BMC Anesthesiology

SYSTEMATIC REVIEW Open Access

Effect of perioperative dexmedetomidine on recovery of postoperative gastrointestinal function in patients with general anesthesia: a systematic review and meta-analysis

Yanping Liu[1†], Hongbin Liang[2†], Yuanyuan Sun[1], Weihua Liu[3], Li Ye[2], Wanyou He[2*] and Hanbing Wang[2*]

Abstract

Background There is controversy surrounding the influence of dexmedetomidine on the recovery of postoperative gastrointestinal dysfunction in patients under general anesthesia. The main purpose of this meta-analysis is to evaluate the effect of dexmedetomidine administration during the perioperative period on the recovery of gastrointestinal function in patients under general anesthesia.

Methods A systematic review and meta-analysis with trial sequential analysis was performed to identify randomized controlled trials comparing dexmedetomidine administration with placebo for the recovery of gastrointestinal function. The primary outcomes were gastrointestinal function; first oral feeding time; incidences of postoperative nausea and vomiting, postoperative nausea, and postoperative vomiting; time to first bowel sound; time to first flatus; and time to first defecation. The secondary outcome was the length of hospital stay.

Results A total of 20 studies comparing 2,470 participants were included in this meta-analysis. Perioperative dexmedetomidine administration did not result in a significant reduction in the time to first oral feeding (MD= -7.91, 95% CI = – 16.45 to 0.62, $P = 0.07$). However, dexmedetomidine administration was associated with a decreased incidence of postoperative nausea and vomiting (RR = 0.72, 95% CI = 0.58 to 0.88, $P = 0.001$), time to first flatus (MD= -6.73, 95% CI= -10.31 to -3.15, $P = 0.0002$), and time to first defecation (MD= -12.01, 95% CI = -22.40 to -1.61, $P = 0.02$).

Conclusions Perioperative dexmedetomidine administration can promote the recovery of gastrointestinal function and reduce the length of hospital stay after abdominal surgery. The optimal dose and timing of dexmedetomidine and the influence on non-abdominal surgery need further investigation.

†Yanping Liu and Hongbin Liang contributed equally as first authors to this research project.

Wanyou He and Hanbing Wang contributed equally as corresponding authors to this research project.

*Correspondence:
Wanyou He
he_wanyou@163.com
Hanbing Wang
wanghanbing2@126.com

Full list of author information is available at the end of the article

Trial registration The study protocol was registered in the PROSPERO database (registration number: CRD42023443708) on July 9, 2023.

Keywords Perioperative administration of dexmedetomidine, Postoperative gastrointestinal function recovery, General anesthesia, Abdominal surgery

Introduction

Postoperative gastrointestinal dysfunction, occurs in 10–30% of patients undergoing abdominal surgery under general anesthesia and has emerged as an important qualitative component of anesthesia and surgical recovery [1]. Postoperative gastrointestinal dysfunction is characterized by the inability to resume a normal diet, accompanied by symptoms such as nausea, vomiting, abdominal distension, and constipation [2]. Research has shown that patients experiencing postoperative gastrointestinal dysfunction also exhibit a range of adverse outcomes such as an average increase of 4 days in the length of hospital stay, a 29% higher incidence of postoperative complications, a 12% increase in the likelihood of requiring re-operation, an 8% increase in re-admission rates, and a four-fold higher mortality rate than patients without postoperative gastrointestinal dysfunction [3].

Postoperative gastrointestinal dysfunction is influenced by a combination of factors related to the type of surgery, general anesthesia, and the patient's age and sex [4], but there are no effective prevention strategies yet available [5]. Opioids remain ubiquitous in the maintenance of general anesthesia, and the management of postoperative pain and are closely correlated with postoperative gastrointestinal dysfunction [6]. In 2018, a joint consensus advocated to reduce the intraoperative opioid utilization to promote recovery after postoperative gastrointestinal dysfunction [5].

Dexmedetomidine, a selective alpha2-adrenergic agonist, is frequently used as an adjunct to anesthesia during the perioperative period owing to its anti-inflammatory properties [7], stress reduction benefits [8], and positive effect on the vagus nerve [9]. These characteristics make dexmedetomidine a potential candidate for preventing postoperative gastrointestinal dysfunction. The 2016 guidelines [10] from the American Society of Anesthesiologists (ASA) support the perioperative use of dexmedetomidine to decrease opioid consumption [11], improve patient prognosis, and expedite patient recovery.

There is a lack of consensus regarding the impact of dexmedetomidine on postoperative gastrointestinal dysfunction in existing literature [12]. On the one hand, some studies have showed that dexmedetomidine could prevent the alteration of intestinal microcirculation during surgery or anesthesia [13] and may be beneficial to the recovery of gastrointestinal function. A meta-analysis of perioperative use of dexmedetomidine showed that it can potentially reduce the time to first flatus and defecation, but the study was limited by its poor evidence owing to the comparator arm which included lidocaine, morphine, or fentanyl that may have impacted gastrointestinal function recovery, hence being unable to differentiate between different types of surgeries [14]. On the other hand, other studies reported that dexmedetomidine cannot shorten the time to first flatus and bowel sounds for patients undergoing elective abdominal hysterectomy [15]. One study even showed a notable suppressive effect on gastrointestinal function in healthy volunteers [16]. Moreover, these past studies included in the analysis demonstrated suboptimal quality as they were limited-scale investigations and lacked Trial Sequential Analysis (TSA) to evaluate the robustness of the meta-analysis outcomes. A multicenter randomized controlled clinical trial showed that intraoperative use of dexmedetomidine can enhance the recovery of postoperative gastrointestinal dysfunction [2], which can benefit for making a consensus in the positive effect of dexmedetomidine. Hence, we conducted an exhaustive review of randomized controlled trials. Our objective was to synthesize the existing evidence and assess the potential of continuous perioperative infusion of dexmedetomidine in enhancing postoperative gastrointestinal dysfunction recovery and shortening the length of hospital stay. Additionally, TSA was employed to appraise the reliability and precision of our meta-analysis findings.

Methods

Registration and protocol

The study protocol was registered in the PROSPERO database (registration number: CRD42023443708) on July 9, 2023, and was conducted in accordance with the PRISMA [17] (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. The PICO format was utilized, where "P" represents patients (adult patients under general anesthesia), "I" represents interventions (administration of dexmedetomidine), "C" represents comparisons (control), and "O" represents outcomes (recovery from postoperative gastrointestinal dysfunction).

Eligibility criteria

The inclusion criteria were randomized controlled clinical trials on adult human subjects (age ≥ 18 years) undergoing surgery that compared the effect of perioperative intravenous dexmedetomidine with a placebo for gastrointestinal function recovery. Additionally, the

selected studies were all original research and reported data analysis results. Different studies evaluated various parameters of postoperative gastrointestinal function recovery. For searching previous studies and the purpose of this meta-analysis, the following parameters were considered as the primary study outcomes: time to first oral feeding; incidences of postoperative nausea and vomiting (PONV), postoperative nausea, and postoperative vomiting; time to first bowel sound; time to first flatus; and time to first defecation. The secondary outcome was the length of hospital stay. Studies were excluded if they reported any interventions not consistent with our aim, did not provide clear details on dexmedetomidine dosage and administration, and were duplicates of previously reported data, and reviews. The adherence to these well-defined criteria ensured the relevance and reliability of the included studies in the meta-analysis.

