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META-ANALYSIS

# Prognostic factors associated with gastrointestinal dysfunction after gastrointestinal tumor surgery: A meta-analysis

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## Abstract

***BACKGROUND***

Explore the risk factors of gastrointestinal dysfunction after gastrointestinal tumor surgery and to provide evidence for the prevention and intervention of gastrointestinal dysfunction in patients with gastrointestinal tumor surgery.

***AIM***

To investigate the potential risk factors for gastrointestinal dysfunction following gastrointestinal tumor surgery and to present information supporting the prevention and management of gastrointestinal dysfunction in surgery patients.

***METHODS***

Systematically searched the relevant literature from PubMed, Web of Science, Cochrane Library, Embase, CNKI, China Biomedical Database, Wanfang Database, and Weipu Chinese Journal Database self-established until October 1, 2022. Review Manager 5.3 software was used for meta-analysis after two researchers independently screened literature, extracted data, and evaluated the risk of bias in the included studies.

***RESULTS***

A total of 23 pieces of literature were included, the quality of which was medium or above, and the total sample size was 43878. The results of meta-analysis showed that the patients were male (OR = 1.58, 95%CI: 1.25-2.01, $P = 0.002$) and ≥ 60 years old (OR = 2.60, 95%CI: 1.76-2.87, $P < 0.001$), physical index ≥ 25.3 kg/m$^2$ (OR = 1.6, 95%CI: 1.00-1. 12, $P = 0.040$), smoking history (OR = 1.89, 95%CI: 1.31-2.73, $P < 0.001$), chronic obstructive pulmonary disease (OR = 1.49, 95%CI: 1.22-

1.83, $P < 0.001$), enterostomy (OR = 1.47, 95%CI: 1.26-1.70, $P < 0.001$), history of abdominal surgery (OR = 2.90, 95%CI: 1.67-5.03, $P < 0.001$), surgical site (OR = 1.2, 95%CI: 1.40-2.62, $P < 0.001$), operation method (OR = 1.68, 95%CI: 1.08-2.62, $P = 0.020$), operation duration (OR = 2.65, 95%CI: 1.92-3.67, $P < 0.001$), abdominal adhesion grade (OR = 2.52, 95%CI: 1.90-3.56, $P < 0.001$), postoperative opioid history (OR = 5.35, 95%CI: 3.29-8.71, $P < 0.001$), tumor TNM staging (OR = 2.58, 95%CI: 1.84-3.62, $P < 0.001$), postoperative blood transfusion (OR = 2.92, 95%CI: 0.88-9.73, $P = 0.010$) is a risk factor for postoperative gastrointestinal dysfunction in patients with gastrointestinal tumors.

***CONCLUSION***

There are many factors affecting gastrointestinal dysfunction in gastrointestinal patients after surgery. Clinical staff should identify relevant risk factors early and implement targeted intervention measures on the basis of personalized assessment to improve the clinical prognosis of patients.

**Key Words:** Gastrointestinal tumor surgery; Postoperative gastrointestinal dysfunction; Intestinal paralysis; Risk factors; Meta-analysis



**Core Tip:** Our study conducted meta-analysis to investigate prognostic factors associated with gastrointestinal dysfunction after surgery for gastrointestinal tumors. Through systematic integration of existing literature, we will further study the survival rate, quality of life, complication rate, and other indicators of patients after surgery and analyze the relationship between them and factors such as patient age, tumor type, and surgical method. It is helpful to provide clinicians with more accurate postoperative management strategies to promote patients' recovery and quality of life. Our study will also provide an important reference basis to enhance the understanding and attention given to the postoperative recovery process.

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## INTRODUCTION

Gastrointestinal tract refers to the digestive tube from the stomach to the anus, including the stomach, small intestine, large intestine and other parts, which is the longest and most important part of the digestive tube[1-3]. Postoperative gastrointestinal dysfunction (POGD), also known as postoperative gastro-anthralgia, is an acute pathophysiological change of the gastrointestinal tract, mainly characterized by gastrointestinal mucosal damage, barrier dysfunction and gastrointestinal motility disorders, manifested by nausea, vomiting, abdominal distension, delayed exhaust or defecation, and may even cause intestinal infection and sepsis. Prolong the hospital stay of patients and increase the economic burden of patients. Studies[4-6] have shown that almost all medium and above surgery (especially abdominal surgery), anesthesia, fluid load, analgesic drugs, postoperative inflammatory response, *etc*., will have varying degrees of influence on postoperative gastrointestinal function. Among them, the incidence of POGD after abdominal surgery ranges from 4% to 32%, and the incidence of gastrointestinal surgery is even higher. Rapid and effective identification of risk factors for POGD is of great importance for formulating prevention and treatment interventions, reducing the incidence of POGD, and reducing the medical burden of patients[7].

