations from the intended intervention and outcome measurement (*Figure 2*).

Given the limited number of included studies (<10), formal assessment of publication bias through funnel plot analysis was not feasible. Potential reporting bias was therefore evaluated qualitatively, considering study design, selective outcome reporting, and completeness of data presentation across studies.

LOS

All six studies (14,15,18-21) reported postoperative LOS. Pooled analysis showed a significant reduction in LOS in patients managed with ERAS (SMD = -1.28; 95% CI: -1.82 to -0.73; $P < 0.001$) (*Figure 3A*). Heterogeneity was substantial ($I^2 = 84\%$), largely reflecting differences in baseline LOS across healthcare systems, with shorter stays in European centers (2–3 days) and longer stays in Asian cohorts (7–10 days). Despite this variability, all studies favored ERAS groups.

Postoperative complications

All six studies (14,15,18-21) reported complication rates and were included in the pooled analysis. The meta-analysis demonstrated a significant reduction in postoperative complications in the ERAS group (RR = 0.59; 95% CI: 0.39–0.90; $P = 0.01$), with no heterogeneity ($I^2 = 0\%$) (*Figure 3B*). Reported complications included urinary retention, wound-related issues, gastrointestinal dysfunction, and minor cardiopulmonary events. Importantly, no study reported an increased incidence of major complications, confirming that ERAS pathways improve safety without additional risk.

Postoperative pain

Three studies provided data on postoperative pain (14,15,18), which was significantly reduced in the ERAS group (SMD = -1.30; 95% CI: -1.94 to -0.66; $P < 0.001$) (*Figure 3C*). This finding is clinically relevant, reflecting earlier mobilization and reduced need for rescue analgesics. Heterogeneity was substantial ($I^2 = 80.5\%$), likely due to differences in pain assessment tools (Numeric Rating Scale *vs.* Visual Analogue Scale) and the timing of evaluation.

Functional recovery

Functional recovery was assessed through three endpoints:

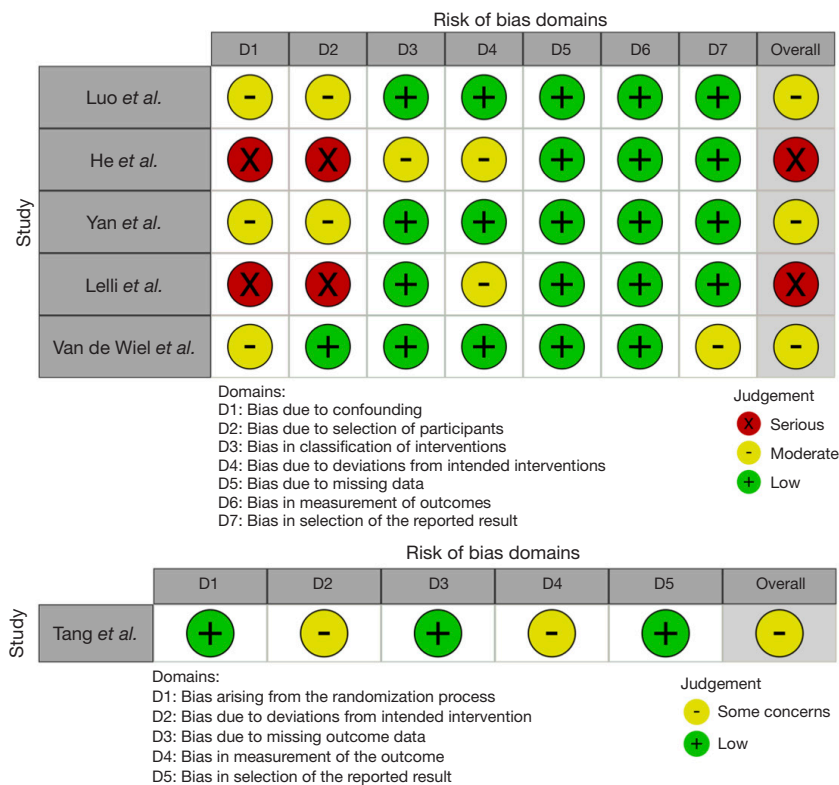


Figure 2 Risk of bias assessment of the included studies. Non-randomized studies were evaluated with the ROBINS-I tool, showing two studies at serious risk of bias (He *et al.*, Lelli *et al.*), three at moderate risk (Luo *et al.*, Yan *et al.*, Van de Wiel *et al.*), while the randomized controlled trial (Tang *et al.*) was assessed with the RoB 2.0 tool and rated as having some concerns. RoB, risk of bias.

