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Author Affiliation:Kahramanmaraş Sutcu Imam
University.**Systemic Inflammatory and Nutritional Indices in
Chronic Subdural Hematoma: A Systematic Review
and Meta-Analysis**

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ADMINISTRATIVE INFORMATION**Support** - This systematic review and meta-analysis received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.**Review Stage at time of this submission** - Completed but not published - The review is complete but not yet submitted for publication: data extraction, ROBINS-I risk-of-bias assessment, meta-analysis, and GRADE certainty-of-evidence assessment have all been finished, and a manuscript draft exists. This protocol is being registered retrospectively, after these stages were completed. The delay occurred because the research team recognized the value of a transparent, publicly accessible registry entry only after data extraction and analysis were substantially complete; prospective registration (e.g., PROSPERO, which requires registration before data extraction begins) was therefore no longer eligible. No eligibility criteria, outcome definitions, or analysis methods were altered based on the results obtained after the fact; the only pre-specified analytic decision applied post hoc was the fallback from a random-effects to a fixed-effects model for the PNI-recurrence pool, made solely due to technical non-convergence with only two studies (unrelated to the direction or magnitude of the result). Methodological rigor consistent with PRISMA 2020 reporting standards was maintained throughout, including a structured PECOS framework, ROBINS-I risk-of-bias assessment, and GRADE certainty rating.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202680065**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 August 2026 and was last updated on 17 August 2026.**INTRODUCTION****Review question / Objective** Population: Adult patients with chronic subdural hematoma (CSDH) treated surgically (burr-hole drainage or craniotomy).

Exposure/Index: Systemic (peripheral blood) inflammatory and nutritional indices (NLR, PLR, SII, SIRI, PNI, NPAR, MLR, RPR, CONUT, GNRI,

NRS-2002, PIV, CRP, eosinophil count, eosinophil-to-platelet ratio, Mini Nutritional Assessment).

Comparator: Low vs. high index level (cut-off or continuous), or patients with vs. without the outcome of interest.

Outcome: Primary — CSDH recurrence/reoperation. Secondary — functional outcome, disease presence/severity, morbidity/mortality/length of hospital stay.

Rationale Chronic subdural hematoma has a relatively high recurrence rate after surgical evacuation. Systemic inflammatory and nutritional indices are inexpensive, widely available blood-based biomarkers increasingly studied as prognostic markers across neurosurgical and oncological conditions. Existing reviews on CSDH biomarkers (a 2023 scoping review and a 2021 meta-analysis) either excluded systemic inflammatory/nutritional indices entirely or focused only on radiological recurrence predictors; a 2022 umbrella review of CSDH recurrence risk factors predates most publications on newer indices such as PIV, NPAR, and RPR. No prior work has systematically and quantitatively synthesized the relationship between systemic inflammatory/nutritional indices and CSDH outcomes.

Condition being studied Chronic subdural hematoma (CSDH) in adult patients undergoing surgical treatment.

METHODS

Search strategy PubMed/MEDLINE was searched using a string combining three blocks: (1) CSDH terms (MeSH: "Hematoma, Subdural, Chronic"; free text: "chronic subdural hematoma/haematoma", "CSDH"), (2) 13 systemic inflammatory/nutritional index terms (NLR, PLR, SII, SIRI, PNI, NPAR, MLR, "inflammatory index/marker*", "hematologic/hematological index*", "blood cell ratio*", "systemic inflammation"), (3) outcome terms ("recurrence/recurrent/residual", "prognosis", "outcome*", "mortality", "functional outcome*"). Search was run on 15 August 2026 and returned 16 results.

Search was supplemented by Web of Science Core Collection and Cochrane CENTRAL (full searches), citation/reference mining (snowballing), and a supplementary cross-check via Elicit/Semantic Scholar. A Scopus search (449 results, run 16 August 2026) was retrieved and processed as a post-hoc supplementary check: after deduplication against the primary search results (17/51 keyword-matched candidates were already captured, cross-validating the primary search strategy), 34 new candidates were screened at title level and the 10 highest-priority candidates were assessed via full text. All 10 were determined ineligible under the pre-specified PECOS criteria (wrong exposure type — local/hematoma-fluid rather than systemic/peripheral-blood biomarkers; wrong outcome type — disease-occurrence/diagnosis case-control design rather than recurrence within an already-diagnosed CSDH cohort; or exposure not meeting the composite-index definition — raw platelet count alone). No

new studies were added to the evidence base as a result of the Scopus search. Embase access was attempted directly via embase.com on 16 August 2026; the research team confirmed it does not have institutional access (no subscription/login available), so no Embase search could be executed. A draft search string was prepared for potential future use should access become available, but it was never run. This remains a disclosed methodological limitation.

Participant or population Adult patients (surgically treated for CSDH). Observational studies (cohort or case-control-type comparisons) only; randomized controlled trials, case reports, and reviews without primary data were excluded.

Intervention Measurement of one or more systemic inflammatory/nutritional indices (see PICO above) in peripheral blood, analyzed as a predictor of CSDH recurrence or other clinical outcomes. This is a prognostic-factor review, not an intervention-effect review; no causal claims are made.

Comparator Low vs. high index value (by reported cut-off or as a continuous variable), or comparison between patients with vs. without the outcome of interest.

