Patients at high risk of postoperative complications in Crohn's disease – A meta-analysis and systematic review.

Keywords
treatment outcome, IBD, abdominal surgery, postsurgical complications, predisposing factors

Abstract

Introduction
The aim of the study is to identify patient-related factors influencing the risk of early postoperative complications in Crohn's disease (CD).

Material and methods
A meta-analysis was conduced based on articles addressing early complications after abdominal surgery for CD. The analysis included the following risk factors: age, sex, hypoalbuminemia, serum CRP levels, anemia, blood leukocyte levels, BMI, smoking, diabetes mellitus and hypertension. A systematic review was performed between 21 November 2021 and 4 December 2021 and repeated after a three and a half years. Outcomes were reported as two effect sizes: odds ratio (OR) w and response ratio (R), both with 95% CI, p-value <0.05 and visualisation in a forest plot. The strength of evidence was determined based on Egger's test p-value, sample size, and I^2 statistic.

Results
The following significant risk factors of early postoperative complications in CD were identified assuming Level I strength of evidence: hypoalbuminemia (OR= 1.82; 95%CI 1.62-2.06), anemia (OR= 1.77; 95% CI 1.47-2.15), age≥40 years (OR= 1.44; 95%CI 1.18-1.77), diabetes (OR=1.28; 95%CI 1.04-1.57), hypertension (OR=1.27; 95% CI 1.06-1.51), smoking (OR=1.23; 95% CI 1.14-1.33). At Level II, included CRP levels (R= 1.58; 95% CI 1.32-1.89), male sex (OR=1.23; 95% CI 1.11-1.37), blood leukocyte levels (R=1.11; 95% CI 1.07-1.15).

Conclusions
These findings suggest that nutritional status, age, comorbidities, and parameters of blood morphology and biochemistry should be carefully considered when assessing the risk of postoperative complications in patients with CD.

MAIN TEXT

Introduction:

Crohn's disease (CD) is a chronic, non-specific inflammatory condition of the gastrointestinal tract. Despite ongoing advances in medical science, its aetiology remains poorly understood, and no definitive cure has yet been discovered. Consequently, CD continues to represent a significant medical and social challenge.

The highest rates are observed in Western industrialised countries, ranging from 10 to 30 cases per 100,000 person-years, with a steady increase noted since the mid-20th century [1-3]. Similar upward trends have been reported in East Asian countries such as Japan, China, and South Korea [1,2]. In contrast, CD remains relatively rare in Africa and South America [2]. Increased vulnerability has been associated with urban residency and northern latitudes [2,3]. The incidence typically peaks in the second and fourth decades of life, with no substantial sex differences [2,3].

Although currently incurable,[4] the course of CD can be managed and its symptoms controlled. Standard pharmacological treatments include corticosteroids, thiopurines (azathioprine, 6-mercaptopurine), methotrexate, anti-TNF agents (infliximab, adalimumab, certolizumab pegol), anti-integrin agents (vedolizumab, natalizumab), and ustekinumab[5].

Pharmacotherapy is often complemented by surgical intervention, which plays a key role in managing CD and its complications. Surgical strategies vary based on the intraoperative findings, with bowel-sparing approaches being the most desirable. The need for surgery increases with disease progression,[6] and up to 80% of patients with CD will undergo at least one surgical procedure during their lifetime[7].

While surgery is effective in inducing remission and resolving complications, major abdominal operations – such as segmental resection of the small or large intestine, strictureplasty, intestinal

bypass, stoma formation, or restoration of bowel continuity – are associated with a high complication rate, exceeding 60%[8].

Patients undergoing surgery are often younger and may present with intestinal malabsorption, secondary malnutrition, and hypoproteinemia. Surgeons must be vigilant regarding both general postoperative risks and those specific to CD. Early postoperative complications include septic events, anastomotic leakage, bleeding, and bowel obstruction. Their occurrence significantly impairs treatment outcomes and patients' quality of life; therefore, particular attention should be paid to all possible methods of complication prevention.

The aim of this study is to identify patient-related factors that influence the risk of early postoperative complications in individuals undergoing abdominal surgery for Crohn's disease.

Methods:

This paper forms part of the research undertaken for the doctoral dissertation of one of the authors, titled "*Multifaceted Assessment of Perioperative Risk Factors in Patients with Crohn's Disease (CD).*"

The data are presented in compliance with the MOOSE (Meta-analyses of Observational Studies in Epidemiology) checklist and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 [9].

Information sources and Search strategy: The first author performed a systematic review of the literature available in PubMed, Cochrane library, Academic Search Ultimate (EBSCO) and Google Scholar databased between 21 November 2021 and 04 of December 2021. The search terms included combinations of the following keywords: "Crohn's disease", OR "Crohn's disorder", OR "IBD", OR "regional enteritis"; AND "complications", OR "outcomes", OR "morbidity", OR "recurrence", OR "relapse", OR "remission", OR "treatment outcome", OR "treatment failure", OR "reoperation"; AND "postoperative", OR "perioperative"; AND "risk factors", OR "contributing

factors", OR "predisposing factors"; AND "surgery", OR "resection". Search was made with and without the use of logical operators ('AND', 'OR').

The study included articles published up to 04 December 2021. A systematic re-examination of the previously searched databases was performed on July 15, 2025, following a three-and-a-half-year interval, employing consistent methodology to refresh the literature review.

Any authors were not contacted to search for unpublished papers. All papers were considered regardless of the language of publication. In order to increase the number of search results, the "related articles" function in PubMed and the reference lists of selected articles were also reviewed.

Eligibility criteria:

After reviewing the titles and abstracts of available papers, articles were included in the meta-analysis according to the PICO formula:

1) Participant: individuals over 15 years of age, of any sex, race, or geographic origin, who underwent abdominal surgery for CD.

2) Intervention: presence of patient-related risk factors (age, sex, hypoalbuminemia, serum CRP levels, anemia, blood leukocyte levels, BMI, nicotinism, diabetes, hypertension)

3) Comparator: absence of the respective risk factor

4) Outcome: any complication that occurred within one month post-surgery as defined by the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) [10](Table I)

The listed complications were graded by severity on a scale of 1 to 5 according to the Clavien–Dindo classification. (Table II)

Inclusion criteria required studies to present precise event counts or odds ratios accompanied by 95% confidence intervals, mean values of the risk factor under investigation in the complication group, and their respective control counterparts.

Studies had to employ one of the following designs: observational study, randomised or non-randomised controlled trial, prospective or retrospective cohort study, case–control study, or cross-sectional study.

Exclusion criteria were: insufficient data or repeated study on the same group of patients; studies conducted on animals; pregnant patients; patients suffering from indeterminate colitis or ulcerative colitis. Types of operations that required disqualification from the study were: cholecystectomies; organ transplants; operations due to perianal disease.

If the follow up was longer than 30 days or difficult to determine or there were no results from a comparison group the study was also excluded.

Data collection process: The obtained studies were reviewed by the first author using the Mendeley Desktop 1.19.8. library and the Microsoft Excel programme. The following data were collected: the title; first author; year of publication; study design; country and type and day of the performed operations; postoperative complications and their risk factors. Any disagreement were resolved by discussion with the fourth author , who was also the Principal Investigator. Articles in a language other than English were translated using Google Translate.

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

Final article: All four authors contributed to and approved the final version of the manuscript..

Statistical analysis: Calculations for the meta-analysis were performed with the Statistica 13.1. Because we assume that the study is heterogeneous in nature, random effect model was used. Two-sided statistical tests with *p*-values of less than 0.05 indicated statistical significance. The results were visualised in forest plots in two effect sizes: OR as statistical measure for dichotomous outcomes, with 95% Confidence Interval and *p*-value less than 0.05. Continuous variables in the form of means with standard deviations were tested with the use of response ratio R with 95% CI, *p*-value <0.05. Chronological cumulative analysis was used to determine the cumulative effect and how its error changed over time when taking subsequent publications into account. Statistical heterogeneity was analysed with I^2 , with I^2> 50% indicating significant heterogeneity. Publication bias was assessed with Egger's test with *p*-value <0.1 indicating significant difference and the result was visualised in a funnel plot. Sensitivity was analysed on sensitivity plots showing changes in the cumulative effect after exclusion of individual studies from the meta-analysis to discover how different values of independent variable will influence the significance of a particular dependent variable.

Evaluation of the strength of evidence: The strength of evidence was determined based on three criteria as indicated previously [11]: Egger's test *p*-value > 0.1, the whole study group over 1,000 patients and I^2< 50%. Briefly, Level I strength of evidence (high-quality) was achieved when all three conditions were met, Level II (moderate-quality), when two were met; Level III (moderate-quality), when one was met and Level IV (low-quality), when none of the three conditions were met.

Results:

In total, 5,157 papers were identified through the database searches. Of these, 45 articles were selected for acceptance in the meta-analysis.

A detailed report on the numbers of identified, screened and selected articles can be found in Figure 1.

Detailed information on the included studies and their quality assessment (New Castle Ottava Scale) are presented in Table III.

No randomised controlled trials were identified; therefore, only cohort studies were qualified for analysis, encompassing data from 28,940 patients. The mean age of patients ranged between 29 and 46 years.