time to first ambulation, removal of urinary catheter, and removal of drain. First ambulation occurred significantly earlier with ERAS (SMD = -2.16; 95% CI: -3.10 to -1.22; P < 0.001) (Figure 4A), corresponding to a mobilization time of 24–36 hours earlier (15,18–20). Urinary catheter removal was also significantly accelerated (SMD = -2.81; 95% CI: -4.12 to -1.50; P < 0.001) (Figure 4B), with most ERAS patients having their catheter removed intraoperatively or on the first postoperative day, compared with days 3–5 in conventional care (15,18–20). Drain removal was similarly favored by ERAS (SMD = -2.58; 95% CI: -4.80 to -0.37; P = 0.02) (15,18,20) (Figure 4C). In ERAS groups, drains were omitted or removed within 24 hours, with no increase in postoperative collections or re-interventions. Collectively, these results highlight the role of ERAS in accelerating functional recovery and reducing reliance on invasive devices.

Hospital costs

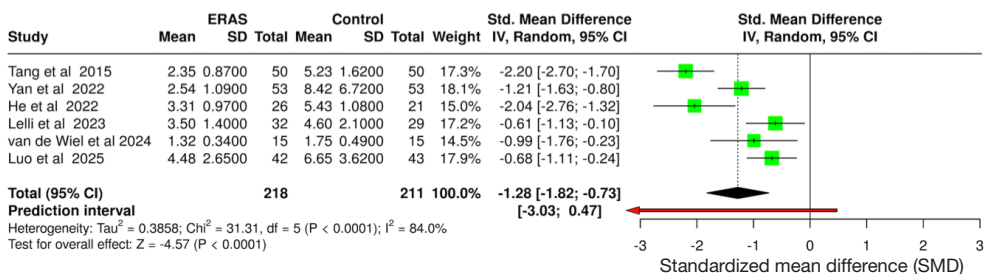
Hospitalization costs were reported in three studies

(16,20,21). The pooled analysis suggested a non-significant trend toward cost reduction in ERAS patients (SMD = -1.73; 95% CI: -3.79 to 0.33; P = 0.1) (Figure 5A), with very high heterogeneity (I² = 97%). This heterogeneity reflects differences in healthcare systems, currencies, and inclusion of direct versus indirect costs. While individual studies reported reductions of up to 20–30% per patient, pooled results do not allow firm conclusions.

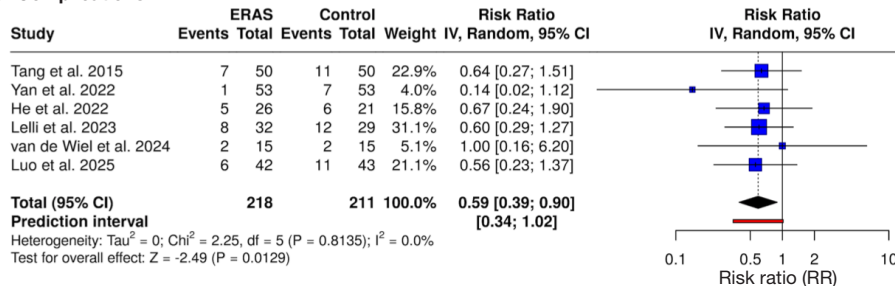
Gastrointestinal recovery

Two endpoints were evaluated: time to first meal and time to first flatus. Time to first oral intake was significantly shorter in ERAS patients (SMD = -1.59; 95% CI: -2.87 to -0.31; P = 0.01) (Figure 5B), with resumption of feeding often on the day of surgery or the following morning, compared with 2–3 days later in conventional care (18–20). Time to first flatus was also reduced (SMD = -1.04; 95% CI: -1.42 to -0.67; P < 0.001) (Figure 5C), indicating faster resolution of postoperative ileus (15,18,20). These results confirm that

A Length of stay



B Complications



C Pain

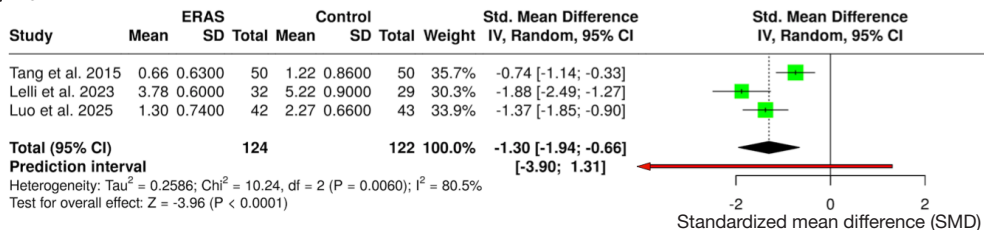


Figure 3 Forest plots of primary outcomes. (A) Length of stay was significantly shorter in the ERAS group. (B) Postoperative complications were significantly reduced with ERAS. (C) Postoperative pain scores were significantly lower with ERAS. CI, confidence interval; ERAS, enhanced recovery after surgery; IV, inverse variance; SD, standard deviation.

