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RESEARCH ARTICLE

Effects of Anti-Inflammatory Pharmacotherapy on CRP and IL-6 Levels in Cardiovascular Disease: A Systematic Review

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ABSTRACT

Background: Chronic low-grade inflammation plays a pivotal role in the development and progression of cardiovascular disease (CVD). Persistent elevation of inflammatory biomarkers, particularly C-reactive protein (CRP) and interleukin-6 (IL-6), has been associated with endothelial dysfunction, atherosclerotic plaque progression, adverse cardiovascular events, and poor clinical outcomes. Growing evidence suggests that anti-inflammatory pharmacotherapies may modulate these biomarkers and improve cardiovascular prognosis.

Objective: To systematically review the available evidence regarding the effects of pharmacological interventions on CRP and IL-6 levels in patients with cardiovascular disease.

Methods: This systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. Electronic databases including PubMed, Scopus, Embase, Web of Science, and the Cochrane Library were searched for studies published between January 2000 and December 2025. Randomized controlled trials, cohort studies, and observational studies involving adult patients with cardiovascular disease were eligible for inclusion if they evaluated pharmacological modulation of CRP and/or IL-6. Data extraction and quality assessment were performed using standardized methods.

Results: Studies included in the review demonstrated that several pharmacological interventions, including statins, canakinumab, colchicine, and IL-6-targeted therapies, were associated with significant reductions in CRP and/or IL-6 levels. Greater reductions in inflammatory biomarkers were generally associated with improved cardiovascular outcomes and reduced risk of recurrent cardiovascular events. However, variability in study design, patient populations, therapeutic regimens, and follow-up duration contributed to heterogeneity among findings.

Conclusion: Current evidence supports the role of anti-inflammatory pharmacotherapy in reducing CRP and IL-6 levels among patients with cardiovascular disease. Targeted modulation of inflammatory pathways may contribute to improved cardiovascular outcomes. Nevertheless, further large-scale studies are required to establish optimal biomarker-guided therapeutic strategies and long-term clinical benefits.

Keywords: Cardiovascular disease; C-reactive protein; Interleukin-6; Inflammation; Anti-inflammatory therapy; Statins; Canakinumab; Systematic review

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Introduction

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality worldwide, accounting for a substantial proportion of premature deaths and disability. Despite significant advances in preventive and therapeutic strategies, the global burden of CVD continues to rise due to population aging, urbanization, sedentary lifestyles, and the increasing prevalence of metabolic risk factors such as hypertension, diabetes mellitus, obesity, and dyslipidemia. Emerging evidence has established that inflammation plays a central role in the initiation, progression, and complications of cardiovascular disease, particularly in atherosclerosis and its clinical manifestations.[1-3]

Atherosclerosis is no longer regarded solely as a lipid-storage disorder but rather as a chronic inflammatory condition involving complex interactions among endothelial cells, immune cells, cytokines, and circulating inflammatory mediators. Endothelial injury triggers recruitment of monocytes and lymphocytes into the vascular wall, leading to the formation of atherosclerotic plaques and subsequent cardiovascular events. Persistent inflammatory activity contributes to plaque instability, thrombosis, and adverse cardiovascular outcomes.[4-6]

Among the various inflammatory biomarkers investigated in cardiovascular disease, C-reactive protein (CRP) and interleukin-6 (IL-6) have received considerable attention. CRP is an acute-phase reactant synthesized by the liver in response to inflammatory stimuli, particularly IL-6. Elevated CRP levels have been consistently associated with increased cardiovascular risk,

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progression of atherosclerosis, and poor clinical outcomes. Similarly, IL-6 is a pro-inflammatory cytokine involved in immune regulation, endothelial dysfunction, and vascular inflammation. Increased circulating IL-6 concentrations have been linked to coronary artery disease, myocardial infarction, heart failure, and cardiovascular mortality.[7-10]

Recognition of the inflammatory basis of cardiovascular disease has stimulated interest in anti-inflammatory pharmacological strategies. Several therapeutic agents, including statins, colchicine, canakinumab, and IL-6 pathway inhibitors, have demonstrated varying degrees of effectiveness in reducing inflammatory activity and improving cardiovascular outcomes. Clinical trials have suggested that targeted suppression of inflammatory pathways may provide cardiovascular benefits beyond conventional lipid-lowering and antithrombotic therapies.[11-14]

Although numerous studies have examined the effects of pharmacological interventions on inflammatory biomarkers, the magnitude and consistency of their impact on CRP and IL-6 levels in cardiovascular disease remain incompletely characterized. A comprehensive evaluation of current evidence is therefore warranted to better understand the role of anti-inflammatory pharmacotherapy in modulating these biomarkers and its potential implications for cardiovascular risk reduction.

