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Meta-analysis of robotic-assisted NOSE versus traditional TWSR in colorectal cancer surgery: postoperative outcomes and efficacy

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Abstract

Background This meta-analysis aimed to assess the safety and efficacy of robotic-assisted natural orifice specimen extraction surgery (NOSE) compared to traditional robotic transabdominal wall specimen retrieval surgery (TWSR) for colorectal cancer.

Methods A systematic search was conducted in three electronic databases (PubMed, Web of Science and Embase) from inception to August 2023. Primary outcomes included postoperative complications, the number of lymph nodes harvested, overall survival and disease-free survival. Secondary outcomes included the postoperative visual analog scale (VAS) score, the additional use of analgesics, the restoration of gastrointestinal function, blood loss, the mean operation time, and length of postoperative hospital stay.

Results In this meta-analysis, a total of 717 patients from 6 observational studies met the inclusion criteria. Compared with the TWSR group, the NOSE group had greater benefits in terms of overall postoperative complications [odds ratios (OR) 0.55; 95% confidence intervals (CI) = 0.34 to 0.89; $P = 0.01$, $I^2 = 0\%$)], the number of lymph nodes harvested [weighted mean differences (WMD) = 1.18; 95% CI = 0.15 to 2.21; $P = 0.02$, $I^2 = 0\%$)], the rate of wound infection (OR 0.17; 95% CI = 0.04 to 0.80; $P = 0.02$, $I^2 = 0\%$), the passed flatus time (WMD = −0.35 days; 95% CI = −0.60 to −0.10; $P = 0.007$, $I^2 = 73\%$), the additional use of analgesics (OR 0.25; 95% CI = 0.15 to 0.40; $P < 0.001$, $I^2 = 0\%$), the diet recovery time (WMD = −0.56; 95% CI = −1.00 to −0.11; $P = 0.01$, $I^2 = 78\%$) and the postoperative VAS score (WMD = −1.23; 95% CI = −1.63 to −0.83; $P < 0.001$, $I^2 = 65\%$). There were no significant differences in the blood loss (WMD = −5.78 ml; 95% CI = −17.57 to 6.00; $P = 0.34$, $I^2 = 90\%$), mean operation time (WMD = 14.10 min; 95% CI = −3.76 to 31.96; $P = 0.12$) ($I^2 = 93\%$), length of postoperative hospital stay (WMD = −0.47 day; 95% CI = −0.98 to 0.03; $P = 0.07$, $I^2 = 51\%$), incidences of postoperative ileus (OR 1.0; 95% CI = 0.22 to 4.46; $P = 1.00$, $I^2 = 0\%$), anastomotic leakage (OR 0.73; 95% CI = 0.33 to 1.60; $P = 0.43$, $I^2 = 0\%$), and intra-abdominal abscess (OR 1.59; 95% CI = 0.47 to 5.40; $P = 0.46$, $I^2 = 0\%$), or 3-year overall survival [hazard ratio (HR) = 1.07, 95% CI = 0.60 to 1.94; $P = 0.81$)] or disease-free survival (HR = 0.94, 95% CI = 0.54 to 1.63; $P = 0.82$, $I^2 = 0\%$).

Conclusion This meta-analysis showed that the NOSE group had better postoperative outcomes than did the TWSR group and that NOSE was a safe and viable alternative to TWSR. More large-sample reviews and further randomized trials are warranted.

Keywords Colorectal cancer, NOSE, TWSR, Meta-analysis

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Introduction

Colorectal cancer (CRC) is one of the most common malignancies in males and females [1]. It ranks as the third most prevalent malignancy worldwide with high morbidity and mortality [2]. Surgical resection remains the most appropriate method for curative treatment [3]. Robotic surgery has been widely used for CRC patients because the development of minimally invasive technology offers better visualization with a three-dimensional magnified view, a stable camera platform and greater dexterity of movements compared to conventional laparoscopic surgery [4]. However, all of the above surgeries require an abdominal incision (approximately 4–8 cm) to extract the surgical specimen, drastically increasing the incidence of incision-related complications such as wound infections, incisional hernias and postoperative pain [5]. NOSE has recently become popular because it avoids an additional long laparotomy incision [6]. Additionally, Franklin et al. [7] showed that NOSE is associated with fewer postoperative complications and faster recovery of gastrointestinal function. However, whether the use of a robotic platform combined with NOSE contributes to reducing postoperative complications, decreasing intraoperative bleeding and improving long-term prognosis remains controversial. Therefore, we conducted this meta-analysis to analyse the safety and feasibility of robotic-assisted NOSE compared with traditional robotic resection for treating CRC.

Materials and methods

Search strategy

A search for relevant articles was performed through electronic medical databases (PubMed, Embase, and Web of Science) for all relevant literature published up to November 2023 addressing robotic surgery with NOSE for the treatment of CRC. The language of publication was restricted to English. The search terms and keywords used to detail the search strategy are provided and shown in *Electronic supplementary material, Content 1*. Our study was designed and completed following the PRISMA guidelines [8].

Inclusion criteria and exclusion criteria

The search strategy differed according to the different requirements of the various databases. We also screened the references of relevant studies to identify potential articles. Studies were included if they conformed to the principles of PICO(S) (participants, interventions, comparisons, outcomes, study design). The inclusion criteria were as follows: (1) Participants: CRC patients undergoing traditional robotic transabdominal wall specimen retrieval surgery (TWSR); (2) Interventions: NOSE via the transrectal, transanal or transvaginal approaches; (3) Comparisons: the clinical effects of traditional robotic transabdominal wall specimen retrieval surgery (NOSE) versus TWSR; (4) Outcomes: intraoperative and postoperative data; and (5) Study type: published retrospective studies in humans. The exclusion criteria were as follows: (1) conference abstracts, case reports or animal studies; and (2) a lack of follow-up data or inability to obtain the original data.

Data extraction and quality assessment

Data extraction was conducted by two independent authors (Zhicheng Zhu and Haitao Yu). These data extracted included patient characteristics (age, sex, BMI, preoperative/

postoperative chemoradiotherapy use), author, country, year of publication, study design, lesion type, specimen extraction site, tumour location, sample size, TNM stage, blood loss, operation time, additional use of analgesics, overall postoperative complications, intra-abdominal abscesses, postoperative ileus, anastomotic leakage, wound infection, the passed flatus time, the diet recovery time, length of postoperative hospital stay, the number of lymph nodes harvested, the postoperative visual analog scale (VAS) score, the 3-year overall survival (OS) and disease-free survival (DFS). The accuracy of the data extraction was ensured by blinded checking of the data by the third author (Tian Xu). Discrepancies were resolved by consensus among all three authors. The overall risk of bias of each study was assessed by two authors (Yu Xia and Zhenda Wan) utilizing the Newcastle–Ottawa Quality Assessment Scale (NOS), with six or more stars indicating high quality, and less than six stars indicating low quality [9].