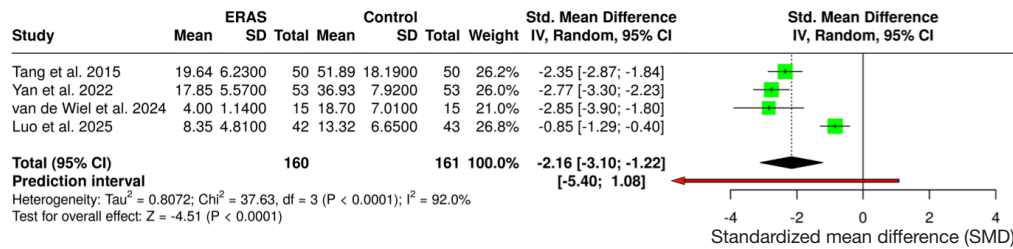
ERAS accelerates gastrointestinal recovery, likely through synergistic interventions, including reduced fasting, carbohydrate loading, early feeding, and mobilization.

Discussion

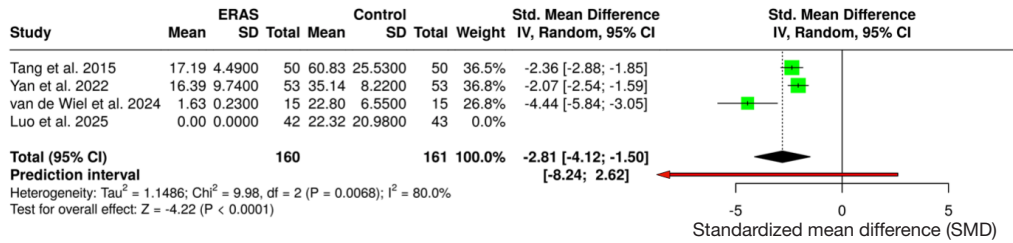
This meta-analysis represents one of the first systematic syntheses dedicated to the application of ERAS protocols in adrenalectomy. By pooling six comparative studies involving 429 patients (14,15,18-21), we found consistent benefits, including reduced LOS, fewer complications, decreased postoperative pain, and accelerated functional recovery, without an increase in perioperative risk. Reduction in LOS emerged as the most consistent and clinically meaningful outcome. All included studies demonstrated a significantly shorter hospital stay in ERAS groups, with a difference of 2–3 days in European centers and up to 5–6 days in Asian

cohorts (14,15,18-21). The pooled analysis confirmed this benefit (SMD = -1.28; P < 0.001), despite high heterogeneity (I² = 84%), which was largely attributable to differences in healthcare systems and baseline practices. ERAS protocols, on average, shortened hospital stays by about 2–3 days in European groups and up to 5–6 days in Asian groups. They also led to earlier mobilization, removal of urinary catheters, and drain removal, typically by around 24–36 hours compared to standard care. These findings align with the consolidated evidence from colorectal and pancreatic surgery, confirming that ERAS principles are transferable to adrenal surgery, despite its lower surgical volume and specific endocrine challenges (14,15,18-21). Substantial heterogeneity was observed across outcomes like LOS, pain, and costs, likely due to differences in healthcare systems, perioperative practices, and ERAS protocols. Due to the limited number of studies, subgroup analyses

A Time to first ambulation



B Time to urinary catheter removal



C Time to drain removal

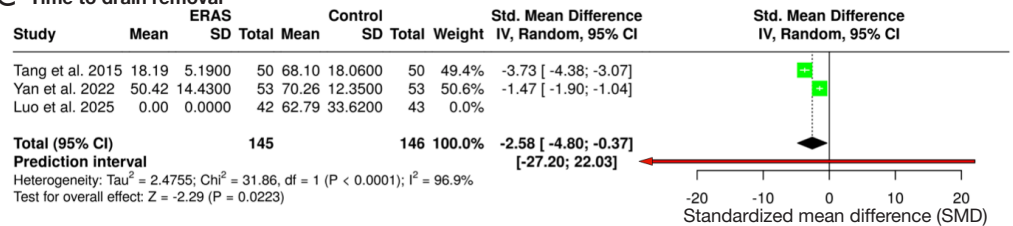


Figure 4 Forest plots of functional recovery outcomes. (A) Time to first ambulation, (B) urinary catheter removal, and (C) drain removal were all significantly shorter in ERAS patients compared to controls. CI, confidence interval; ERAS, enhanced recovery after surgery; IV, inverse variance; SD, standard deviation.

