

Comprehensive Analysis of Baseline Risk Variables for Postoperative Ileus Development in Gastrointestinal Surgery Patients

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Abstract

Background: Postoperative ileus (POI) is a common and significant complication following gastrointestinal surgery, affecting up to 12.5% of patients. It leads to prolonged hospital stays, patient discomfort, and an increased risk of postoperative complications. Despite numerous studies, identifying consistent risk factors for POI remains challenging due to varying definitions and study methodologies. This systematic review and meta-analysis aim to identify baseline risk factors associated with POI following gastrointestinal surgery.

Methods: A systematic review was conducted following PRISMA, MOOSE, and Cochrane Handbook guidelines. Literature from MEDLINE, EMBASE, and the Cochrane Library was searched up to May 2024 for studies evaluating preoperative risk factors for POI in adult gastrointestinal surgery patients. Data extraction and bias assessment were carried out using standardized methods. A meta-analysis was performed for risk factors reported in two or more studies, using random-effects models to calculate pooled odds ratios (OR).

Results: From an initial 2,500 articles, 28 studies were included in the qualitative analysis. The studies collectively involved 57,767 patients, of whom 6,127 developed POI.

Conclusion: Male sex is a significant risk factor for postoperative ileus following gastrointestinal surgery, while prior abdominal surgery does not show a clear association. The findings highlight the need for standardized definitions of POI and further research to confirm the role of comorbid conditions in its development. Understanding these baseline risk factors is crucial for developing strategies to prevent and manage POI effectively.

Introduction

Postoperative ileus remains a significant and frustrating clinical issue for both patients and healthcare providers. This condition affects up to 12.5% of individuals who undergo gastrointestinal surgery (1), leading to patient discomfort, extended hospital stays, and a higher risk of postoperative complications (2). It is no surprise that a 2017 public consultation study highlighted the prevention of postoperative ileus as an unresolved and crucial concern (3).

The causes of postoperative ileus are believed to be multifactorial (4), with risk factors generally categorized into patient-related and procedural factors (5). Previous research aimed at identifying these risk factors or exploring strategies to reduce postoperative ileus has faced challenges, primarily due to inconsistent definitions of the condition and unclear criteria for distinguishing between transient and prolonged forms (1).

Several clinical trials have investigated interventions to reduce the incidence of postoperative ileus, exploring the use of steroids (6), opioid agonists (7), and intravenous lidocaine (8). However, these studies have been limited by the lack of standardized definitions and the absence of a universally accepted core outcome set (9). The creation of a validated gastrointestinal recovery score could significantly advance this research. To develop such a

tool, further investigation is needed into the preoperative and operative factors contributing to postoperative ileus, as well as the outcome variables, interventions, and the natural course of the condition.

The PROgnosis RESearch Strategy (PROGRESS), a UK Medical Research Council-funded initiative, seeks to promote multidisciplinary research aimed at improving care quality outcomes, including the management of postoperative ileus (10). Identifying risk factors and developing a gastrointestinal recovery score to better assess interventions for reducing postoperative ileus aligns with the goals of this initiative, focusing on "prognostic factor research" and "prognostic model research."

This review aims to identify preoperative factors that contribute to the development of postoperative ileus, as part of a broader collaborative effort led by the Association of Coloproctology of Great Britain and Ireland (ACPGBI) to create a gastrointestinal recovery score.

Methods

This review was conducted following the guidelines outlined in the Cochrane Handbook, the MOOSE guidelines for meta-analysis of observational studies in epidemiology, and the PRISMA guidelines for systematic reviews and meta-analyses (11–13). The review was registered on PROSPERO, an international database for prospective systematic reviews.

The primary objective was to compile a list of potential risk factors for the development of postoperative ileus following gastrointestinal surgery through a comprehensive review of the literature. The secondary objective was to conduct a meta-analysis of these risk factors to assess their significance and effect on the likelihood of developing postoperative ileus.

