

# Risk factors for postoperative complications in Crohn's disease: A systematic review and meta-analysis

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

**Background.** Crohn's disease (CD) is a non-specific inflammatory bowel disorder for which no definitive cure is available. The primary management strategy is pharmacological treatment aimed at alleviating symptoms. However, many patients ultimately require surgical intervention to manage complications arising from the disease.

**Objectives.** The aim of this study was to investigate disease-related factors that may increase the risk of early postoperative complications in patients with CD.

**Materials and methods.** A meta-analysis was conducted based on studies examining early surgical and medical complications following abdominal surgery for CD. The analyzed risk factors included disease duration prior to surgery, history of previous surgeries, presence of concurrent perianal disease, intra-abdominal abscess during surgery, and Montreal classification subtypes A1–3, L1–4, and B1–3. A systematic review was performed using 4 major databases: PubMed, Cochrane Library, Academic Search Ultimate (EBSCO), and Google Scholar. Outcomes were assessed using the odds ratio (OR) and response ratio (R), together with 95% confidence intervals (95% CIs). Egger's test was used to evaluate publication bias. Heterogeneity was assessed using the  $I^2$  statistic, with  $I^2 > 50\%$  indicating significant variability.

**Results.** A total of 51 articles met the inclusion criteria. The analysis identified several significant risk-increasing factors: history of previous surgeries (OR = 1.39; 95% CI: 1.23–1.57), Montreal classification group B3 (OR = 1.26; 95% CI: 1.11–1.42), disease duration before surgery (R = 1.10; 95% CI: 1.02–1.18), and group L2 (OR = 1.38; 95% CI: 1.11–1.72). Conversely, factors associated with a reduced risk of postoperative complications included group L1 (OR = 0.81; 95% CI: 0.71–0.92) and group B2 (OR = 0.81; 95% CI: 0.71–0.91).

**Conclusions.** This meta-analysis aggregated data from a broad spectrum of patients and treatment settings across multiple institutions worldwide. Although some risk of bias and heterogeneity was observed, the findings nevertheless highlight the importance of considering disease subtype and progression when assessing the likelihood of postoperative complications in patients with CD. This knowledge may be valuable for optimizing treatment strategies.

**Key words:** Crohn's disease, postoperative complications, risk factors, abdominal surgery, disease progression

## Highlights

- Meta-analysis of 51 studies identifies key risk factors for early postoperative complications in Crohn's disease patients undergoing abdominal surgery.
- Previous surgeries, longer disease duration, Montreal B3 behavior, and L2 location significantly increase the risk of postoperative complications in Crohn's disease.
- Montreal classification subtypes L1 and B2 are associated with a reduced risk of early surgical and medical complications after Crohn's disease surgery.
- Findings emphasize the importance of disease phenotype and progression in surgical risk stratification and treatment planning for Crohn's disease.

## Introduction

Crohn's disease (CD) is classified as a non-specific inflammatory bowel disease characterized by transmural inflammation of the gastrointestinal tract that may occur in any segment, from the mouth to the anus. As the exact etiology of the disease remains unknown, no definitive cure is currently available.<sup>1</sup> The primary approach to managing CD involves pharmacological treatment aimed at alleviating symptoms. Nevertheless, many patients ultimately require surgical intervention, including major intra-abdominal procedures such as adhesiolysis, resection of the small or large intestine, strictureplasty, or drainage of intra-abdominal abscesses, to manage complications arising from the disease.

Although CD can affect any segment of the gastrointestinal tract, it most commonly involves the ileocecal region. Inflammation may lead to intestinal strictures and adhesions in some cases, whereas in others it may result in fistulas or intra-abdominal abscesses. Many patients also develop perianal abscesses and fistulas, which present additional clinical challenges. This heterogeneity of disease presentation is reflected in the Montreal classification system, which evaluates the following parameters: age at disease onset, disease location, and disease behavior. The Montreal classification was first introduced at the World Congress of Gastroenterology in Montreal in 2005.<sup>2</sup>

Research suggests that the severity of CD may be influenced by its specific subtype.<sup>3–5</sup> Indicators such as perianal manifestations, early age at diagnosis, and the ileocolonic subtype may be associated with a more severe disease course.<sup>6,7</sup> Severe disease courses are often accompanied by chronic inflammation, significant malnutrition, and deficiencies in energy and protein, as well as the need for long-term steroid therapy, all of which are recognized risk factors for postoperative complications. Factors associated with a complicated disease course may therefore contribute to an increased risk of unfavorable postoperative outcomes.<sup>8</sup>

## Objectives

When considering treatment options, it is essential to evaluate the likelihood of complications. The aim of this study was to investigate disease-related factors that may influence the risk of early postoperative complications.

## Materials and methods

This paper forms part of the research conducted for the doctoral thesis of one of the authors, entitled "Multifaceted Assessment of Perioperative Risk Factors in Patients with Crohn's Disease (CD)." The findings presented in this study adhere to the guidelines established in the MOOSE (Meta-analysis of Observational Studies in Epidemiology) and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 statements.

## Information sources and search strategy

The first author (J.Ł.) conducted a systematic literature search using the PubMed, Cochrane Library, Academic Search Ultimate (EBSCO), and Google Scholar databases between November 21 and December 4, 2021. The search included the following terms: "Crohn's disease," "Crohn's disorder," "IBD," "regional enteritis," combined with "complications," "outcomes," "morbidity," "recurrence," "relapse," "remission," "treatment outcome," "treatment failure," and "reoperation," as well as "postoperative," "perioperative," "risk factors," "contributing factors," "predisposing factors," "surgery," and "resection". Different combinations of these terms were used with the logical operators "AND" and "OR". The search included articles published up to December 4, 2021. The authors did not contact researchers to obtain unpublished studies. On July 15, 2025, the databases were re-examined after a 3.5-year interval using the same search strategy to update the literature review. Articles published in all languages were considered. To broaden the search results, the "related articles" function in PubMed and the reference lists of the included studies were also screened.

## Eligibility criteria

The selection of articles for the meta-analysis was guided by the PICO framework. Participants: Patients aged >15 years, regardless of race or sex, undergoing abdominal surgery for CD. Intervention: Disease-related risk factors, including disease duration prior to surgery, history of previous surgical procedures, presence of concomitant perianal disease, intra-abdominal abscess during surgery, and disease subtypes A1–3, L1–4, and B1–3 according to the Montreal classification (Table 1). Comparator: Presence vs absence of specific risk factors. Outcome: All complications occurring within 30 days after surgery, as defined by the ACS-NSQIP.<sup>9</sup> (Table 2)

Complications were stratified into 5 severity grades (1–5) according to the Clavien–Dindo classification system (Table 3). Articles were included in the analysis if they met the following criteria: reported exact event

numbers, provided odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs), reported mean values for the analyzed risk factor in the complication group, and included identifiable corresponding data for the control group. The following study designs were eligible for inclusion: observational studies, randomized controlled trials (RCTs), non-randomized controlled trials, prospective cohort studies, retrospective cohort studies, case–control studies, and cross-sectional studies.

Studies were excluded if they contained insufficient data or represented duplicate publications involving the same group of patients. In addition, studies involving animals, pregnant patients, or individuals diagnosed with indeterminate colitis or ulcerative colitis were excluded. Studies were also excluded if they focused on procedures such as cholecystectomy, organ transplantation, or surgeries related to perianal disease. Furthermore, studies with a follow-up period shorter than 30 days, unclear follow-up duration, or lacking outcome data for a comparison group were excluded from the analysis.

