Original Article

Enhanced recovery after surgery (ERAS) might be a standard care in radical prostatectomy: a systematic review and meta-analysis

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Background: Several enhanced recovery after surgery (ERAS) protocols for radical prostatectomy (RP) have been reported in recent years. Nonetheless, there is no sufficient evidence to support the implementation of ERAS as a standard of care modality.

Methods: A search was done in the PubMed, Embase, Clinical Trials.gov, Cochrane Library, CNKI Library databases and reference lists to identify relevant studies from inception until May 2019 to be included in the study. A systematic review of five randomized controlled trials (RCTs), one prospective cohort study and four retrospective studies covering 3,803 patients, comparing ERAS with conventional care was performed. Outcomes of interest for the study were intraoperative outcomes (operation time and blood loss), postoperative outcomes (hospital stay, catheter stay, first defecation and first anal exhaust) and postoperative complications. Random events meta-analyses were performed. Sensitivity analysis was also performed to determine whether the results of the meta-analysis were robust.

Results: Notably, ERAS group had significantly shorter hospital stay [overall standardized mean difference (SMD) =−1.65, 95% confidence interval (CI): −2.53, −0.76, P<0.001], shorter time to first defecation (overall SMD =−1.56, 95% CI: −2.71, −0.42, P=0.008), shorter time to first anal exhaust (overall SMD =−1.23, 95% CI: −1.97, −0.50, P=0.001) and lower incidence of nausea [overall risk ratio (RR) =0.62, 95% CI: 0.40, 0.94, P=0.024] compared to the conventional group. There was no statistical difference in intraoperative outcomes, catheter stay and other postoperative complications between the two groups (P>0.05).

Conclusions: The data presented so far consistently show that ERAS may be utilized as a standard of care in RP treatment.

Keywords: Enhanced recovery after surgery (ERAS); conventional care; radical prostatectomy (RP); hospital stay; postoperative complications; systematic review

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Introduction

Prostate cancer (Pca) is the most common genitourinary tract tumor in men (1). Radical prostatectomy (RP) is a first-line treatment for low and intermediate-risk localized Pca patients (2). RP can be either open or minimally invasive. Currently, minimally invasive RPs are widely applied. These are laparoscopic radical prostatectomy (LRP) and robot-assisted laparoscopic radical prostatectomy (RALP). Particularly, RALP has become the mainstay invasive treatment for localized Pca. Compared to open RP, minimally invasive RP is an effective and widely accepted treatment for localized Pca (3-5). Moreover, it reduces perioperative outcomes such as blood loss (6). However, open RP is still an option in some countries.

Enhanced recovery after surgery (ERAS) is a protocol aimed to reduce perioperative complications as well as the physical and psychological stress of surgical trauma. It is also described as fast-track surgery (FTS), because it accelerates patient rehabilitation, shortens the hospitalization period and reduce the medical costs. It was first performed by Kehlet in 1997 (7). It includes a series of evidence-based procedures, such as surgical, nursing, medical, anesthetic and perioperative managements (8).

A high number of Pca patients are elderly people. As such, comorbidities are very common thus necessitating the reduction of perioperative complications and acceleration of patient's recovery. ERAS has been widely applied in patients undergoing colorectal, breast and gastrointestinal surgery (9-12). However, its application in patients undergoing urological surgery is relatively low (13). To date, there is no meta-analysis to compare the efficacy and safety of ERAS to conventional care in patients undergoing RP. With more data available currently, a systematic review and meta-analysis was performed to assess whether ERAS should be considered as a standard care for patients undergoing RP.

Methods

Search strategy

We performed a comprehensive literature search on Embase, PubMed, the Clinicaltrials.gov (http://clinicaltrials.gov/), the Cochrane Library and CNKI Library to identify clinical trials that compared ERAS and conventional care. The search was done in all data published before May 2019. The search terms included: "ERAS", "Enhanced recovery after surgery", "Enhanced recovery", "perioperative management", "Fast-track surgery", "FTS", "Radical prostatectomy" and "Prostate cancer". We also screened the reference lists of review articles. Additional studies were also retrieved by manual search in relevant journals. We exclusively included studies which were published in English and Chinese.

Inclusion and exclusion criteria

Studies were selected according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (14). Clinical trials that met the four listed criteria were included:

(I) Randomized phase II, III, and IV trials;
(II) Patients who underwent RP;
(III) Participants who had received ERAS compared to conventional care and
(IV) Trails with available events, event rates and sample sizes to enable determination of efficacy and safety of ERAS.

Trials were excluded if:

(I) They involved animal research;
(II) They were reviews only;
(III) Had abstracts only;
(IV) Had overlapping data and
(V) Those studies without standard mean difference (SMD), risk ratio (RR), odds ratio (OR), hazard ratio (HR) and 95% confidence intervals (CIs).

Data extraction and quality assessment

Two reviewers independently did literature screening, data extraction, and quality assessment of the trials. A third reviewer was involved to have a consensus were the two reviewers disagreed. From each article, the first author's name, year of publication, study type, disease type, the number of patients, trial phase, treatment and control arms, the number of patients with intraoperative outcomes, postoperative outcomes and postoperative complications were extracted. The quality of the methodology used in randomized controlled trials (RCTs) was determined by the Jadad criteria (15). The quality of each trial was scored and grouped as either high- or low-quality trial. High-quality trials had scores of more than three (score ≥3) while the low-quality trials had scores of less than two (score ≤2). The Newcastle-Ottawa Scale (NOS) criteria (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) was used to determine the quality of the methodology used in non-randomized trials. Score ranged from 0 to 9 stars. High-