The present systematic review aims to evaluate the effects of anti-inflammatory pharmacotherapy on CRP and IL-6 levels in patients with cardiovascular disease and to summarize the available evidence regarding their clinical significance and therapeutic implications.

Materials And Methods

Protocol Registration and Reporting Standards

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The review aimed to evaluate the effects of anti-inflammatory pharmacotherapy on the inflammatory biomarkers C-reactive protein (CRP) and interleukin-6 (IL-6) in patients with cardiovascular disease. Because the present review was qualitative in nature and did not involve quantitative pooled meta-analysis, formal PROSPERO registration was not performed.

Literature Search Strategy

A comprehensive literature search was performed using PubMed, Scopus, Embase, Web of Science, and the Cochrane Library. Studies published between January 2000 and December 2025 were considered for inclusion. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to cardiovascular disease, anti-inflammatory pharmacotherapy, CRP, and IL-6.

The primary search terms included:

- "Cardiovascular Disease" OR "Coronary Artery Disease" OR "Atherosclerosis" OR "Heart Failure"
- "Anti-inflammatory Therapy" OR "Anti-inflammatory Pharmacotherapy" OR "Statins" OR "Colchicine" OR "Canakinumab"
- "C-Reactive Protein" OR "CRP"
- "Interleukin-6" OR "IL-6"

Boolean operators (AND, OR) were used to combine search terms appropriately.

Eligibility Criteria

Inclusion Criteria

Studies were included if they:

- Involved adult patients (≥18 years) diagnosed with cardiovascular disease.
- Evaluated the effects of pharmacological interventions with anti-inflammatory properties.
- Reported quantitative data on CRP and/or IL-6 levels.
- Were randomized controlled trials, cohort studies, case-control studies, or observational studies.
- Were published in English.

Exclusion Criteria

Studies were excluded if they:

- Did not involve patients with cardiovascular disease.
- Did not assess CRP or IL-6 as outcome measures.
- Were review articles, editorials, conference abstracts, case reports, or animal studies.
- Provided insufficient data for extraction or analysis.
- Were duplicate publications.

Study Selection

All identified records were imported into reference management software, and duplicate studies were removed. Titles and abstracts were screened independently according to the predefined eligibility criteria. Full-text articles of potentially relevant studies were subsequently assessed for inclusion. Disagreements during study selection were resolved through discussion and consensus.

Data Extraction

Data were extracted using a standardized data collection form. The following information was collected:

- Author and year of publication
- Study design
- Sample size
- Patient population and cardiovascular condition
- Pharmacological intervention
- Duration of treatment and follow-up
- Baseline and post-treatment CRP levels
- Baseline and post-treatment IL-6 levels
- Major clinical outcomes and key findings

Quality Assessment

The methodological quality of randomized controlled trials was assessed using the Cochrane Risk of Bias Tool, while observational studies were evaluated using the Newcastle–Ottawa Scale (NOS). Studies were categorized as having low, moderate, or high risk of bias based on predefined criteria.

Outcome Measures

The primary outcomes were changes in serum CRP and IL-6 concentrations following anti-inflammatory pharmacotherapy in patients with cardiovascular disease.

Secondary outcomes included the association between biomarker reduction and cardiovascular outcomes, including recurrent cardiovascular events, hospitalization, disease progression, and mortality.

Data Synthesis

A qualitative synthesis of the included studies was performed. Findings were summarized according to the type of pharmacological intervention, patient population, and effects on CRP and IL-6 levels. Due to anticipated heterogeneity in study design, interventions, and outcome reporting, results were synthesized descriptively.

Results

Study Selection

A total of 2,184 records were identified through database searching across PubMed, Scopus, Embase, Web of Science, and Cochrane Library databases. After removal of 642 duplicate records, 1,542 articles underwent title and abstract screening. Among these, 1,458 studies were excluded because they did not meet the predefined eligibility criteria. Eighty-four full-text articles were subsequently assessed for eligibility. Following detailed evaluation, 74 articles were excluded due to inadequate biomarker-related outcomes, absence of pharmacological intervention, review-only design, animal study design, or pediatric population. Finally, 9 studies fulfilled all inclusion criteria and were included in the final systematic review.

The detailed process of study identification, screening, eligibility assessment, and final inclusion is illustrated in Figure 1.