Through meta-analysis, this study summarized the risk factors of POGD in patients undergoing gastrointestinal surgery, providing a theoretical basis for early assessment and identification of high-risk groups of POGD in patients undergoing gastrointestinal surgery.

## MATERIALS AND METHODS

### *Literature retrieval strategy*

Using the combination of subject words and free words, we searched PubMed, Web of Science, Cochrane Library, Embase, CNKI, China Biomedical Database, Wanfang Database, WiP Chinese Journal, and other databases for relevant studies on the influencing factors of gastrointestinal dysfunction after gastrointestinal surgery. The references included in the literature were also retroactively searched, and the search time range was from the establishment of the database to October 1, 2023.

The search strategies were (Colorectal Neoplasms OR Ileal Neoplasms OR Duodenal Neoplasms OR Stomach Neoplasms OR Jejunal Neoplasms) AND (colorectal neoplasms or ileal neoplasms or duodenal neoplasms or stomach neoplasms or jejunal neoplasms). Surgery OR Opera OR Perioperative Period OR Postoperative) AND (Postoperative

gastrointestinal dysfunction OR ileus OR postoperative ileus OR prolonged ileus OR intestinal paralysis) AND (Factors OR relatives).

### Document inclusion criteria

(1) Age of the study subjects was ≥ 18 years old; (2) Patients with gastrointestinal tumors undergoing elective surgery; (3) The content of the literature studies was the influencing factors or risk factors of postoperative POGD; (4) The study type was cohort study; and (5) Outcome indicators were the risk factors associated with POGD after gastrointestinal tumor surgery.

### Document exclusion criteria

(1) Repeated publication; (2) Unable to obtain the full text; only abstracts; incomplete data literature; (3) Literature with a score of < 7 on the Newcastle-Ottawa Scale (NOS); and (4) Literature on the diagnosis of POGD is not clear.

### Literature screening and data extraction

Two researchers independently searched and screened the literature strictly according to the inclusion and exclusion criteria, extracted data for cross-checking, and, in cases of disagreement, the third researcher arbitrated or discussed it in a group. The main contents of data extraction include the first author, publication years, research location, research type, manual location, sample size, POGD incidence, research factors, etc.

### Literature quality evaluation

NOS was used independently by two researchers to evaluate the quality of the included documents, and a third researcher was jointly assessed when disagreements arose. A total of 8 items were included in 3 aspects, including the selection of research objects, the comparability between groups, and the evaluation of exposure and outcome. The full score was 9, and ≥ 7 was classified as high-quality research, which was included.

### Statistical analysis

Meta-analysis was performed using Review Manager 5.3 software. According to the OR value and 95%CI of the original data in the literature, the combined effect size (ES), ES = LN (OR), and standard error of effect size (SE) = LN (upper limit of interval - lower limit of interval)/3.92. $I^2$ was used to test the heterogeneity of the included literature. If $I^2 \leq 50\%$ and $P \geq 0.1$, it indicated that there was no significant heterogeneity among the studies, and a fixed-effect model was selected for analysis. If $I^2$ is greater than 50% and $P < 0.01$, it indicates heterogeneity among studies. After analyzing the source of heterogeneity, a random effects model is selected for analysis. Sensitivity analysis was conducted by comparing the consistency of the results of the two models and eliminating the literature that had a great influence on the combined results. The funnel plot method was used to analyze the existence of publication bias.

## RESULTS

### Literature retrieval results and included research characteristics

A total of 922 literatures were obtained through the initial examination of the database; 130 literatures were supplemented by other means; 102 duplicated literatures were removed; 125 literatures that were obviously inconsistent with the theme were excluded by reading the abstract and title; 30 literatures were included in the preliminary screening; 7 literatures were excluded after reading the full text; and the full text was carefully read according to the inclusion and exclusion criteria. Finally, a total of 23 eligible pieces of literature were included[4,8-29]. The specific literature screening process is shown in Figure 1.