Table 1. Montreal classification

Clinical factors	Classification
Age at diagnosis [years]	A1, ≤16
	A2, 17–39
	A3, ≤40
Location	L1, ileal
	L2, colonic
	L3, ileocolonic
	L4, isolated upper gastrointestinal tract disease
Behavior	B1, non-stricturing, non-penetrating
	B2, stricturing
	B3, penetrating
	p, perianal disease

## Data collection process

The primary author used Mendeley Desktop v. 1.19.8 (Mendeley Ltd., London, UK) and Microsoft Excel 2010 (v. 14.0.7268.5000; Microsoft Corp., Redmond, USA) to review the selected studies. The extracted data included the study title, authors, year of publication, study design, country of origin, type and date of surgical procedures performed, as well as postoperative complications and their associated risk factors. Any discrepancies were resolved through discussion with the 5<sup>th</sup> author (M.M.), who served as the principal investigator. Articles written in languages other than English were translated using Google Translate (Google LLC, Mountain View, USA).

Table 2. Types of complications considered in the study (according to American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) definitions)

Surgical	Medical/clinical
Surgical site infection, wound dehiscence, anastomotic leak, enterocutaneous fistula, intra-abdominal abscess, generalized sepsis, septic shock, postoperative bowel obstruction, unplanned reoperation, peristomy complications, hemorrhage, hematoma, need for blood transfusion.	Dehydration, fever of unknown origin, urinary tract infection, <i>Clostridioides difficile</i> infection, respiratory complications (unplanned intubation, pneumonia, pulmonary edema, pleural effusion, failure to extubate), urinary complications (acute renal failure, progression of chronic kidney disease), cardiovascular complications (pulmonary embolism, acute coronary syndrome, myocardial infarction, cardiac arrhythmias), neurological complications (stroke, psychotic disorders), venous thrombosis, adrenal insufficiency, liver insufficiency, and death.

Table 3. Clavien–Dindo classification

Grade	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological, surgical, endoscopic, or radiological intervention
II	Deviation from the normal postoperative course requiring pharmacological treatment
IIIa	Complication requiring surgical, endoscopic, or radiological intervention not under general anesthesia
IIIb	Complication requiring surgical, endoscopic, or radiological intervention under general anesthesia
IVa	Life-threatening complication requiring intensive care unit (ICU) management with single-organ failure
IVb	Life-threatening complication requiring ICU management with multiple organ failure
V	Death of the patient

## Quality assessment

The quality of the included studies was assessed by the first author (J.L.) using the Newcastle–Ottawa Scale (NOS). Studies with a score of  $\geq 5$  points were considered to be of high quality.

## Statistical analyses

Statistical analyses for the meta-analysis were performed using Statistica v. 13.1 (StatSoft Inc., Tulsa, USA). Given the anticipated heterogeneity among studies, a random-effects model was applied. All statistical tests were two-tailed, and  $p < 0.05$  was considered statistically significant. The results were presented in forest plots illustrating 2 effect measures. Odds ratios were calculated for dichotomous outcomes and presented with 95% CIs. Continuous variables, expressed as means with standard deviations (SDs), were analyzed using the response ratio (R), defined as the ratio of the mean value in the treatment group to that in the control group, together with 95% CIs. A chronological cumulative analysis was performed to evaluate how the cumulative effect estimate and its standard error (SE) changed over time with each successive publication. Statistical heterogeneity among studies was assessed using the  $I^2$  statistic, with values  $>50\%$  indicating substantial heterogeneity. Publication bias was assessed using Egger's test, with  $p < 0.1$  considered indicative of significant asymmetry, and the results were visualized using funnel plots. Sensitivity analyses were conducted to evaluate the influence of individual studies on the pooled effect estimates by sequentially excluding each study from the analysis.

## Evaluation of the strength of evidence

The strength of evidence was determined based on 3 criteria, as previously described.<sup>10</sup> These criteria included Egger's test  $p \geq 0.1$ , a total study population exceeding 1,000 patients, and  $I^2 < 50\%$ . Level I strength of evidence (high quality) was assigned when all 3 criteria were satisfied; level II (moderate quality) when 2 criteria were met; level III (moderate quality) when 1 criterion was met; and level IV (low quality) when none of the criteria were fulfilled.

## Results

A comprehensive literature search identified a total of 5,157 publications. Of these, 51 articles met the inclusion criteria and were included in the meta-analysis. A detailed overview of the number of records identified, screened, excluded, and included in the analysis is presented in Fig. 1. Detailed characteristics of the included studies, together with their quality assessments using the NOS, are presented in Table 4.<sup>11–61</sup> No randomized controlled trials were

identified; therefore, the meta-analysis was based on cohort studies comprising data from 21,283 patients. The mean age of participants across studies ranged from 29 to 46 years.

Considerable heterogeneity was observed among the included studies. Notably, studies conducted by Celentano et al.,<sup>14</sup> the Italian Society of Colorectal Surgery (SICCR),<sup>15</sup> and Yu et al.<sup>25</sup> focused on cohorts of patients aged  $\geq 16$  years. In contrast, Wang et al.,<sup>11</sup> Tiberi et al.,<sup>16</sup> and O'Brien et al.<sup>17</sup> exclusively analyzed severe postoperative complications classified as  $>3a$  according to the Clavien–Dindo classification. Mege and Michelassi<sup>31</sup> assessed postoperative complications based on rates of acute hospital readmissions. In another study, Mege et al.<sup>42</sup> included only patients undergoing ileocecal resection with anastomosis and a temporary protective stoma.

Among the patient-related risk factors associated with early postoperative complications and identified with level I strength of evidence were previous surgical interventions (OR = 1.39; 95% CI: 1.23–1.57;  $p < 0.001$ ), Montreal classification group B3 (OR = 1.26; 95% CI: 1.11–1.42;  $p < 0.001$ ), and disease duration prior to surgery (R = 1.10; 95% CI: 1.02–1.18;  $p = 0.01$ ). A factor identified with level II strength of evidence that showed statistical significance was Montreal classification group L2 (OR = 1.38; 95% CI: 1.11–1.72;  $p = 0.004$ ). Conversely, factors associated with a decreased risk of postoperative complications and identified with level I strength of evidence included Montreal classification group L1 (OR = 0.81; 95% CI: 0.71–0.92;  $p = 0.001$ ) and group B2 (OR = 0.81; 95% CI: 0.71–0.91;  $p = 0.001$ ). For other risk factors, including intraoperative intra-abdominal abscess, concomitant perianal disease, and Montreal classification groups A1–A3, L3, L4, and B1, no statistically significant associations were observed. Further details of the analyses are presented in Table 5, Fig. 2–7, and Supplementary Fig. 1–8.

Following the initial analysis, an additional analysis of risk factors associated with severe postoperative complications (defined as Clavien–Dindo grade  $\geq IIIa$ ) was performed. However, the available data were sufficient to analyze only prior surgical interventions, which did not show a statistically significant association (OR = 1.55; 95% CI: 0.82–2.96;  $p = 0.181$ ).