Search strategy

From inception until June 30, 2023, a systematic search was conducted using the PubMed and Cochrane Library databases. The search terms utilized were "Dexmedetomidine" [all fields] AND "Gastrointestinal tract" [all fields] OR "Postoperative ileus" [all fields] OR "Ileus" [all fields] OR "Gastrointestinal" [all fields]" OR "Gastroenteric function" [all fields] OR "Flatus" [all fields]" OR "Defecation" [all fields]" OR "Diet" [all fields] OR "Oral feeding" [all fields] OR "Postoperative nausea and vomiting" [all fields] OR "Bowel" [all fields] OR "First bowel sound" [all fields] OR "Defecation" [all fields] OR "Exhaust" [all fields].

Study selection and data collection

Two authors (YP. Liu and HB. Liang) conducted a thorough examination of the titles and abstracts and excluded any duplicate studies to identify potentially eligible ones. In case of discrepancy, a third author (YY. Sun) was consulted to resolve the differences. Additionally, both authors (YP. Liu and HB. Liang) independently assessed the risk of bias in the studies using the second version of the Cochrane risk-of-bias tool for RCTs (RoB 2.0) [18], and any disagreements were resolved through consultation with the third author (YY. Sun). To gather relevant information, the same two authors used a pre-designed data abstraction form, which included details such as the first author, publication year, country, participants age, sample size, surgical procedure, intervention, and outcomes. The specific steps of the selection process are visually presented in Fig. 1.

The outcome indicators extracted for our meta-analyses comprised only the primary and secondary outcomes. These outcomes were presented as counts of positive events or mean difference (MD). In instances where a study reported continuous outcomes as median, we converted these into mean±standard deviation by using

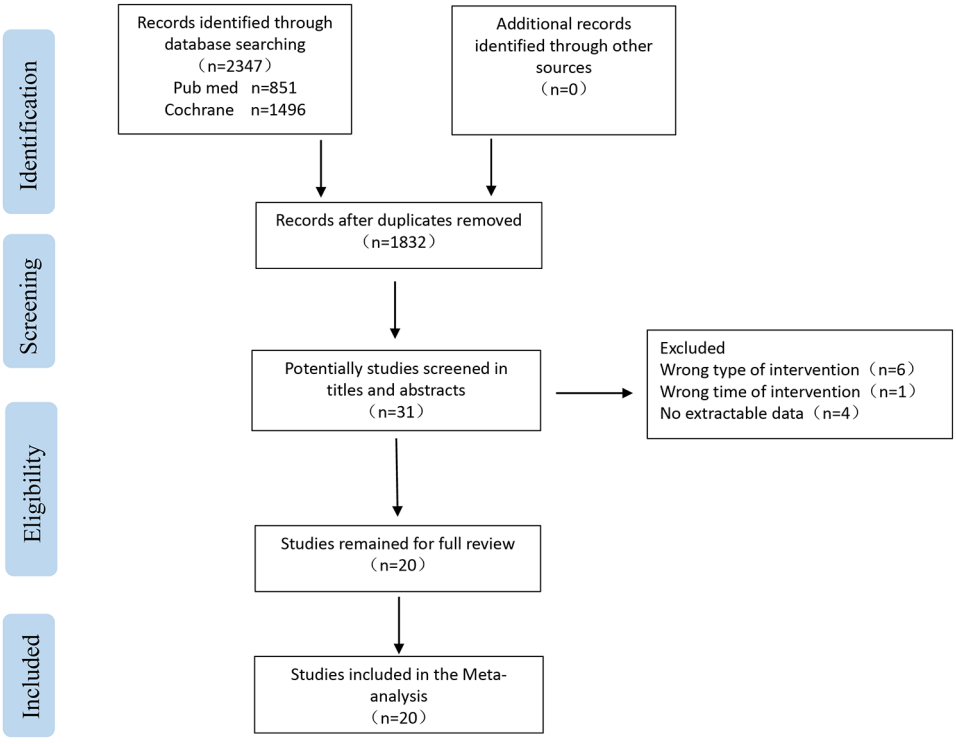

Fig. 1 Flow chart of trial selection

the equation by Wan et a.i [19]. (Cochrane Handbook Chap. 6.5.2.5).

Methodological quality assessment

The methodological quality of the trials included in the study was assessed using the second version of the Cochrane risk-of-bias tool for RCTs (RoB 2.0) [18]. Five domains of bias were evaluated, namely (1) Randomization process, (2) Deviations from intended interventions, (3) Missing outcome data, (4) Measurement of the outcome, (5) Selection of the reported result. Each domain was categorized as having either a low risk of bias, some concerns, or a high risk of bias. Trials that demonstrated a low risk of bias across all domains were categorized as low risk of bias. If at least one domain was identified as raising some concerns, but not at high risk of bias for any domain, they were categorized as some concerns. Trials were classified as high risk of bias if they were judged to be at high risk of bias in at least one domain, or if they were judged to have some concerns for multiple domains in a way that substantially lowers confidence in the result (Fig. 2).

Statistical analysis

Data analysis and synthesis were conducted using Review Manager (Rev Man), version 5.4, provided by The Nordic Cochrane Center in Copenhagen, Denmark. Continuous outcomes were expressed as the MD, while dichotomous outcomes were presented as Risk Ratio (RR). All results were accompanied by their respective effect estimates and 95% confidence intervals (95%CI). Heterogeneity was evaluated using the I^2 statistic [20], classified into three levels: low ($I^2<50\%$), moderate ($I^2=50–75\%$), and high ($I^2>75\%$). $I^2<50\%$ and P value$\geq$0.1 were indicative of non-significant heterogeneity, and a fixed-effects model was employed to pool the data. Conversely, $I^2>50\%$ and $P<0.1$ were indicative of substantial heterogeneity, and a random-effects model was chosen. $P<0.05$ was considered to indicate statistically significant differences. Additionally, a funnel plot analysis was conducted to assess publication bias when 10 or more independent comparisons were included in a pooled analysis. A subgroup analysis of the primary outcome was performed.

Trial sequential analysis [21] was performed using the TSA software (0.9.5.10 beta version; Copenhagen Trial Unit, Copenhagen, Denmark) to assess statistically significant outcomes. TSA was aimed to control the risk of type-1 error and evaluate the robustness and reliability of

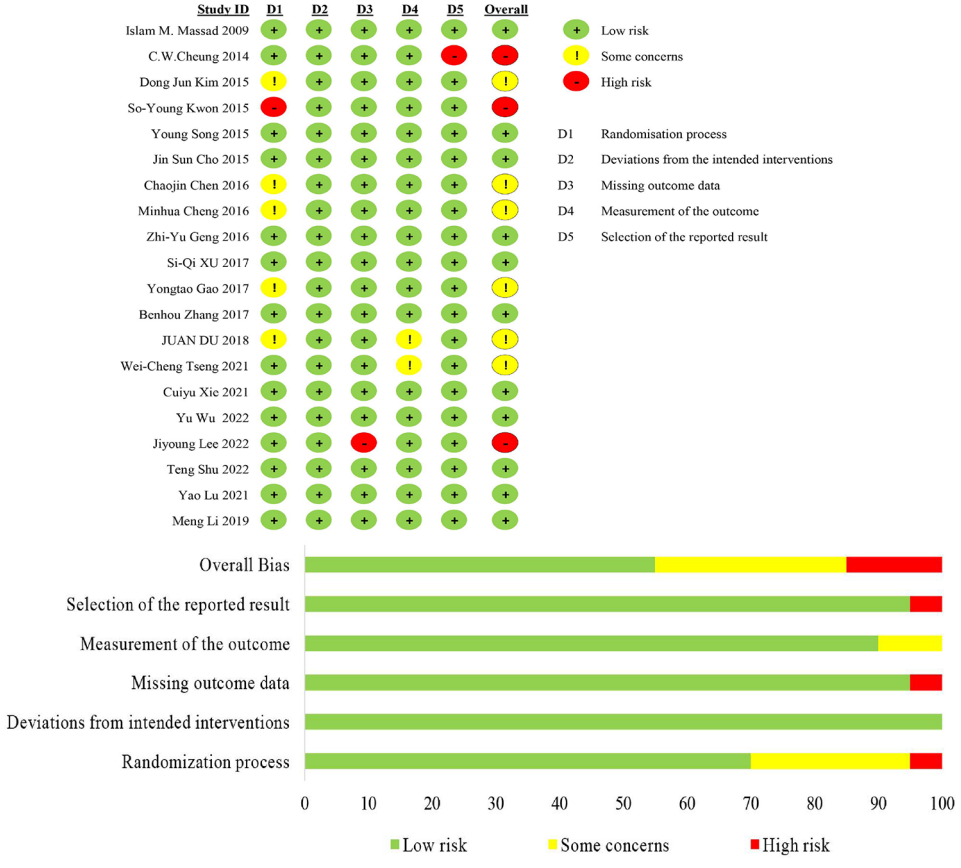

Fig. 2 The risk of bias for the included studies, using version 2.0 of the Cochrane risk-of-bias tool for RCTs (RoB 2.0)