### Basic features of the included literature

A total of 23 cohort studies were included[4,8-29], with a total sample size of 43878 cases and 5300 cases of POGD, and the incidence of POGD ranged from 4.5% to 71.2 percent. The NOS scores of the included literature were all ≥ 7 points, and the quality of the literature met the requirements (Figure 2). The basic characteristics and quality evaluation results of the included literature are shown in Table 1.

### Meta-analysis results

A fixed-effect model was used to analyze 10 factors, including body mass index (BMI) (≥ 25.3 kg/m$^2$), age, smoking history, chronic obstructive pulmonary disease, enterostomy, history of abdominal surgery, surgical site, duration of surgery, abdominal adhesion grade, and TNM stage of tumors. Statistical heterogeneity was not found among the included literatures. A random effects model was used for analysis, and gender, operation mode, postoperative opioid history, postoperative blood transfusion, postoperative body temperature, and preoperative albumin low heterogeneity test were statistically significant ($P < 0.05$). The results showed that, in addition to postoperative body temperature and preoperative hypoalbumin, the other 14 factors were risk factors for postoperative POGD in patients with gastrointestinal tumors (Table 2 and Figure 3).

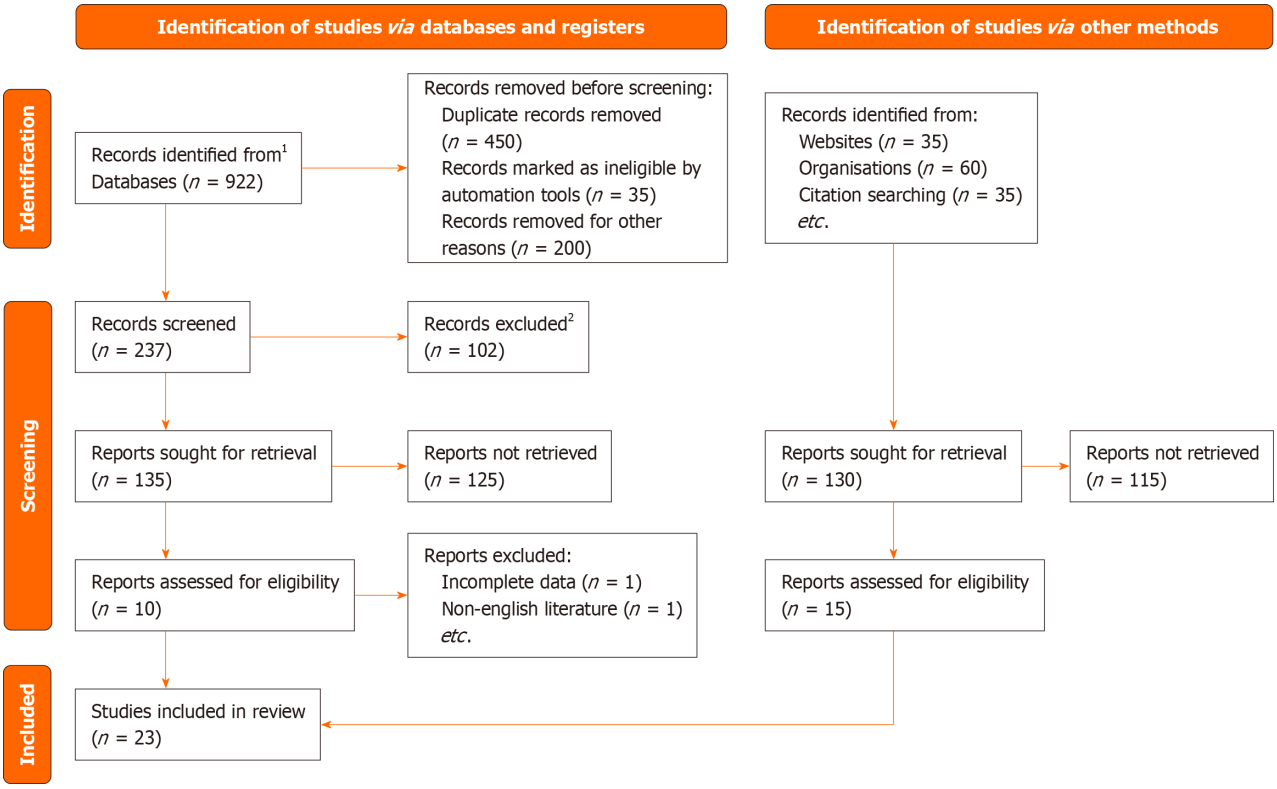


**Figure 1 Flow chart of the literature screening.** [1]Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). [2]If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

### *Sensitivity analysis*

For risk factors with large heterogeneity ($I^2 \geq 50\%$), the source of heterogeneity was further explored by excluding individual studies one by one. The results showed that after the exclusion of individual studies, the statistical heterogeneity among all literature was reduced, and the research results were relatively stable compared with before and after the exclusion, as shown in Table 3.