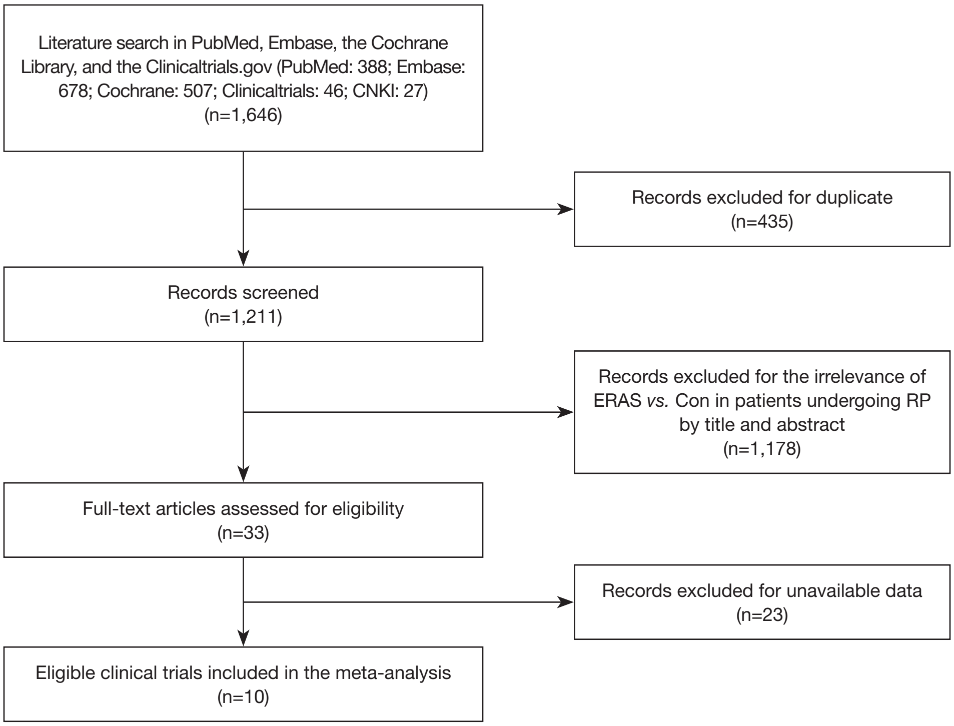

Figure 1 Flow chart for eligible studies. ERAS, enhanced recovery after surgery; Con, conventional group; RP, radical prostatectomy.

quality trials were those with scores of more than seven stars (score ≥7 stars).

Statistical analysis

Data of patients with intraoperative outcomes, postoperative outcomes and postoperative complications was extracted from all the included trials. SMD, RR and 95% CI were calculated to determine the association strength of these two regimens with the outcomes. The Q and I^2 statistics were used to determine the heterogeneity. I^2 of more than fifty percent (I^2>50%) indicated a statistically significant heterogeneity. The random-effect model was used in meta-analyses of the conservative statistics. Subgroup analysis was carried out based on the clinical characteristics. A funnel plot was used to determine any bias in the publications. Begg adjusted rank correlation test (16) and Egger regression test (17) were also performed to assess the publication bias. A sensitivity analysis was performed to determine whether the results of the meta-analysis were robust. STATA statistical version 12.0 software was used to perform all the statistical analyses (Stata Corporation, College Station, Texas, USA). A P value of less than 0.05 (P<0.05) was considered statistically significant. All the P vales were two-sided.

Results

Characteristics of studies included in this study

Our initial search yielded 1,646 potentially relevant clinical trials on ERAS or conventional care in patients who underwent RP. After reviewing and screening, 10 primary studies (18-27) met our inclusion criteria. Among the ten, five were RCTs studies, four were retrospective trials and one was a prospective cohort study. The studies had 3,803 subjects that were pooled for meta-analyses (*Figure 1*). The baseline characteristics of each trial are shown in *Table 1* while the Care elements implemented in ERAS protocol for RP in each trial are shown in *Table 2*. All trials included were open label and had between 50 and 2,610 patients enrolled for the trial. The Jadad quality scores of the included RCTs ranged from 2 to 3 while the NOS quality scores for the prospective cohort study and the retrospective trials ranged from 7 to 8 stars. Base on the eligibility criteria of most of the trials, patients with impaired hepatic, renal or bone marrow function were excluded. A majority of the patients in these trials had an Eastern Cooperative Oncology Group (ECOG) performance-status scores of 0 or 1. This systematic review followed the guidelines of the PRISMA statement.

Table 1 Characteristics of all studies

Study	Country	Surgery type	Trials type	Number (ERAS/Con)	Age (year) (ERAS/Con)	BMI (kg/m^2) (ERAS/Con)	Gleason score (ERAS/Con)	T-stage (ERAS/Con)	PSA (ng/mL) (ERAS/Con)	ASA score (ERAS/Con)	Jadad score	NOS score
Gralla 2007 (18)/ Magheli 2011 (19)	Germany	LRP	RCT	25/25	61.8/62.2	25.8/25.8	6.0/5.9	T1 (25/25)	7.3/10.2	2/2	2	–
Dong 2018 (25)	China	RP	RCT	105/95	66.8/67.0	22.4/22.3	–	T1 (64/56)	–	–	3	–
								T2 (41/39)				
Yu 2018 (26)	China	RALP	RCT	26/25	67.6/72.0	21.9/20.8	≤7 (18/16)	T1 (1/2)	31.6/31.4	–	–	–
							>7 (8/9)	T2 (25/23)				
Zhao 2018 (27)	China	LRP	RCT	76/58	51.5/52.9	24.3/24.2	–	–	–	1–2/1–2	3	–
Okamura 2013 (23)	Japan	RP	Prospective cohort study	1,256/1,354	67.5/67.1	–	–	–	–	–	–	8
Abou 2014 (24)	Canada	RP	Retrospective study	99/100	61.8/62.5	–	6–10	T2–3	–	–	–	7
Sugi 2017 (20)	Japan	RALP	Retrospective study	75/123	68/69	24.3/23.4	7/7	T1 (42/86)	7.1/6.5	2/2	–	7
								T2 (33/37)				
Huang 2018 (21)	China	RALP	Retrospective study	36/37	62.1/63.5	23.1/23.5	≤7 (17/16)	T1 (16/20)	13.4/15.4	1–3	–	7
							>7 (6/7)	T2 (20/17)				
Lin 2019 (22)	China	LRP	Retrospective study	124/164	70.9/70.0	20.3/20.4	≤7 (88/118)	T1–2 (40/52)	44.5/36.8	–	–	7
							>7 (36/46)	T3–4 (40/64)				