statistical findings obtained from our meta-analysis. The statistical parameters were set at 5% alpha, 90% power, and a Z-value of 1.96. For continuous outcomes, to ensure the dependability and conclusiveness of evidence in our meta-analysis, we calculated the MD and variance based on the included studies with low risk. While for dichotomous outcomes, the incidence in the intervention arm (IIA) and incidence in the control arm (ICA) were separately calculated based on all included studies [22].

Results

Study selection

Our initial search yielded 2,347 studies covering the period until June 30, 2023. After excluding duplicate studies and screening titles and abstracts, 31 studies met the eligibility criteria. Subsequently, the full texts of these potentially eligible studies were thoroughly reviewed, leading to the exclusion of 11 studies. Ultimately, 20 studies were included in our meta-analysis. A detailed representation of the selection process and the results of our meta-analysis are shown in Fig. 1.

Study characteristics

The total population included in all the studies in the meta-analysis was 2,470, of which 1,249 were assigned to the DEX group, and 1,221 to the control group. The administration of dexmedetomidine including loading dose, maintenance dose, and duration showed variation among the studies (Table 1). Intraoperative administration of DEX was used in 16 studies [2, 15, 23–36], while three studies [37–39] focused on postoperative analgesia, and one trial [40] employed both intraoperative and postoperative infusion of dexmedetomidine. Among the 20 studies, the loading dose of dexmedetomidine ranged from 0.5 μg/kg to 1 μg/kg over a period of 10–15 min, and the maintenance dose varied from 0.1 μg/kg/h to 0.5 μg/kg/h. Fourteen studies [2, 15, 23–28, 33–35, 38–40] were specific to abdominal surgery, while six [29–32, 36, 37] investigated non-abdominal surgery.

Risk of bias within studies

Among the 20 trials, 11 [2, 15, 23–25, 28, 30, 32, 35–37] were determined to have a low risk of bias, 6 [26, 27, 31, 38–40] were determined to some concerns, while the remaining three [29, 33, 34] were classified as having an overall high risk of bias.

Primary outcomes

Time to first oral feeding

Four studies [2, 24, 27, 28] comprising 931 participants (dexmedetomidine group: 472 participants, Control group: 459 participants) indicated that the administration of dexmedetomidine did not result in a significant reduction in the time to first oral feeding for patients undergoing general anesthesia (MD=−7.91; 95%CI=−16.45 to 0.62, P=0.07, I^2=97%) (Supplementary Fig. 1a). A sensitivity analysis was conducted, excluding the study by Chen et al. [27], which still demonstrated no difference in the outcome, but with reduced heterogeneity (MD=−5.06; 95%CI=−11.27 to 1.16, P=0.11, I^2=83%). TSA (Supplementary Fig. 1b) revealed that the cumulative Z curve crossed the conventional boundary for benefit, but did not reach the TSMB or the RIS, suggesting that these findings may be false positives attributed to random chance.

Postoperative nausea and vomiting

Data from 10 RCTs [23–27, 29–33] involving a total of 867 participants (dexmedetomidine group: 439 participants, Control group: 428 participants) to investigate the incidence of PONV revealed a significant difference between the two groups regarding PONV (RR=0.72; 95%CI=0.58 to 0.88, P=0.001, I^2=14%) (Fig. 3a). Interestingly, when we included the ninth article in our analysis (Fig. 3b), the cumulative Z curve crossed the conventional boundary and the TSMB, indicating sufficient evidence to establish a conclusive finding. Although the cumulative Z curve did not cross the RIS when considering all included studies, additional research was unlikely to alter our conclusion. Based on these findings, the administration of dexmedetomidine was associated with a reduction in the incidence of PONV in patients undergoing surgery. The funnel plot for the PONV suggested the presence of publication bias (Supplementary Fig. 2).

Subgroup analyses were performed to assess the impact of different factors on PONV in the type of surgery (Fig. 4a). In six studies [23–27, 33] involving a total of 499 participants who underwent abdominal surgery, the incidence of PONV was significantly reduced (RR=0.66; 95%CI=0.50 to 0.85, P=0.002, I^2=15%). However, in four studies [29–32] comprising 368 participants who underwent non-abdominal surgery, dexmedetomidine did not show a significant reduction in the incidence of PONV (RR=0.82; 95%CI=0.59 to 1.13, P=0.23, I^2=20%). Moreover, a TSA analysis (Fig. 4b) was performed. The inclusion of the fifth article resulted in the cumulative Z curve crossing the conventional boundary and the TSMB, although did not cross the RIS when considering all included studies. But the accumulated evidence was deemed sufficient to establish a conclusive finding. However, in the non-abdominal surgery group (Fig. 4c), TSA analysis showed that did not enough to drawing a definitive conclusion.

Postoperative nausea

Seven studies [23, 25, 30, 34, 37, 38, 40] comprised 864 participants (dexmedetomidine group: 433 participants,

