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Evaluating The Prognostic Value Of C-Reactive Protein And Albumin Biomarkers In Breast Cancer Patients: Systematic Review

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Abstract

Background: Current prognostic tools for breast cancer, such as TNM staging, have limitations in capturing the systemic inflammatory and nutritional dimensions of the disease, which significantly influence patient outcomes. Inflammatory markers like C-reactive protein (CRP) and albumin, as well as their composite scores, have emerged as promising, cost-effective prognostic tools.

Objective: This systematic review and meta-analysis aimed to comprehensively evaluate the prognostic value of CRP, albumin, the CRP-to-albumin ratio (CAR), and related composite scores (mGPS, PNI) in breast cancer patients, and to synthesize evidence on interventions that modify these biomarkers.

Methods: A PRISMA-compliant systematic review was conducted. A comprehensive search of PubMed and the Cochrane Library (2010–2024) identified observational studies and randomized controlled trials (RCTs) reporting associations between these biomarkers and survival outcomes (OS, PFS, DFS). Data on study characteristics, biomarker measurements, and clinical outcomes were extracted. Quality was assessed using Cochrane RoB 2 tool.

Results: The synthesis of evidence from 27 studies demonstrated robust prognostic significance for CRP and albumin. Elevated CRP predicted shorter progression-free survival in metastatic disease (e.g., during CDK4/6 inhibitor therapy) and increased breast cancer risk in pre-diagnostic settings. Low serum albumin was a strong, independent predictor of worse disease control, DFS, and OS across all stages. Composite scores integrating both markers—notably the modified Glasgow Prognostic Score (mGPS) and CAR—showed superior prognostic power. Patients with mGPS 2 had a more than twofold increased mortality risk (HR = 2.056) and a drastically reduced 10-year OS (22% vs. 71% for mGPS 0). RCTs confirmed the modifiability of CRP through interventions such as weight loss (35–44% reduction), exercise (~30% reduction), and specific supplements (synbiotics, ω-3 fatty acids).

Conclusion: CRP, albumin, and their derived ratios provide significant, independent prognostic information beyond traditional staging in breast cancer. Their integration into clinical practice offers a

simple, cost-effective strategy for enhanced risk stratification, treatment response monitoring, and personalized supportive care. The demonstrated modifiability of these biomarkers through lifestyle and pharmacological interventions opens avenues for novel therapeutic strategies aimed at improving patient outcomes.

Introduction:

Breast cancer is the most common cancer in women globally and a leading cause of cancer-related deaths. It primarily originates in the ductal or lobular epithelium, with risk factors well-documented in Western populations, where screening programs facilitate early detection. However, in developing regions, symptomatic presentation (e.g., breast mass, nipple discharge) remains common. Diagnosis relies on clinical examination, imaging, and biopsy, with treatment options including surgery, chemotherapy, radiation, and targeted therapies guided by tumor characteristics. Despite advancements, prognosis varies significantly based on stage, molecular markers, and treatment response[1].

Epidemiologically, breast cancer accounts for 11.7% of global cancer cases, predominantly affecting women over 40, with a median diagnosis age of 61[2]. Incidence peaked around 2000 but has since declined, particularly in women under 50, due to improved screening and therapies. Mortality rates have dropped in high-income regions, yet disparities persist in low-resource settings. In the U.S., 1 in 8 women will develop breast cancer, underscoring its public health burden. Early detection remains critical, as survival rates correlate strongly with tumor size and stage at diagnosis[1].

Prognosis in breast cancer is heavily influenced by TNM staging, where stages 0–3 are potentially curable, while stage 4 (metastatic) is incurable, with a median survival of ~21.7 months. Tumor size significantly impacts outcomes: <1 cm tumors show 99% 5-year survival, whereas 3–5 cm tumors drop to 86%. Widespread mammography screening has reduced average tumor size (<2 cm), improving survival rates. However, metastatic disease remains a major challenge, highlighting the need for better prognostic biomarkers, such as C-reactive Protein and albumin, to refine risk stratification and personalize treatment[3].

The relationship between chronic inflammation and cancer is complex and bidirectional. The mechanisms through which chronic inflammation might lead to cancer have been detailed elsewhere and include DNA damage and genomic, epigenomic, and cellular alterations and interactions [4], [5]. Regular use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) has been consistently associated with reduced risk of cancers, including breast cancer [6], and reduced breast cancer risk in high-risk women with BRCA1 and BRCA2 mutations [7]. These observations provide indirect evidence of a potential link between inflammation and risk of developing breast cancer[8].