Statistical analysis

Statistical analyses were performed with Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) and STATA14.0 (StataCorp LP, College Station, Texas). Differences in effect sizes were assessed by using weighted mean differences (WMD) with 95% confidence intervals (CI) for continuous variables. Odds ratios (OR) with 95% CI were used to analyse the dichotomous variables. If the original literature only provided the median or interquartile range, we converted it to the mean and standard deviation (SD) according to the instructions from the Cochrane Handbook and Hozo et al. [10, 11]. For the survival analysis, OS and DFS were analysed by using the hazard ratio (HR) and its standard error (SE). If the HR and SE could not be directly calculated, Engauge Digitizer software (version 12.1) was used to extract the data from the Kaplan–Meier survival curves, which were subsequently calculated according to the methods of Tierney et al. [12, 13]. The heterogeneity of the results across studies was analysed with the Q test and I^2. The heterogeneity was absent,then a fixed-effects model was used if $P>0.1$ (for the Q test) and $I^2\leq 50\%$ [14]. Statistically significant heterogeneity was observed, then a random effects model was used when $P<0.1$ (for the Q test) and $I^2>50\%$. Sensitivity analysis was performed by removing one study at a time to estimate whether the final results were significantly affected when heterogeneity was high ($I^2>50\%$). Potential sources of heterogeneity were explored in subgroup analyses. Publication bias was illustrated with funnel plots [15].

Literature selection

A total of 120 potentially relevant studies were obtained by searching three databases (PubMed, Embase and Web of Science). We ultimately selected 6 papers for further in-depth analysis based on multiple factors, such as the removal of duplicate articles and the relevance of the title, abstract or article content (Fig. 1).

The basic characteristics of the included patients

All the included articles were retrospective nonrandomized studies. A total of 717 participants were included in this meta-analysis, with 334 participants in the NOSE group and 383 participants in the TWSR group. All patients were diagnosed with malignant carcinoma. The basic characteristics of the included studies are shown in Table 1. The NOS scores ranged from 0 to 9 points, and no intraoperative conversion to open surgery occurred. Retrospective trials with a low risk of bias (NOS score ≥ 6) were regarded as high-quality studies (*Electronic supplementary material, Table S1*). The basic patient and tumour characteristics are shown in *Electronic supplementary material, Table S2.*

Primary and Secondary Outcomes

Overall postoperative complications

Six studies reported the incidence of overall postoperative complications. According to the pooled analysis of the data, the NOSE group (8.7%) had fewer overall postoperative complications than the TWSR group (14.1%) (OR 0.55; 95% CI = 0.34 to 0.89; $P=0.01$). The fixed-effects model showed no significant heterogeneity ($P=0.98$, $I^2=0\%$) (Fig. 2).

Harvested lymph nodes

Two studies lacked detailed data on the number of harvested lymph nodes. The meta-analysis revealed that 1.18 more lymph nodes were harvested in the NOSE group (WMD = 1.18; 95% CI = 0.15 to 2.21; $P=0.02$). The heterogeneity among the studies was low ($P=0.70$, $I^2=0\%$), and the fixed-effects model was applied (Fig. 3).

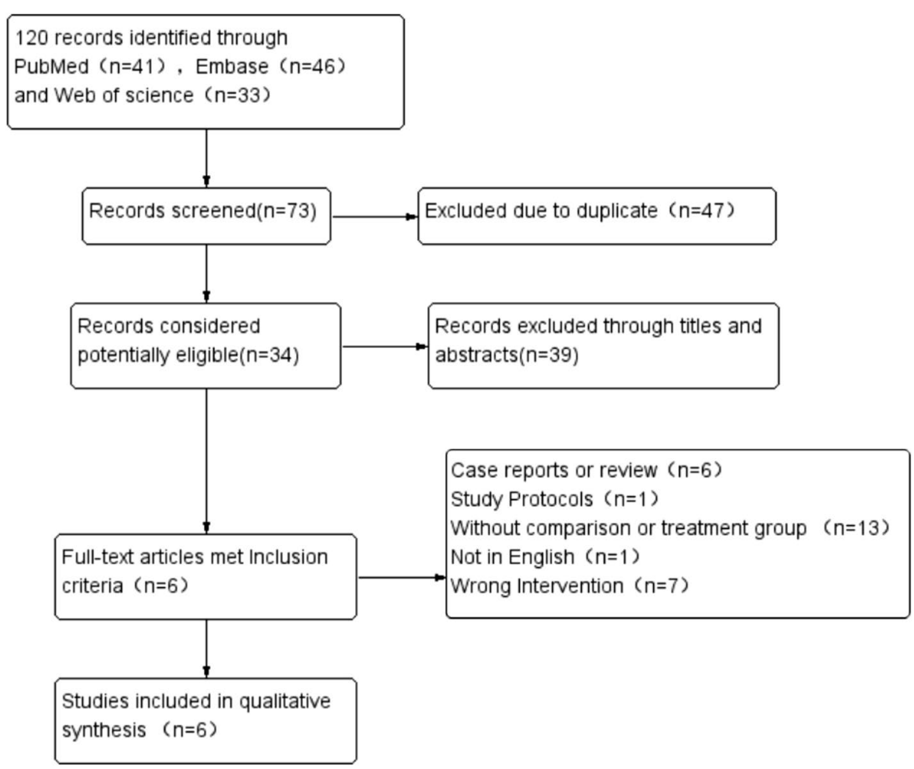

Fig. 1 Flow chart of the literature search strategy

Table 1 The basic characteristics of the included studies. RNR: retrospective nonrandomized study

Author	Year	Country	Study design	Lesion type	Specimen extraction site	Tumor located	Total samples	Sample size NOSE	Sample size TWSR	TNM stage
Aslaner et al. [16]	2022	Turkey	RNR	adenocarcinoma	transanal/transvaginal	sigmoid/rectum	150	57	93	I-II
Gao et al. [17]	2020	China	RNR	malignant carcinoma	transvaginal	sigmoid/rectum	90	45	45	I-III
Ju et al. [18]	2023	China	RNR	adenocarcinoma	transanal	sigmoid/rectum	182	91	91	I-III
Kang et al. [19]	2012	Korea	RNR	adenocarcinoma	transanal	rectum	119	53	66	NR
Li et al. [20]	2023	China	RNR	malignant carcinoma	transanal	sigmoid/rectum	78	39	39	T2-T4
Liu et al. [21]	2020	China	RNR	malignant carcinoma	transanal	rectuml	98	49	49	T1-T3

Anastomotic leakage

All of the studies described the incidence of anastomotic leakage. There was no significant difference between the two groups (OR 0.73; 95% CI = 0.33 to 1.60; P = 0.43). No significant heterogeneity was observed (P = 0.98, I^2 = 0%) (Fig. 4).

Wound infection

Five studied analysed wound infection and revealed that the NOSE group (0%) had no significant difference in the incidence of wound infection compared with the TWSR group (2.8%) (OR 0.17; 95% CI = 0.04 to 0.80; P = 0.02). No significant heterogeneity was observed (P = 1.00, I^2 = 0%) (Fig. 5).