Table 1 Characteristics of the included studies

Author/Year /Country	Age (DEX/Control)	Type of surgery	Sample size (DEX/ Control)	Strategy of DEX doses		Strategy of Control	Outcomes
				Loading /time	Maintenance		
Islam M. Massad[25] 2009（ Jordan）	31.02/32.03	Laparoscopic gynecological	42/39	None	0.5ug/kg/h	Placebo	PONV, PN, PV
C. W. Cheung[34] 2014(China)	61.7/64.4	Elective colorectal surgery	46/50	1.0ug/kg 10min	0.5ug/kg/h	Placebo	PN, PV
Dong Jun Kim[31] 2015(Korea)	74.5/73.5	Elective orthopedic surgery	30/30	None	0.4ug/kg/h	Placebo	PONV
So-Young Kwon[29] 2015(Korea)	66.4/67.1	Elective transurethral resection	30/30	0.5ug/kg	0.5ug/kg/h	Placebo	PONV
Young Song[37] 2015（ Korea）	57/58	Posterior lumbar spinal fusion	53/52				PN, PV
Jin Sun Cho[28] 2015(Korea)	55.1/55.4	Laparoscopic gastrectomy	46/46	0.5ug/kg 10min	0.4ug/kg/h	Placebo	FFL, TOF, LOS
Chaojin Chen[27] 2016（ China）	56.67/60.17	Laparoscopic colorectal	30/30	1ug/kg 10min	0.3ug/kg/h	Placebo	FFL, PONV, TED, TOF, LOS
Minhua Cheng[39] 2016（ China）	56.98/59.09	Abdominal operation	59/54				FFE
Zhi-Yu Geng[23] 2016（ China）	39.6/41.7	Laparoscopic gynecological	65/65	0.5ug/kg/ 10min	0.1ug/kg/h	Placebo	PONV, PN, PV
Si-Qi XU[15] 2017（ China）	48/46.5	Elective abdominal hysterectomy	60/60	0.5ug/kg 10min	0.5ug/kg/h	Placebo	FFL, TBS
Yongtao Gao[38] 2017（ China）	50.4/51.7	Abdominal operation	102/101				FFL, PN, PV
Benhou Zhang[35] 2017(China)	41.12/43.12	Elective open liver resection	26/26	0.5ug/kg 10min	0.3ug/kg/h	Placebo	FFL
JUAN DU[40] 2018(China)	47.2/46.5	Laparoscopic hysterectomy	41/40	None	0.5ug/kg/h	Placebo	PN, PV
Wei-Cheng Tseng[26] 2021(China)	31.29/35.47	Open living donor hepatectomy	17/17	None	0.4 ug/kg/h	Placebo	FFL, PONV, LOS
Cuiyu Xie[30] 2021(China)	44/41	Ambulatory thyroidectomy	84/84	0.5ug/kg 10min	0.1ug/kg/h	Placebo	PONV, PN, PV
Yu Wu[24] 2022(China)	46.89/46.71	Elective laparoscopic Hyster myomectomy	54/52	0.5ug/kg 15min	0.2ug/kg/h	Placebo	FFL, PONV, FFE, TOF
Jiyoung Lee[33] 2022(Korea)	45.3/46.6	Laparoscopic hysterectomy	47/41	None	0.4ug/kg/h	Placebo	PONV
Teng Shu[32] 2022(China)	45.6/46.2	Elective thyroid cancer surgery	40/40	0.5ug/kg 10min	0.5ug/kg/h	Placebo	PONV
Yao Lu[2] 2021(China)	70.1/70.4	Elective abdominal surgery	344/331	0.5ug/kg 15min	0.2ug/kg/h	Placebo	FFL, FFE, TOF
Meng Li[36] 2019(China)	59.27/60.91	Elective lumber spinal surgery	33/33	0.5ug/kg 15min	0.1ug/kg/h	Placebo	FFL

First flatus FFL, Postoperative nausea and vomiting PONV, Postoperative nausea PN, Postoperative vomiting PV, First defecation FFE, Time to first oral feeding TOF, Time to first bowel sounds TBS, Time to first mobilization TFM, Length of hospital stays LOS

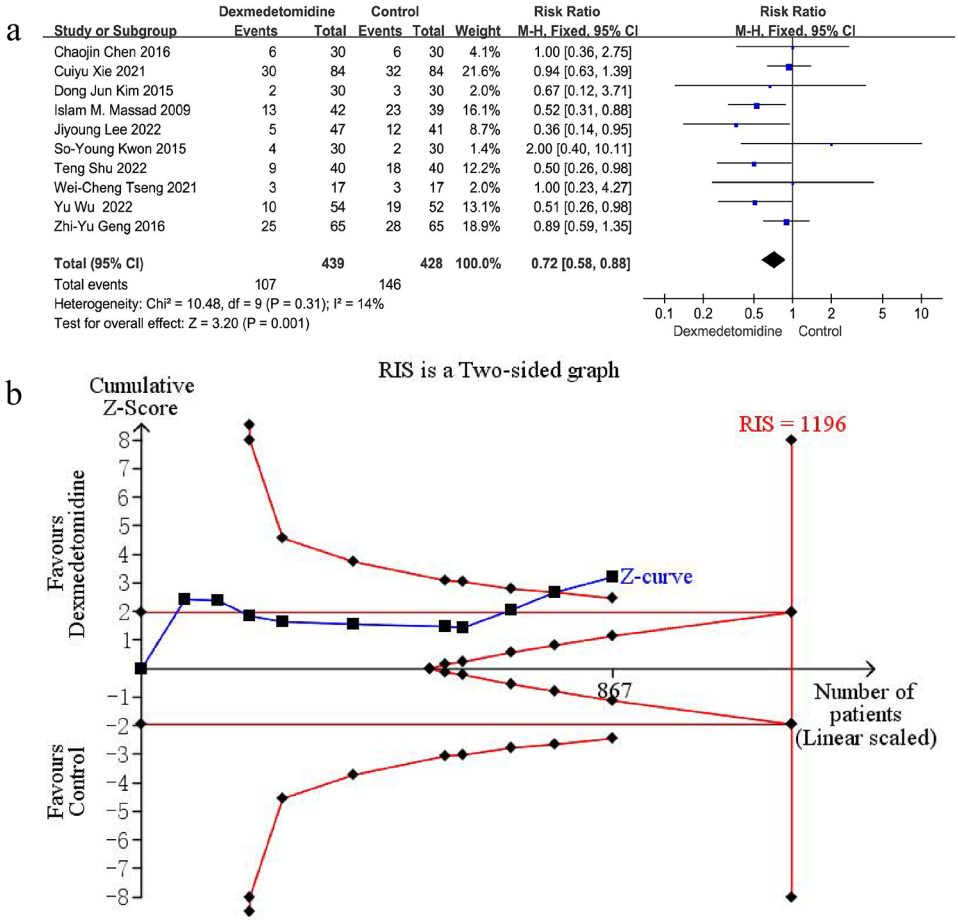

Fig. 3 (**a**) Forest plot for the PONV. (**b**) TSA for the PONV: IIA:24.37, ICA:34.11

Control group: 431 participants) to evaluate postoperative nausea. The forest plot analysis yielded significant results (RR=0.73; 95%CI=0.57 to 0.93, P=0.01, I^2=39%) (Supplementary Fig. 3a).

Postoperative vomiting

The same seven relevant studies [23, 25, 30, 34, 37, 38, 40] with a total of 864 participants were used to assess postoperative vomiting and revealed a significant difference between the two groups (RR=0.57; 95%CI=0.41 to 0.79, P=0.0007, I^2=0%) (Supplementary Fig. 3b).

Time of first flatus

In the meta-analysis, nine RCTs [15, 24, 26–28, 35, 38] were included that comprised 1406 participants, with 710 in the dexmedetomidine group and 696 in the control group. The collective evidence demonstrated a significant reduction in the time to first flatus compared to the control group (MD = -6.73; 95%CI=−10.31 to -3.15, P=0.0002, I^2=96%) (Fig. 5a). A sensitivity analysis was performed by excluding the study conducted by Chen et al. [27], which indicated that the heterogeneity was reduced (MD = -4.97; 95%CI=−7.57 to -2.37, P=0.0002, I^2=91%). Furthermore, we conducted a TSA analysis (Fig. 5b), and when the eighth article was included, the cumulative Z curve crossed the conventional boundary for the benefit and the TSMB, suggesting favorable outcomes. The accumulated evidence was deemed sufficient to establish a conclusive finding.