Measuring systemic chronic inflammatory markers in the blood may be one way of understanding the role of inflammation in breast cancer risk and might provide intermediate outcome markers in prevention studies. Inflammatory markers, such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF- α) are shown to markedly increase in response to infection and tissue damage, as well as in active state of disease [8], [9].

CRP is one of the most lengthily studied inflammation marker in cancer [10]. CRP level above 10 mg/L is commonly recognized as a sign of acute inflammation whereas lower readings are exhibited in low-grade chronic inflammation [11]. For breast cancer (BCa), CRP has been suggested as a long-term prognostic marker due to its consistent association [12], [13]. Pre-treatment elevated CRP upon diagnosis was linked with increased BCa mortality [14]. In post-diagnosis stage, elevated CRP was associated with poorer survival in several cancer including BCa, signifying the implication of inflammation towards cancer progression [10], [15].

Albumin has also been detected as predictive of CRP and this concurred a previous finding among pre-treatment, advanced pancreatic cancer patients that showed that albumin was inversely associated with CRP

(r= −0.387; P < 0.001)[16]. CRP and albumin were commonly produced in the liver, regulated by interleukin-6-promoted inflammation and has been demonstrated to be independent prognostic factor of BCa survival [17]. Elevated CRP levels and low serum albumin during diagnosis significantly and adversely affected BCa survival [14], [18].

C-reactive protein (CRP) and albumin are key biomarkers reflecting systemic inflammation and nutritional status, both of which influence breast cancer progression and outcomes[19]. The CRP-to-albumin ratio (CAR) combines these markers, offering a stronger prognostic tool than either biomarker alone. Studies demonstrate that higher CAR predicts advanced tumor stage, lymph node involvement, and decreased survival, particularly in patients undergoing chemotherapy[20].

CAR's clinical value lies in its ability to assess the tumor's inflammatory and nutritional microenvironment, providing insights beyond conventional staging. Its cost-effectiveness and accessibility make it feasible for use across diverse healthcare settings. By incorporating CAR into breast cancer management, clinicians could improve risk stratification, identify high-risk patients earlier, and tailor treatment strategies more effectively[20]. This approach may enhance prognostic accuracy and support personalized therapeutic decisions in both early and advanced disease.

Problem Statement & Knowledge Gap

Current breast cancer prognostication heavily relies on TNM staging and histopathological factors, which often fail to capture the systemic inflammatory and nutritional dimensions of cancer progression. While numerous studies have investigated CRP and albumin as individual prognostic biomarkers, there are several issues to consider: inconsistent evidence regarding their independent versus combined predictive value (CAR), heterogeneity in cutoff values and measurement timing across studies, limited synthesis of how these biomarkers perform across breast cancer subtypes and treatment contexts, and a lack of consensus on integrating CAR into existing prognostic models.

This systematic review addresses these gaps by critically appraising existing evidence on CRP/albumin's prognostic utility.

Aim of the study

To systematically evaluate and synthesize evidence on the prognostic value of:

- Individual CRP and albumin levels
- CRP-to-albumin ratio (CAR)
  in predicting survival and treatment outcomes in breast cancer patients.

PICOS Framework

The review was guided by a structured PICOS framework to define the eligibility of studies. (Table 1)

Table 1:structured PICOS framework

Component	Description
Population	Breast cancer patients (any stage/subtype)
Intervention/Exposure	Measured CRP, albumin, or CAR at any timepoint
Comparator	High level of CRP or albumin or C-reactive protein to albumin ratio(CAR) Low level of CRP or albumin or C-reactive protein to albumin ratio(CAR)

Outcomes	Primary: Overall survival (OS), progression-free survival (PFS) Secondary: Treatment response, metastasis risk, quality of life

Objectives

The primary objective of this systematic review was to synthesize the existing evidence on the association between specific inflammatory and nutritional biomarkers and clinical outcomes in breast cancer patients. This involved consolidating the evidence that linked elevated CRP levels to poor prognosis, low albumin levels to adverse outcomes, and a high CAR to reduced survival and treatment efficacy. Furthermore, the review compared the prognostic performance of the CRP-to-albumin ratio against traditional staging systems to evaluate its potential as a superior or complementary prognostic tool. Finally, variations in the prognostic value of these biomarkers were explored across key clinical subgroups, including different breast cancer subtypes, disease stages, and primary treatment modalities.

