

INPLASY PROTOCOL

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None.

Neutrophil-to-lymphocyte ratio in relation to the risk of all-cause mortality and cardiovascular events among patients with chronic kidney disease: a systematic review and meta-analysis

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Review question / Objective: Can neutrophil-to-lymphocyte ratio predict the risk of cardiovascular events or all-cause mortality in chronic kidney disease?

Condition being studied: There are many factors that contribute to the setting of the inflammatory status in CKD, including increased production of proinflammatory cytokines, chronic and recurrent infections, oxidative stress and acidosis. Several markers of inflammation such as C-reactive protein, interleukin-6, have been identified as independent predictors of prognosis in CKD patients. These mediators stimulate mesangial and endothelial glomerular cells and subsequently cause an increase in the production and a decrease in the degradation of the mesangial and endothelial extracellular matrix, leading to glomerular hypertension, tubulointerstitial fibrosis and renal scarring. Because chronic inflammation is a major factor in the progression of CKD, evaluating and alleviating the extent of chronic inflammation is important to attenuate the progression of kidney dysfunction. Neutrophil-to-lymphocyte ratio (NLR), which is a very low cost, widely available and standard investigation, has recently emerged as a prognostic marker in cardiac disorders. A growing body of evidence demonstrated NLR was associated with the clinical outcome in CKD patients. However, conclusions of the studies are inconsistent.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 June 2020 and was last updated on 30 June 2020 (registration number INPLASY202060112).

INTRODUCTION

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METHODS

Participant or population: Adults with chronic kidney disease.

Intervention: High neutrophil to lymphocyte ratio and low neutrophil-to-lymphocyte ratio to predict mortality in CKD patients.

Comparator: High neutrophil-to-lymphocyte ratio vs low neutrophil-to-lymphocyte ratio to predict mortality in CKD patients.

Study designs to be included: We will include cohort studies to assess the prognostic value of NLR in CKD.

Eligibility criteria: 1) prospective or retrospective cohort studies; 2) The participants were CKD patients, including end-stage renal disease (ERSD) and dialysis population, and there is no restriction on gender, race, age, occupation; 3) the outcome include any cause of death or the occurrence of major cardiovascular events; 4) providing baseline NLR and multiple adjusted relative

risk (RR) or hazard ratio (HR) with 95% CI for NLR.

Information sources: A comprehensive search was carried out in PubMed, Embase, and Web of Science databases from inception of the study until April 1st, 2020.

Main outcome(s): This meta-analysis indicates a high NLR is related to all-cause mortality and cardiovascular events in patients with chronic kidney disease. Hazard ratios (HRs) with 95% CIs were used as the summary estimate for dichotomous outcomes.

Quality assessment / Risk of bias analysis: A quality assessment of each selected study was carried out by two investigators with a nine-item Newcastle-Ottawa Scale (NOS). The studies are evaluated on three ways using the NOS, namely comparability, selection, and outcome confirmation. The maximum score is nine stars, and NOS scores greater than 6 is considered of high quality. Disagreements between reviewers judgements will be resolved by a third senior reviewer.

Strategy of data synthesis: Data analyses were performed with STATA 15.1. I-squared statistic was used to identify heterogeneity. If $I^2 \geq 50\%$ or $P < 0.05$, a random effect model was applied; otherwise, a fixed effect model was used. In addition, low, moderate, and high levels were nominally applied to define I-squared values as 25%, 50%, and 75%, respectively. Subgroup analyses were conducted to explore the sources of heterogeneity. Publication bias was inspected by a funnel plot. Sensitivity analysis was used to investigate the influence of a single study on the overall risk estimate, and was carried out by sequentially omitting one study. Finally, $P < 0.05$ was considered to be significant difference.

Subgroup analysis: Subgroup analyses were performed according to a priori groupings related to study design, region, age of participants, the value of NLR and CKD stage.

Sensibility analysis: Sensitivity analysis was conducted to investigate the stability of the outcome and was performed by sequentially excluding 1 study at a time.

Country(ies) involved: China.

Keywords: All-cause mortality; Cardiovascular events; Meta-analysis; Neutrophil to lymphocyte ratio.

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