Significant heterogeneity was observed between studies. The studies which adopted only serious complications, i.e. >3a, in the Clavien-Dindo Scale as end points were: Wang et al. (2024) [12], Tiberi et al. (2020) [16] and O'Brien et al. (2020) [17] . Articles which included data on patients operated on with laparoscopic and minimally invasive techniques were: Tiberi et al. (2020) [16], Yoon et al. (2020) [23], Riss et al. (2012) [47], Holubar et al. (2010) [50], and Bergamaschi et al. 2009 [51].

Yu et al. (2019) [24] used a study group with patients aged 16 years or older, and considered complications starting at Grade 2 in the Clavien-Dindo Scale as end points. Mege, Michelassi (2018) [31] and Joyce et al. (2013) [45] estimated the number of postoperative complications based on acute hospital readmissions. Mege et al. (2015) [42] formed the study group from patients after ileocaecal resection with anastomosis and temporary protective stoma. Brouquet et al. (2010) [49] only included patients scheduled for reoperation for recurrent CD.

Among patient-related risk factors for early postoperative complications in Level I strength of evidence, statistically significant were : hypoalbuminemia (OR 1.82; 95%CI 1.62-2.06; $p<0.0001$); anemia (OR 1.77; 95% CI 1.47-2.15 $p<0.0001$); age ≥40 years (OR 1.44; 95%CI 1.18-1.77, $p=0.004$); diabetes (OR=1.28; 95%CI 1.04-1.57 $p=0.0176$); arterial hypertension (OR=1.27; 95% CI 1.06-1.51 $p=0.0081$); smoking (OR=1.23; 95% CI 1.14-1.33 $p<0.0001$).

It should be added that for hypoalbuminemia cut-off points of albumin levels were ≤3.0g/dl in studies by Tiberi [16], Gklavas [19], Kotze [35], Zhou [38], Post [54], Lindor [56], and Yang[48]. In anemia a threshold of HGB levels were <12g/dl for females and <13g/dl for males in studies by Aaltonen [28], Gklavas [19] and Zhao [33]; HCT <36% for females and <39% for males in studies by Yang [48] and Aydinli [29]). In factor age ≥40 years all studies have a cut-off point ≥40 years, apart from Larson [15] and Post [54] with a cut-off point >50 years and Takahashi-Monroy [53] with a cut-off point >60 years).

In Level II strength of evidence statistically significant factors were: CRP concentrations (R=1.58; 95% CI 1.32-1.89 p<0.0001); male sex (OR=1.23; 95% CI 1.11-1.37 p=0.0001) and blood leukocyte concentrations (R=1.11; 95% CI 1.07-1.15 p<0.0001)

The study did not find a statistically significant result for patient BMI≤18.5 as a risk factor.

Detailed results of the statistical calculations are presented in Table IV and Figures 2-11.

Fig.2 Meta-analysis of early postoperative complications for hypoalbuminemia.

Fig.3 Meta-analysis of early postoperative complications for anemia

Fig.4 Meta-analysis of early postoperative complications for patients over 40 years of age

Fig.5 Meta-analysis of early postoperative complications for patients with BMI<18.5

Fig.6 Meta-analysis of early postoperative complications for diabetes

Fig.7 Meta-analysis of early postoperative complications for hypertension

Fig.8 Meta-analysis of early postoperative complications for nicotinism

Fig.9 Meta-analysis of early postoperative complications for serum CRP levels

Fig.10 Meta-analysis of early postoperative complications for male sex

Fig.11 Meta-analysis of early postoperative complications for preoperative blood leukocyte levels

Following the main analysis, a subgroup analysis was conducted for risk factors associated with severe postoperative complications (i.e. Clavien–Dindo score ≥ 3a). Due to limited data, this analysis could only be performed for hypoalbuminaemia. The result was not statistically significant: OR = 1.01; 95% CI: 0.41–2.53; p = 0.979.

Discussion:

Despite ongoing advances in medical science, Crohn's disease still remains a major therapeutic challenge. The treatment of inflammatory bowel disease (IBD) requires extensive interdisciplinary knowledge and close cooperation among specialists from various medical fields, including gastroenterology, surgery, internal medicine, radiology, dermatology, rheumatology, and clinical nutrition.

IBD course may also be influenced by comorbidities such as hypertension and diabetes[57], as well as patient-specific factors including age, disease duration, nutritional status, and overall physiological condition. These variables can significantly affect both the course of treatment and surgical outcomes.

As a result, patients often require long-term therapy, which is associated with an increased risk of complications and treatment failure. Determining the optimal timing for surgical intervention is therefore critical. Continuing ineffective conservative treatment can expose patients to serious complications. For example, corticosteroid therapy may result in steroid resistance or dependence [58] – an important concern from a surgical perspective. When pharmacological treatment fails, early surgical intervention is preferable to prolonged steroid use, which carries a markedly higher

risk of perioperative complications [59-61]. As such, a significant number of CD patients will require surgical intervention during their lifetime.

All surgical procedures carry an inherent risk of complications, and one of the surgeon's key objectives is to minimise this risk. Therefore, identifying clinical conditions and patient-related factors that increase the likelihood of complications is essential. This meta-analysis aimed to assess perioperative risk associated with various patient-specific factors. Our findings indicate that the following factors significantly increase the risk of complications: hypoalbuminemia, anemia, age ≥40 years, smoking, diabetes mellitus, and arterial hypertension (all with Level I strength of evidence); as well as elevated blood leukocyte count and male sex (both with Level II strength of evidence).

Hypoalbuminemia is a recognised risk factor for perioperative complications [59-62]. A 2016 study by Truong et al. found it to be significantly associated with prolonged hospitalisation, increased incidence of surgical site infections, higher risk of enterocutaneous fistulas and higher risk of deep vein thrombosis [59-63]. Albumin serves as both an antioxidant and a transport protein; [60-63] therefore, its deficiency may impair multiple physiological functions [60]. Importantly, low albumin levels may reflect not only malnutrition but also active inflammation, catabolic stress, and systemic illness, all of which negatively impact surgical outcomes [61-64]. It is possible to correct hypoalbuminemia through appropriate nutrition and anti-inflammatory treatment if time, disease course and circumstances allow; however, this should be attempted before the planned operation [59-61,63] as intravenous albumin supply alone does not significantly alter the course of hospitalisation [61]. Our findings support existing literature by confirming hypoalbuminaemia as a significant risk factor for perioperative complications.

Our findings did not indicate a significant relationship between low BMI values (BMI <18.5) and a higher risk of perioperative complications. Nevertheless, our findings showed borderline lack of statistical significance. Previous studies note that malnutrition is one of the most significant risk

factors for surgical complications [4,59-63,65,66]. Operative trauma and the perioperative period place considerable demands on the body, and a well-nourished patient with an adequate protein reserve, will heal more quickly and experience a lower risk of perioperative complications, particularly those related to the healing of intestinal anastomoses or surgical wounds [59-63,65].

In addition, patient age $\geq$ 40 years was also found to be a significant risk factor for perioperative complications. This has also been noted in previous studies; however, the reports often refer to elderly patients with frailty syndrome [20,66-70]. For CD patients, it is important to consider the patient may have remained undiagnosed for a long period [64,66-69,71] later diagnosis will of course be associated with a longer time that the patient was not provided with appropriate care or being monitored. Hence, greater age and disease duration are associated with a greater chance of complications of the disease and therapy. It is also important to note that such patients may have been receiving chronic steroid therapy, which has long-term effects [70-72].

The negative impact of cigarette smoking on CD is well documented [4,66,69,72-74]. A 2008 meta-analysis by Reese et al. found smoking to increase the risk of clinical recurrence after surgical treatment by 2.5 times compared to non-smokers. In addition, cigarette smoking has been found to be a significant contributor to surgical complications [72,73], and it is recommended that compulsive smokers with CD should be routinely advised to quit smoking [76,77,78]. In our analysis, smoking was associated with a 23% increase in postoperative complications.

Our meta-analysis found diabetes to be a statistically significant risk factor for postoperative complications, consistent with previous research [74-76]; indeed, studies have highlighted that it is associated with impaired healing [74-76]. In addition, the metabolic disturbances accompanying diabetes multifactorially worsen the perioperative course, leading to a higher risk of postoperative complications in diabetic patients.

It has long been known that a significant positive correlation exists between hypertension and the risk of perioperative complications, particularly cardiovascular problems, and this risk is increased by perioperative trauma [77]. Sánchez-Guillén et al. report that hypertension and male sex are associated with a higher risk of ileocolic anastomotic leakage [79]. Similarly, our present findings indicate a link between male sex and an increased risk of perioperative complications. However, data on the role of sex as an independent risk factor for perioperative complications in Crohn's disease are inconsistent, with Kimura et al. reporting no such relationship [22]. This issue certainly requires more in-depth research.

One of the primary laboratory markers of inflammation is a pathological increase in the serum leukocyte count. Studies have found a preoperative increase in the serum leukocyte count to be a risk factor for postoperative complications and a longer hospitalization period [80]. Similarly, our findings indicate that an increased serum leukocyte count was also a risk factor for perioperative complications.