### *Publication bias assessment*

The funnel plot method was used to conduct bias analysis for the meta-analysis, with a large number of included studies. The results showed that the distribution of the funnel plot of age was asymmetrical, and there was publication bias. The gender, enterostomy funnel plot distribution is symmetrical; there is no bias in the distribution table. These results indicate that there is a certain publication bias in the literature included in this study, which may be related to the small number of studies included for each risk factor (Figure 4).

## DISCUSSION

The latest expert consensus on the prevention and treatment of POGD points out that once POGD occurs, it will prolong the hospital stay of patients and increase the financial burden of patients[30]. Understanding the risk factors of POGD is of great significance to preventing its occurrence. In this study, 23 studies on the risk factors of POGD after gastrointestinal tumor surgery were analyzed, and the results showed that the risk factors affecting POGD involved individual factors including gender, age, BMI, and smoking history. The associated factors of disease and treatment history included chronic obstructive pulmonary disease, a history of abdominal surgery, and the grade of abdominal adhesion. The factors related to surgery included the operation site, operation mode, operation duration, enterostomy, and TNM grade of the tumor[31]. Treatment-related factors included postoperative opioid use history and postoperative blood transfusion[32]. The correlation between risk factors and the risk of POGD was summarized.

Effects of pathophysiological factors on POGD in patients undergoing surgery for gastrointestinal tumors. The incidence of POGD is higher in men than in women, which is consistent with the conclusion of one study. The reason may be that the hypogastric nerve, pelvic nerve, and spermatic cord may be damaged in male patients during the operation[33]. At the same time, studies have shown that the pain threshold of male patients is higher than that of female patients, and pain leads to increased release of catecholamines, which act on the gastrointestinal tract and inhibit gastrointestinal peristalsis function. The incidence of POGD is higher in patients with a BMI > 25.3 kg/m$^2$, which is consistent with another study on the cause of POGD after colon surgery. Patients with a high BMI may have hyper-

**Table 1 Basic characteristics and quality evaluation results of the included literatures**

| Ref. | Country | Research type | Surgical site | Cases | Incidence of POGD (%) | NOS score |
|---|---|---|---|---|---|---|
| Xu *et al*[13] | China | Retrospective cohort study | Colorectal cancer | 187 | 16. 6 | 7 |
| Huang *et al*[14] | China | Prospective cohort study | Gastric cancer | 296 | 32. 4 | 7 |
| Wang *et al*[17] | China | Retrospective cohort study | Gastric cancer | 83 | 26. 5 | 8 |
| Pu *et al*[24] | China | Retrospective cohort study | Colorectal cancer | 404 | 18. 3 | 7 |
| Wu *et al*[25] | China | Retrospective cohort study | Gastric cancer | 312 | 41. 03 | 8 |
| Liu *et al*[26] | China | Retrospective cohort study | Colorectum | 260 | 31. 6 | 8 |
| Tian *et al*[29] | China | Retrospective cohort study | Small intestine | 247 | 40. 5 | 7 |
| Franko *et al*[8] | America | Retrospective cohort study | Colorectum | 820 | 4. 5 | 8 |
| Kronberg *et al*[9] | America | Retrospective cohort study | Colorectum | 413 | 10.2 | 7 |
| Millan *et al*[10] | Spain | Retrospective cohort study | Colorectal cancer | 773 | 15.96 | 7 |
| Chapuis *et al*[11] | Australia | Retrospective cohort study | Colorectum | 3393 | 14. 0 | 8 |
| Kim MG *et al*[12] | Korea | Retrospective cohort study | Gastric cancer | 389 | 1.8 | 7 |
| Moghadamyeghaneh *et al*[15] | America | Retrospective cohort study | Colon | 27560 | 12.7 | 7 |
| Wolthuis *et al*[16] | Belgium | Retrospective cohort study | Colorectum | 523 | 15. 9 | 7 |
| Courtot *et al*[18] | France | Retrospective cohort study | Right colon cancer | 637 | 17.7 | 8 |
| Kim *et al*[19] | Korea | Retrospective cohort study | Ileum | 220 | 8.1 | 8 |
| Weng *et al*[20] | Russia | Prospective cohort study | Colorectal cancer | 300 | 13. 0 | 8 |
| Sugawara *et al*[21] | Japan | Prospective cohort study | Gastrointestinal tract | 841 | 8.8 | 7 |
| Aktaş *et al*[22] | Turkey | Prospective cohort study | Ileum | 79 | 9. 0 | 7 |
| Sapci *et al*[23] | America | Retrospective cohort study | Colorectal cancer | 5369 | 16. 6 | 8 |
| Greenberg *et al*[27] | America | Retrospective cohort study | Ileum | 261 | 32.6 | 8 |
| Namba *et al*[28] | Japan | Retrospective cohort study | Colorectal cancer | 356 | 13. 5 | 7 |
| Watkins *et al*[4] | South Africa | Retrospective cohort study | Colorectal cancer | 155 | 36. 0 | 8 |