Postoperative ileus

The pooled analysis of five studies revealed no significant difference in terms of the incidence of postoperative ileus (OR 1.0; 95% CI = 0.22 to 4.46; P = 1.00). No significant heterogeneity was observed (P = 0.67, I^2 = 0%) (Fig. 6).

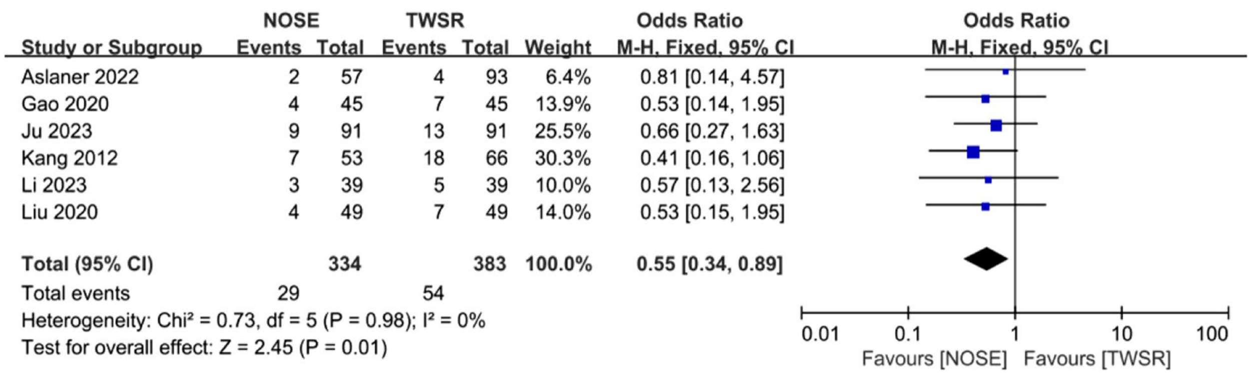

Fig. 2 Forest plot of overall postoperative complications

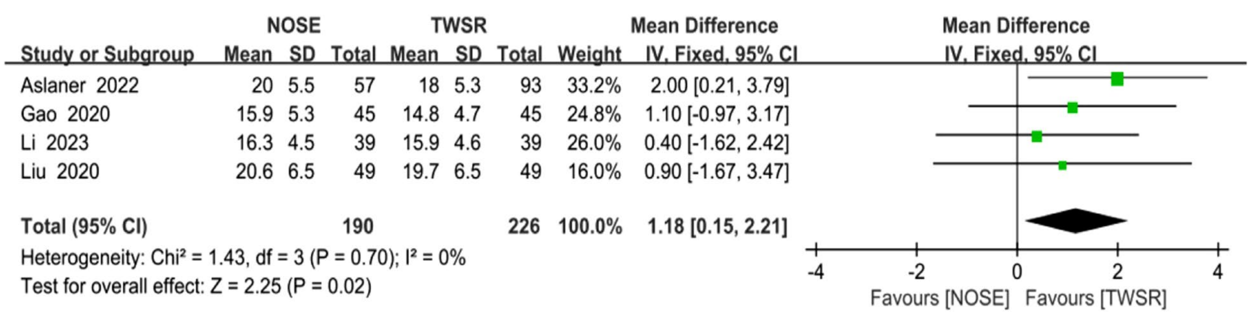

Fig. 3 Forest plot of the number of harvested lymph nodes

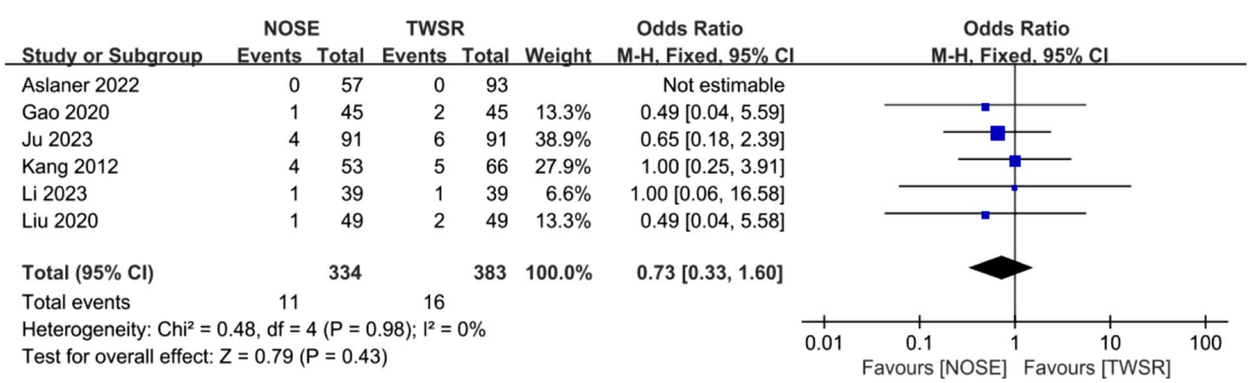

Fig. 4 Forest plot of postoperative anastomotic leakage

Intra-abdominal abscesses

Intra-abdominal abscess rates were not significantly different between the NOSE group and the TWSR group (OR 1.59; 95% CI = 0.47 to 5.40; $P = 0.46$). No significant heterogeneity was observed ($P = 0.95$, $I^2 = 0\%$) (Fig. 7).

Postoperative passed flatus time

All but one of the included studies provided data about gas emission after surgery. The first passed flatus time occurred earlier in the NOSE group than in the TWSR group, and a random effects model was used (WMD = −0.35 days; 95% CI = −0.60 to −0.10; $P = 0.007$). Significant heterogeneity was observed ($P = 0.005$, $I^2 = 73\%$) (Fig. 8).

Additional use of analgesics

According to four studies, the use of additional analgesics in the TWSR group was greater than that in

Study or Subgroup	NOSE Events	NOSE Total	TWSR Events	TWSR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Aslaner 2022	0	57	0	93		Not estimable
Gao 2020	0	45	2	45	22.7%	0.19 [0.01, 4.10]
Ju 2023	0	91	3	91	31.9%	0.14 [0.01, 2.71]
Li 2023	0	39	2	39	22.7%	0.19 [0.01, 4.09]
Liu 2020	0	49	2	49	22.7%	0.19 [0.01, 4.10]
Total (95% CI)		**281**		**317**	**100.0%**	**0.17 [0.04, 0.80]**
Total events	0		9			
Heterogeneity: Chi² = 0.03, df = 3 (P = 1.00); I² = 0%						
Test for overall effect: Z = 2.25 (P = 0.02)						