We also examined the association between patient-related factors and the severity of complications as graded by the Clavien-Dindo classification. A separate analysis focusing on hypoalbuminaemia did not demonstrate a significant correlation with severe complications (defined as Clavien-Dindo grade ≥3a).

Limitations:

The primary objective of this study was to identify patient-dependent factors associated with both mild and severe postoperative complications. Severe complications included anastomotic leakage, wound infections, reoperations, and prolonged postoperative ileus. Although our meta-analysis incorporated a substantial number of high-quality studies, the available data were insufficient to draw definitive conclusions about these severe outcomes, which represents a key limitation of our

work. This underscores the need for further prospective research investigating patient-related risk factors for serious postoperative complications in CD.

Another limitation of this study is the fact that the systematic literature search was conducted by a single author (JŁ), in consultation with another (MM) for conflict resolution. This approach is not consistent with current best practices for systematic reviews, which recommend independent searches by multiple reviewers. The initial literature review also included additional risk factors, such as the type of surgery, pharmacological treatment, and disease-related variables; due to space constraints, those findings will be reported in future publications.

Conclusions:

Our analysis identified several key risk factors for postoperative complications in Crohn's disease: hypoalbuminemia, anemia, age >40 years, smoking, diabetes mellitus, and arterial hypertension. The presence of any of these factors indicates a high-risk patient. It is important to emphasise that all of these factors - except age - are potentially modifiable. Identification of these factors is crucial because with appropriate preoperative optimisation, each of these modifiable factors can be improved or corrected and contribute to enhanced patient care and improved therapeutic outcomes in Crohn's disease.

Additional risk factors include elevated preoperative CRP and leukocyte levels, as well as male sex.

Given the substantial number of high-quality studies included in this meta-analysis, the findings may prove valuable in developing a predictive model for perioperative complications in patients with Crohn's disease.

To date, only a limited number of studies have used meta-analysis to identify predictors of both mild and severe postoperative complications in this population. Further prospective research is warranted in this area.

Patient-related risk factors influencing the risk of early postoperative complications in Crohn's disease.

Risk Factor	Number of patients	OR (95%CI) R (95% CI)	p	I^2	Egger's test (p)	Evaluation of the strength of evidence (Level)
Hypoalbuminemia	11,629	OR = 1.82 (1.62-2.06)	<0.0001	13.66%	0.2062	I
Anemia	2,255	OR = 1.77 (1.47-2.15)	<0.0001	<0.01%;	0.3888	I
Age ≥40	6,025	OR = 1.44 (1.18-1.77)	0.0004	40.30%	0.7946	I
Diabetes	6,225	OR = 1.28 (1.04-1.57)	0.0176	<0.01%	0.5445	I
Hypertension	6,225	OR = 1.27 (1.06-1.51)	0.0081	34.79%	0.5309	I
Smoking	11,621	OR = 1.23 (1.14-1.33)	<0.0001	2.32%	0.4296	I
Serum CRP levels	1,043	R = 1.58 (1.32-1.89)	<0.0001	16.81%	0.0803	II
Male sex	11,341	OR = 1.23 (1.11-1.37)	0.0001	13.90%;	0.0264	II
Blood leukocyte levels	2,586	R = 1.11 (1.07-1.15)	<0.0001	89.86%;	0.7781	II

Table I Types of complications taken into account in the study (By ACS-NSQIP definition)

Type of complication	
Surgical	Medical/clinical
surgical site infection, wound dehiscence, anastomotic leak, enterocutaneous fistula, intraabdominal abscess, generalised sepsis, septic shock, postoperative bowel obstruction, unplanned reoperation, periostomy complications, hemorrhage, hematoma, need for blood transfusion.	dehydration, fever of unknown origin, urinary tract infection, *Clostridioides difficile* infection, respiratory complications (unplanned intubation, pneumonia, pulmonary oedema, 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), nervous system complications (stroke, psychotic disorders), venous thrombosis, adrenal insufficiency, liver insufficiency, and death.

Table II Clavien-Dindo Classification

Clavien-Dindo Classification	
1	deviation from the normal course but not requiring pharmacological, surgical, endoscopic or radiological intervention
2	deviation from the normal course requiring pharmacological intervention
3a	a complication requiring surgical, endoscopic or radiological intervention but without general anesthesia
3b	a complication requiring intervention under general anesthesia
4a	a life-threatening complication requiring ICU treatment with single organ failure
4b	a life-threatening complication requiring ICU treatment with multiple organ failure
5	death of a patient

Table III The articles included in the meta-analysis

Study	Study period	Country/ Region	Study design	No. of patients	Mean/ Median* age	No. of complications	Surgery types	NOS score [a]
Wang et al. 2024 [12]	2017- 2022	China	retrospective analysis	181	39.04	10	intestinal resection: ICR, right hemicolectomy, left-sided colectomy, subtotal colectomy, segmental resection of small bowel	5
Lahes et al. 2022 [13]	2001- 2018	Germany	retrospective analysis	426	41*	158	small bowel or colorectal resection, ileostomy or colostomy, closure of ileostomy or colostomy, or strictureplasty	6
Lavorini et al. 2022 [14]	1994- 2018	Italy	retrospective analysis of a prospectively collected database	307	37*	72	elective primary ileocolic resection	6
Larson et al. 2021 [15]	2012-2017	USA, Switzerland	retrosective review	2,899	38	1,094	right colectomy and index ileocecal resection	7
Tiberi et al. 2020 [16]	2008-2019	Italy	observational retrospective study	133	41.2	6	ileocolic resection	5
O'Brien et al. 2020 [17]	2014-2018	USA	single-institution retrospective observational study	118	40*	19	ileocolic resection	5
Kline et al. 2020 [18]	2008-2018	USA	retrospective clinical and genetic cohort study	269	No inf.	86	ileocolectomy	7
Gklavas et al. 2020 [19]	2010-2018	Greece	single-center retrospective study	153	36*	35	ileocolic resection	7
Dong et al. 2020 [20]	2016-2019	China	retrospective review	202	36.5	66	intestinal resection	7
Duan et al. 2020 [21]	2016-2019	China	retrospective review	129	No inf.	55	small-bowel resection:45; ileocolic resection:44; segmental colectomy:21; other (ostomy closure, strictureplasty, and stoma creation without resection):19	6
Sakurai Kimura et al. 2020 [22]	2012-2018	Brazil	retrospective review	103	40.6	33	abdominal surgeries for CD	5
Yoon et al.	2005-2015	USA, South	retrospective	409	35	166	all laparoscopic	7

2020 [23]		Korea	review				ileocolic resection	
Yu et al. 2019 [24]	2006-2015	South Korea	retrospective study	817	No inf.	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 surg.: 18; abdominoperineal resection or Hartmann's procedure:21	7
Gutie´rrez et al. 2019 [25]	2007-2010	Spain	retrospective review	364	38	100	ileocolic resection with ileocolic anastomosis	6
Nguyen et al. 2019 [26]	2005-2012	USA, Canada	retrospective review of prospectively maintained database	6,082	No inf.	1,315	IBD-related bowel surgery	5
Müller et al. 2018 [27]	2000-2014	Austria	retrospective cohort study	182	31.57	41	laparoscopic intestinal resection: ileocoecal resection:123; colonic resections: 46; segmental small bowel resection: 10; rectal resection:3	7
Aaltonen et al. 2018 [28]	2011-2015	Finland	retrospective study	70	41.5*	14	ileocolic resection:51; ileocolic resection 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
Aydinli et al. 2018 [29]	2015	USA, Turkey	Retrospective study	1,643	41.2	507	ileocolic resection or right hemicolectomy:1191; partial colectomy:375; low	7

							anterior resection:77	
Jouvin et al. 2018 [30]	2002-2013	France, Ireland	retrospective review	360	33	87	all ileocolic resection with additional: small bowel resection:31; small bowl suture:8; strictureplasty:6; colonic resection:18; colonic suture:36; bladder suture:7; other:36	6
Mege, Michelassi 2018 [31]	2004-2016	USA	retrospective review of prospectively maintained database	712	No inf.	70	strictureplasty: 137, stoma-related proc.:62; small-bowel resection: 616; ileocecal resection:388; segmental colectomy:66; proctectomy:64; extensive resection:93; other:72	5
Atasoy et al. 2018 [32]	2001-2016	Turkey	retrospective review	147	36	26	ileocecal resection:105; small bowel resection:13; colectomy:29	6
Zhao et al. 2018 [33]	2013-2016	China	single center, retrospective study	186	No inf.	87	total colectomy:22; segmental colectomy:45; ileocecal resection:47; small bowel resection:72	6
El-Hussuna et al. 2017 [34]	2015 (2-month period)	Denmark/ international 151 centres around the world	Observational prospective cohort study	375	37*	126	right hemicolectomy or ileocaecal resection	7
Kotze et al. 2016 [35]	2007-2014	Brazil	retrospective and observational study,	123	No inf.	45	small bowel resection:39; ileocecal resection:59; total colectomy:7	7
Lee et al. 2016 [36]	1999-2014	South Korea	retrospective review	50	38.4	18	small bowel resection:15; right hemicolectomy:28; combined:7	5
Li et al. 2016 [37]	1998-2014	USA	retrospective review of prospectively maintained database	1,331	41.2	628	small-bowel resection:186; ileocolic resection:687; segmental colectomy:51; total/subtotal colectomy:192; total proctocolectomy:134; stoma creation without resection:52; other (redo ileocolonic anastomosis, strictureplasty,	7