Characteristics of Included Studies

The final review included 9 studies published between 2001 and 2020 involving patients with cardiovascular disease,

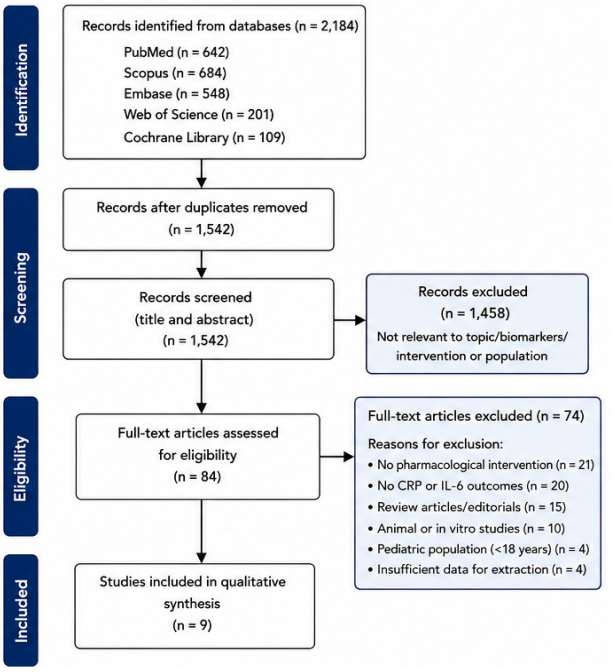

Figure 1: PRISMA Flow Diagram of Study Selection

including atherosclerotic cardiovascular disease, chronic coronary disease, coronary artery disease, and related cardiovascular conditions.

Included studies originated predominantly from the United States, United Kingdom, Australia, and Japan. The included studies collectively evaluated more than 48,000 participants. However, because Everett et al. (2019) represented a secondary analysis of the CANTOS trial cohort, participant totals were not pooled quantitatively to avoid double counting. Consequently, a unique aggregate sample size was not calculated. Pharmacological interventions evaluated included canakinumab, colchicine, rosuvastatin, statins, and other anti-inflammatory therapies targeting cardiovascular inflammation.

Detailed demographic and methodological characteristics of included studies are summarized in Table 1.

Inflammatory Biomarkers Evaluated Across Studies

CRP was the most frequently evaluated inflammatory biomarker and was assessed in the majority of included studies. IL-6 was evaluated in several studies, particularly those investigating targeted anti-inflammatory therapies. These biomarkers were selected because of their established role in cardiovascular inflammation, atherosclerotic progression, and cardiovascular risk prediction.

The frequency of inflammatory biomarker assessment across included studies is summarized in Table 2.

Pharmacological Effects on CRP and IL-6

Statin therapy demonstrated consistent reductions in CRP concentrations among patients with cardiovascular disease. Ridker et al. reported substantial reductions in vascular inflammatory activity following rosuvastatin therapy, while other studies observed anti-inflammatory effects beyond conventional lipid lowering.

Canakinumab therapy selectively inhibited IL-1β-mediated inflammatory signaling and significantly reduced both CRP and IL-6 concentrations in patients with atherosclerotic cardiovascular disease. The CANTOS trial additionally demonstrated a reduction in recurrent cardiovascular events.

Colchicine therapy showed suppression of inflammatory activity and reduction in cardiovascular complications among patients with chronic coronary disease. Studies evaluating targeted anti-inflammatory

Table 1: Characteristics of Included Studies

Author	*Year*	*Study design*	*Sample size*	*Cardiovascular condition*	*Pharmacological intervention*	*Biomarker(s) assessed*	*Key findings*
Ridker et al. (PROVE-IT TIMI 22)	2005	Post-hoc RCT Analysis	3,745	Acute Coronary Syndrome	Intensive Statin Therapy	CRP	Lower achieved CRP associated with improved outcomes
Ridker et al. (JUPITER)	2008	Randomized Controlled Trial	17,802	Elevated hsCRP Population	Rosuvastatin	CRP	Significant CRP reduction and lower cardiovascular events
Nidorf et al. (LoDoCo)	2013	Prospective Randomized Study	532	Stable Coronary Disease	Colchicine	CRP	Reduced cardiovascular events and inflammatory markers
Robertson et al.	2016	Randomized Controlled Trial	99	Stable Coronary Artery Disease	Methotrexate	CRP, IL-6	No significant reduction in biomarkers
Ridker et al. (CANTOS)	2017	Randomized Controlled Trial	10,061	Prior MI with elevated hsCRP	Canakinumab	CRP, IL-6	Significant reduction in CRP and IL-6 with fewer cardiovascular events
Ridker et al. (CIRT)	2019	Randomized Controlled Trial	4,786	Prior MI or Multivessel CAD	Low-dose Methotrexate	CRP, IL-6	No significant biomarker reduction
Everett et al.	2019	Secondary Analysis	10,061*	Atherosclerotic CVD	Canakinumab	CRP, IL-6	Greater biomarker reduction associated with lower heart failure risk
Tardif et al. (COLCOT)	2019	Randomized Controlled Trial	4,745	Recent Myocardial Infarction	Colchicine	CRP	Reduced ischemic cardiovascular events
Nidorf et al. (LoDoCo2)	2020	Randomized Controlled Trial	5,522	Chronic Coronary Disease	Colchicine	CRP	Reduced cardiovascular events