## Discussion

Crohn's disease is an inflammatory disorder of the gastrointestinal tract that may involve any segment of the digestive system and is often accompanied by extraintestinal manifestations. The etiology of CD is complex and not fully understood, with multiple factors contributing to its development. These include genetic predisposition, such as variants in the *NOD2/CARD15* genes,<sup>62</sup> autoimmune responses to intestinal bacterial antigens,<sup>63</sup> environmental factors including smoking, dietary habits, and stress,<sup>64–66</sup> as well as dysbiosis of the intestinal microbiota.<sup>67</sup> A key characteristic of CD is its chronic course, which may lead

**Table 4.** The articles included in the meta-analysis

Study	Study period	Country/region	Study design	Number of patients	Mean/median* age	Number of complications	Surgery types	NOS score <sup>a</sup>
Wang et al., 2024 <sup>11</sup>	2017–2022	China	retrospective analysis	181	39.04	10	ICR; right hemicolectomy; left-sided colectomy; subtotal colectomy; segmental resection of small bowel	5
Lahes et al., 2022 <sup>12</sup>	2001–2018	Germany	retrospective analysis	426	41*	158	small bowel or colorectal resection; ileostomy or colostomy; closure of ileostomy or colostomy; strictureplasty	6
Carmichael et al., 2021 <sup>13</sup>	2013–2019	USA	retrospective review of a prospectively maintained database	474	33*	73	ICR	7
Celentano et al., 2021 <sup>14</sup>	2018–2019	Italy	retrospective, multicenter, observational study	427	42	87	ileoacaecal resection	6
SICCR, 2020 <sup>15</sup>	2018–2019	Italy	retrospective, multicenter, snapshot study	122	no information	48	subtotal colectomy: 55; segmental colectomy: 30; proctectomy: 25	7
Tiberi et al., 2020 <sup>16</sup>	2008–2019	Italy	observational retrospective study	133	41.2	6	ICR	5
O'Brien et al., 2020 <sup>17</sup>	2014–2018	USA	single-institution retrospective observational study	118	40*	19	ICR	5
Kline et al., 2020 <sup>18</sup>	2008–2018	USA	retrospective clinical and genetic cohort study	269	no information	86	ileocelectomy	7
Gklavas et al., 2020 <sup>19</sup>	2010–2018	Greece	single-center retrospective study	153	36*	35	ICR	7
Dong et al., 2020 <sup>20</sup>	2016–2019	China	retrospective review	202	36.5	66	intestinal resection	7
Duan et al., 2020 <sup>21</sup>	2016–2019	China	retrospective review	129	no information	55	small-bowel resection: 45; ICR: 44; segmental colectomy: 21; other (ostomy closure, strictureplasty, and stoma creation without resection): 19	6
Sakurai Kimura et al., 2020 <sup>22</sup>	2012–2018	Brazil	retrospective review	103	40.6	33	abdominal surgeries for CD	5
Yoon et al., 2020 <sup>23</sup>	2005–2015	USA, South Korea	retrospective review	409	35	166	laparoscopic ICR	7
Abdalla et al., 2019 <sup>24</sup>	2013–2015	France	prospective multicenter study	567	no information	165	ICR	6
Yu et al., 2019 <sup>25</sup>	2006–2015	South Korea	retrospective study	817	no information	204	small bowel surgery: 252; ileocecal resection with or without small bowel surgery: 247; right hemicolectomy with or without small bowel resection: 178; total colectomy with or without small bowel surgery: 66; total proctocolectomy with or without small bowel surgery: 35; left hemicolectomy/anterior resection or low anterior resection with or without small bowel surgery: 18; abdominoperineal resection or Hartmann's procedure: 21	7

**Table 4.** The articles included in the meta-analysis – cont.

Study	Study period	Country/region	Study design	Number of patients	Mean/median* age	Number of complications	Surgery types	NOS score <sup>a</sup>
Gutierrez et al., 2019 <sup>26</sup>	2007–2010	Spain	retrospective review	364	38	100	ICR with ileocolic anastomosis	6
Bouquot et al., 2019 <sup>27</sup>	1998–2016	France	retrospective review	524	no information	186	ICR	6
Müller et al., 2018 <sup>28</sup>	2000–2014	Austria	retrospective cohort study	182	31.57	41	laparoscopic intestinal resection: an ileocolic resection: 123 colonic resections: 46; segmental small bowel resection: 10; rectal resection: 3	7
Aaltonen et al., 2018 <sup>29</sup>	2011–2015	Finland	retrospective study	70	41.5*	14	ICR 51; ICR and small bowel resection: 3; small bowel resection: 6; sigmoidectomy with colorectal anastomosis: 3; subtotal colectomy with ileosigmoidal anastomosis: 1; colectomy with ileorectal anastomosis: 6	6
Jouvin et al., 2018 <sup>30</sup>	2002–2013	France, Ireland	retrospective review	360	33	87	all ICR with additional: small bowel resection: 31; small bowel suture: 8; strictureplasty: 6; colonic resection: 18; colonic suture: 36; bladder suture: 7; other: 36	6
Mege and Michelassi, 2018 <sup>31</sup>	2004–2016	USA	retrospective review of prospectively maintained database	712	no information	70	strictureplasty: 137, stoma-related procedure: 62; small-bowel resection: 616; ileocecal resection: 388; segmental colectomy: 66; proctectomy: 64; extensive resection: 93; other: 72	5
Atasoy et al., 2018 <sup>32</sup>	2001–2016	Turkey	retrospective review	147	36	26	ileocecal resection: 105; small bowel resection: 13; colectomy: 29	6
Zhao et al., 2018 <sup>33</sup>	2013–2016	China	single-center, retrospective study	186	no information	87	total colectomy: 22; segmental colectomy: 45; ileocecal resection: 47; small bowel resection: 72	6
de Buck van Overstraeten et al., 2017 <sup>34</sup>	1998–2013	Belgium, the Netherlands	cohort analysis	538	31*	121	ileocecal resection	7
Kotze et al., 2016 <sup>35</sup>	2007–2014	Brazil	retrospective and observational study	123	no information	45	small bowel resection: 39; ileocecal resection: 59; total colectomy: 7	7
Li et al., 2016 <sup>36</sup>	1998–2014	USA	retrospective review of prospectively maintained database	1,331	41.2	628	small-bowel resection: 186; ICR: 687; segmental colectomy: 51; total/subtotal colectomy: 192; total proctocolectomy: 134; stoma creation without resection: 52; other (redo ileocolic anastomosis, strictureplasty, ileostomy revision): 159	7
Zhou et al., 2016 <sup>37</sup>	2012–2014	China	retrospective review	73	36.14	25	intestinal resection and anastomoses, with or without a covering stoma	7
Yamamoto et al., 2016 <sup>38</sup>	2008–2013	Japan, Italy, Brazil	international multicenter retrospective review	231	33	55	all ICR with primary anastomosis	7

Table 4. The articles included in the meta-analysis – cont.