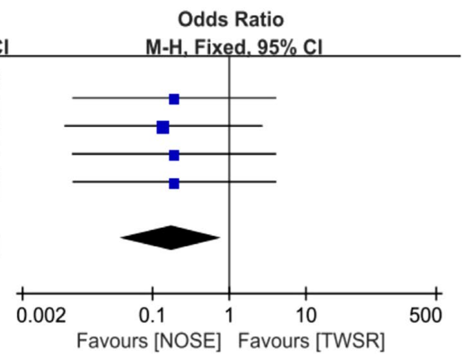

Fig. 5 Forest plot of the incidence of postoperative wound infection

Study or Subgroup	NOSE Events	NOSE Total	TWSR Events	TWSR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Aslaner 2022	0	57	0	93		Not estimable
Gao 2020	0	45	1	45	43.1%	0.33 [0.01, 8.22]
Ju 2023	2	91	1	91	28.4%	2.02 [0.18, 22.71]
Li 2023	0	39	0	39		Not estimable
Liu 2020	1	49	1	49	28.5%	1.00 [0.06, 16.45]
Total (95% CI)		**281**		**317**	**100.0%**	**1.00 [0.22, 4.46]**
Total events	3		3			
Heterogeneity: Chi² = 0.79, df = 2 (P = 0.67); I² = 0%						
Test for overall effect: Z = 0.00 (P = 1.00)						

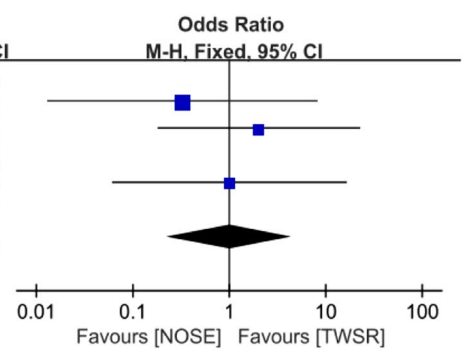

Fig. 6 Forest plot of postoperative ileus incidence

Study or Subgroup	NOSE Events	NOSE Total	TWSR Events	TWSR Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Aslaner 2022	0	57	0	93		Not estimable
Gao 2020	1	45	1	45	23.7%	1.00 [0.06, 16.50]
Kang 2012	2	53	2	66	41.5%	1.25 [0.17, 9.22]
Li 2023	1	39	0	39	11.6%	3.08 [0.12, 77.91]
Liu 2020	2	49	1	49	23.2%	2.04 [0.18, 23.29]
Total (95% CI)		**243**		**292**	**100.0%**	**1.59 [0.47, 5.40]**
Total events	6		4			
Heterogeneity: Chi² = 0.36, df = 3 (P = 0.95); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						

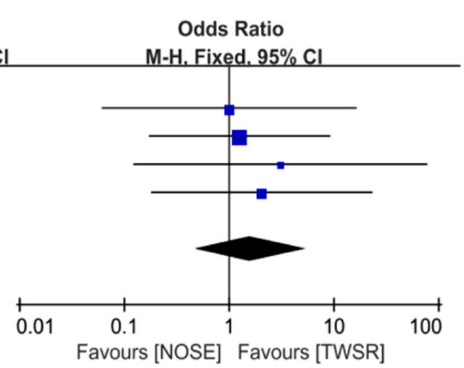

Fig. 7 Forest plot of the rates of postoperative intra-abdominal abscesses

the NOSE group (OR 0.25; 95% CI = 0.15 to 0.40; P < 0.001). No significant heterogeneity was observed ($P = 0.98$, $I^2 = 0\%$) (Fig. 9).

The diet recovery time

Four studies provided data about the soft diet recovery time after surgery. The first eating time was earlier in the NOSE group (WMD = − 0.56; 95% CI = − 1.00 to − 0.11; $P = 0.01$). As significant heterogeneity was observed, the random effects model was applied ($P = 0.003$, $I^2 = 78\%$) (Fig. 10).

Operation time

The operative time was not significantly longer in the NOSE group than in the TWSR group (WMD = 14.10 min; 95% CI = − 3.76 to 31.96; $P = 0.12$). Due to the high heterogeneity, the random effects model was adopted (P < 0.001, $I^2 = 93\%$) (Fig. 11).

Intraoperative blood loss

Five studies reported the intraoperative blood loss. The pooled data showed no significant difference in our meta-analysis (WMD = − 5.78 ml; 95% CI = − 17.57 to 6.00; $P = 0.34$), however, high heterogeneity was observed (P < 0.001, $I^2 = 90\%$); thus, a random effects model was used (Fig. 12).

