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Circulating biomarkers and imaging-defined myosteatosis: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 June 2026 and was last updated on 23 June 2026.

INTRODUCTION

Review question / Objective To determine whether, given the methods currently used to diagnose myosteatosis, any circulating biomarker can be established as a reliable correlate of imaging-defined myosteatosis or imaging-derived muscle quality in adults. Specific objectives: (1) to synthesise compatible effect-measure families without conflating survival outcomes; (2) to compare cancer and non-cancer settings where data allow; (3) to quantify the impact of risk of bias, measurement heterogeneity, transformed data, and source discrepancies; and (4) to determine whether the available evidence is consistent enough to support any biomarker for prospective clinical validation.

Rationale Myosteatosis (imaging-detected skeletal-muscle fat infiltration) is a clinically important marker of muscle quality associated with adverse outcomes, but direct imaging-based assessment requires appropriate scans, segmentation, and anatomical standardisation. Accessible circulating biomarkers (e.g., albumin, CRP, NLR, PLR, PNI, haemoglobin, creatinine-to-cystatin C ratio) have been proposed as correlates, yet the literature is fragmented across populations, imaging modalities and anatomical levels, operational definitions and cut-offs, and effect measures. Whether any consistent biomarker–myosteatosis association can be established against this methodological heterogeneity is unclear.

Condition being studied Myosteatosis — abnormal accumulation of lipid within and between skeletal-muscle fibres — operationalised as reduced muscle radiodensity (attenuation) on CT, increased intramuscular/intermuscular adipose tissue, or an analogous MRI or peripheral quantitative CT measure of skeletal-muscle quality, in adult cancer and non-cancer populations.

METHODS

Participant or population Adults (≥18 years) in cancer or non-cancer populations (community/

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general, hepatic, critical illness, systemic sclerosis, cardiovascular, and other disease-specific cohorts). Paediatric studies excluded.

Intervention At least one pre-specified candidate circulating biomarker, including serum albumin, C-reactive protein, the neutrophil-to-lymphocyte ratio, the platelet-to-lymphocyte ratio, the prognostic nutritional index, haemoglobin, and the creatinine-to-cystatin C ratio (additional candidate analytes are enumerated in the search strategy).

Comparator Where applicable, participants with versus without myosteatosis, or lower versus higher biomarker level; for continuous analyses, the association across the biomarker range. As an observational association review, no interventional comparator applies.

Study designs to be included Cohort and analytical cross-sectional studies reporting an extractable association between a circulating biomarker and an imaging-defined myosteatosis / muscle-quality phenotype. Case reports, reviews, narrative-only reports, paediatric, and non-human studies were excluded.

Eligibility criteria Eligible reports enrolled adults in cancer or non-cancer populations; measured at least one pre-specified candidate circulating biomarker; assessed myosteatosis or skeletal-muscle quality using CT, MRI, or peripheral quantitative CT; and reported an extractable biomarker–imaging association. Cohort and analytical cross-sectional designs were eligible. Excluded from quantitative synthesis: studies reporting only muscle quantity, sarcopenia without a separable myosteatosis measure, narrative significance without an extractable estimate, or survival associations without a biomarker–myosteatosis estimate. Paediatric studies, case reports, reviews, and non-human studies were excluded.

Information sources PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov, from inception to 11 August 2025; reference lists of eligible reports. No language or date restrictions.

Main outcome(s) The presence, severity, or continuous imaging measure of myosteatosis or skeletal-muscle quality (e.g., muscle radiodensity/attenuation, intramuscular/intermuscular adipose tissue), analysed as its association with circulating biomarkers. Mortality, recurrence, complications, and treatment outcomes were outside the quantitative question.

Quality assessment / Risk of bias analysis Risk of bias was assessed independently by two reviewers, with disagreements resolved by discussion. QUIPS (Quality In Prognosis Studies) was the primary domain-based instrument (six domains: study participation, attrition, prognostic factor measurement, outcome measurement, confounding, and statistical analysis/reporting). The Newcastle-Ottawa Scale (cohort and adapted cross-sectional versions) was applied as a supplementary study-level sensitivity instrument only. Study-level QUIPS judgements were extended to individual effect estimates using pre-specified rules (greater concern for unadjusted effects, data-driven thresholds, non-standard or indirect definitions, transformed summary statistics, and unresolved source discrepancies).

Strategy of data synthesis For analysis families with at least two compatible independent estimates, random-effects models were fitted by restricted maximum likelihood (REML); ratio measures on the log scale and correlations after Fisher-z transformation. The primary 95% confidence interval used a modified Hartung-Knapp procedure with a variance safeguard and k−1 degrees of freedom. Effect-measure families were never combined across estimand types; any family with $I^2 > 75\%$ and fewer than four studies was labelled hypothesis-generating. Heterogeneity was summarised with tau^2, Cochran Q, and I^2 (interpreted only as a flag for $k \leq 5$); prediction intervals were reported only for $k \geq 5$. Certainty was graded with a rules-based adapted GRADE approach for prognostic-factor evidence. Pooled estimates, modified Hartung-Knapp intervals, and heterogeneity statistics were verified by independent re-computation in Python (Fisher-z transformation; Paule-Mandel sensitivity estimator).

Subgroup analysis Pre-specified mixed-effects subgroup analyses evaluated albumin by cancer status and categorical NLR by cancer type (colorectal vs other), using interaction p-values with Holm correction and a common residual tau^2.

Sensitivity analysis Sensitivity analyses restricted estimates by QUIPS and NOS risk, confounding and reporting domains, measurement standardisation, and source quality; leave-one-out and influence diagnostics assessed the stability of every pooled estimate. Funnel-plot and Egger tests were not performed because no family reached ten studies.

Language restriction None.

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Country(ies) involved Taiwan.

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