Study	Study period	Country/region	Study design	Number of patients	Mean/median* age	Number of complications	Surgery types	NOS score <sup>a</sup>
Kristo et al., 2016 <sup>39</sup>	1997–2012	Austria	retrospective review	234	no information	39	type of resection – ileocolic: 192; small bowel: 28; colonic: 45; rectal: 1	6
Ding et al., 2015 <sup>40</sup>	2011–2013	USA	retrospective review	164	no information	64	stoma-related: 69; small-bowel resection: 20; ICR: 113; partial colectomy: 9; subtotal colectomy: 15; total colectomy: 11; anterior resection: 2	6
Kulaylat et al., 2015 <sup>41</sup>	2005–2012	USA	multicenter retrospective review	7,631	41.8	2,099	enterectomy: 1,091; ileocectomy: 3,190; partial colectomy: 1,915; total abdominal proctocolectomy: 1076; proctectomy: 359	7
Mege et al., 2015 <sup>42</sup>	2000–2012	France	retrospective review	80	33.5*	15	fecal diversions: 80; covering loop ileostomies: 17; lateral stapling of the sigmoid colon for enterocolonic fistula: 9; left hemi-colectomy for an extended inflammatory mass: 3; complementary small bowel resection: 1; urinary diversion with double J catheter to identify the ureter in an inflammatory mass: 1; liver biopsy for cirrhosis suspicion: 1; no stricturoplasties were performed	5
Scarpa et al., 2015 <sup>43</sup>	2000–2013	Italy	retrospective observational review	146	no information	21	total colectomy: 12; ileal resection: 20; colonic resection: 26; ICR: 87; ileal stricturoplasty: 15	7
Connelly et al., 2014 <sup>44</sup>	2007–2012	USA	retrospective review	143	no information	41	ileocectomy	5
Myrelid et al., 2014 <sup>45</sup>	no information	Sweden, UK, Spain, Norway, Denmark	retrospective review	298	no information	92	small bowel resection: 36; ICR: 185; colonic resection: 43; stoma closure: 29; strictureplasty alone: 5; including strictureplasty: 20; including severe adhesiolysis: 54	6
Bobanga et al., 2014 <sup>46</sup>	2004–2013	USA	retrospective review	142	39	51	ileocectomy or right hemicolectomy	5
Bellolio et al., 2013 <sup>47</sup>	1990–2010	Canada	retrospective review	434	no information	53	ICR	6
Bafford et al., 2013 <sup>48</sup>	1999–2010	USA	retrospective review of prospectively maintained database	196	40.9	45	ICR: 127; small bowel resection: 26; segmental colectomy: 13; low anterior resection: 18; protective stomas: 12	6
Huang et al., 2012 <sup>49</sup>	2005–2010	USA	retrospective descriptive study	130	no information	26	small bowel resection: 17, ICR: 78, partial colectomie: 20, total abdominal colectomie: 22, other bowel cases: 23	6

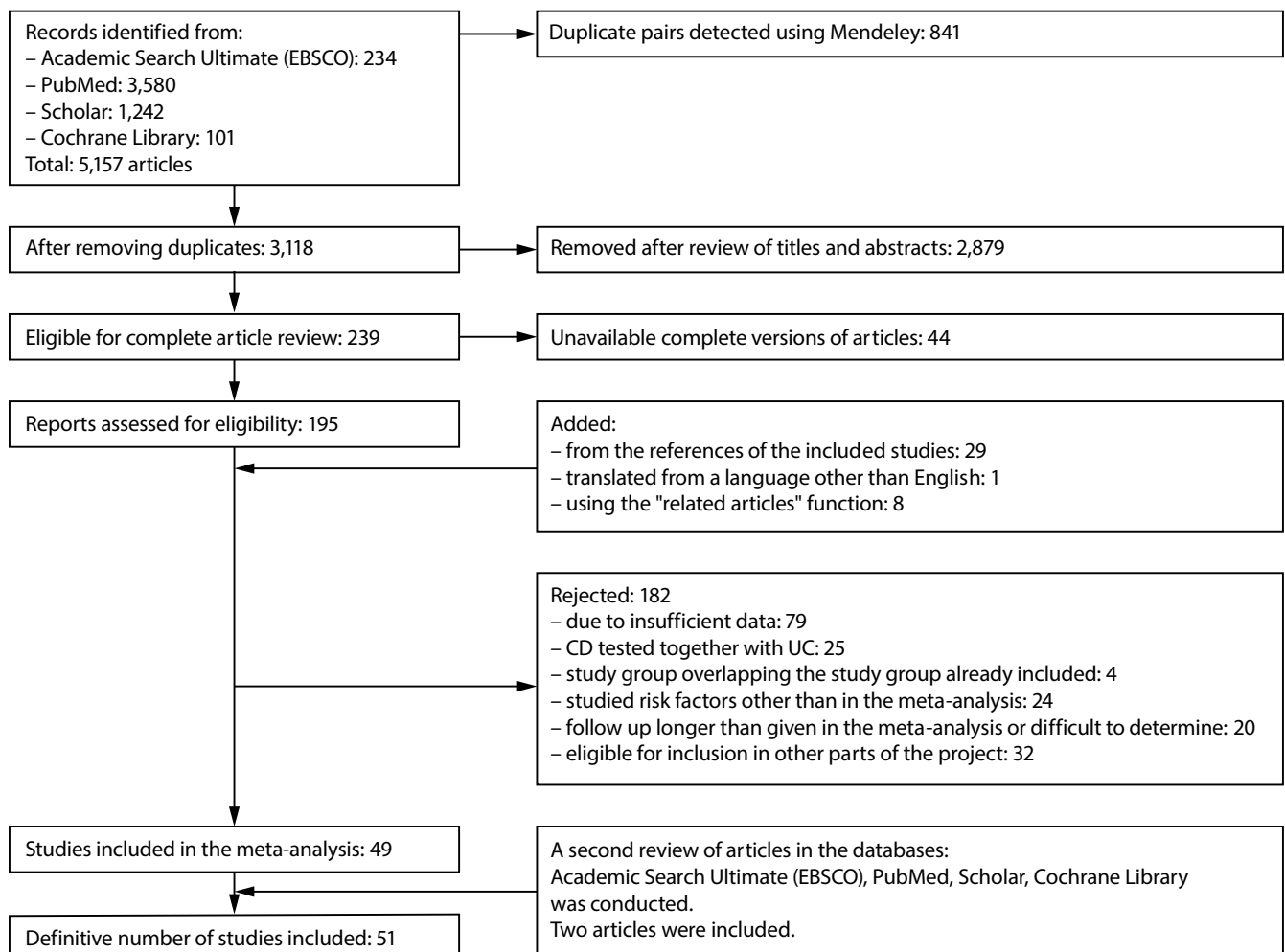
Table 4. The articles included in the meta-analysis – cont.