POGD: Postoperative gastrointestinal dysfunction; NOS: Newcastle-Ottawa Scale.

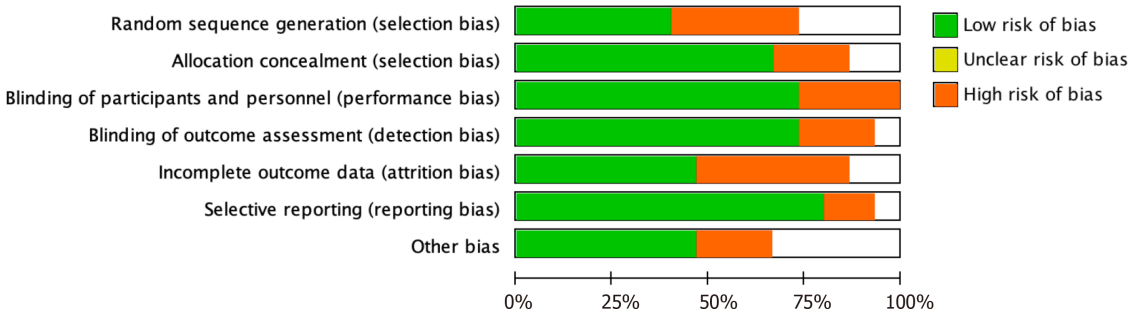


**Figure 2 Literature quality evaluation chart.**

glycemia, glucose metabolism disorder, intestinal epithelial cell dysfunction, and thus intestinal infection susceptibility and mucosal barrier dysfunction. At the same time, studies[34-36] have shown that the higher the BMI, the higher the incidence of POGD and the greater the impact on the postoperative recovery of patients. This study shows that age ≥ 60 years old is one of the risk factors for POGD, which is consistent with the results of the meta-analysis of the study. The reason may be that the older the patients, the autoimmune function will be relatively lower, and the recovery ability of the body will be reduced after surgery. The study's conclusion was that people who had smoked in the past were more likely to have POGD. This was in line with the findings of other relevant studies. This could be because smoking increased the release of reactive oxygen species, which damaged cell and tissue levels and harmed normal tissue perfusion. At the same time, increasing oxidative stress induces blood tube damage and further leads to the occurrence of