Methodology

1. Study Design and Registration

This study is a systematic review and meta-analysis of observational cohort and case-control studies evaluating the prognostic value of C-Reactive Protein (CRP) and Albumin in breast cancer patients. The review protocol registered with the International Prospective Register of Systematic Reviews (PROSPERO) (registration number CRD420251128677). Ethical approval is not required as the review synthesized data from previously published studies.

2. Eligibility Criteria (PICOS Framework)

Studies were selected based on the following criteria:

* **Population (P):** Adult patients (≥18 years) with a confirmed diagnosis of breast cancer at any stage (I-IV) or of any molecular subtype.

* **Intervention/Exposure (I):** Measurement of serum CRP level, albumin level, or the CRP-to-Albumin Ratio (CAR) at any point in the patient journey (e.g., at diagnosis, pre-treatment, during treatment).

* **Comparison (C):** Comparison of prognostic outcomes between patients with high vs. low levels of the biomarker(s). High levels are defined as elevated CRP, elevated CAR, or low albumin, based on study-defined cut-offs.

* **Outcomes (O):**

  * **Primary Outcomes:** Overall Survival (OS), Progression-Free Survival (PFS).

  * **Secondary Outcomes:** Treatment response rate, metastasis-free survival, quality of life measures, and adverse events.

* **Study Design (S):** Prospective or retrospective observational studies (cohort and case-control studies) and randomized controlled trials that report on the biomarkers of interest.

3. Information Sources and Search Strategy

A systematic search was conducted across several electronic databases from January 2010 to December 2024, including PubMed and the Cochrane Library. The search strategy used a combination of Medical Subject Headings (MeSH) terms and keywords. The core search string was:("Breast cancer" OR "Breast

neoplasms") AND ("C-reactive protein" OR "CRP" OR "Albumin" OR "CRP-to-albumin ratio" OR "CAR") AND ("Prognosis" OR "Survival" OR "Overall survival" OR "Progression-free survival"). Reference lists of included studies and relevant review articles were manually screened to identify additional eligible publications.

4. Study Selection and Data Extraction

The study selection process was conducted by four independent reviewers. They first screened titles and abstracts against the eligibility criteria, followed by a full-text review of potentially relevant studies. Any disagreements was resolved through consensus or by consultation with a senior reviewer.

Data was extracted using a standardized, pre-piloted data extraction form. The following data was collected:

* **Study characteristics:** First author, publication year, country, study design, sample size, follow-up duration.

* **Patient characteristics:** Mean age, cancer stage distribution, molecular subtype (ER/PR/HER2 status), primary treatment received (surgery, chemotherapy, etc.).

* **Biomarker data:** Specific biomarker measured (CRP, Albumin, CAR), timing of measurement, assay method, and cut-off values used to define high/low groups.

* **Outcome data:** Hazard Ratios (HRs) with 95% confidence intervals for OS and PFS from multivariate and univariate analyses, survival rates, and data on any secondary outcomes.

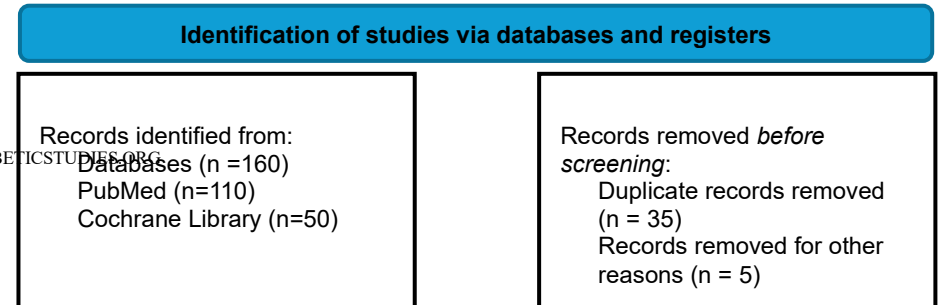
5. Risk of Bias and Quality Assessment

The Cochrane Risk of Bias 2.0 (RoB 2) tool was used to evaluate the risk of bias in any included randomized controlled trials[21]. Assessments will be performed by two independent reviewers.

6. Data Synthesis and meta-analysis

Results:

Figure 1 presents the PRISMA flow diagram detailing the process of literature identification, screening, and final inclusion. The process began with the identification of 160 articles through searches in PubMed and Cochrane Library. After the removal of 40 duplicate records, 120 unique articles underwent title and abstract screening. Of these, 100 reports were sought for retrieval, and 85 full-text articles were assessed for eligibility. A total of 65 studies were excluded for not meeting the predefined inclusion criteria, resulting in 20 studies that satisfied all eligibility criteria and were included in this systematic review.