A systematic review was performed using MEDLINE (via OvidSP), EMBASE (via OvidSP), and Cochrane Library databases, following a predefined protocol, up until May 2017.

Inclusion and Exclusion Criteria

Studies were eligible for inclusion if they evaluated baseline (preoperative) factors and their association with the development of postoperative ileus after gastrointestinal surgery in adult patients. To ensure broad coverage of the literature, the definition of postoperative ileus was accepted as provided by the authors of individual studies, rather than being predetermined by the research team. No restriction was placed on the publication date, and only studies published in English were included. Both retrospective and prospective cohort or case-control studies, as well as randomized controlled trials, were eligible for inclusion. However, case series, case reports, commentaries, and editorials were excluded due to potential bias.

Data Extraction

Article titles and abstracts were imported into Covidence, an online tool for screening and data extraction (www.covidence.org), and screened independently by two authors (PVS and/or ML and/or DV). Disagreements were resolved through discussion. Full-text articles were reviewed by two authors for each study, and bibliographies of included studies were manually searched to identify additional relevant studies. Two authors independently extracted data from each included study using a standardized Microsoft Excel template. Information was collected on study design, sample size, surgical approach (laparoscopic or open), underlying conditions (e.g., cancer, inflammatory bowel disease), and the definition of postoperative ileus. Patient characteristics, both modifiable (e.g., smoking status) and non-modifiable (e.g., gender, age), along with physiological characteristics (e.g., white blood cell count) and disease-related characteristics (e.g., indication for surgery), were also documented.

Statistical Analysis

Studies reporting odds ratios and 95% confidence intervals were selected as many studies provided odds ratios derived from logistic regression but did not include raw data.

Results

The initial search yielded 2,500 unique articles. After screening, 200 full-text papers were reviewed, and following further evaluation, 28 studies were included in the qualitative analysis,

These studies included data from 57,76 patients, 6,127 of whom developed postoperative ileus. The studies comprised 6 prospective cohort studies and 21 retrospective cohort studies. The characteristics of these studies are summarized in Table 1.

All included studies provided a definition of postoperative ileus, which was generally a composite measure involving aspects such as diet tolerance, absence of abdominal distention, and the passage of stool or flatus.

Twelve studies examined the relationship between sex and postoperative ileus. Seven studies found no significant correlation between sex and the development of postoperative ileus (4,15–20), while five studies observed a positive association with male sex (5,21–24). Larger studies that employed multivariate regression methods were more likely to report a significant association. Nine studies explored the link between age and postoperative ileus. Three studies found no association with increasing age (15,16,25), while three others found an association when age thresholds of 65 or 70 years were applied (26,27,28). Three studies using multivariate analysis showed a significant relationship between older age and a higher risk of postoperative ileus (17,22,23). Eight studies assessed whether prior abdominal surgery was a risk factor. Five found no relationship (4,17,21,29,30), while three found a positive association (25,31,32). Again, larger studies using multivariate regression were more likely to identify a significant connection.

Respiratory disease and chronic obstructive pulmonary disease (COPD) were commonly identified as risk factors for postoperative ileus, with three studies supporting this finding (21,22,29) and one study showing no association (17). Cardiac disease and congestive heart failure were positively associated with postoperative ileus in two studies (22,29), but no relationship was found in a large retrospective cohort. Renal failure or dialysis did not appear to be risk factors for postoperative ileus (22,23,29). However, one study identified pre-existing constipation as a significant risk factor (odds ratio (OR) 3.67, 95% confidence interval (CI) 1.40–9.67) (22). Seven studies assessed obesity, with two reporting a positive association between obesity and postoperative ileus (33,34), but this was not consistent across other studies (16,27,29,33,35). Two studies found no relationship between weight and postoperative ileus (15,16). Smoking was linked to increased rates of postoperative ileus in a retrospective study (23).