							ileostomy revision):159	
Zhou et al. 2016 [38]	2012-2014	China	retrospective review	73	36.14	25	intestinal resection and anastomoses, with or without a covering stoma	7
Yamamoto et al. 2016 [39]	2008-2013	Japan, Italy, Brazil	international multicentre retrospective review	231	33	55	all ileocolonic resections with primary anastomosis	7
Ding et al. 2015 [40]	2011-2013	USA	retrospective rview	164	No inf.	64	stoma related: 69; small-bowel resection:20; ileocolic resection:113; partial colectomy:9; subtotal colectomy:15; total colectomy:11; anterior resection:2;	6
Kulaylat et al. 2015 [41]	2005-2012	USA	multicentre retrospective review	7,631	41.8	2,099	enterectomy:1091; ileocolectomy:3190; partial colectomy:1915; total abdominal/proctocolectomy:1076; proctectomy:359	7
Mege et al. 2015 [42]	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 [43]	2000-2013	Italy	retrospective observational review	146	No inf.	21	total colectomy: 12; ileal resection: 20; colonic resection: 26; ileo-colonic resection: 87; ileal stricturoplasty: 15	7
Connelly et al. 2014 [44]	2007-2012	USA	retrospective review	143	No inf.	41	ileocolectomy	5
Joyce et al. 2013 [45]	2001-2007	USA	retrospective review	691	No inf.	168	segmental bowel resection: stomach: 1; duodenum: 2; jejunum: 33; ileum:	5

							497; terminal ileum: 356; colon: 455; rectum: 105; ileal pouch anal anastomosis: 12; strictureplasty: 81	
Bafford et al. 2013 [46]	1999-2010	USA	retrospective review of prospectively maintained database	196	40.9	45	ileocolic resection: 127; small bowel resection: 26; segmental colectomy: 13; low anterior resection: 18; protective stomas: 12	6
Riss et al. 2012 [47]	1998-2008	Austria	retrospective review	182	No inf.	25	ileocolic resection: 153; small bowel resection: 25; rectal resection: 2; colonic resection: 24; closure of bowel fistula: 32; strictureplasty: 16; others: 8	5
Yang et al. 2012 [48]	1991-2010	South Korea	retrospective review of prospective database	350	29	81	abdominal surgery	6
Brouquet et al. 2010 [49]	1998-2008	France	retrospective, observational study of prospective database	61	41*	23	ileocolonic resection: 54; small bowel resection: 7	7
Holubar et al. 2010 [50]	1997-2008	USA	retrospective review of prospective database	92	41	31	both laparoscopic-assisted and hand-assisted laparoscopic surgery; total colectomy and included total proctocolectomy with or without anastomosis or stoma, total abdominal colectomy with or without anastomosis or stoma, and subtotal colectomy with or without anastomosis or stoma; segmental colectomy subgroup	7
Bergamaschi et al. 2009 [51]	1992-2006	USA, France	retrospective review	80	40*	6	all ileocolic resections with intracorporeal anastomosis	7
Sampietro et al. 2009 [52]	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	5

							strictureplasties	
Takahashi -Monroy 2005 [53]	1979-1997	Mexico	retrospective review	34	46	11	ileocecal resection: 17, total colectomy with ileo-rectal anastomosis: 5, Intestinal resection: 4, left hemicolectomy: 3, total colectomy with Hartmann pouch: 2, total non-restorative proctocolectomy: 2, primary perforation closure: 1	5
Post et al. 1991 [54]	1981-1989	Germany	retrospective review of prospectively maintained database	368	33.1	46	gastroenterostomy:4; jejunal resection:11; ileal resection:83; strictureplasty: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 [55]	1978-1983	USA	retrospective study of prospectively maitained database	130	No inf.	39	ileocolic resection: 88; subtotal colectomy: 21; abdominoperineal resection of the rectum: 10; small bowel resection only: 11; either temporary loop ileostomy or a permanent Brooke type ileostomy performed: 45	5
Lindor et al. 1985 [56]	1982	USA	retrosective review	124	33*	16	bowel resections: 116; bowel bypass procedures: 5; resection of diseased bowel in combination with bowel bypass: 3.	5

[a] - NOS -Newcastle Ottawa Scale

Table IV Patient-related risk factors.

Risk Factor	Number of patients	OR (95%CI) for dichotomous variables R (95% CI) for continuous variables	p	I^2	Egger's test (p)	Evaluation of the strength of evidence (Level)
Hypoalbuminemia	11,629	OR = 1.82 (1.62-2.06)	<0.0001	13.66%	0.2062	I
Anemia	2,255	OR = 1.77 (1.47-2.15)	<0.0001	<0.01%;	0.3888	I
Age ≥40	6,025	OR = 1.44 (1.18-1.77)	0.0004	40.30%	0.7946	I
Diabetes	6,225	OR = 1.28 (1.04-1.57)	0.0176	<0.01%	0.5445	I
Hypertension	6,225	OR = 1.27 (1.06-1.51)	0.0081	34.79%	0.5309	I
Smoking	11,621	OR = 1.23 (1.14-1.33)	<0.0001	2.32%	0.4296	I
Serum CRP levels	1,043	R = 1.58 (1.32-1.89)	<0.0001	16.81%	0.0803	II
Male sex	11,341	OR = 1.23 (1.11-1.37)	0.0001	13.90%;	0.0264	II
Blood leukocyte levels	2,586	R = 1.11 (1.07-1.15)	<0.0001	89.86%;	0.7781	II
BMI<18.5	3,808	OR = 1.29 (0.99-1.67)	0.0578	22.73%;	0.3848	-

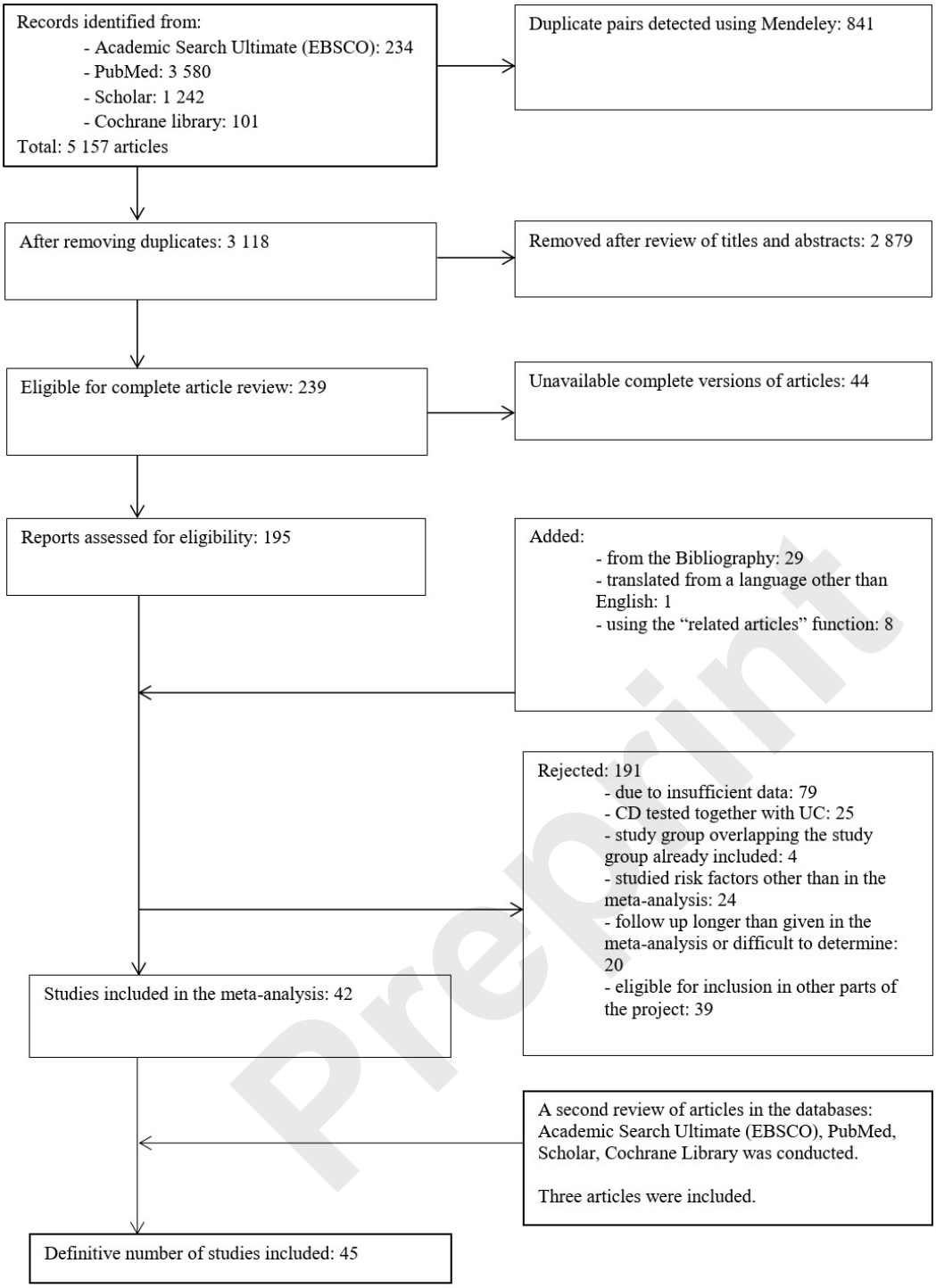

Fig.1 PRISMA 2020 flow diagram.