Time to first defecation

A total of 954 participants from four selected studies [2, 24, 27, 39] were enrolled in the meta-analysis, with 487 participants in the dexmedetomidine group and 467 participants in the control group. The overall analysis indicated significant difference (MD = -12.01, 95%CI = -22.40 to -1.61, P=0.02, I^2=95%) (Supplementary Fig. 4a). Subsequently, a sensitivity analysis was performed by excluding the study conducted by Chen et al. [27], which resulted in a significant difference and reduced heterogeneity (MD=−5.81; 95%CI = -8.64 to -2.97, P<0.01, I^2=45%). The results of the TSA are presented in Supplementary Fig. 4b. The inclusion of the fourth article revealed that the cumulative Z curve crossed the conventional boundary for benefit, but did not reach the TSMB or the RIS, suggesting that these findings may be false

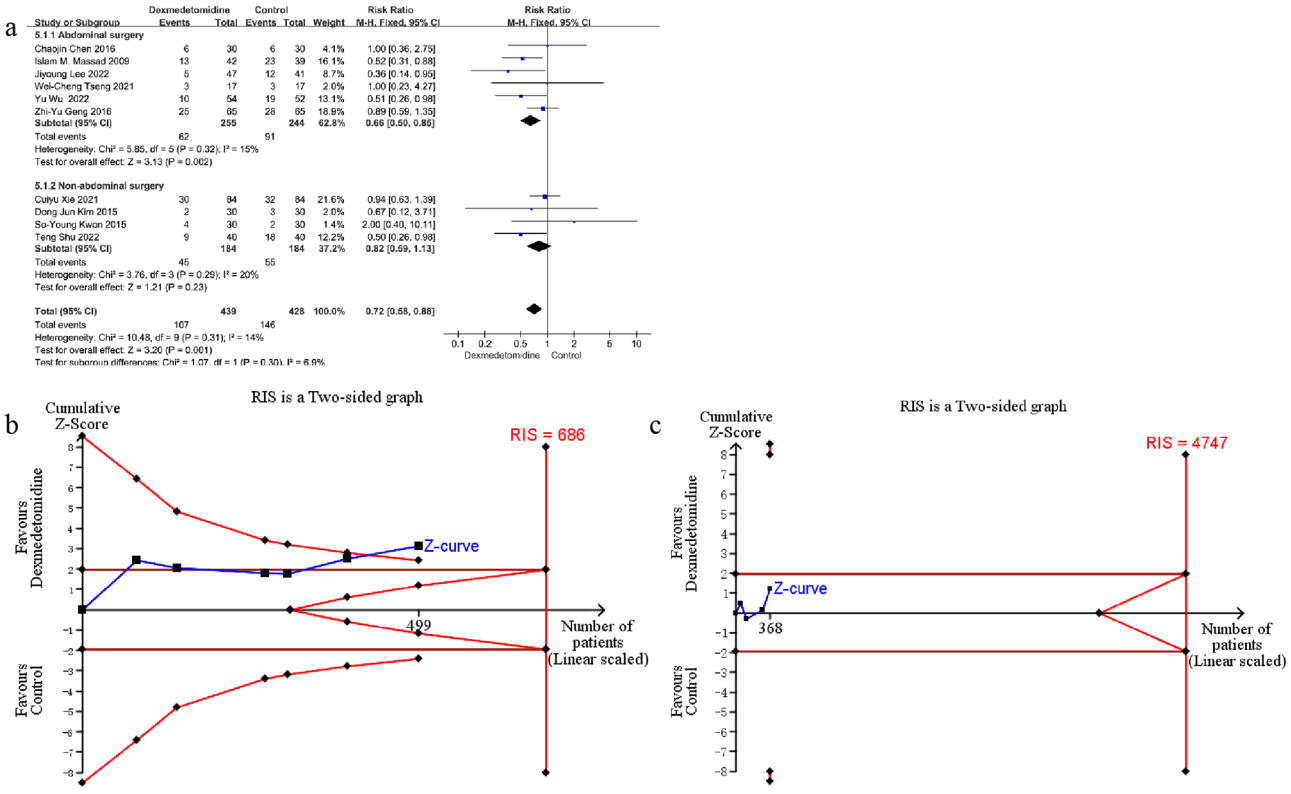

Fig. 4 Forest plot and TSA of the PONV by the subgroups of the type of surgery. (**a**) Forest plot for the subgroup about the type of surgery. (**b**) TSA for the group of abdominal surgery: IIA:24.31, ICA:37.3. (**c**) TSA for the group of non-abdominal surgery: IIA:24.46, ICA:30.0

positives attributed to random chance. Consequently, no definitive conclusion can be drawn from these results.

Secondary outcomes

The length of hospital stays

Three studies [26–28] including 184 participants (dexmedetomidine group: 91 participants, Control group: 93 participants) reported length of stay outcomes. The length of stay outcomes that we included were only about the length of postoperative hospital stay. The meta-analysis (Supplementary Fig. 5a) showed significant difference between the two groups (MD = -1.06, 95%CI = -1.87 to -0.24, P=0.01, I^2=67%). The TSA (Supplementary Fig. 5b) also showed sufficient evidence to establish a conclusion.

Discussion

This systematic review and meta-analysis of 20 RCTs suggested that perioperative administration of dexmedetomidine can facilitate the recovery of gastrointestinal function and shorten the length of hospital stay for patients after abdominal surgery with firm evidence from TSA. For the parameters of gastrointestinal function considering the included studies, we found that the incidence of PONV decreased when dexmedetomidine is administered solely during the intraoperative period, but the time to first flatus and first defecation shortened when dexmedetomidine is administered during the perioperative period.

The pathophysiological basis of postoperative gastrointestinal dysfunction involves a multifaceted interplay of elements, including the inflammatory response, ischemia-reperfusion injury, and postoperative opioid utilization. Gastrointestinal motility primarily relies on the activation of parasympathetic nerves and the suppression of sympathetic nerves [24]. Dexmedetomidine functions as an agonist for α2-adrenergic receptors, which are notably abundant on the membranes of smooth muscle cells in the intestines [24]. Perioperative stress and pain prompt increased catecholamine release, triggering the activation of the renin-angiotensin system. This, in turn, induces sustained contraction of visceral blood vessels, leading to a redistribution of organ-specific blood flow and subsequent compromise in organ perfusion, notably within the gastrointestinal mucosa [13]. Activation of opioid receptors within the gastrointestinal tract culminates in the suppression of acetylcholine and other mediator releases, resulting in decreased luminal water content and inhibited gastrointestinal motility [41]. Dexmedetomidine demonstrates the potential to mitigate the inflammatory response [42] by interacting with α2-adrenoceptors resulting in the suppression of

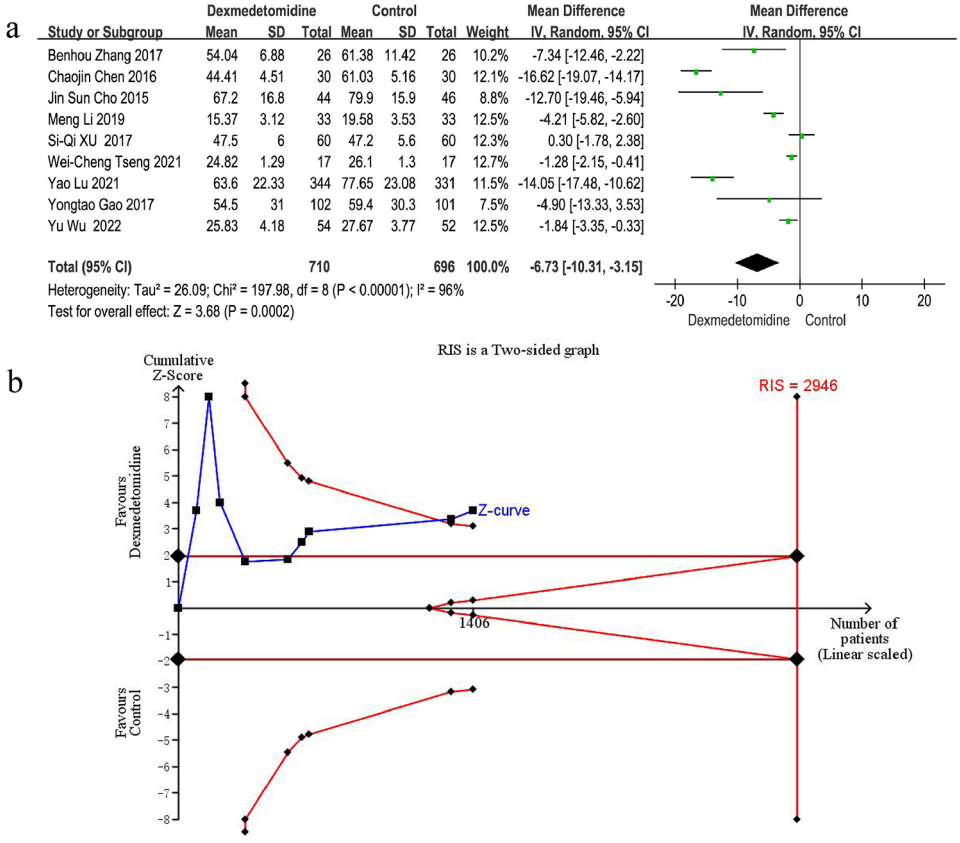

Fig. 5 (**a**) Forest plot for the time to first flatus. (**b**) TSA for the time to first flatus