Study	Study period	Country/region	Study design	Number of patients	Mean/median* age	Number of complications	Surgery types	NOS score <sup>a</sup>
Riss et al., 2012 <sup>50</sup>	1998–2008	Austria	retrospective review	182	no information	25	ICR: 153; small bowel resection: 25; rectal resection: 2; colonic resection: 24; closure of bowel fistula: 32; stricturoplasty: 16; others: 8	5
Yang et al., 2012 <sup>51</sup>	1991–2010	South Korea	retrospective review of a prospective database	350	29	81	abdominal surgery	6
Pinto et al., 2011 <sup>52</sup>	2001–2008	USA	retrospective analysis based on a prospectively collected database	130	no information	49	ICR: 74; ileocelectomy with other procedure: 25; total abdominal colectomy: 12; extended right colectomy: 8; proctocolectomy: 3; left colectomy: 2; low anterior resection: 2	6
Brouquet et al., 2010 <sup>53</sup>	1998–2008	France	retrospective, observational study of a prospective database	61	41*	23	ICR: 54; small bowel resection: 7	7
Holubar et al., 2010 <sup>54</sup>	1997–2008	USA	retrospective review of a prospective database	92	41	31	laparoscopic-assisted and hand-assisted laparoscopic surgery; proctocolectomy with or without anastomosis or stoma; total abdominal colectomy with or without anastomosis or stoma; subtotal colectomy with or without anastomosis or stoma; segmental colectomy	7
Nasir et al., 2010 <sup>55</sup>	2005–2008	USA	retrospective review of prospectively maintained database	370	41.7	106	ileocecectomy: 104; right hemicolectomy: 49; transverse colectomy: 3; left hemicolectomy 4; sigmoid colectomy: 19; subtotal colectomy with ileorectostomy: 14; stricturoplasty: 28; stoma reversal: 37; other: 17	6
Bergamaschi et al., 2009 <sup>56</sup>	1992–2006	USA, France	retrospective review	80	40*	6	all ICR with intracorporeal anastomosis	7
Sampietro et al., 2009 <sup>57</sup>	1993–2007	Italy, UK	retrospective review	393	39.7	22	In 393 consecutive patients with small bowel CD, a total of 865 jejunoileal segments were treated by using 318 minimal bowel resections and 367 stricturoplasties.	5
Takahashi-Monroy, 2005 <sup>58</sup>	1979–1997	Mexico	retrospective review	34	46	11	ileocecal resection: 17; total colectomy with ileorectal anastomosis: 5; intestinal resection: 4; left hemicolectomy: 3; total colectomy with Hartmann pouch: 2; total non-restorative proctocolectomy: 2; primary perforation closure: 1	5

**Table 4.** The articles included in the meta-analysis – cont.

Study	Study period	Country/region	Study design	Number of patients	Mean/median* age	Number of complications	Surgery types	NOS score <sup>a</sup>
Post et al., 1991 <sup>59</sup>	1981–1989	Germany	retrospective review of prospectively maintained database	368	33.1	46	gastroenterostomy: 4; jejunal resection: 11; ileal resection: 83; strictuoplasty: 70; ileocecal resection/right hemicolectomy: 212; resection of previous anastomosis: 51; colic resection: 99; proctectomy/proctocolectomy: 3; closure of ileostomy/colostomy; closure of enteric fistula: 66; closure of vesical/genital fistula: 29; other: 28	5
Heimann et al., 1985 <sup>60</sup>	1978–1983	USA	retrospective study of prospectively maintained database	130	no information	39	ICR: 88; a subtotal colectomy: 21; abdominoperineal resection of the rectum: 10; small bowel resection only: 11; either temporary loop ileostomy or a permanent Brooke-type ileostomy: 45	5
Lindor et al. 1985 <sup>61</sup>	1982	USA	retrospective review	124	33*	16	bowel resections: 116; bowel bypass procedures: 5; resection of diseased bowel in combination with bowel bypass: 3	5

NOS – Newcastle–Ottawa Scale; ICR – ileocolic resection.



**Fig. 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow diagram

Table 5. Disease-related risk factors

Risk factor	Number of patients	OR (95%CI) for dichotomous variables R (95% CI) for continuous variables	p-value	I <sup>2</sup>	Egger's test (p-value)	Evaluation of the strength of evidence (level)
Previous surgery	9,939	OR = 1.39 (1.23–1.57)	<0.001	19.74%	0.119	I
Group B3 (according to Montreal classification)	7,982	OR = 1.26 (1.11–1.42)	<0.001	16.32%	0.418	I
Disease duration before surgery	3,485	R = 1.10 (1.02–1.18)	0.01	11.31%	0.489	I
Group L2	5,956	OR = 1.38 (1.11–1.72)	0.004	35.62%	0.002	II
Group L1	5,954	OR = 0.81 (0.71–0.92)	0.001	<0.01%	0.26	I
Group B2	6,586	OR = 0.81 (0.71–0.91)	0.001	<0.01%	0.543	I
Intraoperative abscess	5,055	OR = 0.99 (0.84–1.18)	0.952	4.34%	0.709	–
Concomitant perianal disease	4,420	OR = 1.26 (0.98–1.62)	0.074	49.17%	0.424	–
Group A1	1,988	OR = 0.84 (0.61–1.16)	0.279	<0.01%	0.426	–
Group A2	2,010	OR = 1.1 (0.81–1.5)	0.549	33.74%	0.629	–
Group A3	2,403	OR = 0.99 (0.7–1.41)	0.959	30.89%	0.311	–
Group L3	5,422	OR = 1.12 (0.99–1.27)	0.061	<0.01%	0.056	–
Group L4	2,699	OR = 0.94 (0.61–1.48)	0.8	32.80%	0.636	–
Group B1	5,744	OR = 0.96 (0.81–1.14)	0.659	<0.01%	0.827	–

OR – odds ratio; 95% CI – 95% confidence interval; R – response ratio.