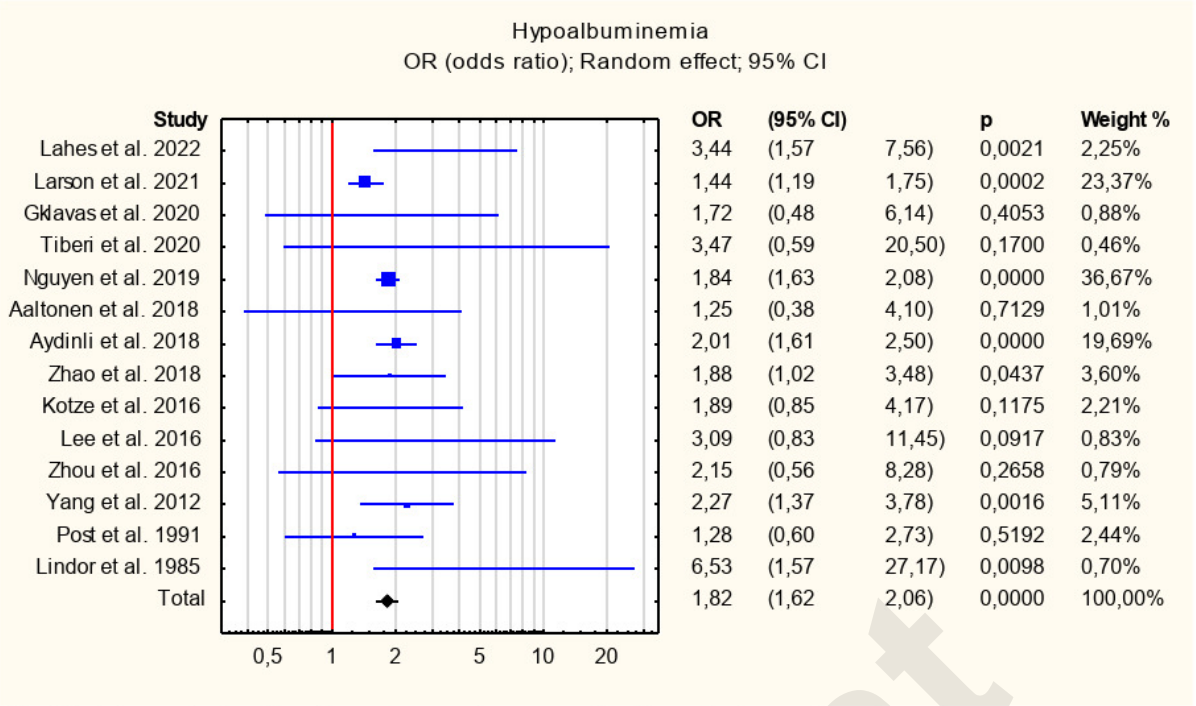

Fig.2 Meta-analysis of early postoperative complications for hypoalbuminemia.

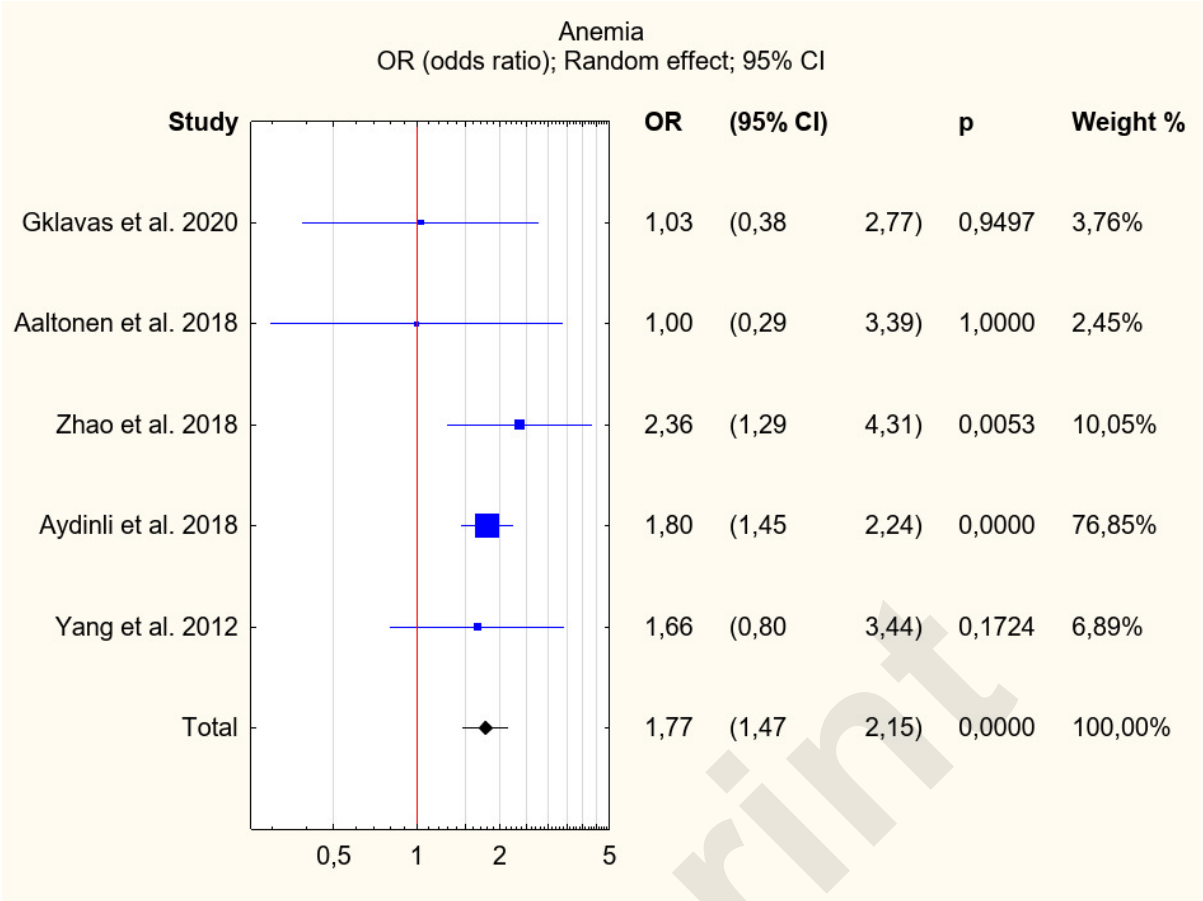

Fig.3 Meta-analysis of early postoperative complications for anemia.

