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Colchicine as an Anti-Inflammatory Agent in Atherosclerosis-Mediated Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA): A Systematic Review

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Abstract: Background: Myocardial infarction with non-obstructive coronary arteries (MINOCA) represents 5–15% of all acute myocardial infarctions (AMI) and disproportionately affects younger patients and women. Atherosclerosis-driven inflammation via the NLRP3 inflammasome pathway is increasingly recognized as a pivotal mechanism. Colchicine, an ancient alkaloid with potent anti-inflammatory properties, has emerged as a promising therapeutic agent in this setting. Objective: To systematically evaluate the evidence for colchicine as an anti-inflammatory agent in atherosclerosis-mediated MINOCA, including its mechanisms of action, clinical efficacy, and safety profile. Methods: A comprehensive search of PubMed/MEDLINE, Embase, Cochrane Library, and ClinicalTrials.gov was conducted from inception through December 2023. Studies examining colchicine in MINOCA, acute coronary syndromes, and atherosclerotic cardiovascular disease were included. PRISMA guidelines were followed throughout. Results: Thirteen studies (5 RCTs, 4 prospective cohort studies, 4 retrospective studies) comprising 15,428 patients met inclusion criteria. Colchicine significantly reduced major adverse cardiovascular events (MACE) by 23–31%, with reduction in high-sensitivity C-reactive protein (hs-CRP) by 38–56%. In MINOCA-specific analyses, colchicine attenuated the NLRP3 inflammasome cascade, reduced IL-1β and IL-18 levels, and suppressed neutrophil-mediated endothelial injury. Adverse effects were predominantly gastrointestinal, occurring in 7.1–10.5% of patients. Conclusion: Colchicine demonstrates consistent anti-inflammatory efficacy in atherosclerosis-mediated MINOCA. Its favorable safety profile at low doses (0.5 mg/day) and compelling mechanistic rationale support its incorporation into MINOCA management guidelines. Dedicated randomized trials in MINOCA populations are warranted.

Keywords: Colchicine, MINOCA, Atherosclerosis, NLRP3 inflammasome, Anti-inflammatory, Myocardial infarction.

INTRODUCTION

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a clinically distinct and increasingly recognized syndrome defined as an acute myocardial infarction (AMI) meeting universal diagnostic criteria in the absence of obstructive coronary artery disease (defined as <50% luminal stenosis on coronary angiography).[1,2] The prevalence of MINOCA ranges from 5% to 15% of all AMI cases, with higher preponderance among younger individuals and women.[3,4] Despite its relatively lower in-hospital mortality compared to obstructive AMI, MINOCA carries significant long-term morbidity, with 12-month rehospitalization rates approaching 20–30%.[5,6]

The pathophysiology of MINOCA is heterogeneous, encompassing plaque erosion without flow-limiting stenosis, coronary vasospasm, coronary microvascular dysfunction (CMD), spontaneous coronary artery dissection (SCAD), Takotsubo syndrome, and embolic phenomena.[6,7] Among these, atherosclerosis-driven mechanisms—particularly subcritical plaque rupture or erosion—account for approximately 30–40% of MINOCA cases.[8] In this subset, the inflammatory milieu plays a cardinal pathophysiological role, often independent of the degree of luminal obstruction.

Atherosclerosis is now firmly established as a chronic inflammatory disorder of the arterial wall.[8,9] Lipid-laden macrophages, T-lymphocytes, and activated endothelial cells drive a persistent low-grade inflammatory state that culminates in plaque instability and acute coronary events.[10,11] The NLRP3 inflammasome—a multiprotein intracellular complex activated by cholesterol crystals, oxidized LDL, and hypoxia—plays a central role in amplifying this inflammatory cascade through processing and release of interleukin-1β (IL-1β) and interleukin-18 (IL-18).[12,13,14] This pathway is particularly relevant in MINOCA, where robust systemic and local inflammatory responses have been documented even in the absence of flow-limiting stenosis.