sympathetic nerve activation [43] and subsequent release of catecholamines [44]. However, existing literature also proposes that the crux of dexmedetomidine's impact on perioperative gastrointestinal function revolves around its opioid-sparing ability [24]. The incorporation of dexmedetomidine during surgical procedures resulted in decreased post-craniotomy analgesic requirements [45]. When dexmedetomidine was used in conjunction with narcotics and opioids, a synergistic enhancement of its intrinsic effect can transpire, consequently leading to a reduction in its dosage [46].

Our meta-analysis covered various types of surgeries. Previous studies have highlighted that patients undergoing abdominal surgery were susceptible to postoperative gastrointestinal dysfunction, which contributes to increased hospitalization expenses and economic burden [47]. Therefore, mitigating postoperative gastrointestinal dysfunction has emerged as the primary focus to curtail medical costs and improve patient outcomes [47]. To delve deeper into the impact of dexmedetomidine on gastrointestinal functional recovery in patients undergoing various surgical procedures, we conducted a distinct subgroup analysis for abdominal and non-abdominal surgery. Given that all included studies classified the surgery type as abdominal surgery except for the PONV parameter, further subdivision into subgroups for other parameter analysis was deemed unnecessary. In addition, it was reasonable to conclude that dexmedetomidine administration during the perioperative period can promote the recovery of gastrointestinal function after abdominal surgery. For the PONV parameter, we stratified patients into two distinct groups based on the type of surgery: those who underwent abdominal surgery [23–27, 33] and those underwent non-abdominal surgery [29–32]. The forest plot analysis for the non-abdominal surgery [29–32] subgroup revealed no significant difference, while the TSA analysis showed inconclusive findings. These results were distinct from those reported in previous studies. For instance, Song et al.'s [37] study, which focused on patients undergoing posterior lumbar fusion, showed an effective reduction in PONV with postoperative dexmedetomidine administration. Nevertheless, this reduction may be attributed to the patient inclusion criteria, as they enrolled patients with at least three risk factors for PONV. Within the subgroup of non-abdominal surgeries [29–32], variations in anesthesia protocols were noted across the studies. Xie et al. [30] reported using azasetron 10 mg at the end of the surgery, while Kim et al. [31] and Kwon et al.'s [29] studies did not administer any pre-emptive antiemetic. Furthermore,

Shu et al.'s [32] study administered ondansetron intravenously 10 min before surgery. These inconsistencies in antiemetic approaches warrant further investigation to determine the specific impact of dexmedetomidine on PONV in patients undergoing non-abdominal surgery.

Despite an extensive search of the database, we were unable to identify a reliable study documenting the optimal dose of dexmedetomidine. Furthermore, the maintenance and loading doses of dexmedetomidine varied among the included studies, leading to the inability to reach a definitive conclusion regarding the optimal dose based on our analysis. Additionally, the utilization of dexmedetomidine differed across various periods; among the included studies three [38–40] administered dexmedetomidine after the surgery, one study [41] administered dexmedetomidine both during and after surgery, and the remaining studies were intraoperative. Notably, regarding the time of first flatus, Gao et al. [38] administered dexmedetomidine after surgery, but exclusion of this study did not impact the overall results. However, regarding the time of first defecation, Cheng et al. [39] administered dexmedetomidine after surgery, but the forest plots showed there was also has significant difference between two groups upon its exclusion (MD=−13.24; 95%CI = -15.34 to -11.14, P <0.001, I^2=97%). Regarding the first oral feeding, length of hospital stay and PONV, all included studies provided continuous intraoperative dexmedetomidine infusion. This difference prevented further subgroup analysis. Moreover, we refrained from specifically subdividing the maintenance dose point of dexmedetomidine infusion for subgroup analysis. Consequently, we speculated that further research is needed to explore the dose-response effect and assessed the impact of different periods of dexmedetomidine administration on gastrointestinal function recovery. For the time to first bowel sounds, the studies we included were insufficient to conduct further analysis.

The forest plot illustrated the time to first oral feeding, revealing a significant degree of heterogeneity (I^2=97%) (Supplementary Fig. 1). However, upon excluding the study conducted by Chen et al. [27], the heterogeneity diminishes (I^2=83%). Regarding first flatus, the forest plot showed high heterogeneity (I^2=96%) (Fig. 5). However, upon exclusion of Chen et al.'s [27] study, the heterogeneity was significantly reduced (I^2=91%). The time to first defecation exhibited substantial heterogeneity (I^2=95%) (Supplementary Fig. 4). After the exclusion of Chen et al.'s study [27], the heterogeneity decreased to I^2=45%. We hypothesized that this discrepancy might be attributed to the administration of 2 mg morphine at the end of the surgery in Chen et al.'s [27] study. Opioids such as morphine have been associated with increased intestinal permeability, potentially facilitating bacterial translocation and leading to bacterial dysbiosis [48]. Previous research has also indicated that morphine can exert inhibitory effects on gastrointestinal function, resulting in reduced gastrointestinal motility and delayed gastric emptying [49]. When more than 2 mg hydromorphone is administered intravenously, the recovery time of gastrointestinal function is delayed [50]. Although only 2 mg of morphine was administered in this study, we cannot disregard its potential influence.

In the case of the 20 articles included in this meta-analysis, several exclusion criteria warrant acknowledgment. Certain studies opted to omit participants with prior instances of PONV [23, 25] or individuals who had undergone antiemetic or glucocorticoid therapy within 24/48 h before the surgical procedure [23, 25]. This measure was adopted to gauge the specific impact of dexmedetomidine on PONV, effectively mitigating patient susceptibility and the influence of concurrent medications on outcome variables. Furthermore, selected correlated investigations used controls concerning patients' preoperative conditions to minimize their effect on the evaluation of postoperative gastrointestinal function. This approach involved the exclusion of patients with pre-existing gastrointestinal dysfunction [2, 24, 25, 27, 30, 39], previous abdominal surgeries [2, 24, 26, 27], or individuals with a history of prolonged opioid [15, 24, 33, 34, 41] or psychotropic drug [15, 23, 29, 30, 34, 35, 37] usage before surgery. It is imperative to acknowledge that these diverse exclusion criteria could potentially impact our findings.

Limitations

This systematic review and meta-analysis has several potential limitations that warrant consideration. First, the TSA analysis established the MD and variance based on studies characterized by a low risk of bias, with 11 of 20 studies (55%) falling into this category. Thus, the chosen TSA model may lack objectivity. Second, this study did not analyze adverse events associated with perioperative dexmedetomidine administration in patients undergoing surgery. Third, the meta-analysis failed to differentiate the utilization of opioid analgesics among the various postoperative pain management drugs in the included studies. Fourth, notable heterogeneity was observed in the pooled outcomes of the meta-analysis, and sensitivity analysis had minimal influence on the heterogeneity. Finally, the control of non-treatment factors among the included studies is inconsistent, such as the exclusion criteria, which may also affect our conclusions. These limitations should be addressed in future research.