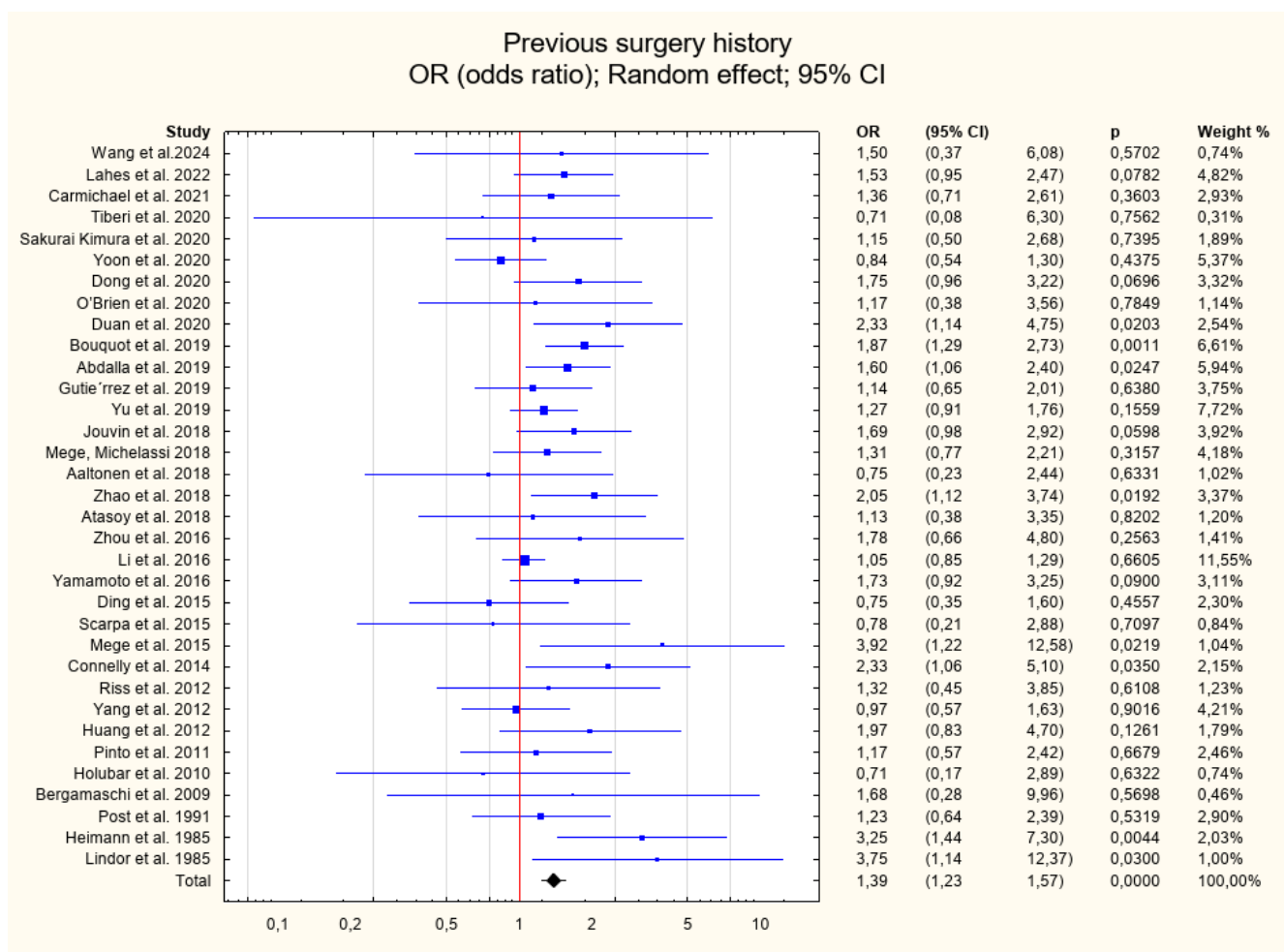


Fig. 2. Meta-analysis of early postoperative complications associated with previous surgery

OR – odds ratio; 95% CI – 95% confidence interval.

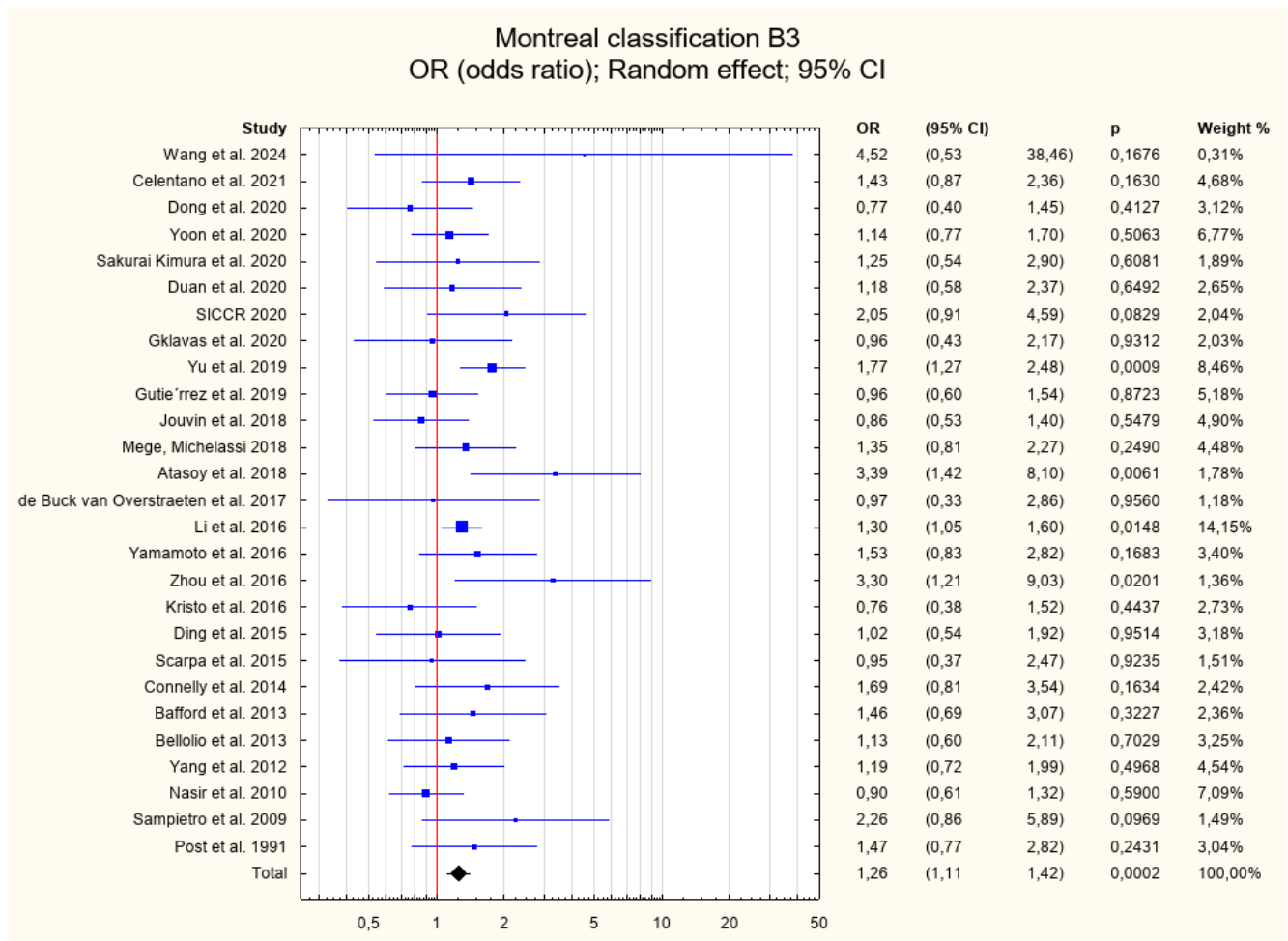


Fig. 3. Meta-analysis of early postoperative complications associated with Montreal classification group B3

OR – odds ratio; 95% CI – 95% confidence interval.

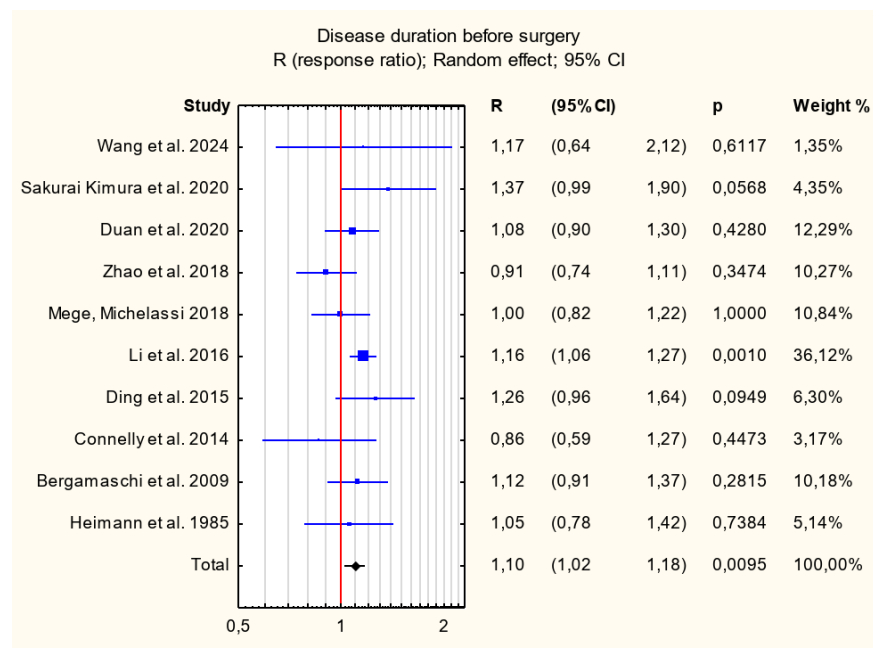


Fig. 4. Meta-analysis of early postoperative complications associated with disease duration prior to surgery

OR – odds ratio; 95% CI – 95% confidence interval.

