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Prognostic Value of the Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score in Patients with Urothelial Carcinoma: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202690114

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 September 2026 and was last updated on 25 September 2026.

INTRODUCTION

Review question / Objective Is a low pretreatment hemoglobin, albumin, lymphocyte, and platelet (HALP) score associated with worse survival outcomes, recurrence, and adverse clinicopathological features in patients with urothelial carcinoma?

Rationale Systemic inflammation and nutritional status play important roles in cancer progression and prognosis. The HALP score is a simple composite index calculated from routinely available blood tests, reflecting both nutritional status and systemic inflammatory response. Several studies have reported associations between a low HALP score and poor outcomes in patients with bladder cancer treated with radical cystectomy, transurethral resection, or systemic therapy, and in patients with UTUC treated with radical nephroureterectomy. However, these studies are retrospective, have limited sample sizes, and use different cut-off values, and no meta-analysis has

specifically evaluated the prognostic value of the HALP score in urothelial carcinoma.

Condition being studied Urothelial carcinoma (UC), including non-muscle-invasive, muscle-invasive, and metastatic bladder cancer and upper tract urothelial carcinoma (UTUC).

METHODS

Search strategy PubMed:

(HALP[tiab] OR "hemoglobin, albumin, lymphocyte"[tiab] OR "haemoglobin, albumin, lymphocyte"[tiab] OR "hemoglobin-albumin-lymphocyte-platelet"[tiab] OR "haemoglobin-albumin-lymphocyte-platelet"[tiab]) AND ("Urinary Bladder Neoplasms"[Mesh] OR "Carcinoma, Transitional Cell"[Mesh] OR "Ureteral Neoplasms"[Mesh] OR urothelial[tiab] OR "bladder cancer"[tiab] OR "bladder carcinoma"[tiab] OR "upper tract"[tiab] OR cystectomy[tiab] OR nephroureterectomy[tiab])

Embase:

(halp:ti,ab OR 'hemoglobin, albumin, lymphocyte':ti,ab OR 'haemoglobin, albumin, lymphocyte':ti,ab OR 'hemoglobin-albumin-lymphocyte-platelet':ti,ab) AND ('bladder cancer'/exp OR 'urothelial carcinoma'/exp OR urothelial:ti,ab OR 'bladder cancer':ti,ab OR 'upper tract':ti,ab OR cystectomy:ti,ab OR nephroureterectomy:ti,ab)

Web of Science:

TS=(HALP OR "hemoglobin, albumin, lymphocyte" OR "haemoglobin, albumin, lymphocyte" OR "hemoglobin-albumin-lymphocyte-platelet") AND TS=(urothelial OR "bladder cancer" OR "bladder carcinoma" OR "upper tract" OR cystectomy OR nephroureterectomy)

Cochrane Library:

(HALP OR "hemoglobin, albumin, lymphocyte"):ti,ab,kw AND (urothelial OR bladder):ti,ab,kw.

Participant or population Adult patients (aged 18 years or older) with histologically confirmed urothelial carcinoma of the bladder or upper urinary tract, regardless of disease stage or treatment modality (surgery, intravesical therapy, chemotherapy, immunotherapy, or antibody-drug conjugates).

Intervention Low pretreatment HALP score, as defined by the cut-off value used in each study. The HALP score is calculated as: hemoglobin (g/L) × albumin (g/L) × lymphocyte count (/L) / platelet count (/L).

Comparator High pretreatment HALP score according to the same cut-off value.

Study designs to be included Prospective or retrospective cohort studies that report the association between the pretreatment HALP score and survival, recurrence, or treatment response.

Eligibility criteria Inclusion criteria: (1) patients with histologically confirmed urothelial carcinoma; (2) HALP score measured before treatment; (3) patients stratified into low and high HALP groups by a defined cut-off value; (4) reporting of HRs with 95% CIs for at least one survival or recurrence outcome, ORs for treatment response, or sufficient data to estimate them; (5) full-text articles published in English.