LRP, laparoscopic radical prostatectomy; RP, radical prostatectomy; RALP, robot-assisted laparoscopic radical prostatectomy; RCT, randomized controlled trial; Con, conventional group; ERAS, enhanced recovery after surgery.

Table 2 Care elements implemented in ERAS protocol for RP

ERAS elements	Eligible trials								
	Gralla 2007/ Magheli 2011	Dong 2018	Yu 2018	Zhao 2018	Okamura 2013	Abou 2014	Sugi 2017	Huang 2018	Lin 2019
Preoperative interventions									
Patient education/ counseling	√	√	√	√		√		√	√
Shortened fasting	√			√		√		√	√
Bowel preparation	√		√				√	√	
Optimized diets	√			√		√	√		
Prophylactic antibiotics					√				√
Prophylactic anticoagulation									√
Prophylactic antiemesis									√
Intraoperative interventions									
Prophylactic antibiotics	√				√				
Pneumoperitoneum	√								
Scrotal jockstrap	√								
Epidural anesthesia/ nonsteroidal analgesic painkillers	√		√						√
Intravenous fluid restriction			√				√	√	√
Prevention of hypothermia			√	√					√
Use of drain-age tubes					√	√			√
Postoperative interventions									
Nonsteroidal analgesic painkillers	√						√	√	
Intravenous fluid restriction	√							√	√
Early oral feeding	√	√	√	√	√	√		√	√
Early ambulation	√	√	√	√	√	√	√	√	√
Prophylactic medication					√				√
Early drainage tube removal			√	√	√	√			√

ERAS, enhanced recovery after surgery; RP, radical prostatectomy.

Table 3 Data of intraoperative outcomes

Study	Operation time (min ± SD)		Blood loss (mL ± SD)	
	ERAS	Con	ERAS	Con
Gralla 2007/Magheli 2011	240±64.7	220.1±57.0	275.2±315.2	156.9±71.8
Okamura 2013	227±74	215±67	1,226±974	1,209±880
Sugi 2017	219±63.0	225±67.3	200±207.9	200±349.5
Huang 2018	135±32	147±29	191±64	179±65
Lin 2019	102±24	106±32.1	151.1±32.5	164.3±41.5
Yu 2018	283±57.7	273.5±70.4	197.2±165.2	187.9±125.2

ERAS, enhanced recovery after surgery; Con, conventional group; SD, standard deviation.

Table 4 Data of postoperative outcomes

Study	Hospital stay (days ± SD)		Catheter stay (days ± SD)		First defecation (days ± SD)		Pain (n)		First anal exhaust (days ± SD)	
	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con
Gralla 2007/ Magheli 2011	3.6±1.2	6.7±0.9	11.4±10.7	9.6±6.9	3.6±1.2	6.7±0.9	4	15	–	–
Okamura 2013	13.6±6.1	15.3±7.1	8.3±7.1	8.7±5.3	–	–	–	–	–	–
Abou 2014	2±0.2	3±0.4	–	–	–	–	–	–	–	–
Sugi 2017	10.5±3.3	9±6.9	6±2.3	6±7.4	2.6±1.0	3±1.3	–	–	–	–
Huang 2018	7.3±1.6	9.8±2.0	–	–	–	–	–	–	2.6±1.1	3.6±1.5
Lin 2019	3.8±1.7	9.2±2.7	6.5±0.5	6.6±0.7	0.7±0.2	3.4±1.5	–	–	0.4±0.3	1.3±1.0
Dong 2018	8.6±1.5	14.7±1.7	–	–	–	–	–	–	2.7±0.4	3.8±0.4
Yu 2018	9.3±2.2	12.8±6.8	11.1±3.4	14.8±4.6	–	–	–	–	1.2±0.5	1.6±0.5
Zhao 2018	6.2±1.3	7.1±1.5	–	–	3.4±0.6	4.0±1.0	–	–	2.0±0.4	2.3±0.5

SD, standard deviation.

Findings—intraoperative outcomes (operation time and blood loss)

A total of 3,270 subjects treated with either ERAS or conventional care in six trials were included for the analysis of operation time and blood loss (data shown in *Tables 3,4*). An SMD of 0.00 (95% CI: −0.19, 0.20, I^2=63.4%) were obtained from analysis of the operation times of patients under ERAS and conventional care. In the analysis of blood loss, an SMD of −0.00 (95% CI: −0.19, 0.19, I^2=60.2%) were obtained (*Figure 2*). These results showed no statistical difference in both the operation time and blood loss between ERAS and conventional care groups (P=0.987).

Although the results of intraoperative outcomes indicated statistically significant heterogeneity, the sensitivity analysis showed that the results of intraoperative outcomes were robust (*Figure S1*).