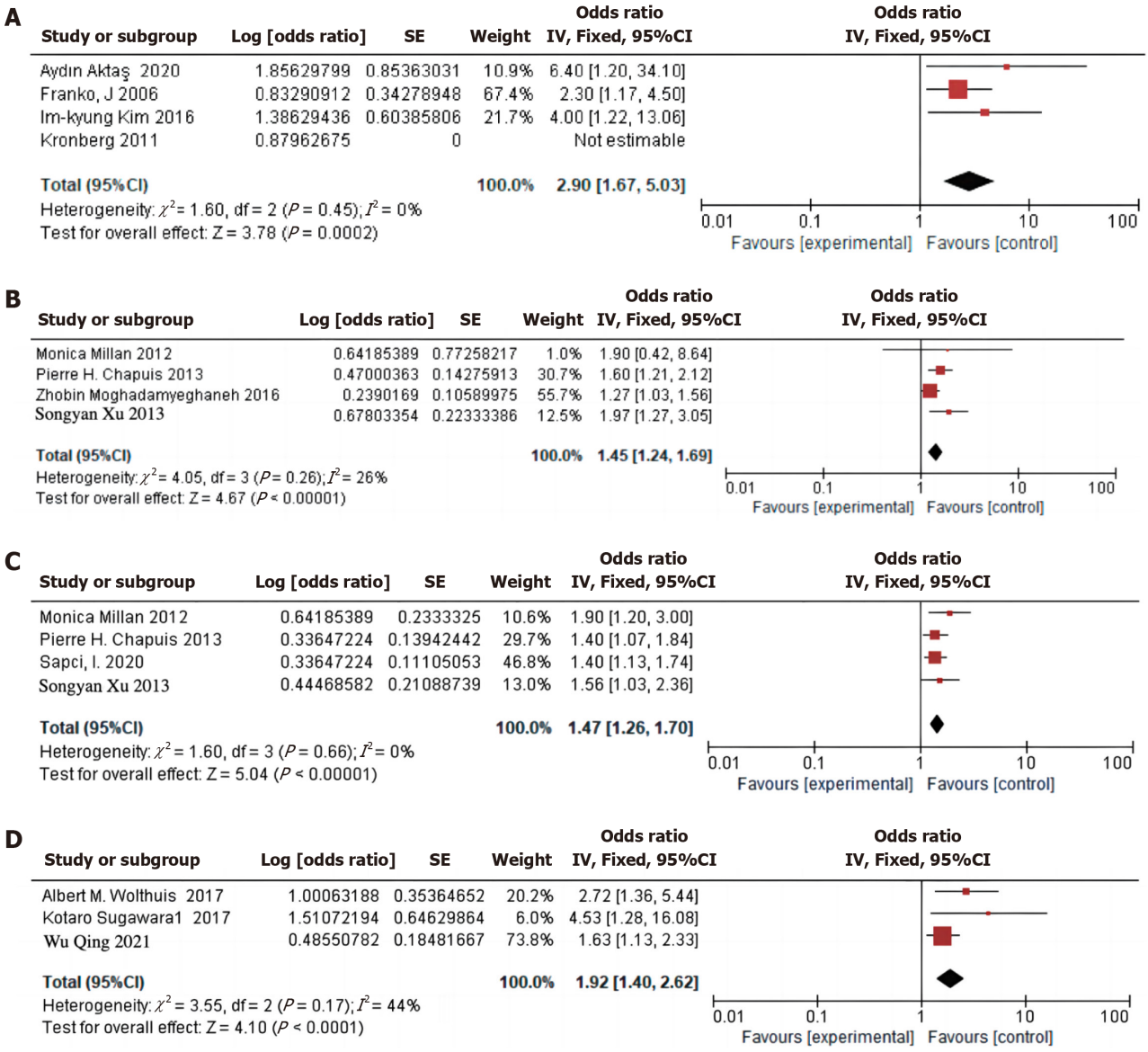


**Figure 3 Meta-analysis of the effects of gastrointestinal dysfunction after gastrointestinal tumor surgery.** A: Meta-analysis of the correlation between abdominal surgery history and postoperative postoperative gastrointestinal dysfunction (POGD) for gastrointestinal tumors; B: Meta-analysis of postoperative POGD in patients with chronic obstructive pulmonary disease and gastrointestinal tumors; C: Meta-analysis of the correlation between POGD after enterostomy and gastrointestinal tumors; D: Meta-analysis of the correlation between surgical site and postoperative POGD in gastrointestinal tumors.

POGD[37].

Effect of combined disease and treatment history on POGD in patients undergoing surgery for gastrointestinal tumors. The incidence of postoperative POGD is higher in patients with chronic obstructive pulmonary disease, which may be due to the fact that patients with this history need to take drugs for a long time, which may lead to gastrointestinal dysfunction[38]. Patients with a history of abdominal surgery have a higher incidence of POGD, which is consistent with the results of a study on the occurrence of postoperative POGD in patients with gastric cancer. In patients with a history of abdominal surgery, the normal intestinal anatomical structure is destroyed, and intestinal adhesions are present. Meanwhile, the more serious intestinal adhesions are, the longer the operation time needs to be removed and the intestinal cavity opening time will increase, and the incidence of POGD will increase[39].