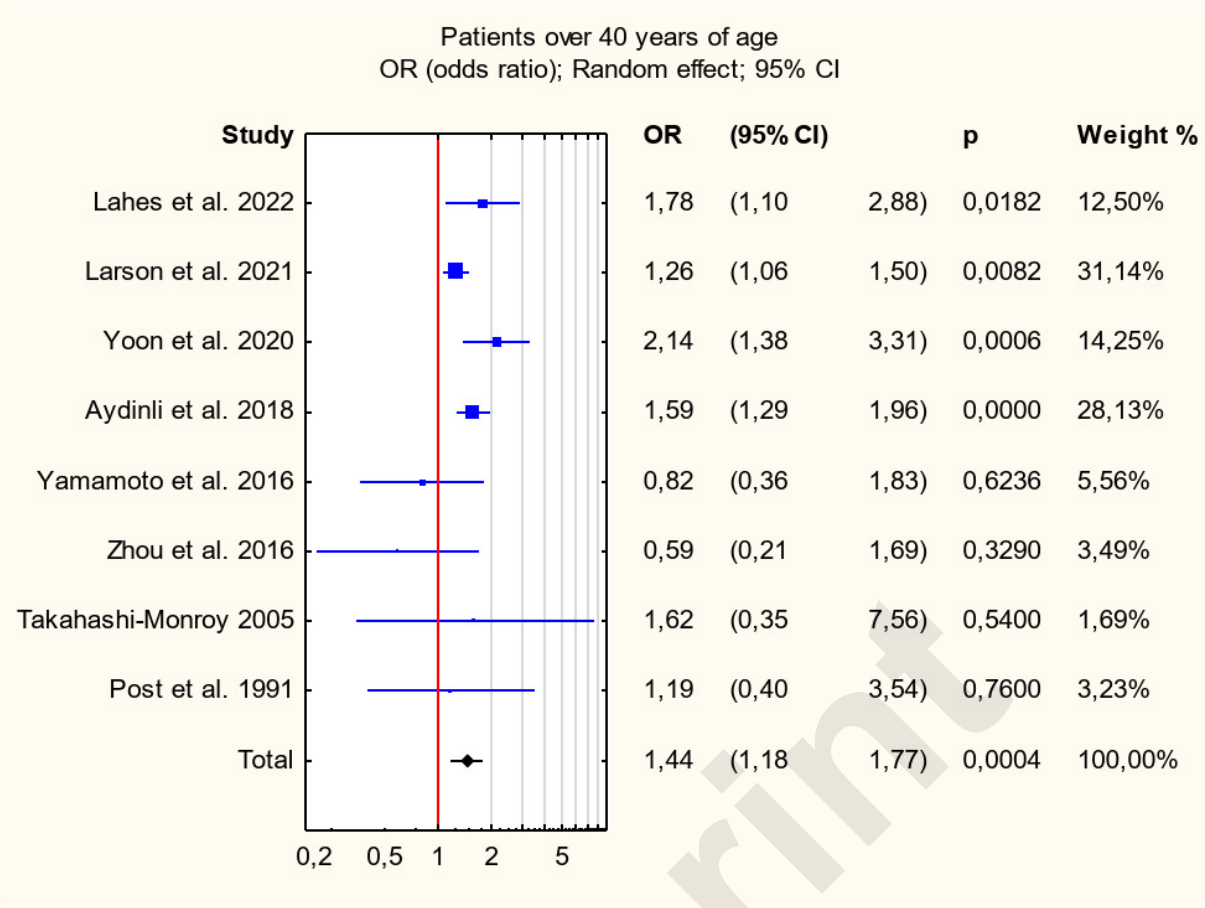

Fig.4 Meta-analysis of early postoperative complications for patients over 40 years of age.

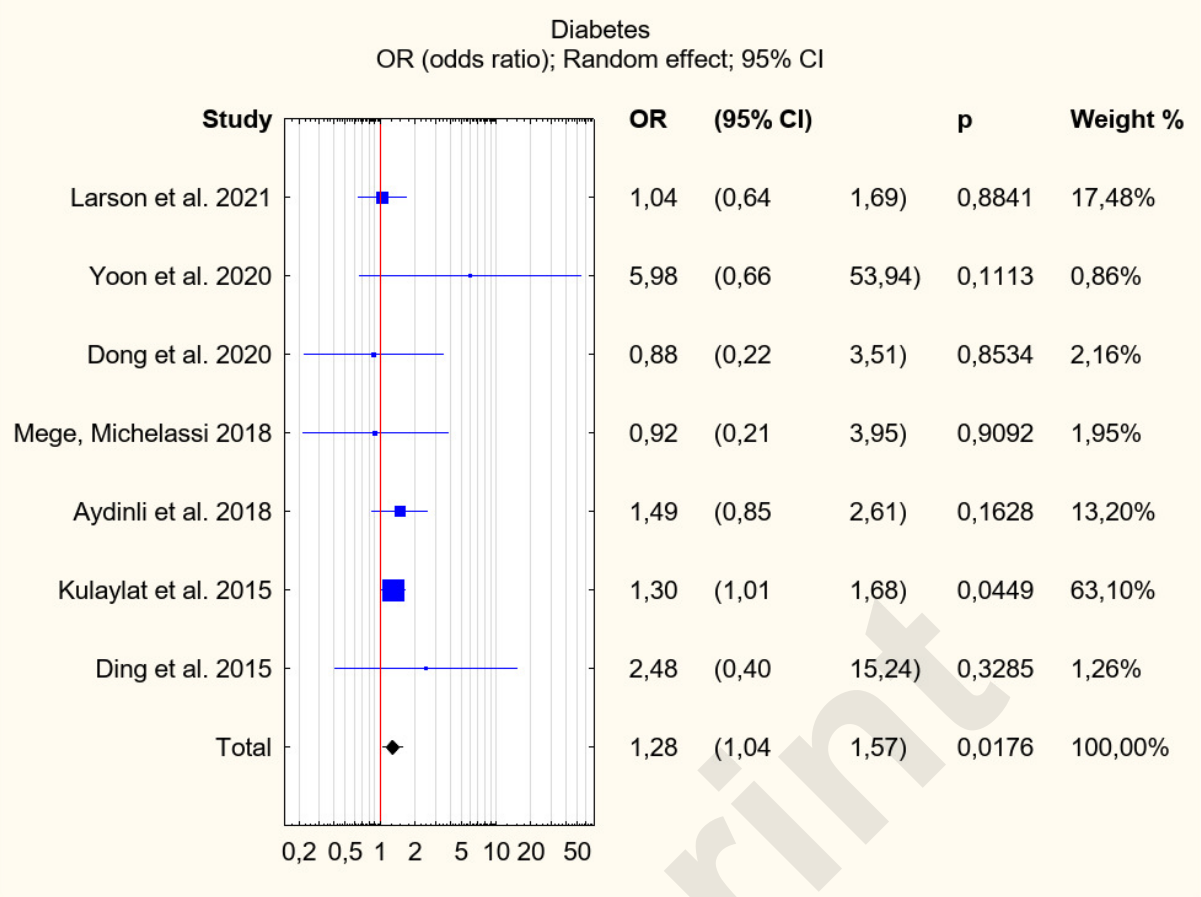

Fig.5 Meta-analysis of early postoperative complications for diabetes.

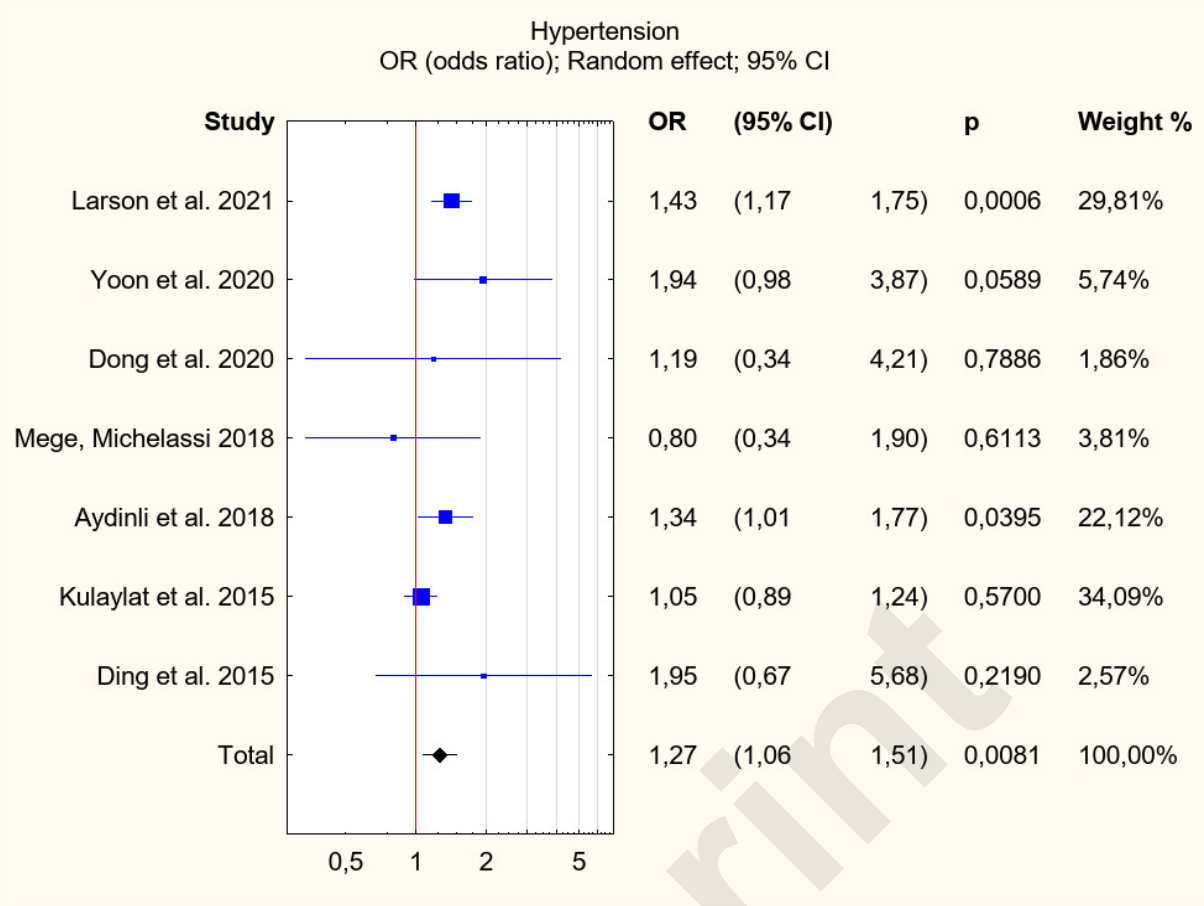

Fig.6 Meta-analysis of early postoperative complications for hypertension.