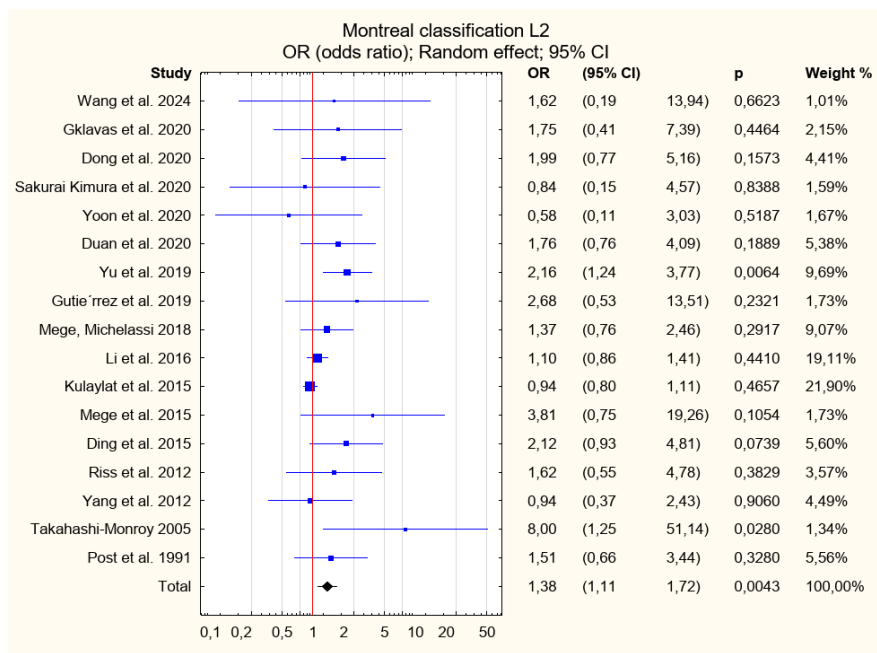


Fig. 5. Meta-analysis of early postoperative complications associated with Montreal classification group L2

OR – odds ratio; 95% CI – 95% confidence interval.

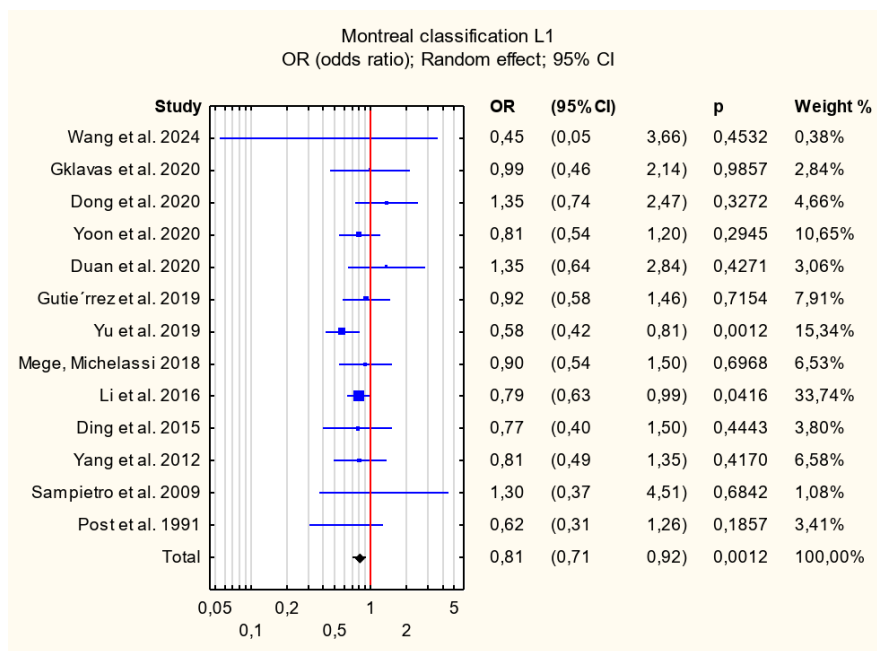


Fig. 6. Meta-analysis of early postoperative complications associated with Montreal classification group L1

OR – odds ratio; 95% CI – 95% confidence interval.

to various complications related both to the disease itself and to its management, particularly surgical treatment.<sup>68</sup>

This meta-analysis aimed to identify disease-related risk factors associated with the occurrence of complications after surgery in patients with CD. Disease duration prior to surgical intervention emerged as a statistically significant predictor of early postoperative complications (class I evidence; R = 1.10; 95% CI: 1.02–1.18; p = 0.01).

Previous studies have also demonstrated the association between longer disease duration and postoperative complications. For example, Hossne et al.<sup>69</sup> reported that disease duration was a significant risk factor for postoperative complications, a finding similarly observed by Sakurai Kimura et al.<sup>22</sup> The available literature further supports the notion

that prolonged disease duration is associated with an increased risk of surgical complications.<sup>70</sup> This relationship may be explained by the fact that patients with a longer disease course are particularly susceptible to complications resulting from chronic inflammation, malabsorption, and subsequent nutritional deficiencies, all of which may impair the healing of surgical wounds and intestinal anastomoses.<sup>71</sup> Prolonged inflammation may also contribute to the development of complications requiring additional surgical interventions, such as fistulas or intestinal strictures.<sup>23,68,69,71</sup> Moreover, repeat surgical procedures are generally associated with a higher risk of complications due to the compromised quality of abdominal tissues, which makes safe surgical dissection and preparation more challenging.<sup>72,73</sup>

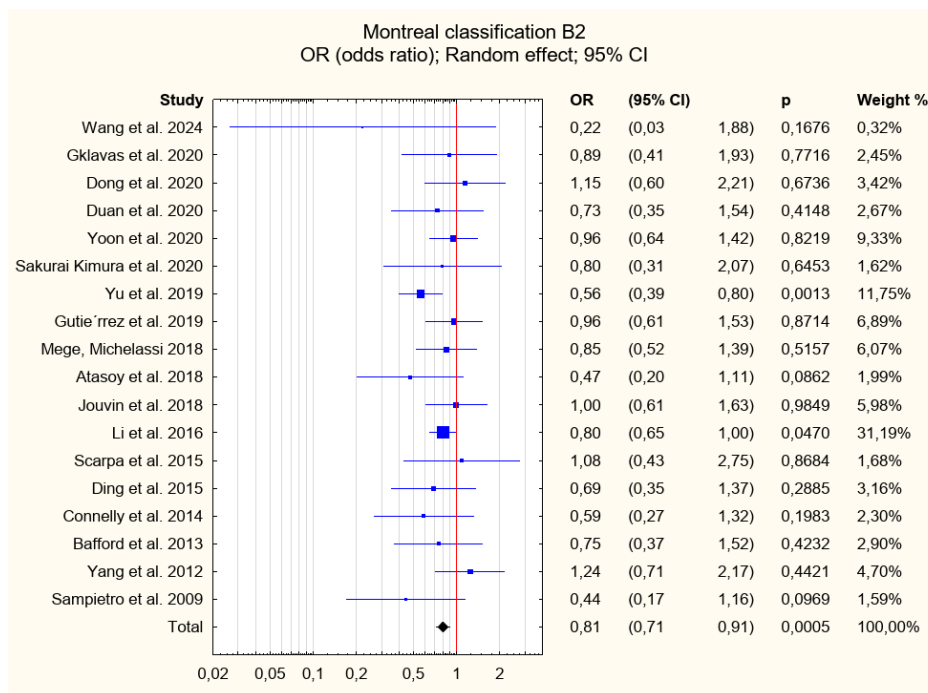


Fig. 7. Meta-analysis of early postoperative complications associated with Montreal classification group B2

OR – odds ratio; 95% CI – 95% confidence interval.