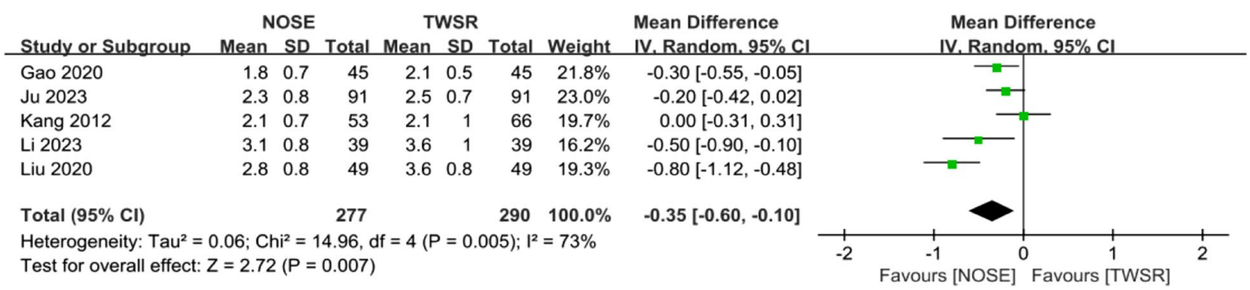

Fig. 8 Forest plot of the first postoperative passed flatus time

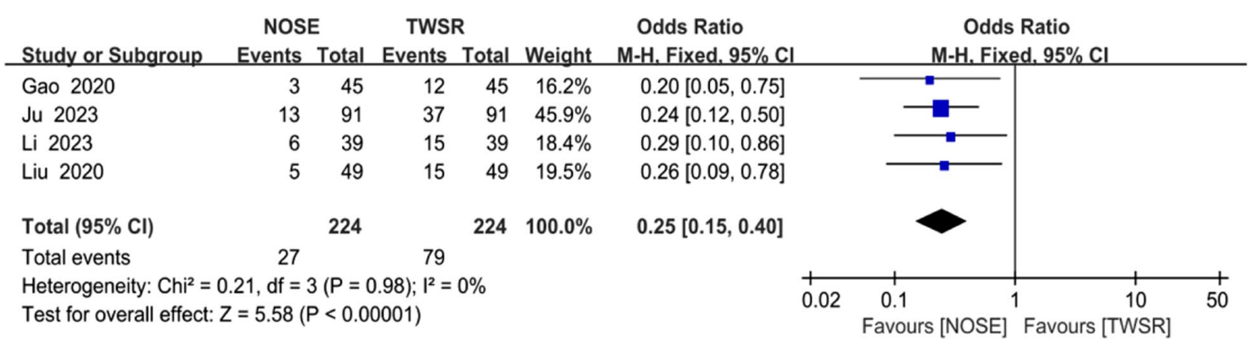

Fig. 9 Forest plot of the additional use of analgesics

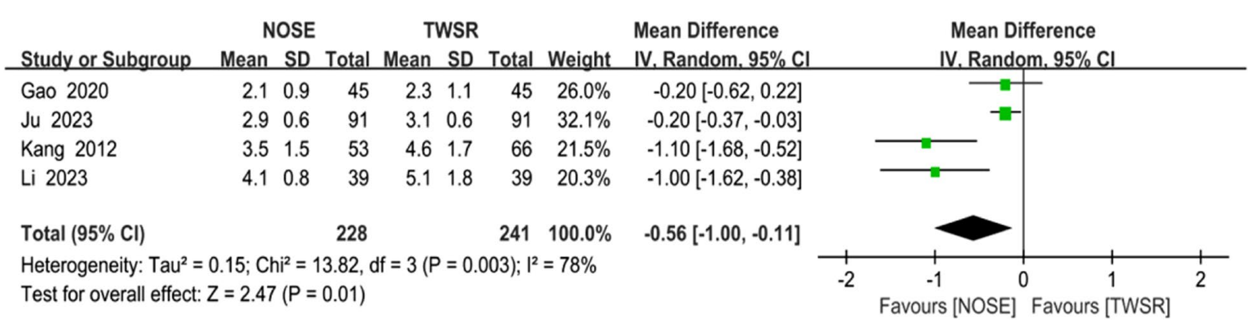

Fig. 10 Forest plot of the soft diet recovery time

The length of hospital stay

The length of hospital stay was recorded in all studies. Compared with that in the TWSR group, the length of hospital stay in the NOSE group was not significantly different (WMD = −0.47 days; 95% CI = −0.98 to 0.03; $P = 0.07$), and a random effects model was adopted owing to the high heterogeneity ($P = 0.07$, $I^2 = 51\%$) (Fig. 13).

Postoperative VAS score

Of the six studies, four evaluated the first day of postoperative pain using a visual analogue scale (VAS). The NOSE group had significantly lower VAS pain scores (WMD = −1.23; 95% CI = −1.63 to −0.83; P < 0.001). A random effects model was used due to the high heterogeneity ($P = 0.04$, $I^2 = 65\%$) (Fig. 14).

OS and DFS

Four studies reported the Kaplan–Meier survival curves of OS and DFS between the two groups. For the HR and 95% CI, one study had direct data, whereas this data was lacking in the other three studies. Using Engauge Digitizer and Tierney's method, we obtained the natural logarithm HR and SE. The pooled results revealed no significant difference between the NOSE and TWSR groups in terms of OS (HR = 1.07, 95% CI = 0.60 to 1.94; $P = 0.81$; heterogeneity test: $P = 0.94$, $I^2 = 0\%$) or DFS (HR = 0.94,