or meta-regression were not feasible; therefore, pooled estimates should be interpreted cautiously. In contrast to the substantial heterogeneity observed for LOS, the pooled analysis demonstrated a significant reduction in postoperative complications with ERAS (RR =0.59; P=0.0129), with no heterogeneity across studies (I²=0%) (14,15,18-21). This consistency across studies represents a major strength of the analysis and suggests that ERAS not only accelerates recovery but also improves overall surgical safety. Given the distinct perioperative risks and recovery patterns associated with hormonally active tumors, the heterogeneity of surgical indications across studies represents a potential confounder and should be considered when interpreting pooled outcomes. Comparable findings have been reported in colorectal, hepatobiliary, and thoracic surgery, where ERAS has been associated with fewer infectious and cardiopulmonary complications through better fluid management, normothermia, and early

mobilization (4,22,23).

Three studies reported data on postoperative pain (14,15,18), showing a significant reduction in ERAS patients (SMD =-1.30; P<0.001). Although heterogeneity was high (I²=80.5%), reflecting the use of different assessment tools and timing of evaluation, the direction of effect was consistent. The adoption of multimodal, opioid-sparing analgesia and the use of regional techniques are likely responsible for this improved pain control, which directly facilitates early mobilization and reduces opioid-related adverse effects (14,15,18).

ERAS also significantly improved functional recovery. Patients mobilized 24–36 hours earlier, had urinary catheters and drains removed sooner, often on postoperative day 0–1 compared to days 3–5 in conventional care, and achieved autonomy more rapidly (15,18-20). Importantly, earlier removal of invasive devices did not increase the risk of urinary or wound complications. These results mirror