Findings—postoperative outcomes (hospital stay, catheter stay, first defecation and first anal exhaust)

Hospital stay

A total of 3,803 subjects treated with either ERAS or conventional care in nine trials were included for the analysis of hospital stay (data shown in *Tables 3,4*). An SMD of −1.65 (95% CI: −2.53, −0.76, I^2=98.7%) was obtained from analysis of hospital stay of patients under ERAS and conventional care (*Figure 3*). The results showed that ERAS group had a shorter hospital stay than conventional

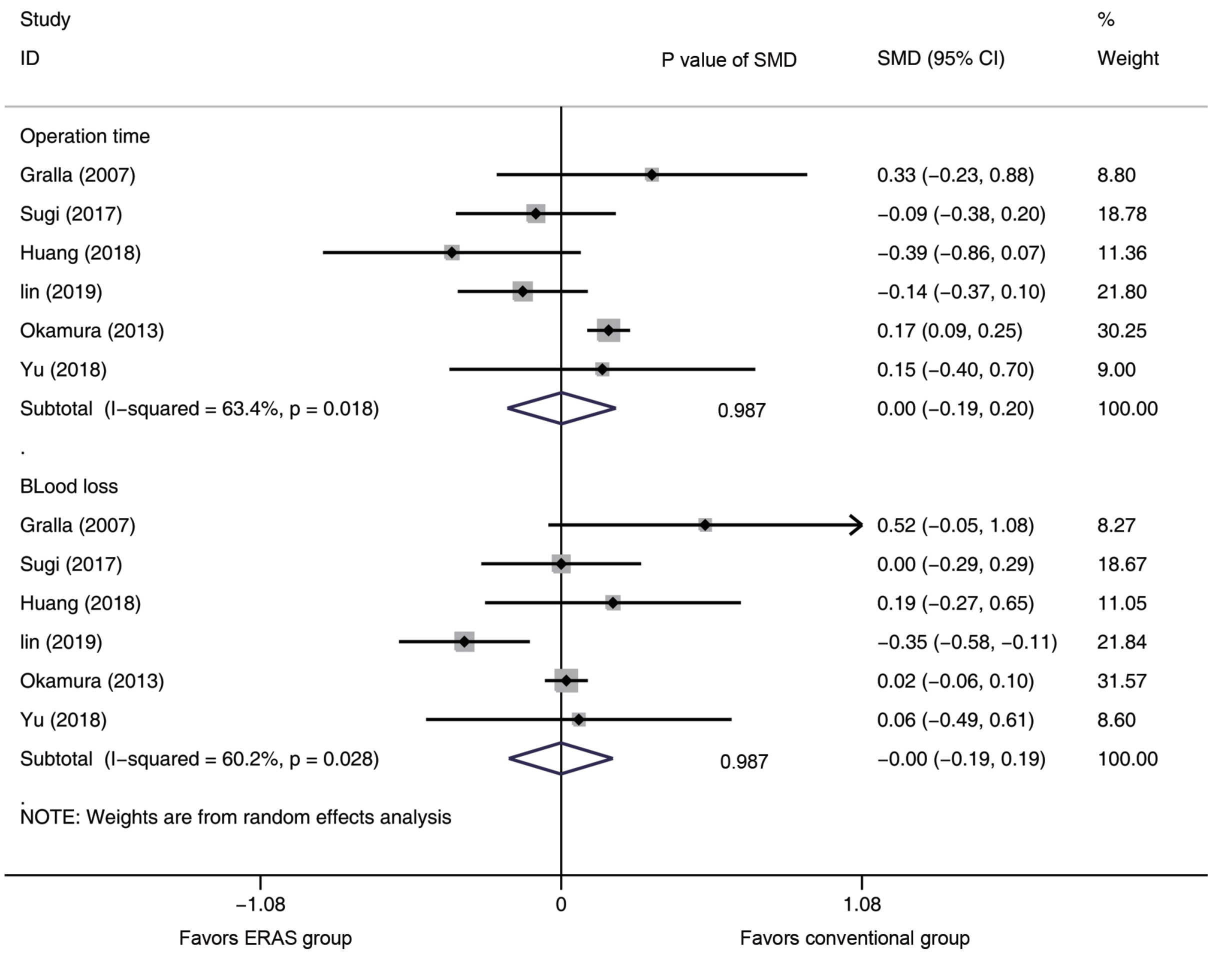

Figure 2 Annotated forest plot for meta-analysis of intraoperative outcomes of ERAS and conventional groups. Summary of intraoperative outcomes (operation time and blood loss) SMD between ERAS and conventional groups were calculated using the random effect model. Size of squares is directly proportional to the amount of information available. ERAS, enhanced recovery after surgery; SMD, standard mean difference; CI, confidence interval; P, P value of the Q test for heterogeneity.

care groups (P<0.001). As the results indicated statistically significant heterogeneity, subgroup analysis was performed to find sources of heterogeneity. The nine trials were first separated in three groups (LRP, RALP and RP) based on their surgery sub-type. However, the results still showed heterogeneity (*Table 5*) indicating that the difference in surgery sub-types was not the source of heterogeneity. However, the sensitivity analysis showed that the results of hospital stay were robust (*Figure S2*).

Catheter stay

A total of 3,197 subjects treated with either ERAS or conventional care in five trials were included for the analysis of catheter stay (data shown in *Tables 3,4*). In the analysis of catheter stay, an SMD of −0.12 (95% CI: −0.31, 0.07, I^2=59.8%) were obtained (*Figure 3*). The results showed no statistical difference in catheter stay between ERAS and conventional care groups (P=0.204).