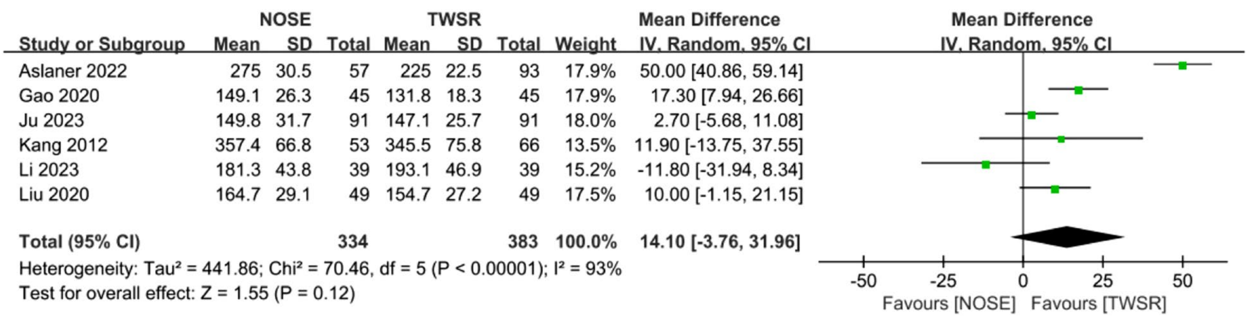

Fig. 11 Forest plot of the operation time

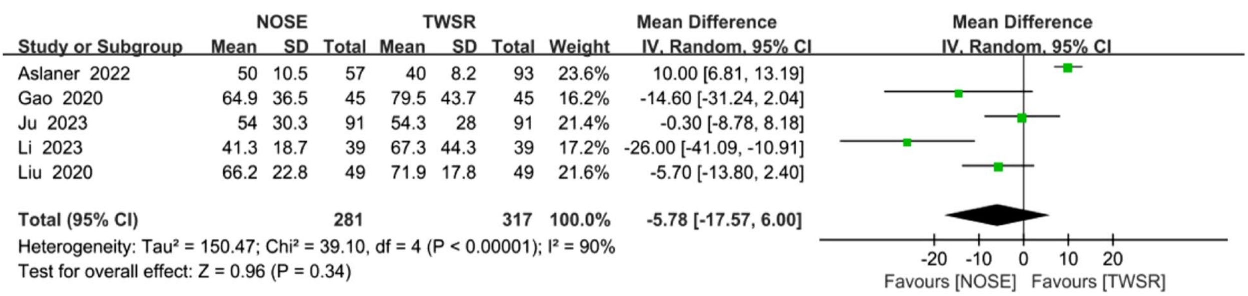

Fig. 12 Forest plot of the intraoperative blood loss

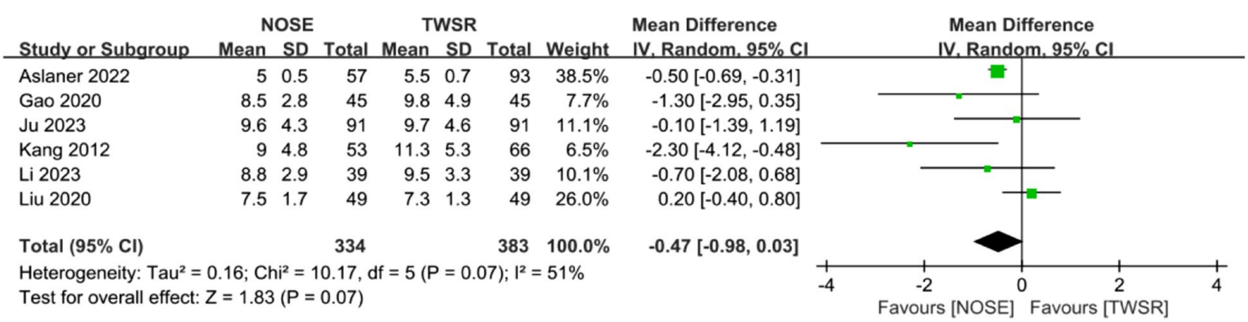

Fig. 13 Forest plot of the length of postoperative hospital stay

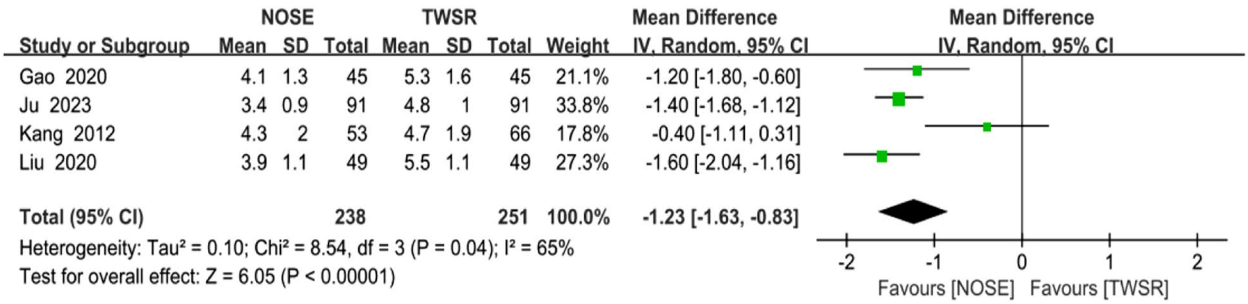

Fig. 14 Forest plot of the postoperative VAS score on Day 1

95% CI = 0.54 to 1.63; $P = 0.82$; heterogeneity test: $P = 0.81$, $I^2 = 0\%$). The fixed-effects model was adopted for two studies due to the low heterogeneity (Fig. 15).

Sensitivity and subgroup analyses

The purpose of the sensitivity analysis and subgroup analyses was to determine the stability of the results and the possible sources of heterogeneity, respectively. We conducted a sensitivity analysis to compare the passed flatus time, soft diet recovery time, operative time, amount of interoperative blood loss, length of hospital stay and Day 1 VAS score. All the results were stable according to the sensitivity analysis (Fig. 16).

Subgroup analyses were conducted based on patients' history of abdominal surgery. A history of abdominal surgery was associated with a shorter hospital stay in the NOSE group compared with the TWSR group (WMD = −0.94 days; 95% CI = −1.82 to −0.07; $P = 0.03$; $I^2 = 26\%$), but similar findings were not observed for patients with no history of abdominal surgery (WMD = −0.21 days; 95% CI = −0.89 to 0.47; $P = 0.54$; $I^2 = 79\%$). There were no differences in the operation time between patients with a history of abdominal surgery (WMD = 6.07 min; 95% CI = −5.75 to 17.88; $P = 0.31$; $I^2 = 67\%$) and patients with no history of abdominal surgery (WMD = 30.13 min; 95% CI = −9.07 to 69.33; $P = 0.13$; $I^2 = 97\%$). Similarly, there were no difference in the amount of intraoperative blood loss between patients with a history of abdominal surgery (WMD = −12.67 ml; 95% CI = −29.06 to 3.71; $P = 0.13$; $I^2 = 78\%$) and patients with no history of abdominal surgery (WMD = 2.61 ml; 95% CI = −12.75 to 17.97; $P = 0.74$; $I^2 = 92\%$). Patients in the NOSE group who had a history of abdominal surgery had an earlier passed flatus time than did those in the TWSR group (WMD = −0.23 days; 95% CI = −0.40 to −0.06; $P = 0.008$; $I^2 = 30\%$). Subgroup analysis of the postoperative VAS scores revealed that patients in the NOSE group who had a history of abdominal

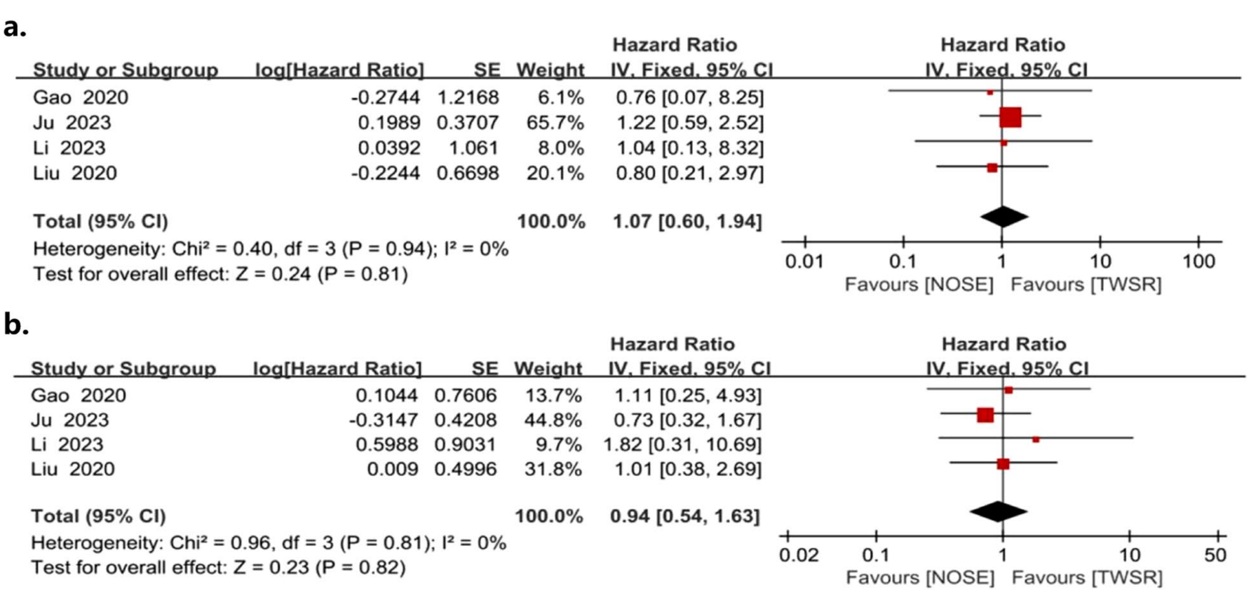

Fig. 15 Forest plot of 3-year overall survival (**a**) and 3-year disease-free survival (**b**)