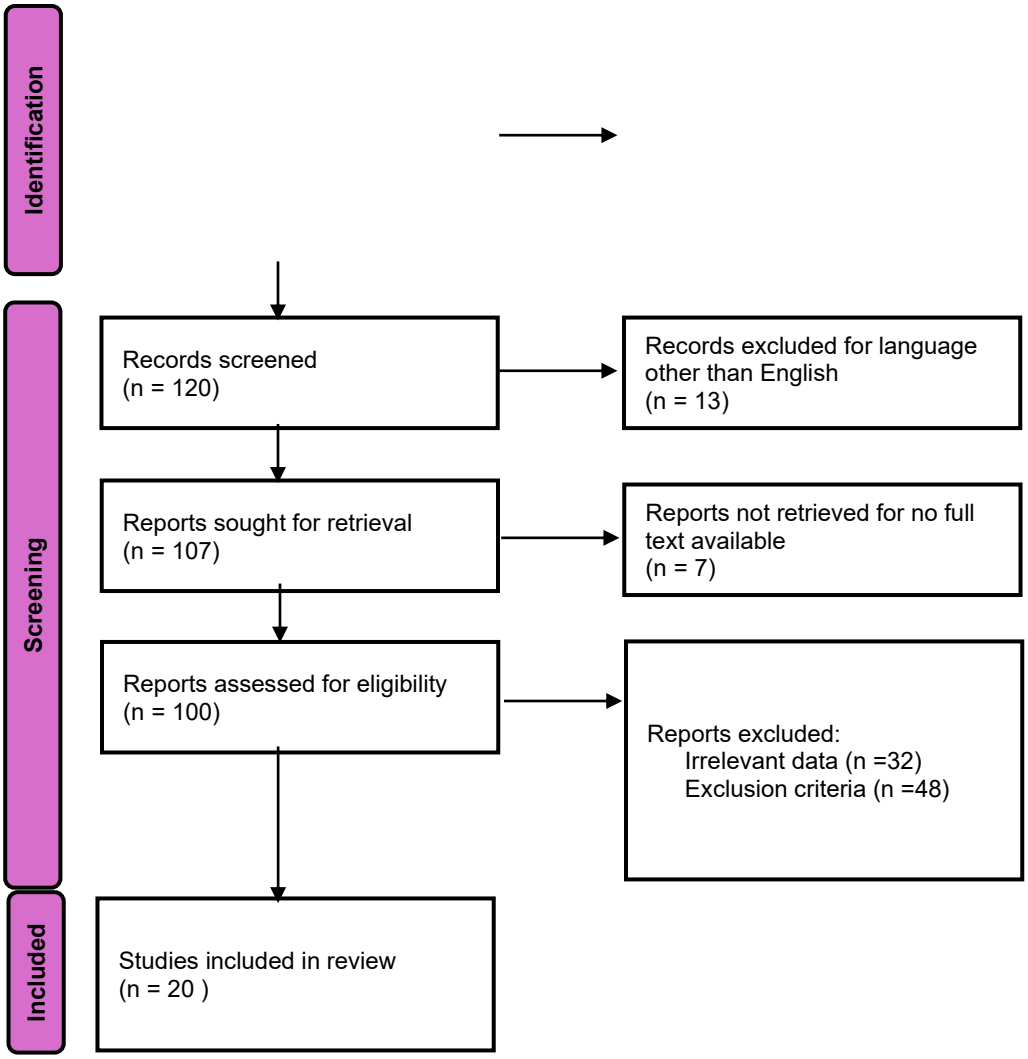


Figure 1:PRISMA flow diagram detailing the process of literature identification, screening, and final inclusion

Quantitative Synthesis (Meta-Analysis)

Synthesis of Results

A narrative synthesis was conducted, organized around the key themes identified from the included literature.