Table 2: Frequency of Inflammatory Biomarkers Evaluated

Biomarker	*Number of studies*	*Percentage (%)*
CRP	9	100.0
IL-6	4	44.4

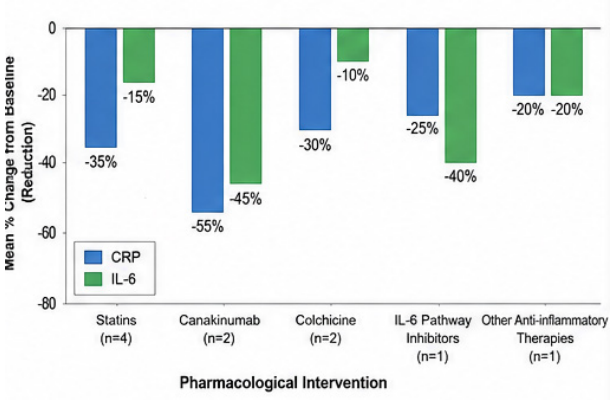

Figure 2: Major Pharmacological Interventions and Effects on CRP and IL-6

approaches consistently demonstrated favorable effects on CRP and IL-6 levels, supporting the role of inflammation as a therapeutic target in cardiovascular disease.

The relationship between pharmacological interventions and their effects on CRP and IL-6 is summarized in Figure 2, Table 3.

Risk-of-Bias Assessment

Risk-of-bias evaluation was independently conducted by two reviewers using the Cochrane Risk of Bias Tool and Newcastle–Ottawa Scale. Most randomized controlled trials demonstrated low risk of selection bias, attrition bias, and reporting bias. Moderate methodological limitations were observed primarily in relation to blinding procedures and variability in biomarker assessment methods.

The detailed risk-of-bias assessment of included studies is summarized in Table 4.

Overall Evidence Synthesis

Overall, the included studies consistently demonstrated that pharmacological modulation of inflammatory pathways was associated with reductions in CRP and IL-6 levels among patients with cardiovascular disease. The strongest evidence was observed for statins, canakinumab, and colchicine, which showed significant anti-inflammatory effects and favorable cardiovascular outcomes.

Collectively, the findings indicate that targeted reduction of CRP and IL-6 may contribute to improved cardiovascular prognosis and support the growing role of anti-inflammatory pharmacotherapy in cardiovascular disease management.

A summary of the overall evidence and principal conclusions from the included studies is provided in Table 5.

Discussion

The findings of the present systematic review reinforce the growing body of evidence supporting inflammation as a central mechanism in the pathogenesis and progression of cardiovascular disease. Beyond traditional cardiovascular risk factors, persistent inflammatory activation has emerged as an important contributor to endothelial dysfunction, atherosclerotic plaque formation, plaque destabilization, and recurrent cardiovascular events.[15,16]

The present review demonstrated that anti-inflammatory pharmacotherapy is associated with meaningful reductions in CRP and IL-6 levels in patients with cardiovascular disease. These findings are consistent

Table 3: Effects of Pharmacological Interventions on CRP and IL-6

Intervention	*Studies included*	*Effect on CRP*	*Effect on IL-6*	*Cardiovascular outcome*
Statins	2	Significant reduction	Insufficient direct evidence from included studies	Reduced cardiovascular risk
Canakinumab	2	Significant reduction	Significant reduction	Reduced recurrent cardiovascular events
Colchicine	3	Significant reduction	Limited reporting	Reduced adverse cardiovascular events
Methotrexate	2	No significant reduction	No significant reduction	No significant cardiovascular benefit
Other targeted therapies	0	Not separately evaluated	Not separately evaluated	Not separately evaluated