Conclusions

Based on the systematic review and meta-analysis, perioperative administration of dexmedetomidine appears to facilitate the recovery of gastrointestinal function

and shorten the length of hospital stay after abdominal surgery. These findings from the chosen TSA model provided substantial confirmation evidence to support. While we cannot deny that dexmedetomidine facilitates the recovery of gastrointestinal function by mitigating opioid consumption and ameliorating stress or other associated effects, further large-scale, standardized, randomized controlled studies are needed to explore the optimal dose and different administration times of dexmedetomidine for postoperative gastrointestinal dysfunction recovery. Furthermore, future research should also focus on the effect of perioperative dexmedetomidine administration on non-abdominal surgery.

First flatus FFL, Postoperative nausea and vomiting PONV, Postoperative nausea PN, Postoperative vomiting PV, First defecation FFE, Time to first oral feeding TOF, Time to first bowel sounds TBS, Time to first mobilization TFM, Length of hospital stays LOS.

Abbreviations

DEX	Dexmedetomidine
ASA	American Society of Anesthesiologists
TSA	Trial Sequential Analysis
PONV	Postoperative nausea and vomiting
MD	Mean difference
RR	Risk ratio
95%CI	95% confidence intervals
TSMB	Trial sequential monitoring boundary
RIS	Required information size
FFL	First flatus
PN	Postoperative nausea
PV	Postoperative vomiting
FFE	First defecation
TOF	Time to first oral feeding
TBS	Time to first bowel sounds
TFM	Time to first mobilization
LOS	Length of hospital stays

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-024-02868-0.

Supplementary Material 1

Acknowledgements

The authors gratefully acknowledge the assistance of Hong Zheng, Professor of West China Hospital, Sichuan University, for the guidance on writing assistance and language help, and the Institute of Anesthesia and Neuroscience of Foshan First People's Hospital for the guidance.

Author contributions

Yanping Liu: Conceptualization, Methodology, Software, Writing – original draft, Validation, Writing – review & editing. Hongbin Liang: Conceptualization, Methodology, Software, Writing – original draft. Yuanyuan Sun: Writing – review & editing, Data curation. Weihua Liu: Conceptualization, Data curation. Li Ye: Data curation. Wanyou He: Visualization, Investigation, Software. Hanbing Wang: Supervision, Writing – review & editing.

Funding

This work was supported by the National Natural Science Foundation of China [grant number 82001197] and the Foundation of Guangdong Province [grant number 2021B1515120050].

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Nursing, The First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital, Jinan City 25000, China
[2]Department of Anesthesiology, The First People's Hospital of Foshan, Lingnan Road 81#, Foshan City 528000, China
[3]Shandong First Medical University & Shandong Academy of Medical Science, Jinan City 25000, China

Received: 19 February 2024 / Accepted: 19 December 2024
Published online: 28 December 2024

References

1. Venara A, Neunlist M, Slim K, Barbieux J, Colas PA, Hamy A, Meurette G. Postoperative ileus: pathophysiology, incidence, and prevention. J Visc Surg. 2016;153:439–46.
2. Lu Y, Fang PP, Yu YQ, Cheng XQ, Feng XM, Wong GTC, Maze M, Liu XS. Effect of intraoperative dexmedetomidine on recovery of gastrointestinal function after abdominal surgery in older adults: a randomized clinical trial. JAMA Netw Open. 2021;4:e2128886.
3. Tevis SE, Carchman EH, Foley EF, Harms BA, Heise CP, Kennedy GD. Postoperative ileus–more than just prolonged length of stay? J Gastrointest Surg. 2015;19:1684–90.
4. Zhong Y, Cao Z, Baumer D, Ajmani V, Dukes G, Chen YJ, Ayad SS, Wischmeyer PE. Incidence and risk factors for postoperative gastrointestinal dysfunction occurrence after gastrointestinal procedures in US patients. Am J Surg. 2023;226:675–81.
5. Hedrick TL, McEvoy MD, Mythen MMG, Bergamaschi R, Gupta R, Holubar SD, Senagore AJ, Gan TJ, Shaw AD, Thacker JKM, Miller TE, Wischmeyer PE, Carli F, Evans DC, Guilbert S, Kozar R, Pryor A, Thiele RH, Everett S, Grocott M, Abola RE, Bennett-Guerrero E, Kent ML, Feldman LS, Fiore JF Jr. Perioperative Quality Initiative (POQI) 2 workgroup. American society for enhanced recovery and perioperative quality initiative joint consensus statement on postoperative gastrointestinal dysfunction within an enhanced recovery pathway for elective colorectal surgery. Anesth Analg. 2018Jun;126(6):1896–907.
6. Adams TJ, Aljohani DM, Forget P. Perioperative opioids: a narrative review contextualising new avenues to improve prescribing. Br J Anaesth. 2023;130:709–18.
7. Lewis K, Alshamsi F, Carayannopoulos KL, Granholm A, Piticaru J, Al Duhailib Z, Chaudhuri D, Spatafora L, Yuan Y, Centofanti J, Spence J, Rochwerg B, Perri D, Needham DM, Holbrook A, Devlin JW, Nishida O, Honarmand K, Ergan B, Khorochkov E, Pandharipande P, Alshahrani M, Karachi T, Soth M, Shehabi Y, Møller MH, Alhazzani W, GUIDE group. Dexmedetomidine vs other sedatives in critically ill mechanically ventilated adults: a systematic review and meta-analysis of randomized trials. Intensive Care Med. 2022;48:811–40.
8. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. Clin Pharmacokinet. 2017;56:893–913.
9. He G-Z, Bu N, Li Y-J, Gao Y, Wang G, Kong Z-D, Zhao M, Zhang SS, Gao W. Extra loading dose of dexmedetomidine enhances intestinal function recovery after colorectal resection: a retrospective cohort study. Front Pharmacol. 2022;13:806950.
10. Kaye AD, Chernobylsky DJ, Thakur P, Siddaiah H, Kaye RJ, Eng LK, Harbell MW, Lajaunie J, Cornett EM. Dexmedetomidine in enhanced recovery after