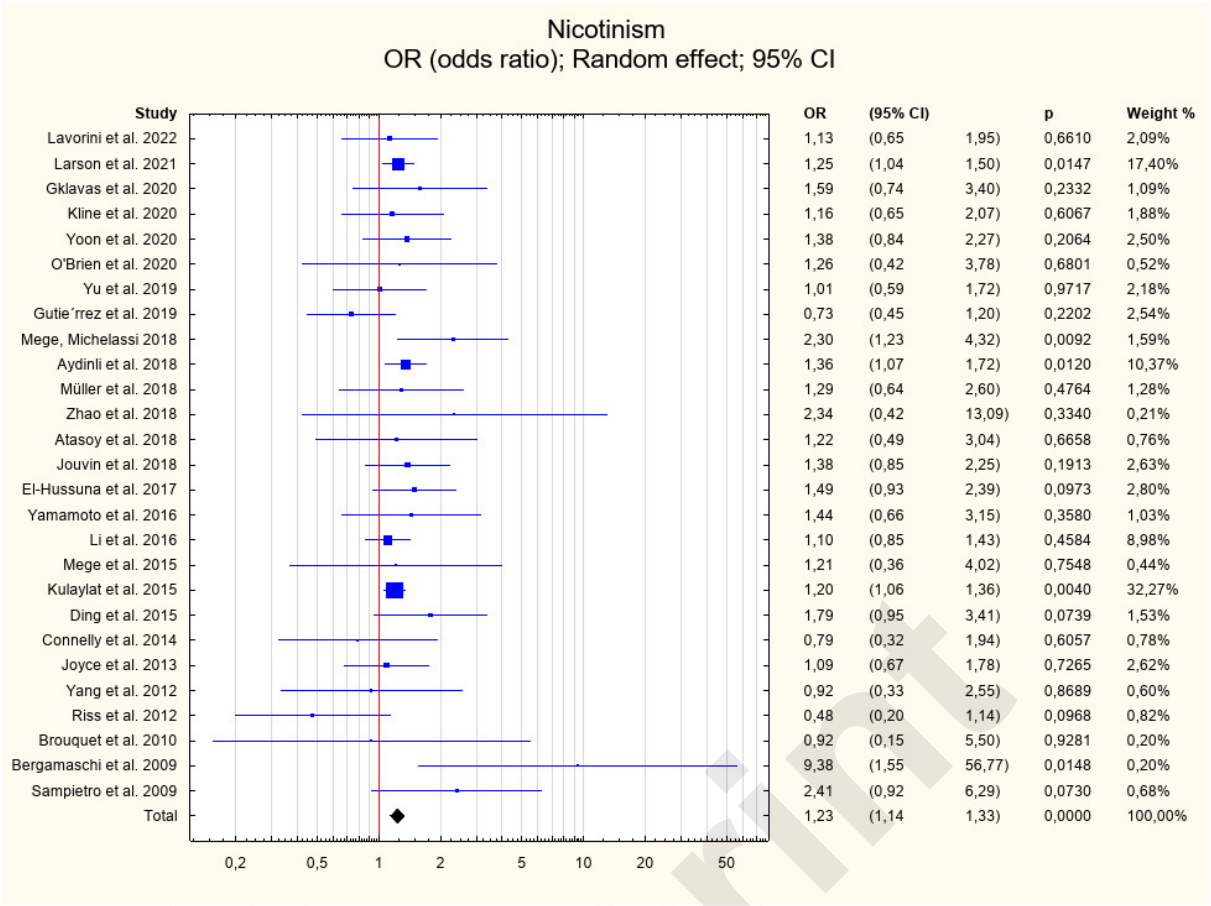

Fig.7 Meta-analysis of early postoperative complications for smoking.

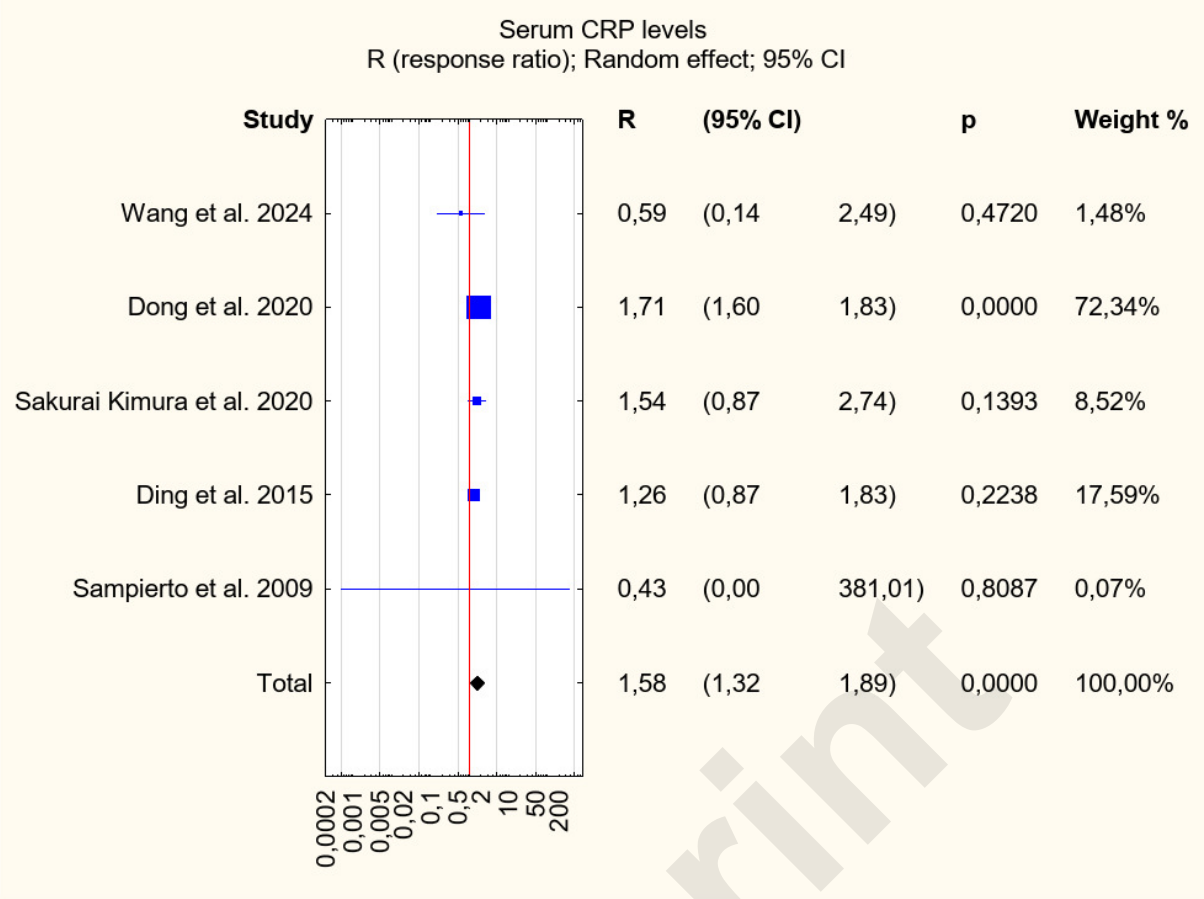

Fig.8 Meta-analysis of early postoperative complications for serum CRP levels.