First defecation

Six hundred and seventy subjects treated with either ERAS or conventional care in four trials were included for the analysis of first defecation (data shown in *Tables 3,4*). An SMD of −1.56 (95% CI: −2.71, −0.42, I^2=97.4%) were obtained (*Figure 3*). The results showed that ERAS groups had a shorter time to first defecation compared to the conventional care groups (P=0.008). The results indicated statistically significant heterogeneity. Subgroup analysis was

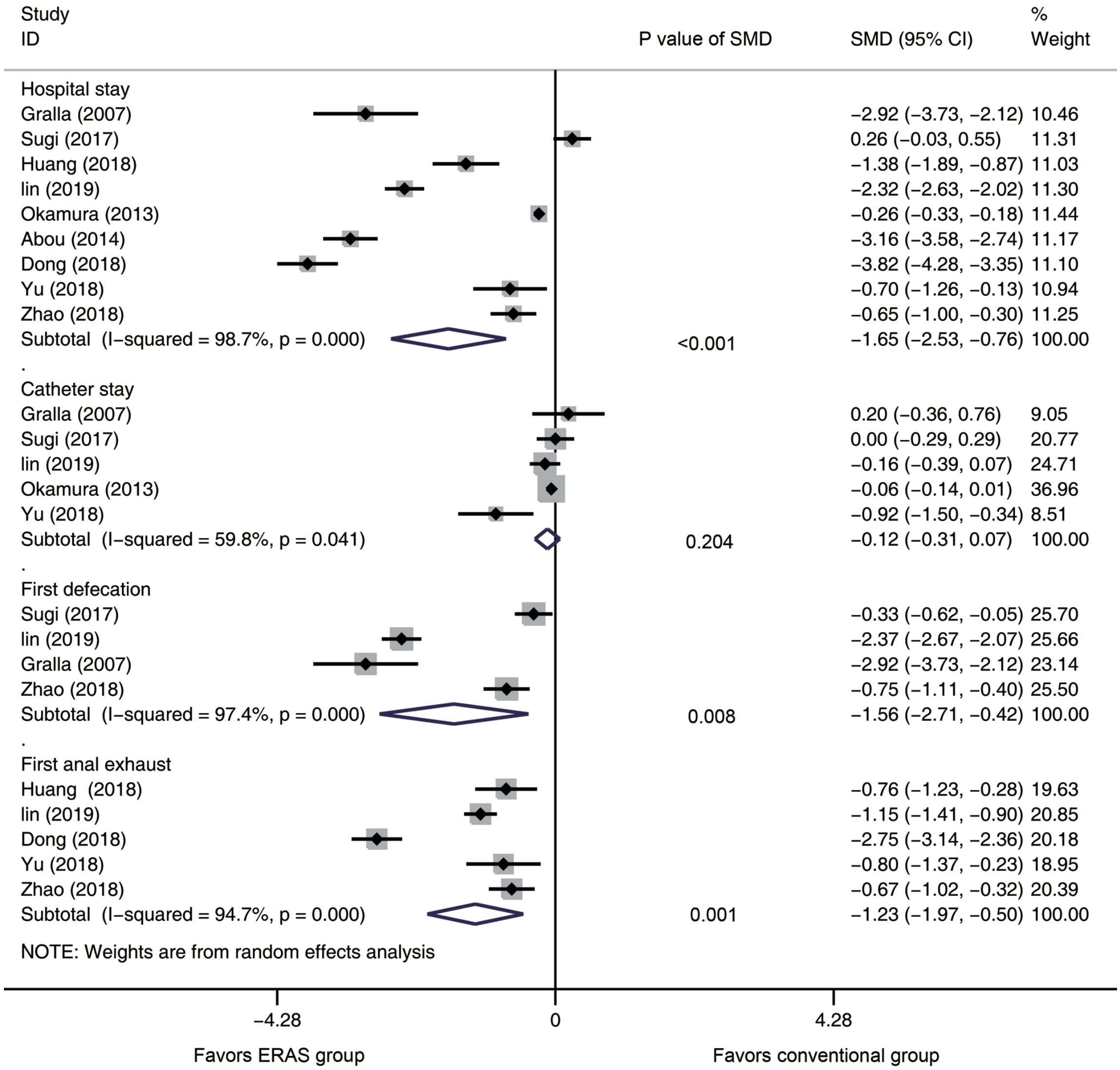

Figure 3 Annotated forest plot for meta-analysis of postoperative outcomes of ERAS and conventional groups. Summary of postoperative outcomes (hospital stay, catheter stay, first defecation and first anal exhaust) SMD between ERAS and conventional groups were calculated using the random effect model. Size of squares is directly proportional to the amount of information available. ERAS, enhanced recovery after surgery; SMD, standard mean difference; P, P value of the Q test for heterogeneity.

performed to find sources of heterogeneity. The four trials were first separated in two groups (LRP and RALP) based on their surgery sub-type. However, the results still showed heterogeneity (*Table 5*) indicating that the difference in surgery sub-types was not the source of heterogeneity. But sensitivity analysis showed that the results of first defecation were robust (*Figure S3*).

First anal exhaust

Seven hundred and forty-eight subjects treated with either ERAS or conventional care in 5 trials were included for the analysis of first anal exhaust (data shown in *Tables 3,4*). An SMD of −1.23 (95% CI: −1.97, −0.50, I^2=94.7%) were obtained (*Figure 3*). The results showed that ERAS group had a shorter time to first anal exhaust than conventional care groups (P=0.001). The results indicated statistically significant heterogeneity. Subgroup analysis was performed to find sources of heterogeneity. The five trials were first separated in three groups (LRP, RALP and RP) based on their surgery sub-type. However, the results still showed

Table 5 Subgroup analysis of operation time, first defecation and first anal exhaust

Subgroup analysis	N	RR (95% CI)	P values	Test for heterogeneity		
				Chi^2	P_h	I^2
First defecation						
LRP	3	−1.98 (−3.26, −0.71)	0.002	54.64	<0.001	96.3%
RALP	1	−0.34 (−0.62, −0.05)	0.023	–	–	–
First anal exhaust						
LRP	2	−0.93 (−1.40, −0.46)	<0.001	4.76	0.029	79.0%
RALP	2	−0.78 (−1.14, −0.41)	<0.001	0.01	0.913	0%
RP	1	−2.75 (−3.14, −2.36)	<0.001	–	–	–
Hospital stay						
LRP	3	−1.94 (−3.26, −0.61)	0.004	59.98	<0.001	96.7%
RALP	3	−0.59 (−1.64, −0.46)	0.271	32.98	<0.001	93.9%
RP	3	−2.40 (−4.96, 0.15)	0.065	385.13	<0.001	99.5%

LRP, laparoscopic radical prostatectomy; RP, radical prostatectomy; RALP, robot-assisted laparoscopic radical prostatectomy; N, number of trials; RR, risk ratio; CI, confidence interval; P_h, P value of the Q test for heterogeneity.

heterogeneity (*Table 5*) indicating that the difference in surgery sub-types was not the source of heterogeneity. But sensitivity analysis showed that the results of first anal exhaust were robust (*Figure S4*).