Higher American Society of Anesthesiologists (ASA) status was associated with postoperative ileus in two large studies. Milan et al. reported an odds ratio of 1.6 for ASA II and 7.0 for ASA IV, though with large confidence intervals (29). Similarly, Moghadamyeghaneh et al. found an increased risk of postoperative ileus for patients with ASA scores above II (OR 1.2, 95% CI 1.07–1.36) (22). A raised white blood cell count (above $12 \times 10^9/\text{mm}^3$) was identified as a risk factor in one small retrospective study (36), but this finding was not corroborated in a larger retrospective study using multivariate analysis (22).

Table 1. Study characteristics.

Study	Study design	Surgical population	Operative approach	Patients (n)	Rate of POI (%)
Akiyoshi <i>et al</i> (2011) ³³	Prospective cohort	Colorectal resection	Laparoscopic	1,194	1.08
Artinyan <i>et al</i> (2008) ⁴	Retrospective cohort	Abdominal surgery	Open	88	100
Bakker <i>et al</i> (2015) ⁴⁵	Prospective cohort	Colorectal resection	Mixed	816	11.64
Barletta <i>et al</i> (2011) ¹⁵	Retrospective cohort	Colorectal resection	Mixed	279	8.60

Bickenbach <i>et al</i> (2013) ³⁵	Retrospective cohort	Gastric cancer resection	Not reported	1,853	8.60
Bisanz <i>et al</i> (2008) ¹⁶	Retrospective cohort	Abdominal surgery	Not reported	101	43.56
Chapuis <i>et al</i> (2013) ⁵	Retrospective cohort	Colorectal resection	Mixed	2,400	14.00
Englesbe <i>et al</i> (2010) ⁴⁶	Prospective cohort	Colorectal resection	Mixed	1,553	5.34
Franko <i>et al</i> (2006) ³¹	Retrospective cohort	Colorectal resection	Laparoscopic	820	4.52
Grosso <i>et al</i> (2012) ²⁶	Retrospective cohort	Colorectal resection	Mixed	446	5.38
Hamel <i>et al</i> (2000) ³⁰	Retrospective cohort	Colorectal resection	Laparoscopic	85	17.64
Huang <i>et al</i> (2015) ²⁷	Prospective cohort	Gastric cancer resection	Mixed	296	32.43
Ichikawa <i>et al</i> (2016) ⁴⁷	Retrospective cohort	Colorectal resection	Laparoscopic	172	2.91
Juarez-Parra <i>et al</i> (2015) ¹⁷	Retrospective cohort	Colorectal resection	Mixed	95	21.11
Kim <i>et al</i> (2013) ²⁸	Retrospective cohort	Gastric cancer resection	Laparoscopic	389	1.80
Kronberg <i>et al</i> (2011) ²⁵	Retrospective cohort	Colorectal resection	Laparoscopic	413	10.17
Le <i>et al</i> (2011) ²¹	Retrospective cohort	Ileal pouch–anal anastomosis	Open	91	21.98
Millan <i>et al</i> (2012) ²⁹	Retrospective cohort	Colorectal resection	Mixed	773	15.91
Moghadamyeghaneh <i>et al</i> (2016) ²²	Retrospective cohort	Colorectal resection	Mixed	27,560	12.69
Murphy <i>et al</i> (2016) ²³	Retrospective cohort	Colorectal resection	Mixed	9,734	14.01
Petros <i>et al</i> (1995) ¹⁸	Retrospective cohort	Colorectal resection	Open	358	16.20
Pikarsky <i>et al</i> (2002) ³⁴	Retrospective cohort	Colorectal resection	Laparoscopic	162	12.34
Tian <i>et al</i> (2017) ¹⁹	Retrospective cohort	Colorectal resection	Mixed	5,533	7.95
Valenti <i>et al</i> (2007) ⁴⁸	Retrospective cohort	Colorectal resection	Open	273	9.15
Vather <i>et al</i> (2013) ²⁰	Prospective cohort	Colorectal resection	Mixed	255	19.61
Vather <i>et al</i> (2015) ²⁴	Prospective cohort	Colorectal resection	Mixed	327	26.91
Yamamoto <i>et al</i> (2013) ³²	Retrospective cohort	Colorectal resection	Laparoscopic	1,701	2.70

POI, postoperative ileus.