surgery (ERAS) protocols for postoperative pain. Curr Pain Headache Rep. 2020;24:21.
11. Liu Y, Liang F, Liu X, Shao X, Jiang N, Gan X. Dexmedetomidine reduces perioperative opioid consumption and postoperative pain intensity in neurosurgery: a meta-analysis. J Neurosurg Anesthesiol. 2018;30:146–55.
12. Jessen Lundorf L, Korvenius Nedergaard H, Møller AM. Perioperative dexmedetomidine for acute pain after abdominal surgery in adults. Cochrane Database Syst Rev. 2016;2:CD010358.
13. Yeh YC, Sun WZ, Ko WJ, Chan WS, Fan SZ, Tsai JC, Lin TY. Dexmedetomidine prevents alterations of intestinal microcirculation that are induced by surgical stress and pain in a novel rat model. Anesth Analg. 2012;115:46–53.
14. Behera BK, Misra S, Jena SS, Mohanty CR. The effect of perioperative dexmedetomidine on postoperative bowel function recovery in adult patients receiving general anesthesia. Minerva Anestesiol. 2022;88:51–61.
15. Xu SQ, Li YH, Wang SB, Hu SH, Ju X, Xiao JB. Effects of intravenous lidocaine, dexmedetomidine and their combination on postoperative pain and bowel function recovery after abdominal hysterectomy. Minerva Anestesiol. 2017;83:685–94.
16. Iirola T, Vilo S, Aantaa R, Wendelin-Saarenhovi M, Neuvonen PJ, Scheinin M, Olkkola KT. Dexmedetomidine inhibits gastric emptying and oro-caecal transit in healthy volunteers. Br J Anaesth. 2011;106:522–7.
17. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6:e1000100.
18. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
19. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14:135.
20. Melsen WG, Bootsma MCJ, Rovers MM, Bonten MJM. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. Clin Microbiol Infect. 2014;20:123–9.
21. Shah A, Smith AF. Trial sequential analysis: adding a new dimension to meta-analysis. Anaesthesia. 2020;75:15–20.
22. Duan X, Coburn M, Rossaint R, Sanders RD, Waesberghe JV, Kowark A. Efficacy of perioperative dexmedetomidine on postoperative delirium: systematic review and meta-analysis with trial sequential analysis of randomised controlled trials. Br J Anaesth. 2018;121:384–97.
23. Geng ZY, Liu YF, Wang SS, Wang DX. Intra-operative dexmedetomidine reduces early postoperative nausea but not vomiting in adult patients after gynaecological laparoscopic surgery: a randomised controlled trial. Eur J Anaesthesiol. 2016;33:761–6.
24. Wu Y, Cai Z, Liu L, Wang J, Li Y, Kang Y, An N. Impact of intravenous dexmedetomidine on gastrointestinal function recovery after laparoscopic hysteromyomectomy: a randomized clinical trial. Sci Rep. 2022;12:14640.
25. Massad IM, Mohsen WA, Basha AS, Al-Zaben KR, Al-Mustafa MM, Alghanem SM. A balanced anesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med J. 2009;30:1537–41.
26. Tseng WC, Lin WL, Lai HC, Chen TW, Chiu YC, Chen PH, Wu ZF. Adjunctive dexmedetomidine infusion in open living donor hepatectomy: a way to enhance postoperative analgesia and recovery. Int J Clin Pract. 2021;75:e14002.
27. Chen C, Huang P, Lai L, Luo C, Ge M, Hei Z, Zhu Q, Zhou S. Dexmedetomidine improves gastrointestinal motility after laparoscopic resection of colorectal cancer: a randomized clinical trial. Med (Baltim). 2016;95:e4295.
28. Cho JS, Kim HI, Lee KY, An JY, Bai SJ, Cho JY, Yoo YC. Effect of intraoperative dexmedetomidine infusion on postoperative bowel movements in patients undergoing laparoscopic gastrectomy: a prospective, randomized, placebo-controlled study. Med (Baltim). 2015;94:e959.
29. Kwon SY, Joo JD, Cheon GY, Oh HS, In JH. Effects of dexmedetomidine infusion on the recovery profiles of patients undergoing transurethral resection. J Korean Med Sci. 2016;31:125–30.
30. Xie C, Zhang C, Sun H, Lu Y. Effects of dexmedetomidine on postoperative nausea and vomiting in adult patients undergoing ambulatory thyroidectomy: a randomized clinical trial. Front Med (Lausanne). 2021;8:781689.
31. Kim DJ, Kim SH, So KY, Jung KT. Effects of dexmedetomidine on smooth emergence from anaesthesia in elderly patients undergoing orthopaedic surgery. BMC Anesthesiol. 2015;15:139.
32. Shu T, Xu S, Ju X, Hu S, Wang S, Ma L. Effects of systemic lidocaine versus dexmedetomidine on the recovery quality and analgesia after thyroid cancer surgery: a randomized controlled trial. Pain Ther. 2022;11:1403–14.
33. Lee J, Hwang HW, Jeong JY, Kim YM, Park C, Kim JY. The effect of low-dose dexmedetomidine on pain and inflammation in patients undergoing laparoscopic hysterectomy. J Clin Med 2022;11.
34. Cheung CW, Qiu Q, Ying ACL, Choi SW, Law WL, Irwin MG. The effects of intra-operative dexmedetomidine on postoperative pain, side-effects and recovery in colorectal surgery. Anaesthesia. 2014;69:1214–21.
35. Zhang B, Wang G, Liu X, Wang TL, Chi P. The opioid-sparing effect of perioperative dexmedetomidine combined with oxycodone infusion during open hepatectomy: a randomized controlled trial. Front Pharmacol. 2017;8:940.
36. Li M, Wang T, Xiao W, Zhao L, Yao D. Low-dose dexmedetomidine accelerates gastrointestinal function recovery in patients undergoing lumbar spinal Fusion. Front Pharmacol. 2019;10:1509.
37. Song Y, Shim JK, Song JW, Kim EK, Kwak YL. Dexmedetomidine added to an opioid-based analgesic regimen for the prevention of postoperative nausea and vomiting in highly susceptible patients: a randomised controlled trial. Eur J Anaesthesiol. 2016;33:75–83.
38. Gao Y, Deng X, Yuan H, Leng Y, Zhang T, Xu X, Tian S, Fang J, Ouyang W, Wu X. Patient-controlled intravenous analgesia with combination of dexmedetomidine and sufentanil on patients after abdominal operation: a prospective, randomized, controlled, blinded, multicenter clinical study. Clin J Pain. 2018;34:155–61.
39. Cheng M, Shi J, Gao T, Shen J, Zhao C, Xi F, Li W, Li Q, Yu W. The addition of dexmedetomidine to analgesia for patients after abdominal operations: a prospective randomized clinical trial. World J Surg. 2017;41:39–46.
40. Du J, Li JW, Jin J, Shi CX, Ma JH. Intraoperative and postoperative infusion of dexmedetomidine combined with intravenous butorphanol patient-controlled analgesia following total hysterectomy under laparoscopy. Exp Ther Med. 2018;16:4063–9.
41. Farmer AD, Holt CB, Downes TJ, Ruggeri E, Del Vecchio S, De Giorgio R. Pathophysiology, diagnosis, and management of opioid-induced constipation. Lancet Gastroenterol Hepatol. 2018;3:203–12.
42. Mei B, Li J, Zuo Z. Dexmedetomidine attenuates sepsis-associated inflammation and encephalopathy via central α2A adrenoceptor. Brain Behav Immun. 2021;91:296–314.
43. Kontak AC, Victor RG, Vongpatanasin W. Dexmedetomidine as a novel countermeasure for cocaine-induced central sympathoexcitation in cocaine-addicted humans. Hypertension. 2013;61:388–94.
44. Yuan D, Liu Z, Kaindl J, Maeda S, Zhao J, Sun X, Xu J, Gmeiner P, Wang HW, Kobilka BK. Activation of the α2B adrenoceptor by the sedative sympatholytic dexmedetomidine. Nat Chem Biol. 2020;16:507–12.
45. Song J, Ji Q, Sun Q, Gao T, Liu K, Li L. The opioid-sparing effect of intraoperative dexmedetomidine infusion after craniotomy. J Neurosurg Anesthesiol. 2016;28:14–20.
46. Naaz S, Ozair E. Dexmedetomidine in current anaesthesia practice- a review. J Clin Diagn Res. 2014;8:GE01–4.
47. Traeger L, Koullouros M, Bedrikovetski S, Kroon HM, Moore JW, Sammour T. Global cost of postoperative ileus following abdominal surgery: meta-analysis. BJS Open 2023;7.
48. Rueda-Ruzafa L, Cruz F, Cardona D, Hone AJ, Molina-Torres G, Sánchez-Labraca N, Roman P. Opioid system influences gut-brain axis: dysbiosis and related alterations. Pharmacol Res. 2020;159:104928.
49. Akbarali HI, Inkisar A, Dewey WL. Site and mechanism of morphine tolerance in the gastrointestinal tract. Neurogastroenterol Motil. 2014;26:1361–7.
50. Barletta JF, Asgeirsson T, Senagore AJ. Influence of intravenous opioid dose on postoperative ileus. Ann Pharmacother. 2011;45:916–23.

Publisher's note