Findings—postoperative complications

Several different adverse events and toxicities were reported (data shown in *Table 6*). In the meta-analysis, patients treated with either ERAS or conventional care from ten studies were included for analysis of postoperative complications. ERAS group had significant lower incidence of nausea than the conventional care group (overall RR =0.62, 95% CI: 0.40, 0.94, P=0.024). However, there was no statistical difference of other postoperative complications listed in *Table* 7 between ERAS and conventional care arms (P>0.05).

Publication bias

The shape of the funnel plot did not display any evidence of apparent asymmetry. Furthermore, the formal tests showed no substantial publication bias. The Egger's test had a P value of 0.463 while the Begg's test had a P value of 0.115 (*Figure S5*).

Discussion

In recent years, minimally invasive RP and open RP have been widely used for the management of Pca patients. Minimally invasive RP is advantageous because it minimizes operative injuries and reduces complications compared to open surgery. However, there seemed to be no significant difference in efficacy between these two sub-types of RP (4,28,29). In some countries, open RP is still an option for Pca patients. Currently, many medical centers have implemented the ERAS into RP programs. The ERAS protocol is a standardized perioperative care pathway aimed at minimizing the stress of surgery, reduce postoperative morbidity, shorten hospital stay and accelerate recovery. ERAS has been widely implemented in abdominal and gynecologic surgery (7,30,31). Nonetheless, results from clinical trials are not compelling enough to support any definitive conclusions about the superiority of ERAS in RP programs. In this study, we performed a systematic review and meta-analysis on the efficacy and safety of ERAS and conventional care for Pca patients undergoing RP from 10 primary studies. Among the ten, five were RCTs, four were retrospective trials and one was a prospective cohort study. Results indicated that the ERAS group had significantly shorter hospital stay, shorter time to first defecation, shorter time to first anal exhaust, and lower incidence of nausea

Table 6 Data of postoperative complications

Study	Ileus		Wound infection		Nausea		Lymphocele		Urine leakage		Pneumonia		Urinary tract infection		Deep venous thrombosis		Urinary retention	
	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con	ERAS	Con
Gralla 2007/Magheli 2011	–	–	–	–	–	–	–	–	–	–	0	1	–	–	–	–	0	1
Okamura 2013	–	–	–	–	–	–	13	10	116	141	–	–	–	–	–	–	–	–
Abou 2014	0	2	–	–	–	–	0	2	–	–	–	–	–	–	–	–	–	–
Sugi 2017	3	5	2	2	0	2	1	1	–	–	–	–	–	–	–	–	1	3
Huang 2018	1	3	1	1	2	4	1	1	1	2	0	2	0	1	0	1	–	–
Lin 2019	–	–	–	–	6	7	–	–	0	2	2	4	2	3	0	1	–	–
Dong 2018	–	–	–	–	7	14	–	–	–	–	–	–	3	6	0	1	–	–
Yu 2018	0	1	1	2	2	5	–	–	1	1	–	–	1	2	0	0	–	–
Zhao 2018	–	–	–	–	14	16	–	–	–	–	–	–	3	6	–	–	–	–

ERAS, enhanced recovery after surgery; Con, conventional group.

compared to the conventional group. However, there was no statistical difference in intraoperative outcomes, catheter stay and other postoperative complications between ERAS and conventional group.

Overall survival (OS) and recurrence-free survival (RFS) are the key outcomes for evaluating the efficacy of a surgery. However, the trials included in this meta-analysis did not assess the OS nor RFS, because they were all short-term studies. As such, long-term clinical trials are needed to compare the OS and RFS of these two groups. ERAS group had significantly shorter hospital stay compared to the conventional care group (P<0.001). However, the difference in intraoperative outcomes and catheter stay between ERAS and conventional care arms was not significant (P>0.05). Hospital stay is an important outcome for any surgery. Sugi 2017 reported that there was no significant difference in hospital stay between these two groups (P>0.05) (data shown in *Tables 3,4*) (20). Contrary to these findings, the ERAS group had a significantly shorter hospital stay period compared to the conventional group (P<0.05) in 8 trials used in this study (19,21-27). Similarly, Lin 2018 compared the hospitalization costs between these two groups and found out that the ERAS group could significantly reduce the hospitalization costs compared to the conventional care group (6.1 *vs.* 7.2 thousand USD, P<0.001) (22).

Meta-analysis results also revealed that the ERAS group had significantly shorter times to first defecation (P=0.008) and first anal exhaust compared to the conventional group (P=0.001). Time to first defecation and anal exhaust were two indicators of postoperative recovery of intestinal function. The ERAS protocol suggested omission of preoperative bowel preparation, preoperative carbohydrate loading, and restricted fluid therapy. Evidently, ERAS group had a better postoperative intestinal function recovery than the conventional group.