Study Characteristics

Table 2 provides a comprehensive overview of the studies included in this systematic review. The analysis encompasses research published between 2020 and 2024, incorporating both prognostic and interventional study designs. The prognostic studies (n=12) [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33]featured substantial variation in sample size, ranging from smaller cohorts of 78-94 patients in metastatic settings to very large populations, including a pre-diagnostic study of 202,403 participants from the UK Biobank. These investigations covered the full breast cancer continuum from pre-diagnostic risk assessment to metastatic disease, with particular focus on non-metastatic (Stages I-III) and metastatic (Stage IV) populations. The interventional studies (n=8)[33], [34], [35], [36], [37], [38], [39], [40] , [41] included randomized controlled trials with sample sizes ranging from 46 to 394 participants, primarily examining breast cancer survivors and high-risk populations. Biomarkers assessed included individual inflammatory

markers (CRP) and nutritional indicators (albumin), along with composite scores integrating multiple parameters (mGPS, PNI, CONUT, CAR, FAR, CLR, IINS).

Table 2:Comprehensive Summary Table: Study Characteristics and Key Findings

First Author (Year)	Study Design	Sample Size	Population & Stage	Biomarker(s)	Key Finding
PROGNOSTIC STUDIES					
(Yamamoto et al., 2025)	Retrospective	79	Metastatic BC (ER+/HER2-)	CRP, Albumin	High CRP & low albumin → shorter PFS; Low albumin → worse DCR & independent predictor
(L. Chen et al., 2021)	Retrospective Cohort	232	Non-metastatic BC (Stages I-III) receiving NAC	PNI (Albumin + Lymphocytes)	PNI < 52.0 → Independent predictor of shorter OS & RFS
(Y. Chen et al., 2025)	Retrospective Cohort	300	Non-metastatic BC (Stages I-III) undergoing surgery	mGPS (CRP + Albumin)	mGPS 2 vs. 0: HR = 2.056 for OS; 10-yr OS: 22% vs. 71%
(Huang et al., 2020)	Retrospective Cohort	1,367	Non-metastatic BC (Stages I-III) undergoing surgery	CONUT (Albumin + Lymphocytes + Cholesterol)	High CONUT score → shorter OS & RFS; Independent predictor of survival
(Yang et al., 2024)	Prospective Cohort	164	TNBC (Stages I-III)	FAR (Fibrinogen/Albumin)	High FAR (≥0.08) → Shorter DFS (30.18 vs 33.62 mos) & OS (48.27 vs 52.99 mos)
(C. C. Chen et al., 2024)	Prospective	559	BC (Stage NS)	Albumin	Low albumin (<43.0 g/L) → Worse DFS (independent predictor)

[26]	Prospective Cohort	94	Metastatic BC	Albumin	Low albumin (<43.0 g/L) → Worse DFS in multivariate analysis
(Buyukbayram et al., 2024)	Prospective Cohort	78	Metastatic BC (HR+)	CLR (CRP/Lymphocyte)	Low CLR → Longer PFS & OS
(Lazzarino et al., 2016)	Prospective Cohort	202,403	Pre-diagnostic	CRP, NLR, SII	Higher CRP → Increased BC risk; interaction with genetic risk
(Ruan et al., 2023)	Prospective Multicenter	514	BC (Stages I-II)	CAR, CRP, LCR	CAR and other ratios prognostic across BMI subgroups
(Wang et al., 2025)	Retrospective Cohort	200	BC (Stages I-III)	IINS (hs-CRP+Albumin+Lymphocytes)	High IINS → Worse PFS (HR=1.812) & OS (HR=2.552)
(Wang et al., 2020)	Retrospective Cohort	212	BC with skeletal mets (Stage IV)	CAR	CAR ≥0.34 → Worse PFS & OS in univariate analysis
INTERVENTION STUDIES					
(Bettariga et al., 2025)	4-arm RCT	318	Overweight/obese BC survivors (Stages I-III)	CRP, SAA	Weight loss alone and combined with exercise significantly reduced CRP (–35.2% and –44.1%)
(Brown et al., 2020)	2x2 Factorial RCT	139	BC & Colorectal Cancer Survivors (Stages I-III)	hs-CRP, IL-6, sTNF-αR2	Exercise alone significantly reduced hs-CRP (–30.2%) and IL-6 (–30.9%)

