INPLASY PROTOCOL

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None declared.

Meta-analysis of the neutrophil-to-lymphocyte ratios in inflammatory bowel disease and its disease activity

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Review question / Objective: **The neutrophil-to-lymphocyte ratio (NLR) is associated with the severity of inflammatory bowel disease (IBD). Therefore, we conducted a meta-analysis to evaluate the clinical significance of NLR in patients with IBD and its complications.**
Condition being studied: **Inflammatory bowel disease (IBD), characterized by chronic or relapsing inflammation of the gastrointestinal (GI) tract, is thought to be a relatively common enteropathy worldwide with the highest annual incidence rate of 24.3 per 100,000 person-years for ulcerative colitis (UC) in Europe and the lowest incidence rate of 5 per 100,000 person-years for Crohn's disease (CD) in Asia and the Middle East. Inflammatory Bowel Disease (IBD), which includes both Crohn's disease (CD) and ulcerative colitis (UC), is caused by a complex interplay involving genetic predisposition, environmental factors and an infectious agent. As a systemic disease, people with IBD usually present with a range of clinical features, including fever, malnutrition, and parenteral manifestations. Its clinical manifestations are characterized by recurrent abdominal pain, diarrhea, mucous pus, and blood stool. In addition, most patients with IBD have persistent intestinal mucosal immune system abnormalities, and one-third of patients may have moderate or low fever. The incidence of inflammatory bowel diseases has increased worldwide, and it is now estimated that between 1 and 1.3 million Americans are currently diagnosed with IBD.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 May 2021 and was last updated on 03 May 2021 (registration number INPLASY202150014).

INTRODUCTION

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to evaluate the clinical significance of NLR in patients with IBD and its complications.

Condition being studied: Inflammatory bowel disease (IBD), characterized by chronic or relapsing inflammation of the gastrointestinal (GI) tract, is thought to be a relatively common enteropathy worldwide with the highest annual incidence rate of 24.3 per 100,000 person-years for ulcerative colitis (UC) in Europe and the lowest incidence rate of 5 per 100,000 person-years for Crohn's disease (CD) in Asia and the Middle East. Inflammatory Bowel Disease (IBD), which includes both Crohn's disease (CD) and ulcerative colitis (UC), is caused by a complex interplay involving genetic predisposition, environmental factors and an infectious agent. As a systemic disease, people with IBD usually present with a range of clinical features, including fever, malnutrition, and parenteral manifestations. Its clinical manifestations are characterized by recurrent abdominal pain, diarrhea, mucous pus, and blood stool. In addition, most patients with IBD have persistent intestinal mucosal immune system abnormalities, and one-third of patients may have moderate or low fever. The incidence of inflammatory bowel diseases has increased worldwide, and it is now estimated that between 1 and 1.3 million Americans are currently diagnosed with IBD.

METHODS

Participant or population: Patients with IBD (Inflammatory bowel disease). We initially searched 876 articles, 857 of which were excluded after scanning the titles, abstracts, duplications, and publication types.

Intervention: No.

Comparator: No.

Study designs to be included: No restriction. A comprehensive literature search was conducted by searching the PubMed, Web of Science, Embase, and the Cochrane Library from their inception to April 1, 2021. We used the standard mean difference (SMD) with a 95% confidence interval (CI) to estimate the pooled effect and used subgroup analysis to investigate heterogeneity.

Eligibility criteria: In this essay, two investigators confirmed all correlative studies, and eligible researches were selected by the assessment. At the first level, the titles and abstracts of the identified studies were screened. Full tests were then carefully reviewed. The primary information extracted from each study was as follows: first author, publication year, study region, sample type, number of participants, diagnostic criteria for IBD. mean with SD or median with IQR of NLR, and/or PLR. If important original- data were unavailable in some articles, we contacted the corresponding author by e- mail to obtain further details.

Information sources: As of April 1, 2021, all relevant studies were searched by the electronic database, including PubMed, Web of Science, Embase, and the Cochrane Library. The main search terms were: ("Inflammatory Bowel Disease" OR "Bowel Diseases, Inflammatory" OR "IBD" OR "Ulcerative colitis" OR "Colitis, Ulcerative" OR "UC" OR "Crohn's disease" OR "CD"), AND ("neutrophil to lymphocyte ratio" OR "neutrophil lymphocyte ratio" OR “NLR").

Main outcome(s): The neutrophil-to-lymphocyte ratio. A total of six studies reported the difference 393 UC patients and 429 healthy controls (HCs) in NLR. In active UC patients, we accounted the NLR values is more than HCs (SMD = 1.54, 95% CI = 0.81-2.27, P < 0.001), with high heterogeneity (I2 = 95%, P < 0.001). The same is that the NLR value of inactive UC patients is significantly higher than HCs (SMD = 0.62, 95% CI = 0.04-1.21, P = 0.038), with high heterogeneity (I2 = 93.5%, P < 0.001).

Strategy of data synthesis: Results were expressed as standardized mean differences (SMDs) with 95% confidence intervals (CIs). 0.2–0.5, a small effect; 0.5–

0.8, a medium effect; and ≥ 0.8, a large effect. Heterogeneity among studies was investigated using I2, with I2 > 50% being regarded as significant heterogeneity. The random-effects model was used when significant heterogeneity was observed; otherwise, the fixed-effects model was used. A P-value of less than 0.05 was considered statistically significant. We also conducted a sensitivity analysis to investigate the influence of a single study on the overall risk estimate by omitting one study in turn. Begg's funnel plot and Egger's linear regression tests were performed to assess publication bias. All data were collected using STA TA software (version 14.0; STATA Corp., College Station, TX, USA).

Subgroup analysis: Eleven studies comprising 915 active UC patients and 663 inactive UC patients in NLR. The NLR values in active UC patients were significantly higher than those in inactive UC patients (SMD = 0.96, 95% CI = 0.57-1.34, P < 0.001), with high heterogeneity (I2 = 91.6%, P < 0.001). Six studies reported an association between NLR and CD patients in 616 active CD patients and 483 inactive CD patients. The combined SMD was 0.61 (95% CI: 0.06-1.16, P = 0.030), with high heterogeneity (I2 = 92.1%, P < 0.001).

Sensitivity analysis: The sensitivity analysis of NLR between IBD and HCs showed that the pooled SMD did not materially change when each study was sequentially excluded.

Country(ies) involved: China.

Keywords: Inflammatory bowel disease, Crohn's disease, ulcerative colitis, Neutrophil- to-lymphocyte ratio, Meta-analysis.

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