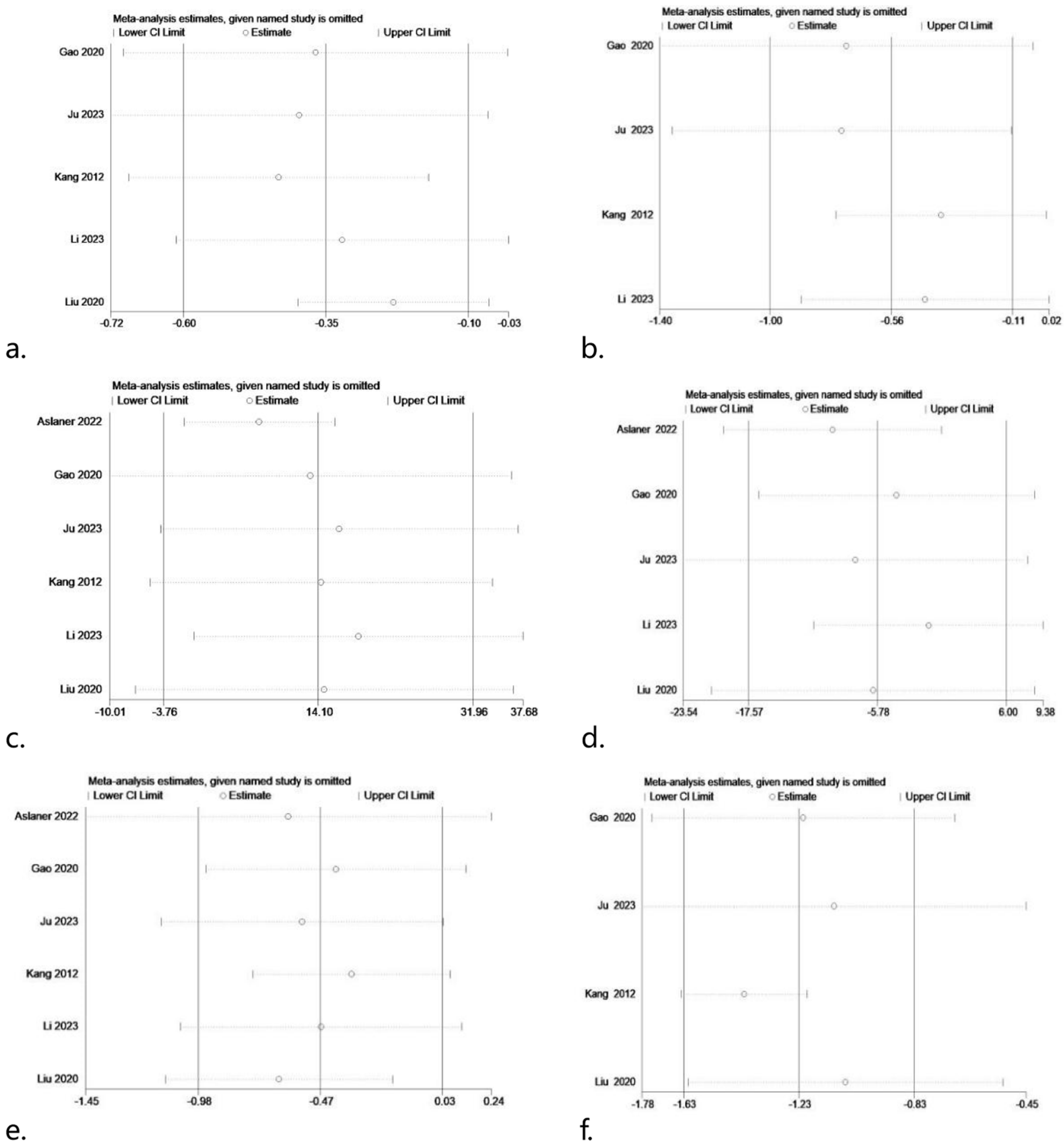

Fig. 16 Sensitivity analysis: **a.** Passed flatus time; **b.** soft diet recovery time; **c.** operative time; **d.** amount of interoperative blood loss; **e.** length of postoperative hospital stay; and **f.** postoperative VAS score on Day 1

surgery had less pain than did those in the TWSR group (WMD = −1.07; 95% CI = −1.62 to −0.53; P = 0.0001; I^2 = 70%) (*Electronic supplementary material, Table S3*).

Publication bias

In our study, a funnel plot of overall postoperative complications was generated to detect publication bias. All of the included studies were within the 95% CI, and the scatter points in the funnel plot were almost all symmetrically distributed according to the Begg's test (Pr > |z| = 0.707 > 0.05) and Egger's test (P > |t| = 0.517 > 0.05) results. Therefore, we concluded there was no publication bias (Fig. 17).

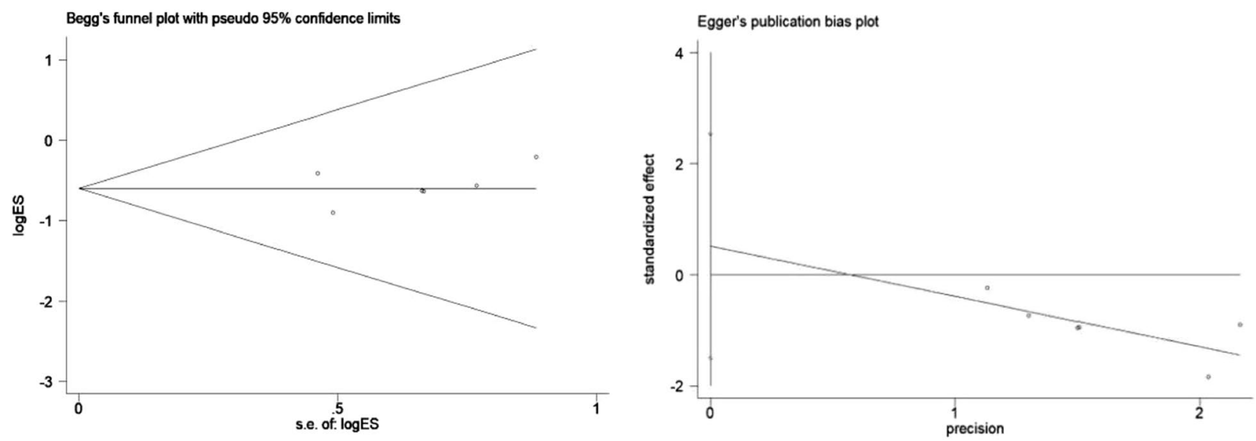

Fig. 17 Funnel plot based on overall postoperative complications

Discussion

NOSE is a more refined minimally invasive technique than conventional methods and can solve major clinical problems with small incisions [22]. NOSE is widely used in clinical practice to extract surgical specimens, mainly via the use of the transvaginal, transurethral, transoral, and transanal approaches [23]. Transanal and transvaginal extraction are the most common approaches used in gastrointestinal surgery [24, 25].

Postoperative complications not only determine patients' satisfaction with medical quality but are also crucial indicators of technological maturity [26]. Our systematic meta-analysis showed that the NOSE group had more advantages in terms of overall postoperative complications, the postoperative VAS score on Day 1, the additional use of analgesics and the incidence of incision infection than did the TWSR group. The decreased use of analgesics in the NOSE group was closely related to the elimination of the mini-laparotomy incision, which decreases the risk of abdominal wall, vessel and nerve injury and reduces postoperative somatic pain [27]. This superiority ensures patients remain in bed for a shorter period of time, which reduces abdominal wall infections and promotes the recovery of gastrointestinal function due to the use of less analgesics. This analysis also revealed consistent results in accelerating postoperative gastrointestinal motility, including a decreased postoperative diet recovery time and decreased first passed flatus time. Some studies have also shown that the incidence of postoperative complications, the time to patients first leaving the bed, the passed flatus time and the diet recovery time with NOSE laparoscopic surgery were significantly lower than those with conventional laparoscopic surgery [28, 29]. The above related benefits should be attributed to the clinical application of NOSE, which replaces the mini-laparotomy incision and significantly reduces associated postoperative complications. However, our research did not reveal significant differences in the length of postoperative hospital stay or the incidences of postoperative ileus or intra-abdominal abscesses between the NOSE group and TWSR group.