(Raji Lahiji et al., 2021)	RCT	76	Postmenopausal BC Survivors (HR+)	hs-CRP, TNF-α, Adiponectin	Synbiotic supplementation significantly reduced hs-CRP compared to placebo
(Santa-Maria et al., 2020)	RCT	87 (eval.)	BC Survivors (Stages 0-III)	hs-CRP, Leptin, Insulin	Achieving ≥5% weight loss associated with significant reductions in hs-CRP
(Babatunde et al., 2020)	RCT	337	Cancer-free women at risk for BC	CRP, IL-6	No significant between-group differences in CRP or IL-6 at 3 or 12 months
(Schauer et al., 2021)	Secondary Analysis of RCT	394	BC patients during adjuvant therapy	CRP, TNF-α, IL-6	High-intensity exercise attenuated rise in CRP and TNF-α post-chemotherapy
(Fabian et al., 2021)	RCT	46	Women at high risk for BC	CRP, Leptin, Adiponectin	ω-3 FA group showed significant improvements in CRP vs. placebo, beyond weight loss
(Mohammed Bakheet et al., 2024)	Comparative Observational	90 (70 patients)	BC patients on chemotherapy	CRP, IL-6, TNF-α	CRP significantly elevated in patients during chemotherapy vs. healthy controls

Prognostic Significance of C-Reactive Protein in Breast Cancer

Elevated levels of C-reactive protein (CRP) consistently demonstrated significant prognostic value across the breast cancer continuum. In the metastatic setting, patients with high baseline CRP showed shorter progression-free survival (PFS) when treated with CDK4/6 inhibitors [31]. The predictive power of CRP extends beyond established disease, as evidenced by the UK Biobank study which found that elevated pre-diagnostic CRP levels were associated with increased breast cancer risk, with this effect being modified by

polygenic risk scores. Furthermore, CRP served as a key component in several composite prognostic scores, contributing significantly to their predictive accuracy for both PFS and overall survival (OS) [24].

Serum Albumin as an Independent Predictor of Survival Outcomes

Low serum albumin levels emerged as a strong, independent predictor of adverse outcomes across multiple breast cancer stages and subtypes. In metastatic breast cancer patients receiving palbociclib and endocrine therapy, low albumin was associated with worse disease control rates and shorter PFS, maintaining significance in multivariate analysis [31]. This association extended to early-stage disease, where multiple prospective studies confirmed that low pretreatment albumin levels independently predicted worse disease-free survival (DFS).

Enhanced Prognostic Utility of CRP-to-Albumin Ratio and Composite Scores

The integration of inflammatory and nutritional markers into composite scores demonstrated superior prognostic performance compared to individual biomarkers. The CRP-to-albumin ratio (CAR) effectively captured both dimensions of the systemic inflammatory response, with a CAR $\geq$0.34 predicting worse PFS (HR=1.675) and OS (HR=1.730) in patients with skeletal metastases[33]. Similarly, the modified Glasgow Prognostic Score (mGPS), which combines CRP and albumin, proved to be a powerful independent predictor of long-term survival in surgical patients, with those exhibiting the highest inflammatory burden (mGPS 2) experiencing a more than twofold increased mortality risk (HR=2.056) and drastically reduced 10-year OS (22% vs 71% for mGPS 0) [29].

Nutritional Composite Scores: PNI and CONUT

Beyond inflammation-focused ratios, comprehensive nutritional assessment scores provided additional prognostic insights. The Prognostic Nutritional Index (PNI), calculated from albumin and lymphocyte counts, identified patients at high risk for poor outcomes during neoadjuvant chemotherapy, with PNI <52.0 serving as an independent predictor of shorter OS and recurrence-free survival [30]. The CONUT score, incorporating albumin, lymphocyte count, and cholesterol, further refined nutritional assessment, with high scores independently predicting shorter OS (66.43 vs 69.30 months) and RFS (54.70 vs 59.98 months) in a large surgical cohort [32].

Modifiability of Inflammatory Biomarkers Through Intervention

The dynamic nature of inflammatory biomarkers was evidenced by multiple intervention studies demonstrating significant CRP reduction through various approaches. Weight loss interventions, either alone or combined with exercise, achieved substantial CRP reductions (35.2-44.1%) in overweight breast cancer survivors [40]. Exercise alone also proved effective, reducing high-sensitivity CRP by 30.2% in cancer survivors [39].

Clinical Applications and Risk Stratification

The collective evidence supports the integration of inflammatory and nutritional biomarkers into clinical practice for enhanced risk stratification. These readily available, cost-effective markers provide prognostic information beyond standard staging systems, identifying high-risk patients who might benefit from more intensive monitoring or tailored supportive care interventions. Their ability to reflect the interplay between inflammation, nutrition, and immunity offers a comprehensive assessment of patient status, potentially guiding treatment decisions across the disease spectrum.