Exclusion criteria: (1) reviews, case reports, letters, editorials, and animal studies; (2) conference abstracts without sufficient data; (3) studies of non-urothelial histology or benign urological conditions; (4) overlapping patient populations, in which case only the largest or most recent study will be included.

Information sources PubMed/MEDLINE, Embase, Web of Science Core Collection, and the Cochrane Library will be searched from inception to the date of the final search. The reference lists of included studies and relevant reviews will be manually screened to identify additional eligible studies.

Main outcome(s) Overall survival (OS), expressed as HRs with 95% CIs. Multivariable-adjusted HRs will be preferred when available.

Additional outcome(s) Cancer-specific survival (CSS), recurrence-free survival (RFS), progression-free survival (PFS), intravesical recurrence after radical nephroureterectomy, response to neoadjuvant chemotherapy, and the association between the HALP score and clinicopathological features (e.g., tumor stage, grade, lymph node status), expressed as HRs or ORs with 95% CIs.

Data management Search results will be imported into EndNote, and duplicates will be removed. Two reviewers will independently screen titles and abstracts, followed by full-text assessment. Data will be extracted independently by two reviewers using a standardized form, including first author, publication year, country, study design, sample size, age, sex, tumor location (bladder or upper tract), disease stage, treatment modality, HALP cut-off value and method of determination, follow-up duration, and HRs or ORs with 95% CIs for each outcome (univariable and multivariable). Disagreements will be resolved by discussion or by consultation with a third reviewer. When HRs are not directly reported, they will be estimated from Kaplan-Meier curves using the method described by Tierney et al.

Quality assessment / Risk of bias analysis The methodological quality of included studies will be assessed independently by two reviewers using the Newcastle-Ottawa Scale (NOS); studies scoring 7 or higher will be considered high quality. The certainty of evidence for each outcome will be rated using the GRADE approach.

Strategy of data synthesis Log-transformed HRs and their standard errors will be pooled using the inverse-variance method; ORs will be pooled for treatment response and clinicopathological features. Outcomes reported in at least two studies will be pooled. Heterogeneity will be assessed using Cochran's Q test and the I^2 statistic. A random-effects model will be used when $I^2 > 50\%$ or $P < 0.10$; otherwise, a fixed-effect model will be applied. Outcomes that cannot be pooled will be described narratively. Statistical analyses will be performed using R software (meta package) or

Stata. A two-sided P value < 0.05 will be considered statistically significant.

Subgroup analysis Where data allow, subgroup analyses will be performed according to tumor location (bladder cancer vs UTUC), disease stage (non-muscle-invasive, muscle-invasive, or metastatic), treatment modality (surgery vs systemic therapy), HALP cut-off value, region, and type of analysis (univariable vs multivariable).

Sensitivity analysis Leave-one-out sensitivity analyses will be conducted by sequentially removing each study. Additional sensitivity analyses will be restricted to high-quality studies (NOS ≥ 7) and to studies reporting multivariable-adjusted HRs. Publication bias will be assessed using funnel plots and Egger's test when at least 10 studies are available; otherwise, it will be discussed qualitatively.

Language restriction English.

Country(ies) involved China.

Other relevant information This review will be conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. Any amendments to this protocol will be documented and reported in the final publication.

Keywords HALP score; hemoglobin; albumin; urothelial carcinoma; bladder cancer; prognosis; meta-analysis.

Dissemination plans The results will be submitted to a peer-reviewed journal for publication.

Contributions of each author

Author 1 - Guowei Liu - Conceived the review, designed the search strategy, performed literature screening and data extraction, conducted the statistical analysis, and drafted the manuscript.

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Author 2 - He Zhang - Independently performed literature screening, data extraction, and quality assessment.

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Author 3 - Jinsheng Wu - Supervised the study, resolved disagreements as the third reviewer, and critically revised the manuscript.

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