Another potential advantage of ERAS would be the reduction of the frequencies of postoperative complications. Huang 2018 reported that ERAS could significantly reduce the incidence of pain compared to the conventional group (data shown in *Tables 3,4*, P=0.004) (21). In the same line, Okamura 2013 reported that there was significantly lower incidence of fever above 38 ℃ in ERAS group compared to the conventional group (1.9% *vs.* 3.5%, P=0.014) (23). Similarly, Gralla 2007 reported that there was significantly lower incidence of penoscrotal complications in the ERAS group compared to the conventional group (5 *vs.* 12, P=0.04) (18). However, trials included for this study were not enough to accurately assess these complications between

Table 7 Meta-analysis results of the incidences of postoperative complications between ERAS and conventional groups in patients undergoing RP

Postoperative complications	N	RR (95% CI)	P values	Test for heterogeneity		
				Chi^2	P_h	I^2
Ileus	4	0.57 (0.20, 1.62)	0.293	1.36	0.714	0%
Wound infection	3	1.00 (0.27, 3.71)	0.998	0.63	0.731	0%
Nausea*	6	0.62 (0.40, 0.94)	0.024	2.39	0.793	0%
Lymphocele	4	1.24 (0.59, 2.58)	0.570	1.53	0.676	0%
Urine leakage	4	0.88 (0.70, 1.10)	0.263	0.82	0.846	0%
Pneumonia	3	0.46 (0.12, 1.76)	0.260	0.50	0.780	0%
Urinary tract infection	5	0.48 (0.22, 1.04)	0.061	0.61	0.961	0%
Deep venous thrombosis	3	0.36 (0.06, 2.24)	0.272	0.03	0.986	0%
Urinary retention	2	0.46 (0.07, 2.88)	0.409	0.06	0.802	0%

*, there had statistically difference between two arms. ERAS, enhanced recovery after surgery; RP, radical prostatectomy; CI, confidence interval; N, number of trials; RR, risk ratio; P_h, P value of the Q test for heterogeneity.

the two groups. As such, no definite conclusion could be drawn. Nonetheless, pooled meta-analysis results revealed that the ERAS group had significant lower incidence of nausea compared to the conventional care group. However, there were no significant differences in other postoperative complications between ERAS and conventional groups (P>0.05) (data shown in *Table 7*).

Heterogeneity is an important aspect in meta-analysis. In this study, statistical analysis revealed that heterogeneity was present in most aspects. Subgroup analysis performed indicated that the difference in surgery sub-types was not the source of heterogeneity. Although the sources of heterogeneity were not found, sensitivity analysis results indicated that the overall significance of the pooled estimates were not affected by any trial included in the study. Similarly, Begg's and Egger's tests were used to detect any publication bias that would introduce false positives in meta-analysis (17). No evidence of publication bias was detected. These results indicated that all the conclusions of this study were credible and verifiable.

However, this study is limited by several factors. The number of studies used was low because of lack of enough high-quality RCTs. As such, some complications could not be accurately assessed. Further to this, the trials included in this study were short-term studies, had inconsistent ERAS protocols and were open labelled. All these were factors that could have affected the outcomes of the study. In future studies, more rigorous long-term experiments needed to be designed to enable precise meta-analysis of all aspects between the ERAS and conventional care groups.

Conclusions

Evidently, the ERAS group had significantly shorter hospital stay, shorter time to first defecation, shorter time to first anal exhaust and lower incidence of nausea compared to the conventional care group. Both groups had similar incidences of other postoperative complications. Based on the consistence of the data presented so far in this and previous studies, ERAS has the potential to be used as a standard of care for Pca patients undergoing RP.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm.2020.04.03). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for 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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Supplementary

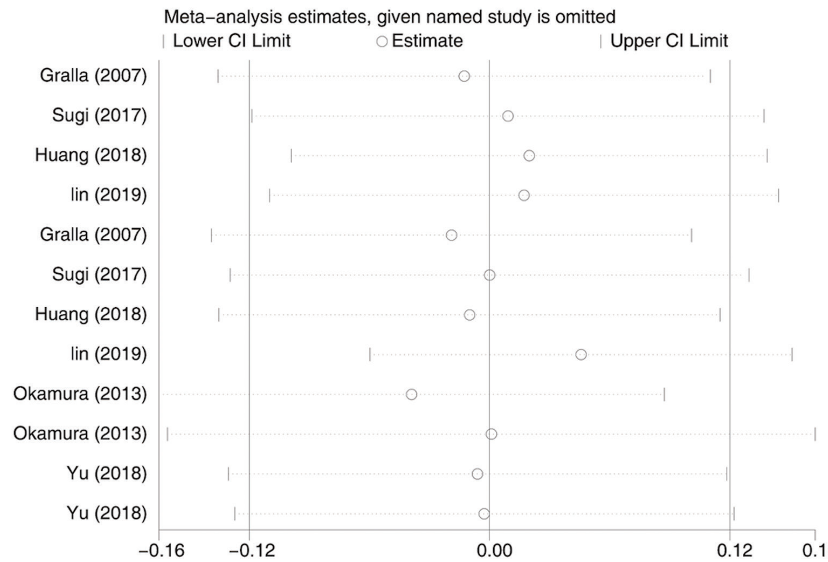

Figure S1 Sensitivity analysis of intraoperative outcomes.