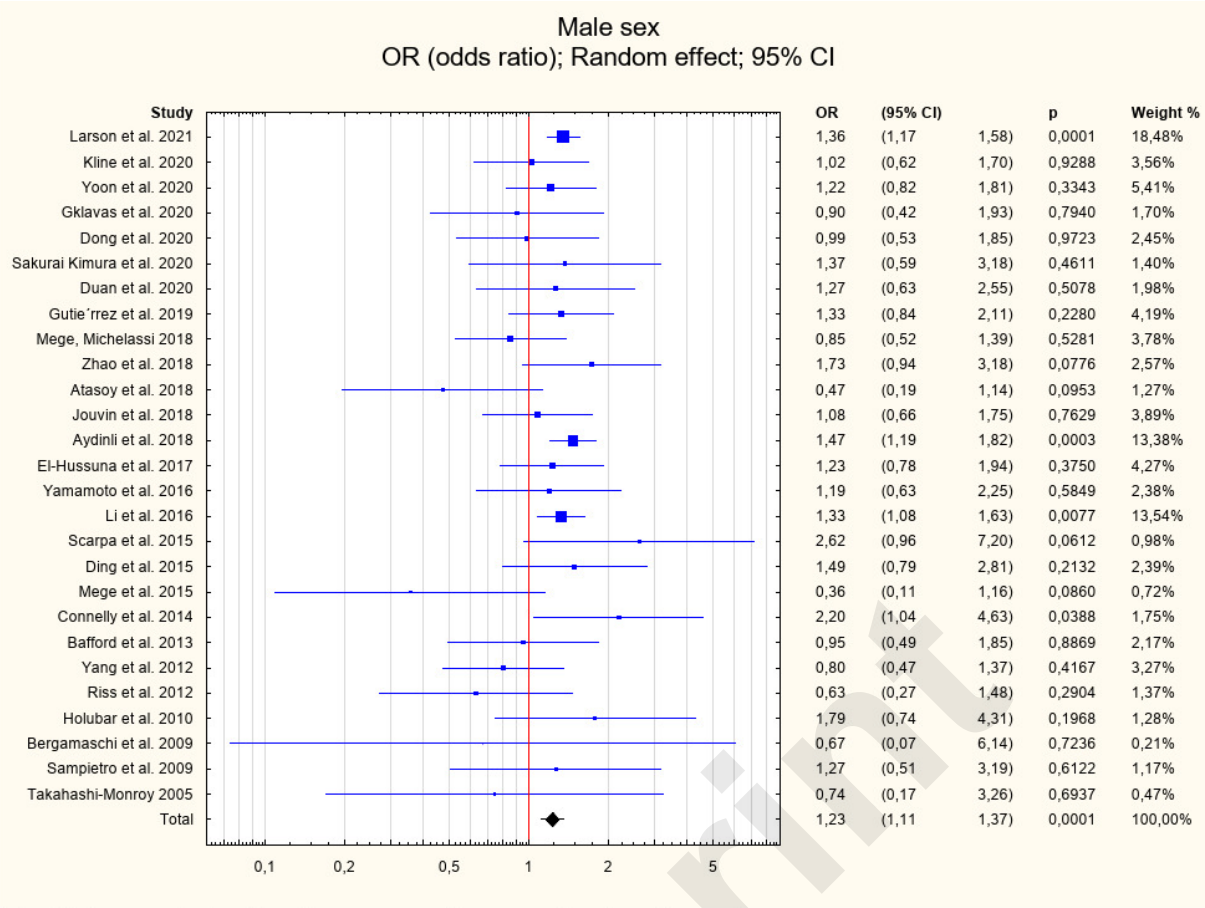

Fig.9 Meta-analysis of early postoperative complications for male sex.

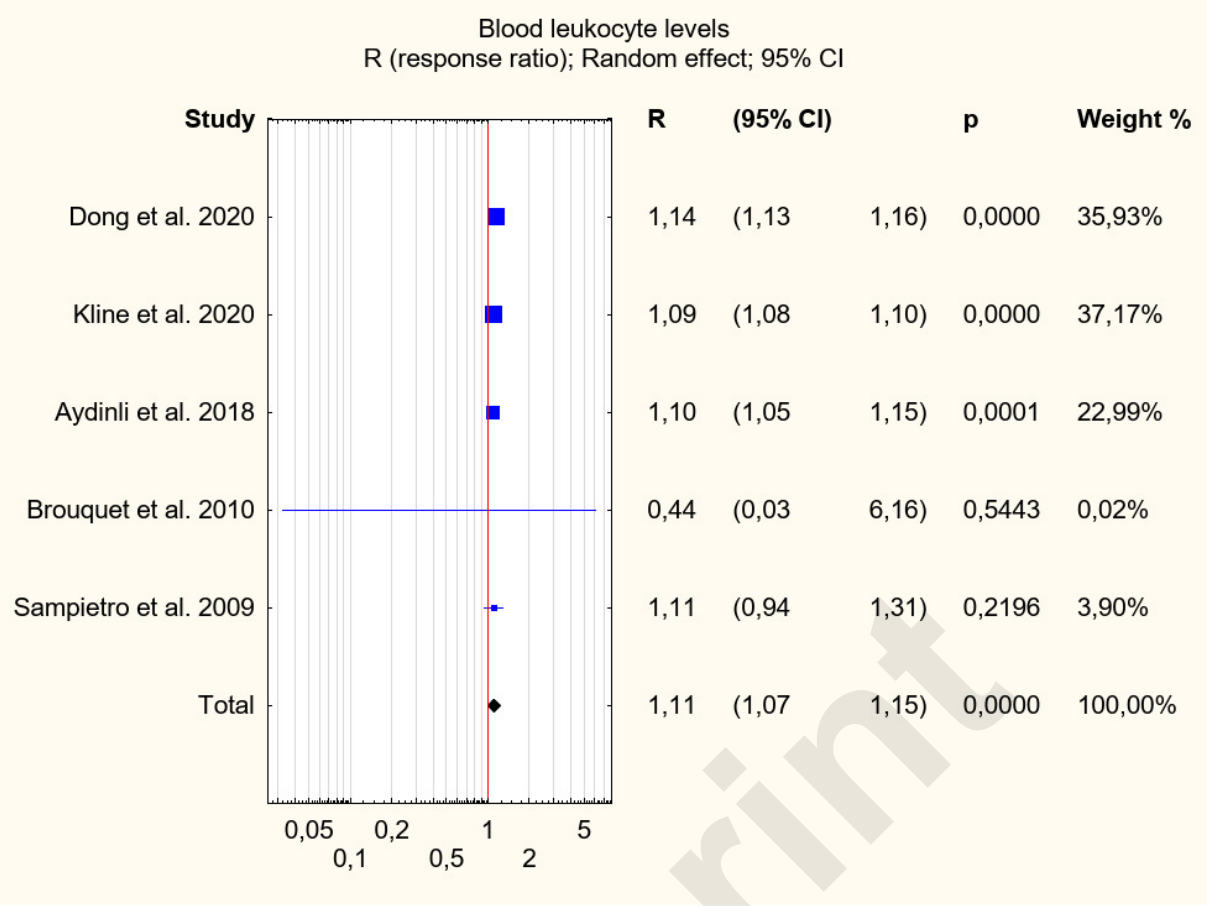

Fig.10 Meta-analysis of early postoperative complications for preoperative blood leukocyte levels.

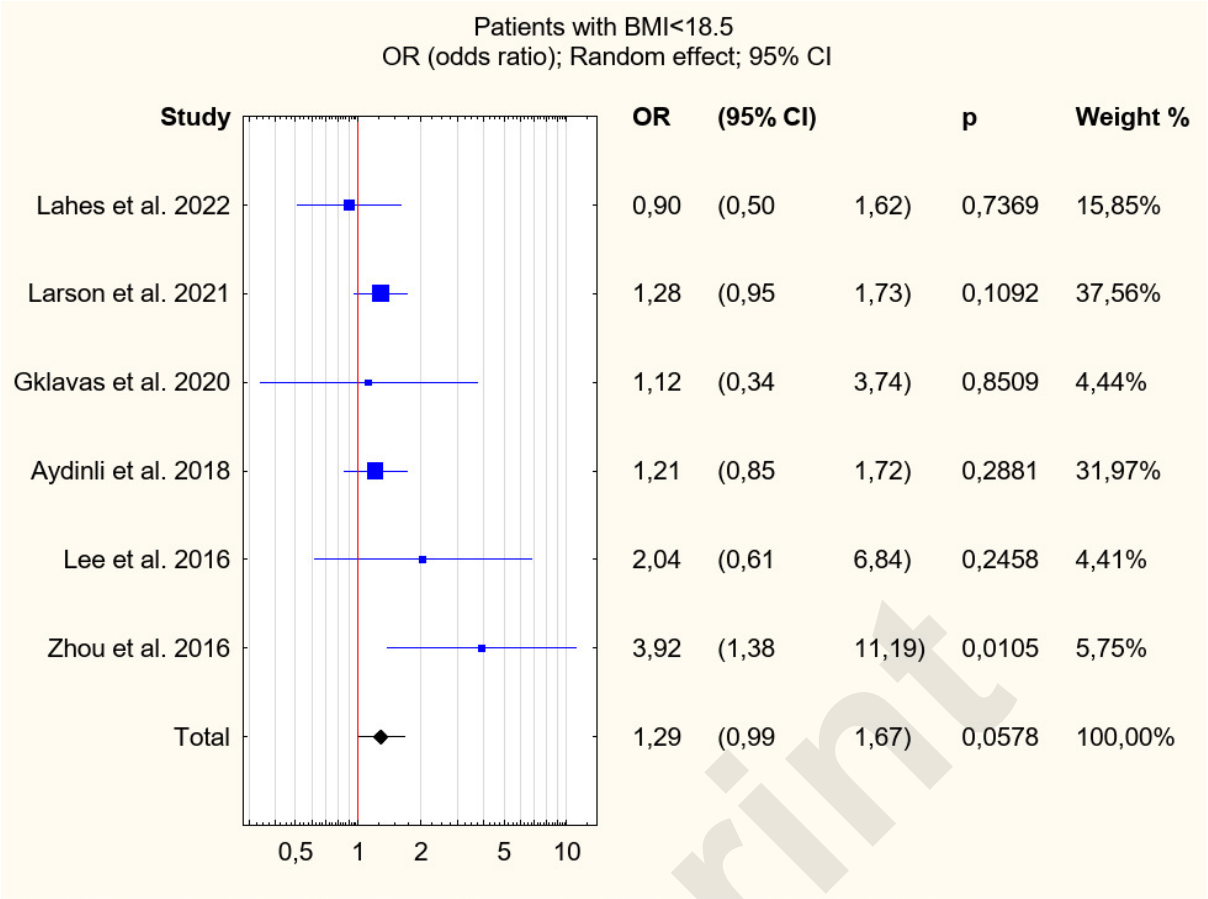

Fig.11 Meta-analysis of early postoperative complications for patients with BMI<18.5.