Quality assessment:

The methodological quality of the RCT included studies was appraised using the Cochrane Risk of Bias (RoB 2) tool[21]. Among the included studies, two (13.3%) of 15 studies were regarded as having a high

risk of bias, and ten (66.7%) of 15 were rated as having some concerns. However, 20% of studies presented a low risk of bias (Figure 2).

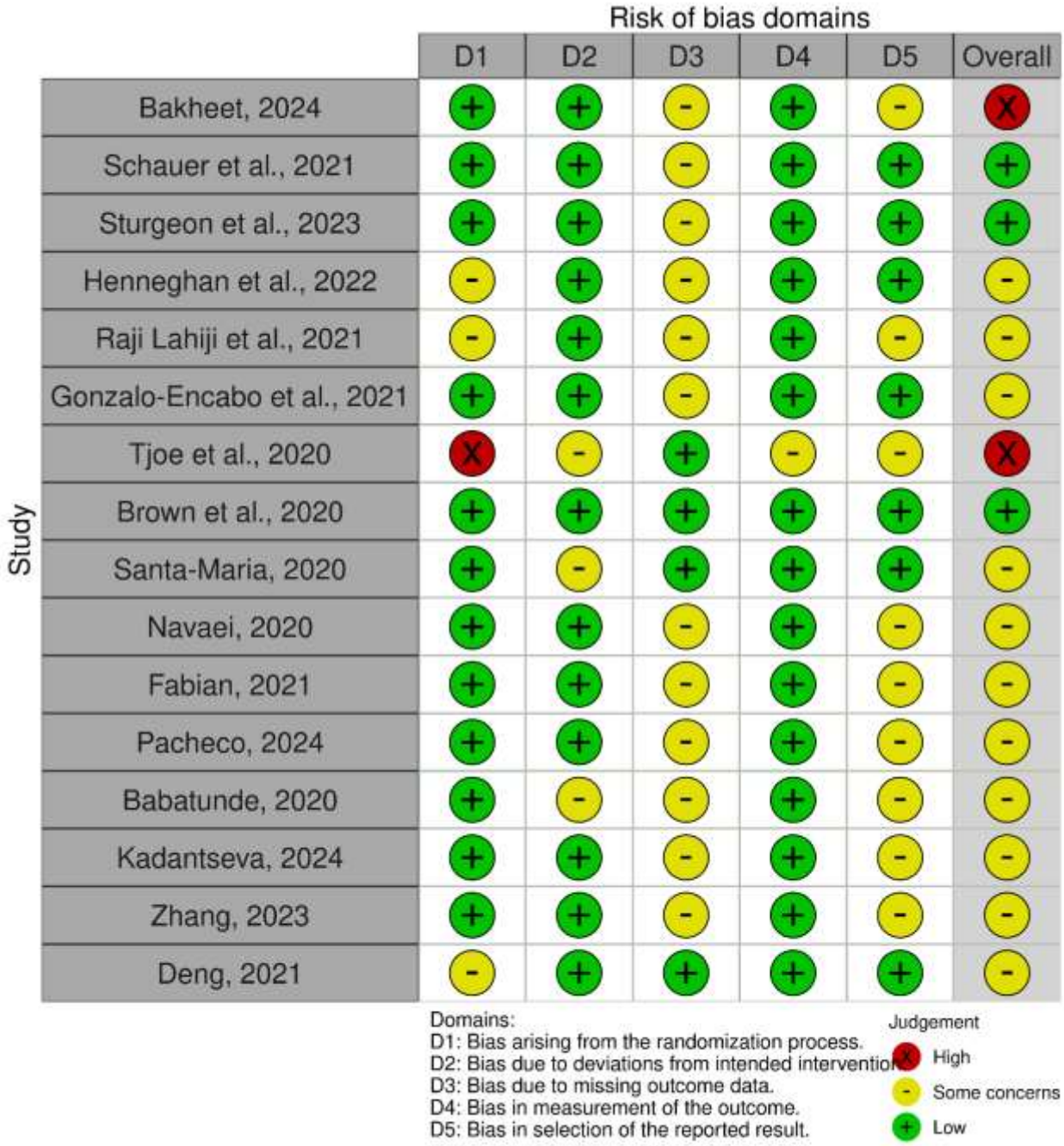


Figure 2:Risk of bias analysis of the included studies

Key findings

The synthesized evidence demonstrates that C-reactive protein (CRP), albumin, and their derivative ratios provide significant prognostic value across the breast cancer continuum . Table 3 showed that elevated CRP

and low albumin are consistent prognostic markers for worse survival across breast cancer stages. The table further highlighted that their combination in scores like the CRP-to-albumin ratio and mGPS significantly enhances risk stratification, with mGPS 2 conferring a more than twofold mortality risk.