Study designs to be included Observational studies (cohort studies, case-control-type comparisons). Excluded: randomized controlled trials where the exposure was a therapeutic agent, case reports, systematic/scoping reviews without primary data, studies assessing only local (hematoma fluid) biomarkers, studies assessing only raw cell counts without a composite index, studies focused only on coagulation parameters (PT/aPTT/fibrinogen), and studies where full-text access could not be obtained to verify eligibility.

Eligibility criteria Inclusion: adult CSDH patients treated surgically; at least one systemic inflammatory/nutritional index reported; an effect estimate (OR/aOR or extractable raw data) for at least one outcome of interest.

Exclusion: case reports; RCTs testing a pharmacological/anesthetic exposure; studies without primary data; studies assessing only local/hematoma-fluid biomarkers; studies unable to be verified via full text.

Information sources PubMed/MEDLINE, Web of Science Core Collection, Cochrane CENTRAL, Elicit/Semantic Scholar (supplementary), Scopus (search run and fully processed as a post-hoc supplementary check — see Search strategy and

limitations above). Embase access was attempted (16 August 2026) but the research team confirmed it has no institutional subscription; no search could be executed. PubMed/MEDLINE, Web of Science Core Collection, Cochrane CENTRAL, Elicit/Semantic Scholar (supplementary), Scopus (search run and fully processed as a post-hoc supplementary check — see Search strategy and limitations above). Embase was not accessible (institutional access not available).

Main outcome(s) Primary: CSDH recurrence/reoperation. Secondary: functional outcome, morbidity, mortality, length of hospital stay.

Data management Screening and full-text eligibility assessment were conducted primarily by a single reviewer (with AI-assisted screening support), which does not fully meet the Cochrane-recommended standard of two independent reviewers. This is explicitly disclosed as a methodological limitation. A second independent risk-of-bias review is being considered as a future addition.

Quality assessment / Risk of bias analysis ROBINS-I (Risk Of Bias In Non-randomised Studies of Interventions) was applied as a single-reviewer preliminary assessment for studies with accessible full text. A second independent reviewer has not yet been involved; this is disclosed as a limitation.

Strategy of data synthesis For each index-outcome combination, the number of independent studies was counted a priori. Combinations with ≥ 3 independent studies were pooled by generic inverse-variance meta-analysis (random-effects, REML; pre-specified fallback to fixed-effect model in case of technical non-convergence related to small study number). Combinations with < 3 studies were reported narratively using Synthesis Without Meta-analysis (SWiM). Heterogeneity was assessed via I^2 , Cochran's Q, and τ^2 . Analyses were conducted in jamovi (v2.7, MAJOR module). Leave-one-out sensitivity analysis and GRADE certainty-of-evidence assessment were additionally performed for both pooled estimates.

Subgroup analysis No formal subgroup analyses were pre-specified given the limited number of pooled studies (2-3 per combination). Where studies used differing recurrence definitions (imaging-based asymptomatic growth vs. symptomatic/reoperation-requiring growth) or mixed acute/chronic populations, this heterogeneity is discussed narratively rather than via formal subgroup meta-analysis.

Sensitivity analysis Leave-one-out sensitivity analysis was performed for both pooled estimates (NLR-recurrence and PNI-recurrence), removing one study at a time and recalculating pooled estimates using both fixed-effect and DerSimonian-Laird random-effects formulas.

Language restriction No formal language restriction was pre-specified; all identified studies to date were published in English.

Country(ies) involved Turkey.

Other relevant information This review has several disclosed methodological limitations: (1) retrospective registration (see above); (2) single-reviewer screening and data extraction; (3) Embase access was attempted directly (16 August 2026) and confirmed unavailable due to lack of institutional subscription, so no Embase search could be executed; a supplementary Scopus search (n=449) was completed post-hoc and cross-validated the primary search strategy (17/51 keyword-matched candidates were already captured by the primary search) but did not add any new eligible studies after full-text screening of the 10 highest-priority candidates; (4) both pooled meta-analyses were rated as Very Low certainty (GRADE) due to small study numbers, high inconsistency (NLR pool), and imprecision; (5) possible patient-cohort overlap could not be definitively ruled out for three pairs of studies sharing overlapping authorship/institutions: Matsubara et al. 2023 and Yagi et al. 2025 (eosinophil-platelet ratio), both included in the narrative synthesis, plus a third publication from the same research group (Yagi et al. 2023, excluded on exposure-type grounds) that reinforces this concern; Serrato et al. 2024 (GNRI), included as supportive/sensitivity-level evidence, and a title/author-overlapping 2026 publication excluded from the review; and Zhu et al. 2023 (PNI), one of only two studies in the primary quantitative PNI-recurrence pooled estimate, and a same-year, same-author-team publication excluded from the review on outcome-type grounds. Cohort independence was not confirmed directly with the study authors; this is disclosed as an unresolved limitation and is discussed further in the manuscript. These limitations are transparently reported in the manuscript's Discussion/Limitations section.

Keywords chronic subdural hematoma; recurrence; neutrophil-to-lymphocyte ratio; prognostic nutritional index; systemic inflammation; meta-analysis.

Dissemination plans Results will be submitted for peer-reviewed publication (target journal: Turkish Neurosurgery).

Contributions of each author

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