Anastomotic leakage is a possible life-threatening complication, and some studies [30, 31] have suggested that it might be more related to the level of anastomosis than to other complications, regardless of whether traditional open surgery or other minimally invasive surgeries are used. Chen et al. [32] also reported that a longer operation time is an independent risk factor for anastomotic leakage in a total of 636 patients who underwent robotic radical rectal cancer surgery. Our results indicate that postoperative anastomotic leakage and the mean operation time were not significantly different. Therefore, we believe that NOSE possesses sufficient safety for CRC patients. Conventional surgical techniques, including preoperative bowel preparation, prophylactic use of antibiotics, transanal lavage and rational surgical drain placement, also play important roles in reducing the occurrence of intestinal fistulas [33, 34]. Moreover, there is a short learning curve for NOSE for experienced surgeons [35]. Hence, the operative time is determined by the surgeons' medical skills instead of the surgical method. Ye et al. [36] revealed that robotic-assisted NOSE resulted in less intraoperative blood loss than laparoscopic-assisted NOSE. Hisada et al. [37] found no significant differences in bleeding volume between laparoscopic resection with NOSE and conventional laparoscopic surgery. In this context, there were no significant between-group differences regarding intraoperative blood loss. Therefore, with the help of robotic systems, which provide a three-dimensional perspective and stability, we assumed that robot surgery has more advantages in decreasing intraoperative blood loss compared to any natural specimen extraction method.

Tumor dissemination and metastasis significantly influence the survival prognosis following gastrointestinal surgery, necessitating their reduction as a priority for surgeons [38, 39]. The safe and effective removal of tumor specimens from the abdominal cavity is one of the important contents to reduce recurrence. A wound protector or specimen bag is usually used for specimen extraction to prevent intraperitoneal tumour dissemination regardless of whether a transabdominal incision or transnatural orifice is used [40]. In our study, the TWSR group usually made a small incision in the abdominal wall to remove the specimen. The NOSE group inserted a sterile plastic sheath into the abdominal cavity via a natural orifice that has been disinfected and rinsed with saline solution, or removed the specimen through the natural orifice using a plastic bag (*show in Electronic supplementary material, Table S2*), followed by a thorough rinse of the abdominal cavity. This process reduced the opportunity for the specimen to contact the abdominal cavity and reduced the risk of tumor dissemination and metastasis. Zhou et al. [25] revealed that NOSE does not increase the risk of natural orifice port-site recurrence, and the long-term survival outcomes of laparoscopic-assisted NOSE are the same as those of laparoscopic surgery with an abdominal incision. Xu et al. [22] also confirmed that the long-term oncological prognosis (5-year DFS and OS) of laparoscopic surgery combined with NOSE seems to be equivalent to that of conventional laparoscopic surgery. Our meta-analysis revealed no significant differences in 3-year OS or 3-year DFS between the two groups. Furthermore, our meta-analysis revealed that more lymph nodes were harvested in the NOSE group than in the TWSR group. Hence, we believe that robotic-assisted NOSE is a safe and mature technology for improving long-term outcomes after CRC surgery and is widely accepted.

The most commonly used prognostic factor for CRC patients is TNM stage [41]. Jo et al. reported that advanced TNM stage was related to worse OS and recurrence-free survival [42]. For some patients with advanced CRC, appropriate preoperative neoadjuvant therapy can reduce lesions and provide the opportunity for surgical resection. Continuing postoperative adjuvant therapy can prolong the survival time [43, 44]. In our investigation, five out of six studies involving 598 CRC patients reported TNM stages of T3 and T4. Except for two studies that did not report the use of chemoradiotherapy, some patients in the other four studies were treated with preoperative or postoperative chemoradiotherapy and achieved good results. These positive benefits are consistent with many other studies [45, 46]. Therefore, not all late-stage tumours are absolute contraindications for surgery, and additional adjuvant therapy may be necessary.

Postoperative quality of life (PQOL) is also a pivotal indicator of surgical efficacy [47]. As most current retrospective studies overlook the PQOL assessment, only one study reported this in our included studies, suggesting that the patients in the NOSE group had better body image, cosmetic outcomes, somatic function, role function, emotional function, social function, etc., than those in the non-NOSE group. Other studies [47, 48] have also revealed that patients in the laparoscopic-assisted NOSE group had satisfactory body image and cosmetic outcomes and a greater quality of life than those in the conventional laparoscopic-assisted surgery group according to the European Organization for Research and Treatment (EORTC) QLQ-C30 scale and the Pelvic Floor Distress Inventory-20 (PFDI-20). Therefore, we believe that NOSE plays a positive role in PQOL. Of course, obtaining more follow-up data is necessary.

Our meta-analysis still contains certain limitations. 1) Only retrospective non-randomized controlled trials with relatively small sample sizes were included in this meta-analysis and large sample size studies are needed to further validate our conclusions. 2) The quality of the studies included in the meta-analysis was determined and many of the included studies lacked relevant data; therefore, high-quality trials are required to strengthen our results. 3) In our meta-analysis, we needed to indirectly obtain HRs through survival curves. This may cause estimation bias. 4) Objective factors, including individual differences among the patients, differences in the measurement methods and surgical methods, and differences in the technical level or experience of the medical staff performing the surgeries, could have resulted in assessment bias and are difficult to avoid.

Conclusions

In summary, this systematic meta-analysis has shown the benefits of NOSE versus TWSR for radical CRC, including the incidence of postoperative overall complications, number of lymph nodes harvested, the postoperative VAS score, additional use of analgesics, the rate of wound infection and the restoration of gastrointestinal function (soft diet recovery time and passed flatus time). However, there were no significant differences in terms of blood loss, the mean operation time, the length of postoperative hospital stay, the incidences of postoperative ileus, anastomotic leakage, and intra-abdominal abscesses or long-term prognosis. The NOSE group was superior to the TWSR group in certain subgroup analyses. In summary, the safety and feasibility of NOSE for the treatment of colorectal tumours was demonstrated. Considering the low level of evidence in the comparisons, more multicentre, large sample, randomized controlled studies are needed to verify the results of our study.

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

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Authors' contributions
Shixiong Zhan and Zhenda Wan conceived the idea and designed the study; Zhicheng Zhu and Haitao Yu collected and extracted the study data. Shixiong Zhan performed the data analysis and interpretation; Shixiong Zhan and Tian Xu wrote the manuscript; and Zhenda Wan and Yu Xia critically reviewed and revised the manuscript.

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Availability of data and materials
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Declarations

Ethics approval and consent to participate
No ethical approval and patient consent are required because all analyses were based on previous published studies.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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