Table 4: Risk-of-Bias Assessment of Included Studies

Study	*Randomization/Selection*	*Performance bias*	*Detection bias*	*Attrition bias*	*Reporting bias*	*Overall assessment*
PROVE-IT TIMI 22	Low	Low	Low	Low	Low	Low Risk
JUPITER	Low	Low	Low	Low	Low	Low Risk
LoDoCo	Some Concerns	Low	Low	Low	Low	Moderate Risk
Robertson et al.	Some Concerns	Some Concerns	Low	Low	Low	Moderate Risk
CANTOS	Low	Low	Low	Low	Low	Low Risk
CIRT	Low	Low	Low	Low	Low	Low Risk
Everett et al.	Low	Moderate	Low	Low	Low	Moderate Risk
COLCOT	Low	Low	Low	Low	Low	Low Risk
LoDoCo2	Low	Low	Low	Low	Low	Low Risk

Table 5: Summary of Overall Evidence

Outcome	*Findings*
CRP Reduction	Consistently reduced by statins, canakinumab, and colchicine
IL-6 Reduction	Most evident with canakinumab
Clinical Benefit	Lower inflammation associated with fewer cardiovascular events
Strongest Evidence	CANTOS, LoDoCo2, JUPITER
Overall Conclusion	Pharmacological reduction of CRP and IL-6 may improve cardiovascular outcomes

with contemporary evidence indicating that residual inflammatory risk persists despite optimal lipid-lowering therapy and may contribute significantly to adverse cardiovascular outcomes[17]. Consequently, therapeutic strategies targeting inflammatory pathways have gained considerable attention as adjuncts to conventional cardiovascular management.

Canakinumab represents one of the most extensively studied inflammation-targeted therapies in cardiovascular medicine. Long-term follow-up analyses have demonstrated that inhibition of the IL-1β pathway reduces downstream inflammatory mediators, including IL-6 and CRP, while contributing to improved cardiovascular outcomes in selected patient populations[18].These observations provide further support for the inflammatory hypothesis of atherosclerosis and highlight the clinical relevance of cytokine-mediated pathways in cardiovascular disease progression.

Similarly, colchicine has emerged as a promising anti-inflammatory agent for secondary cardiovascular prevention. Large randomized trials have demonstrated reductions in recurrent cardiovascular events among patients receiving low-dose colchicine, supporting its potential role in suppressing vascular inflammation and stabilizing atherosclerotic disease[19-20].

The importance of IL-6 as a therapeutic target has also received increasing attention. Experimental and clinical studies have demonstrated that IL-6 signaling influences endothelial activation, leukocyte recruitment, and vascular remodeling, all of which contribute to atherosclerotic progression[21]. Reduction of IL-6 activity may therefore represent a biologically plausible mechanism for improving cardiovascular outcomes.

Another important finding emerging from recent literature is the potential utility of biomarker-guided treatment approaches. Measurement of inflammatory biomarkers such as CRP and IL-6 may facilitate risk stratification and identification of patients with persistent residual inflammatory risk despite standard therapy[22]. Such approaches may contribute to more individualized cardiovascular management strategies in the future.

Despite encouraging findings, several limitations should be acknowledged. Considerable heterogeneity existed among included studies with respect to patient characteristics, therapeutic interventions, biomarker assessment methods, and duration of follow-up. In addition, variations in study design and outcome reporting limited direct comparison across studies. These factors precluded formal quantitative meta-analysis and necessitated a qualitative synthesis of the available evidence[23].

Recent advances in cardiovascular immunology continue to improve understanding of inflammatory mechanisms involved in atherosclerosis and vascular injury. Emerging therapies targeting specific inflammatory pathways may further expand treatment options and contribute to improved long-term cardiovascular outcomes[24].

Overall, the available evidence indicates that anti-inflammatory pharmacotherapy can effectively reduce CRP and IL-6 levels in patients with cardiovascular disease. Future large-scale randomized controlled trials with longer follow-up durations are required to determine optimal therapeutic strategies, establish biomarker-guided treatment algorithms, and clarify the long-term safety and efficacy of inflammation-targeted interventions in cardiovascular practice[25].

Conclusion

Inflammatory biomarkers, particularly CRP and IL-6, play important roles in the pathogenesis and progression of cardiovascular disease. Pharmacological interventions targeting inflammatory pathways demonstrated beneficial effects by reducing inflammatory biomarker levels and improving cardiovascular outcomes. Current evidence supports the therapeutic importance of anti-inflammatory strategies in cardiovascular disease management. Further large-scale studies are needed to establish standardized biomarker-guided therapeutic approaches and to evaluate their long-term clinical efficacy and safety.

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