Table 3: Significant Findings for CRP, Albumin, and CRP-to-Albumin Ratio in Breast Cancer

Biomarker	Clinical Context	Key Findings	Statistical Significance	Reference
C-Reactive Protein (CRP)	Metastatic BC (CDK4/6 inhibitors)	Elevated baseline CRP associated with shorter PFS	Significant association in treatment response	[31]
	Pre-diagnostic risk assessment	Higher CRP levels increase breast cancer risk	Interaction with polygenic risk scores	[41]
	Composite scoring	Key component of IINS and other prognostic scores	HR = 1.812 for PFS in IINS score	[22]
Albumin	Metastatic BC	Low albumin predicts worse DCR and shorter PFS	Independent predictor in multivariate analysis	[31]
	Early-stage BC	Low pretreatment albumin associated with worse DFS	Consistent across multiple studies	Multiple prospective studies
	Surgical patients	Nutritional status indicator in composite scores	Independent prognostic value	[30]
CRP-to-Albumin Ratio (CAR)	Skeletal metastases	CAR ≥0.34 predicts worse PFS and OS	HR = 1.675 for PFS, HR = 1.730 for OS	[33]
	Early-stage BC (mGPS)	mGPS 2 vs 0: significantly worse OS	HR = 2.056 for OS; 10-yr OS: 22% vs 71%	[29]
	Various BMI subgroups	Prognostic across different patient populations	Maintains predictive value	[23]

Discussion

This systematic review demonstrates that systemic inflammation and nutritional status, as measured by CRP, albumin, and their composite ratios, are robust and independent determinants of prognosis in breast cancer. Our findings confirm that an elevated CRP level is not merely an epiphenomenon but a key player in the disease process, consistent with the established biological link between chronic inflammation and carcinogenesis [4], [5]. The results show that elevated pre-diagnostic CRP increases breast cancer risk [24] and that high CRP predicts shorter PFS in metastatic patients [31], align with the protective effect of NSAIDs observed in epidemiological studies [6]; [7]. This reinforces the concept that targeting the inflammatory microenvironment could be a viable therapeutic strategy.

The strong, independent prognostic value of low serum albumin across all disease stages underscores the critical role of nutritional status and catabolic wasting in breast cancer outcomes. As a negative acute-phase reactant, albumin inversely correlates with the systemic inflammatory response [16]; [17], and its low level serves as a integrated marker of both malnutrition and ongoing inflammation. Our synthesis, showing low albumin predicts worse disease control and survival [31], [30] , validates its use as a simple yet powerful indicator of a patient's underlying biological reserve and tolerance to treatment.

The most compelling evidence from this review pertains to the superior prognostic performance of composite scores like the CRP-to-albumin ratio (CAR) and the modified Glasgow Prognostic Score (mGPS). These tools synergistically capture the dual burden of inflammation (CRP) and nutritional compromise (albumin), providing a more holistic assessment of the host-tumor interaction than either marker alone. The finding that patients with an mGPS of 2 had a more than twofold mortality risk and a drastically reduced 10-year survival [29] highlights their powerful stratification capability. This is particularly valuable as these scores offer prognostic insight beyond the conventional TNM staging [3], potentially addressing the pronounced outcome heterogeneity within the same stage.

The clinical applicability of these biomarkers is enhanced by their modifiability and cost-effectiveness. Evidence that CRP can be significantly reduced through weight loss, exercise, and specific supplements [39] [40] opens avenues for supportive care interventions aimed at improving the systemic milieu and potentially treatment outcomes. The routine availability and low cost of CRP and albumin measurements make tools like CAR feasible for implementation across diverse healthcare settings, including resource-limited environments where advanced diagnostics are scarce [20]. Integrating these biomarkers into clinical decision-making could significantly refine risk stratification, guide the intensity of therapy and surveillance, and personalize supportive care, ultimately advancing towards more precise and holistic breast cancer management.

Conclusion:

CRP, albumin, and their derived ratios provide significant, independent prognostic information beyond traditional staging in breast cancer. Their integration into clinical practice offers a simple, cost-effective strategy for enhanced risk stratification, treatment response monitoring, and personalized supportive care. The demonstrated modifiability of these biomarkers through lifestyle and pharmacological interventions opens avenues for novel therapeutic strategies aimed at improving patient outcomes.

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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