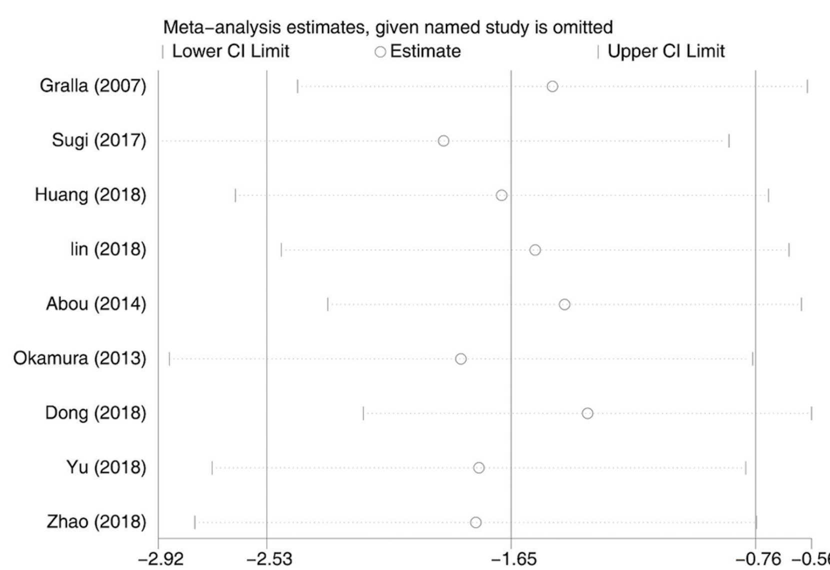

Figure S2 Sensitivity analysis of hospital stay outcome.

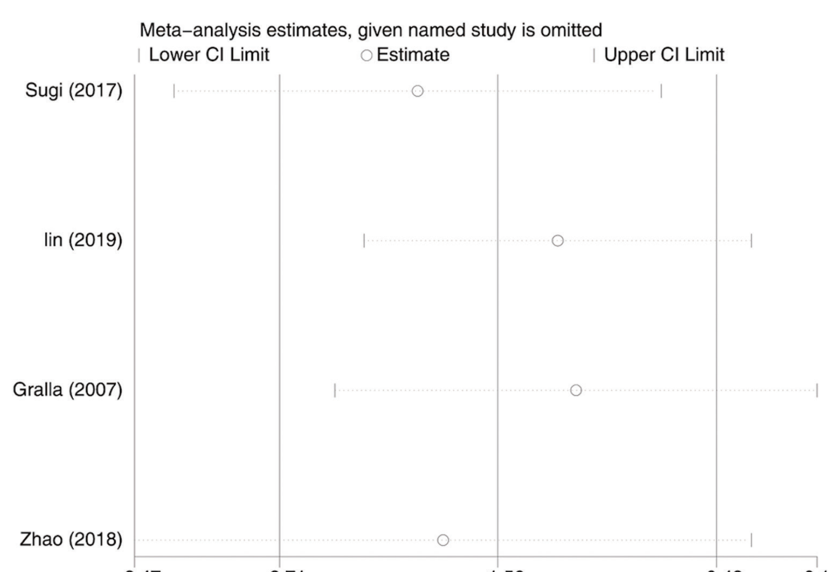

Figure S3 Sensitivity analysis of time to first defecation outcome.

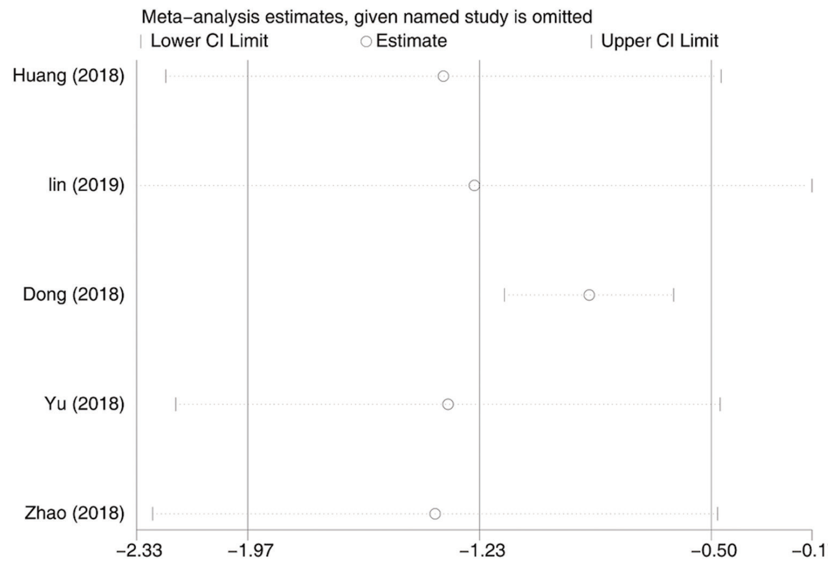

Figure S4 Sensitivity analysis of time to first anal exhaust outcome.

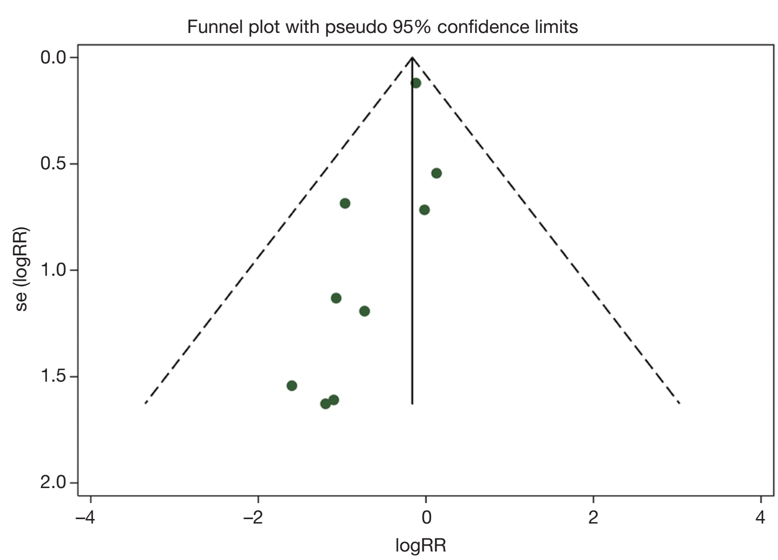

Figure S5 Publication bias risk. RR, risk ratio; se, standard error of the mean.