Effect of surgery-related factors on POGD in patients undergoing surgery for gastrointestinal tumors. At present, surgical treatment is the primary treatment for gastrointestinal tumors, and the risk of POGD occurrence in patients undergoing open surgery is higher than that in patients undergoing laparoscopic surgery. The possible reason is that laparoscopic surgery is minimally invasive and less traumatic, which can reduce the exposure time of patients' intestinal cavities and the stimulation of viscera in the abdominal cavity during surgery[40]. The results of the study showed that the incidence of POGD was higher in patients with TNM stage ≥ III, which was consistent with the results of another study. The later the TNM stage of the tumor, the bigger the resection area, which meant it was more likely to damage abdominal tissue and cause infections and adhesions. People with stage III or higher had to have extensive lymph node dissection[41]. It not only prolongs the operation time but also easily damages lymphatic vessels, leading to obstruction of lymphatic reflux and increasing the risk of POGD[42]. At the same time, different tumor locations have different effects

**Table 2 Meta-analysis of factors affecting gastrointestinal dysfunction in patients after gastrointestinal surgery**

| Research factor | Inclusion study | Heterogeneity test | | Effect model | Meta-analysis results | |
|---|---|---|---|---|---|---|
| | | *P* value | $I^2$ (%) | | OR (95%CI) | *P* value |
| Body mass index (≥ 25.3 kg/m$^2$) | 4 studies[14,20,23,27] | 0.59 | 0 | Immobilization | 1.06 (1.00-1.12) | 0.040 |
| Age | 9 studies[9,14,15,20,22,23,25-27] | 0.17 | 40 | Immobilization | 2.25 (1.76-2.87) | < 0.001 |
| Smoking history | 4 studies[4,10,13,21] | 0.56 | 0 | Immobilization | 1.89 (1.31-2.73) | < 0.001 |
| Chronic obstructive pulmonary disease | 4 studies[10,11,13,15] | 0.26 | 26 | Immobilization | 1.45 (1.24-1.69) | < 0.001 |
| Enterostomy | 4 studies[10,11,13,23] | 0.66 | 0 | Immobilization | 1.47 (1.26-1.70) | < 0.001 |
| History of abdominal operation | 6 studies[8,9,14,19,20,22] | 0.45 | 0 | Immobilization | 2.90 (1.67-5.03) | < 0.001 |
| Surgical site | 7 studies[10,13,14,16,21-23] | 0.17 | 44 | Immobilization | 1.92 (1.40-2.62) | < 0.001 |
| Operation duration | 7 studies[11,14,15,25,27-29] | 0.21 | 36 | Immobilization | 2.65 (1.92-3.67) | < 0.001 |
| Grade of abdominal adhesion | 4 studies[20,22,27,29] | 0.33 | 0 | Immobilization | 2.52 (1.90-3.56) | < 0.001 |
| Tumor TNM staging | 2 studies[14,25] | 0.78 | 0 | Immobilization | 2.58 (1.84-3.62) | < 0.001 |
| Gender (male) | 15 studies[4,10-13,15-18,20,21,23,25,27,28] | < 0.001 | 81 | Random | 1.58 (1.25-2.01) | 0.002 |
| Mode of operation | 9 studies[14-16,21-26] | 0.35 | 87 | Random | 1.68 (1.08-2.62) | 0.020 |
| Postoperative opioid use history | 7 studies[9,14,17,20,25-27] | 0.13 | 51 | Random | 5.35 (3.29-8.71) | < 0.001 |
| Postoperative transfusion | 6 studies[11,18,20,22,28,29] | 0.09 | 64 | Random | 2.92 (0.88-9.73) | < 0.001 |
| Postoperative body temperature | 2 studies[17,25] | < 0.001 | 99 | Random | 5.72 (0.76-42.96) | 0.090 |
| Preoperative low albumin (< 30 g/L) | 6 studies[9,13-15,24,29] | < 0.001 | 96 | Random | 0.37 (0.08-1.72) | 0.210 |