Discussion

This is the inaugural systematic review examining the links between baseline demographic and physiological factors and the development of postoperative ileus in patients undergoing gastrointestinal surgery. The review highlights significant inconsistency in the way postoperative ileus is defined across clinical studies, which limits the ability to consolidate and interpret the findings from various reports. A total of 28 studies were included, with some evidence indicating a relationship between postoperative ileus and factors such as age, male sex, prior abdominal surgery, obesity, and pre-existing respiratory conditions. However, meta-analysis results were hindered by variability in how factors and outcomes were categorized, with a statistically significant relationship observed only for male sex.

Postoperative ileus is a major clinical issue, being one of the most prevalent complications following gastrointestinal surgery, affecting up to 12.5% of patients. Despite extensive research, its mechanisms remain not fully understood. It is traditionally classified into two phases: an immediate neurogenic phase triggered by excessive inhibitory reflexes from nerve activation during surgery, and a prolonged inflammatory phase driven by immune responses (37,38). Although several interventions have been explored to address the pathophysiology of postoperative ileus, the lack of a standardized definition and limited understanding of baseline risk factors complicate the evaluation of these treatments.

To effectively evaluate strategies for preventing postoperative ileus, it is essential to develop a consensus-based gastrointestinal recovery score and deepen our understanding of the risk factors at play. This study contributes to the objectives of the Medical Research Council-funded PROGRESS initiative by addressing both 'prognostic factor research' and 'prognostic model research' (10). Identifying patients at high risk for postoperative ileus remains crucial, as understanding the mechanistic processes underlying this condition may lead to the development of more targeted interventions.

Evidence from this review suggests an association between postoperative ileus and factors such as age, male sex, prior abdominal surgery, obesity, and respiratory disease, indicating that these variables should be systematically recorded and adjusted for in future research. Male sex emerged as the only factor with a significant association with postoperative ileus in the meta-analysis, supported by five studies. This relationship may be linked to increased surgical duration or bowel manipulation due to factors like greater visceral fat or a narrower pelvic structure in men. Increased age, reported in six studies, may be linked to delayed colonic transit and heightened sensitivity to anesthetics or opioid analgesia (39). Obesity, identified in two studies, could correlate with longer surgical procedures, a greater likelihood of open surgery, or higher anesthetic and opioid requirements. Furthermore, pre-existing respiratory disease was associated with higher rates of postoperative ileus in three studies, potentially due to increased opioid use in these patients to prevent respiratory complications.

Recent studies published after our search criteria support several of these findings. Hain et al. (40) found male sex and age as independent risk factors for postoperative ileus, with conversion to open surgery and intra-abdominal infections also contributing. Wolthius et al. (1) identified male sex and prior abdominal surgery as key risk factors for postoperative ileus, with a trend towards higher rates associated with age and body mass index. Rybakov et al. (41) found positive associations with body mass index and prior abdominal surgery, as well as a trend towards higher postoperative ileus rates in male patients. Additionally, Sugawara (42) found a significant link between male sex and postoperative ileus, with trends for higher rates in older patients, those with higher body mass index, and those with respiratory conditions. However, these studies may share similar biases to those in the current review, and thus their findings should be interpreted cautiously.

Further data from the Ileus Management International (IMAGINE) cohort (44) and the randomized trial 'A placebo-controlled trial of intravenous lidocaine in accelerating gastrointestinal recovery after colorectal surgery' (ALLEGRO) could provide additional

insights into patient risk stratification. However, a large prospective cohort study with standardized definitions of postoperative ileus and robust data on risk factors will likely be necessary to accurately answer this question. Despite advancements in other areas of surgical care, the ability to predict and prevent postoperative ileus has seen limited progress. As a complication following most gastrointestinal surgeries, it is crucial for researchers and funding bodies to focus on this condition.

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