Additionally, the presence of Montreal classification group B3 (penetrating disease with fistula formation) was identified as a statistically significant risk factor for postoperative complications (level I evidence; OR = 1.26; 95% CI: 1.11–1.42;  $p < 0.001$ ). Montreal classification group L2 was also identified as a significant risk factor for postoperative complications in this cohort (OR = 1.38; 95% CI: 1.11–1.72;  $p = 0.004$ ). However, there is no clear consensus regarding the Montreal classification as a prognostic indicator of disease progression. A study by Tajra et al.<sup>74</sup> found no association between disease progression as defined by the Montreal classification and the risk of postoperative complications. Conversely, Lin et al.<sup>75</sup> suggested that categorizing patients based on colonic involvement may provide a more reliable predictor of clinical outcomes than the Montreal classification. This issue warrants further investigation, particularly in light of reports suggesting that the Montreal classification may be associated with a statistically significant increase in the need for emergency surgical interventions.<sup>74</sup>

In our study, Montreal classification groups L1 (OR = 0.81; 95% CI: 0.71–0.92;  $p = 0.001$ ) and B2 (OR = 0.81; 95% CI: 0.71–0.91;  $p = 0.001$ ) were associated with a reduced risk of postoperative complications. Historically, it has been suggested that patients presenting with stricturing disease experience a milder clinical course both before and after surgery compared with those with penetrating disease manifestations such as fistulas and abscesses, although the supporting evidence remains limited. The Montreal classification for CD reflects this assumption by assigning the most severe disease behavior category to fistulizing (penetrating) disease regardless of the presence of strictures. Patients are classified as having stricturing disease only when strictures occur in isolation. Consequently, the Montreal classification may underestimate the true

prevalence of strictures. One proposed mechanism suggests that fistulas and abscesses develop at sites where transmural bowel inflammation coincides with increased intraluminal pressure in intestinal segments proximal to a stricture.<sup>76</sup>

Another variable identified in this analysis as a statistically significant risk factor for postoperative complications was a history of prior surgical interventions (level I evidence; OR = 1.39; 95% CI: 1.23–1.57;  $p < 0.001$ ). Patients with a long disease duration and a history of previous surgical procedures represent a distinct subgroup that poses particular challenges in surgical management.<sup>70</sup> This observation is supported by the findings of Kotze et al.,<sup>70</sup> who reported that a longer interval between the diagnosis of CD and surgical intervention is significantly associated with an increased risk of postoperative complications. Each subsequent surgical procedure may lead to the formation of intra-abdominal adhesions,<sup>77</sup> which in patients with CD may be particularly extensive and technically challenging during surgery.<sup>70,78</sup> Clinicians involved in the surgical management of inflammatory bowel disease are well aware that extensive adhesions substantially increase the risk of intraoperative full-thickness intestinal injury.<sup>77,78</sup> This represents a significant challenge, as the surgical management of CD should aim to avoid unnecessary intestinal resections whenever possible.<sup>70,78</sup>

The analysis of risk factors such as intraoperative intra-abdominal abscess, perianal involvement, and selected Montreal classification categories (A1–A3, L3, L4, and B1) did not demonstrate statistically significant associations with postoperative complications. In contrast, Bechara et al.<sup>79</sup> reported that factors including ileocecal disease location, the presence of fistulas, and perianal disease involvement (L3B3p) were associated with an increased risk of surgical recurrence of CD.<sup>79</sup>

A possible explanation for the lack of statistical significance observed for the aforementioned Montreal classification categories may be the considerable variability in disease progression associated with these phenotypes. In a study by Tajra et al.,<sup>74</sup> the presence of strictures in the jejunum and ileum, perianal lesions in patients with CD, and age at diagnosis were reported to be significantly associated with an increased likelihood of surgical intervention. However, the authors did not evaluate the risk of postoperative complications.

According to Martinez-Sanchez et al.,<sup>80</sup> CD with perianal involvement is associated with a poorer prognosis, particularly in cases with rectal involvement, and is linked to a higher frequency of biological therapy use and hospital admissions, especially among patients with complex perianal disease. However, the study did not demonstrate a corresponding increase in the number of abdominal surgeries in this patient group. Furthermore, the prevalence of biological therapy among patients with perianal disease was higher than among those without perianal involvement (42.8% vs 30.7%). The discrepancy between the findings of the present meta-analysis and those reported in the cited study highlights the need for further investigations involving larger patient cohorts to provide sufficient statistical power for a more comprehensive analysis.

## Limitations of the study

Several important limitations of this study should be acknowledged. The primary methodological limitation was that the literature review was conducted by a single researcher, a constraint related to the doctoral nature of the project. To minimize potential errors, the process was supervised by the principal investigator, and all included studies underwent thorough verification. Nevertheless, the inherent risk of subjective bias associated with single-reviewer study selection cannot be excluded. Another methodological limitation was the re-examination and inclusion of additional studies 3.5 years after the initial literature search. Although this approach allowed the meta-analysis database to be updated, it may have introduced additional sources of bias. Furthermore, the aggregated data reflect treatment outcomes from diverse clinical centers, where unmeasured institutional factors may substantially influence therapeutic results. Differences in the interpretation of study endpoints across centers may further affect the reliability of the presented findings.

## Conclusions

In summary, the findings of the present meta-analysis indicate that prolonged disease duration, penetrating disease behavior with fistula formation (Montreal classification group B3), and a history of prior surgical interventions are significant risk factors associated with an increased likelihood of postoperative complications in patients with

CD. Further investigation of factors influencing surgical complications remains warranted. Future studies, particularly prospective investigations as well as those examining immunological, microbial, and genetic determinants, may help refine the identification of predictors of postoperative outcomes in this patient population. Addressing these challenges may play an important role in optimizing surgical management and reducing the risk of postoperative complications. In particular, a better understanding of the effects of chronic inflammation and the impact of gastroenterological therapies on postoperative healing – especially with regard to intestinal anastomoses – may facilitate the identification of more precise predictors of postoperative recovery. Ultimately, this may support the development of clinically applicable predictive models, enabling more personalized treatment strategies and improving patient outcomes and quality of life.

## Supplementary data

The supplementary materials are available at <https://doi.org/10.5281/zenodo.18467011>. The package contains the following files:

Supplementary Fig. 1. Meta-analysis of early postoperative complications for intraoperative abscess.

Supplementary Fig. 2. Meta-analysis of early postoperative complications for concomitant perianal disease.

Supplementary Fig. 3. Meta-analysis of early postoperative complications for Montreal classification group A1.

Supplementary Fig. 4. Meta-analysis of early postoperative complications for Montreal classification group A2.

Supplementary Fig. 5. Meta-analysis of early postoperative complications for Montreal classification group A3.

Supplementary Fig. 6. Meta-analysis of early postoperative complications for Montreal classification group L3.


Supplementary Fig. 7. Meta-analysis of early postoperative complications for Montreal classification group L4.


Supplementary Fig. 8. Meta-analysis of early postoperative complications for Montreal classification group B1.


## Use of AI and AI-assisted technologies


Not applicable.


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