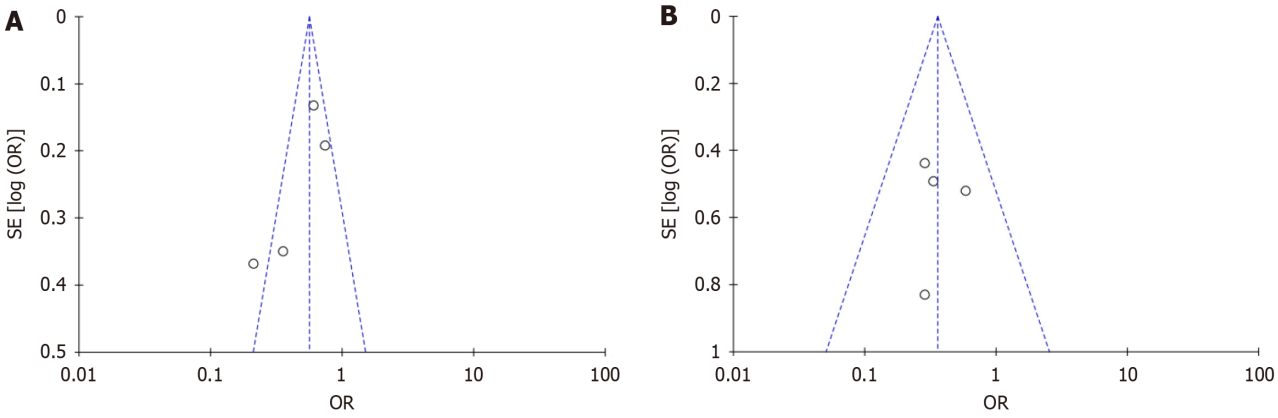


**Figure 4 Publication bias analysis.** A: Publication bias funnel plot of abdominal surgery history and postoperative postoperative gastrointestinal dysfunction (POGD) for gastrointestinal tumors; B: Publication bias funnel plot of postoperative POGD in patients with chronic obstructive pulmonary disease.

on the occurrence of postoperative POGD. The lower the tumor, the more likely it is that the middle rectal artery and lower rectal artery will be damaged when they are free from the mesocentery. This means that the intestine and anastomosis won't get enough blood after surgery, which slows down the recovery of gastrointestinal function[43].

This study showed that preoperative low albumin (< 30 g/L) and postoperative body temperature ≥ 38 °C were not correlated with the occurrence of postoperative POGD after gastrointestinal tumors, which was consistent with the results of a study on the risk factors of postoperative POGD after gastric cancer. Preoperative low albumin (< 30 g/L) was a risk factor in some studies, but it could not be identified as a risk factor for POGD in this study, perhaps because the association between the two became statistically insignificant when more studies were included. However, because of its association with advanced age, this risk factor suggested a decline in nutrition and bodily function. Postoperative body temperature ≥ 38 °C is mostly caused by the absorption of inflammatory factors, postoperative infection, and drug allergy; its normal condition will not exceed 38.5 °C, and it can subside after a period of time. Therefore, more high-quality related studies are needed to explore whether these two indicators are risk factors.

**Table 3 Exclusion of risk factors of postoperative postoperative gastrointestinal dysfunction for gastrointestinal tumors**

| Risk factor | Before exclusion | | | After exclusion | | |
|---|---|---|---|---|---|---|
| | Model | OR (95%CI) | *P* value | Model | OR (95%CI) | *P* value |
| Gender | Random | 1. 65 (1.36-2.00) | 0. 002 | Immobilization | 1.41 (1.29-1.54) | < 0. 001 |
| Mode of operation | Random | 1. 68 (1.08-2.62) | 0. 020 | Immobilization | 2.73 (1.96-3.81) | < 0. 001 |
| Opioid use history | Random | 4. 78 (2.30-9.92) | < 0. 001 | Immobilization | 1.47 (1.17-1.92) | 0. 010 |
| Hemorrhage | Random | 2. 92 (0.88-9.73) | < 0. 001 | Random | 2.92 (0.88-9.73) | 0. 080 |

## CONCLUSION

In summary, males, age ≥ 60 years old, BMI ≥ 25.3 kg/m$^2$, history of smoking, history of chronic obstructive pulmonary disease, TNM stage III or above, enterostomy, history of abdominal surgery, surgical site, surgical method, surgical duration, abdominal adhesion grade, and postoperative blood transfusion were risk factors for postoperative POGD for gastrointestinal tumors. However, due to the limited number and quality of the included studies, the above conclusions need to be verified by more high-quality studies.

## FOOTNOTES

**Author contributions:** Song J wrote the manuscript; Zhou C collected the data; Zhang T guided the study. All authors reviewed, edited, and approved the final manuscript and revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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