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**ADMINISTRATIVE INFORMATION****Support - No.****Review Stage at time of this submission - Completed but not published.****Conflicts of interest - None declared.****INPLASY registration number: INPLASY202510063****Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 January 2025 and was last updated on 18 January 2025.**INTRODUCTION**

**Review question / Objective** Thus, this meta-analysis was conducted to thoroughly assess the relationship between HALP scores and survival outcomes in digestive system cancer patients by synthesizing data from currently available studies.

**Rationale** Digestive system cancers are a major global health burden, necessitating reliable and cost-effective prognostic biomarkers for clinical decision-making. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score, an integrated immune-nutrition marker, has emerged as a potential prognostic tool in various malignancies. This meta-analysis evaluated the prognostic value of the HALP score in patients with digestive system cancers.

**Condition being studied** Cancer remains a major global health challenge, with malignancies across various organ systems causing significant

morbidity and mortality. Among these, the digestive system, as the primary pathway for nutrient absorption, is particularly vulnerable to malignant transformation, often profoundly disrupting the body's balance. Due to the high incidence and mortality rates of digestive system cancers, extensive efforts have been devoted to improving patient outcomes. In recent years, biomarkers derived from routine blood tests, such as the systemic inflammation response index (SIRI) and pan-immune-inflammation value (PIV), have demonstrated potential in aiding diagnosis and management. These biomarkers provide practical, cost-effective tools for clinical decision-making.

**METHODS**

**Search strategy** We conducted a comprehensive search of PubMed, PMC, and Web of Science databases between September 2024 and November 2024 for relevant English articles published up to November 2024. Two researchers independently searched using the keywords:

("hemoglobin, albumin, lymphocyte, and platelet" OR "HALP") AND ("cancer" OR "tumor" OR "neoplasm" OR "carcinoma"). The reference lists of relevant articles were also reviewed and screened simultaneously.

**Participant or population** The study population consisted of clinical patients diagnosed with digestive system cancers.

**Intervention** Patients were categorized into high and low HALP groups using appropriate cutoff values, and prognostic analyses were conducted.

**Comparator** Patients were categorized into high and low HALP groups using appropriate cutoff values, and prognostic analyses were conducted.

**Study designs to be included** Non-randomized study will be included.

**Eligibility criteria** (1). The study population consisted of clinical patients diagnosed with digestive system cancers. (2). Blood tests were performed prior to treatment, and HALP scores were calculated based on the results. (3). Patients were categorized into high and low HALP groups using appropriate cutoff values, and prognostic analyses were conducted. (4). Studies explicitly defined prognostic endpoints and provided Hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). (5). Studies with clearly defined populations, appropriate statistical analyses, and explicit prognostic endpoints were included. (6). Non-clinical studies, reviews, commentaries, conference abstracts, and similar publications were excluded.

**Information sources** We conducted a comprehensive search of PubMed, PMC, and Web of Science databases.

**Main outcome(s)** Our study demonstrates that higher HALP scores are associated with better survival outcomes.

**Additional outcome(s)** Our study demonstrates that the prognostic value of HALP scores are applicable to multiple cancer types and treatment strategies.

**Data management** The extracted information included fundamental study characteristics such as author name, year of publication, sample size, patient age, sex, study type, cancer type, cancer stage, and HALP cutoff values. Prognostic data for various endpoints were also collected, including overall survival (OS), progression-free survival

(PFS), disease-free survival (DFS), recurrence-free survival (RFS), and cancer-specific survival (CSS).

**Quality assessment / Risk of bias analysis** The quality of the included studies was systematically assessed using the Newcastle-Ottawa Scale (NOS), ensuring the reliability and validity of the analysis. Publication bias was examined by using Egger's test.

**Strategy of data synthesis** HRs with 95% CIs were calculated to evaluate the prognostic significance of the HALP score across various survival outcomes, including OS, DFS, RFS, CSS, and PFS. A random-effects model based on the DerSimonian-Laird method was applied to account for potential between-study heterogeneity.

**Subgroup analysis** This Study was grouped according to treatment strategy, cancer type, cutoff value, sample size, and study region.

**Sensitivity analysis** Sensitivity analyses were conducted to assess the robustness of the pooled estimates by sequentially omitting individual studies.

**Language restriction** English.

**Country(ies) involved** China.

**Keywords** HALP, Cancer, Meta-analysis, Prognosis, Biomarker.

**Contributions of each author**

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Author 2 - Jingting Liu.

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