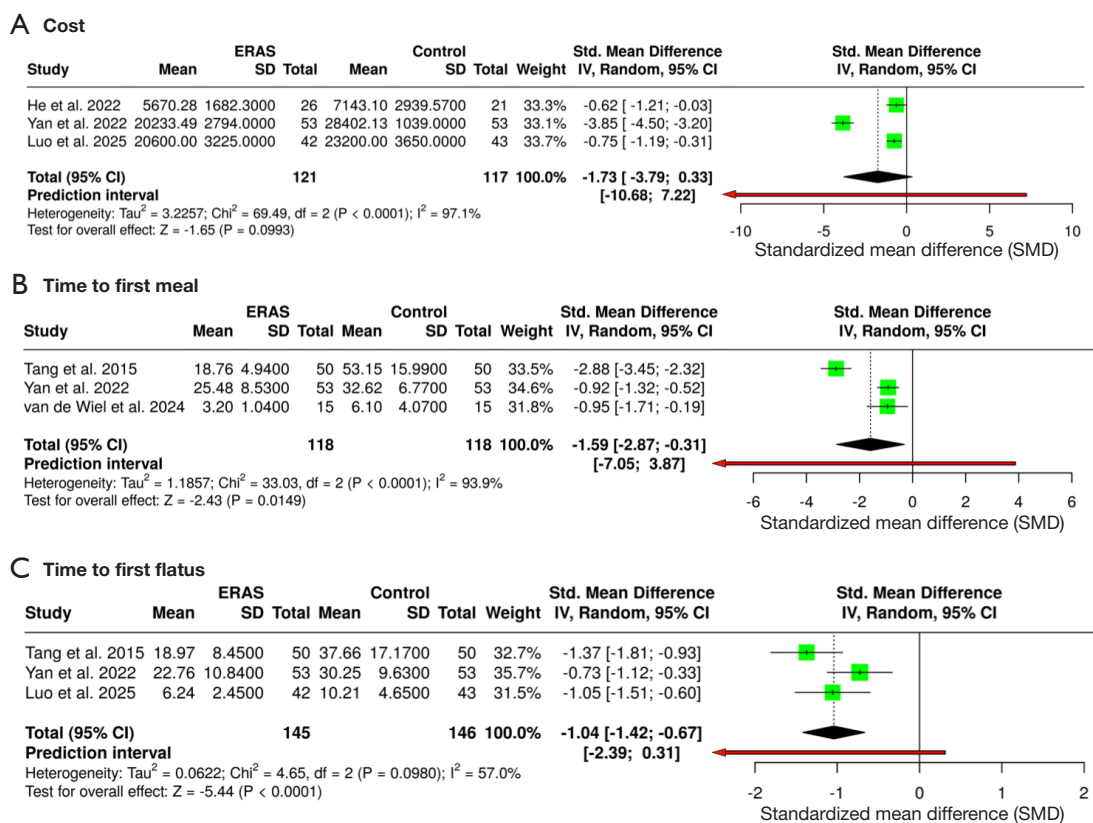


Figure 5 Forest plots of secondary outcomes. (A) Hospital costs showed a non-significant trend toward reduction with ERAS. (B) Time to first oral intake and (C) time to first flatus were significantly shorter in ERAS patients. CI, confidence interval; ERAS, enhanced recovery after surgery; IV, inverse variance; SD, standard deviation.

the experience in urology and gynaecology, where early ambulation and device avoidance represent key drivers of accelerated recovery (24,25).

The time to oral intake was significantly shorter in ERAS patients compared with those in conventional care (SMD = -1.59; 95% CI: -2.87 to -0.31; $P=0.01$). In the included studies, feeding was resumed on the evening of surgery or on the first postoperative day in the ERAS cohorts, whereas patients managed with standard care typically restarted oral intake only after 2–3 days (18–20). These findings confirm the safety of early enteral feeding in adrenal surgery and support its role as an effective strategy to enhance recovery. The results are consistent with the ERAS concept, which involves shortened preoperative fasting, carbohydrate loading, and early mobilization to help preserve gastrointestinal function and reduce postoperative catabolism (18–20).

Time to first flatus was also significantly reduced in ERAS patients (SMD = -1.04; 95% CI: -1.42 to -0.67;

$P<0.001$), indicating faster resolution of postoperative ileus (15,18,20). This effect is clinically relevant, as restoration of bowel function is a key determinant of overall recovery and readiness for discharge. The earlier return of gastrointestinal activity likely reflects the synergistic effects of ERAS measures, including opioid-sparing analgesia, restricted fluid administration, and early ambulation. Collectively, these results demonstrate that ERAS pathways accelerate gastrointestinal recovery in adrenalectomy, contributing substantially to the overall reduction in hospital stay observed in our meta-analysis (15,18,20). Hospitalization costs were evaluated in three studies, with individual analyses reporting savings of up to 20–30% per patient in ERAS cohorts (15,20,21). However, the pooled analysis did not reach statistical significance (SMD = -1.73; $P=0.1$), with very high heterogeneity ($I^2=97\%$) due to differences in healthcare systems, currencies, and methodologies (15,20,21).

Nonetheless, the consistent trend toward reduced

costs supports the potential of ERAS to optimize resource utilization, as has been extensively demonstrated in other surgical specialties (5,26). Taken together, our results confirm that ERAS in adrenalectomy is safe and effective, improving perioperative outcomes and functional recovery. However, the quality of evidence remains limited. Only one RCT was included, while most studies were retrospective with variable RoB. Furthermore, the ERAS protocols differed between studies, reflecting the lack of standardised guidelines for adrenalectomy. This heterogeneity likely contributed to variability in certain outcomes, in particular LOS and pain. Future research should aim to conduct multicentre, RCTs dedicated specifically to adrenalectomy; develop and validate a standardised ERAS protocol tailored to adrenal surgery, including clearly defined core elements; investigate outcomes in specific subgroups, such as patients with pheochromocytoma, primary aldosteronism, or incidentalomas; assess long-term outcomes, quality of life, and patient satisfaction, which remain under-explored in endocrine surgery and perform robust cost-effectiveness analyses, considering not only direct hospital expenditure, but also indirect costs and patient burden. Future research on ERAS in adrenal surgery should go beyond traditional perioperative outcomes and focus more on patient-centered measures. Important indicators include functional independence, patient-reported outcome measures (PROMs), quality of life, time to resume normal daily activities, return to work, and length of sick leave. These factors are particularly relevant for this patient group but are often overlooked in current studies. Including these outcomes would provide a more complete understanding of the true impact of ERAS protocols beyond standard metrics like hospital stay duration.

Conclusions

ERAS protocols for adrenalectomy are associated with faster recovery, reduced postoperative pain, fewer complications, and potentially lower costs, without compromising safety. Although the current evidence base is limited and heterogeneous, our findings support the feasibility and potential benefits of implementing ERAS in adrenal surgery. These results also highlight the need for standardized ERAS guidelines specific to adrenalectomy and for high-quality prospective studies to further validate and consolidate this approach.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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