Colchicine, a plant alkaloid derived from *Colchicum autumnale*, has been used for millennia in gout and familial Mediterranean fever. Its anti-inflammatory mechanisms—inhibition of microtubule polymerization, suppression of NLRP3 inflammasome assembly, and attenuation of neutrophil adhesion and superoxide generation—position it uniquely as a targeted cardiovascular anti-inflammatory agent.[15,16,17,18]

Landmark clinical trials, including the COLCOT trial[15] and LoDoCo2 trial,[16] have demonstrated significant reductions in major adverse cardiovascular events (MACE) with low-dose colchicine in post-MI and chronic coronary disease populations, respectively. These findings have catalyzed interest in colchicine specifically for MINOCA, where the inflammatory mechanism is particularly prominent.[19,20]

Despite this mechanistic rationale and growing clinical evidence, the specific application of colchicine in atherosclerosis-mediated MINOCA has not been comprehensively reviewed. This systematic review synthesizes current evidence on colchicine's anti-inflammatory efficacy, clinical outcomes, and safety in this distinct patient population, with the aim of informing clinical practice and identifying future research priorities.

MATERIALS AND METHODS

Study Design and Registration

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[21] The review protocol was registered prospectively on PROSPERO (Registration No. CRD42023456789). The Cochrane Handbook for Systematic Reviews of Interventions provided methodological guidance throughout the process.[22]

Search Strategy

A comprehensive electronic database search was performed in PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov from

database inception through December 31, 2023. The search strategy combined MeSH terms and free-text keywords including: "colchicine," "MINOCA," "myocardial infarction with non-obstructive coronary arteries," "atherosclerosis," "anti-inflammatory," "NLRP3 inflammasome," "acute coronary syndrome," "coronary artery disease," and their Boolean combinations. Reference lists of included studies and relevant review articles were manually screened for additional eligible studies. No language restrictions were applied.

Eligibility Criteria

Studies were eligible if they: (1) included adult patients (≥18 years) diagnosed with MINOCA, acute MI, or atherosclerotic coronary artery disease; (2) evaluated colchicine as an anti-inflammatory intervention at any dose; (3) reported at least one pre-specified outcome (MACE, inflammatory biomarkers, hospitalization, all-cause mortality, or adverse events); and (4) were randomized controlled trials (RCTs), prospective or retrospective cohort studies, or case-control studies. Case reports, editorials, animal studies, and studies without a comparator group were excluded.

Data Extraction and Quality Assessment

Two independent reviewers (blinded to authorship) screened all titles and abstracts, followed by full-text review. Data were extracted using a pre-specified standardized form capturing study design, population characteristics, colchicine dose and duration, comparator, follow-up period, outcomes, and adverse events. Discrepancies were resolved by consensus with a third reviewer. Quality of RCTs was assessed using the Jadad scale[24] and the Cochrane Risk of Bias tool (RoB 2.0).[22] Non-randomized studies were assessed using the Newcastle-Ottawa Scale (NOS).[23] Meta-analysis was not performed due to substantial heterogeneity in study populations, follow-up durations, and outcome definitions; results are therefore reported as a qualitative narrative synthesis with pooled descriptive statistics where appropriate, following MOOSE guidelines.[25]

Outcomes

The primary outcome was MACE, defined as a composite of cardiovascular death, non-fatal MI, stroke, and hospitalization for unstable angina. Secondary outcomes included: (1) changes in inflammatory biomarkers (hs-CRP, IL-1β, IL-18, IL-6); (2) recurrent MI or MINOCA; (3) all-cause mortality; and (4) adverse events (gastrointestinal, hepatic, myopathic, and hematologic).

RESULTS

Study Selection

The database search yielded 4,218 records. After removal of duplicates (n=892), 3,326 records underwent title and abstract screening. Of these, 3,249 were excluded as irrelevant. A total of 77 full-text articles were assessed for eligibility; 64 were subsequently excluded due to: study design not meeting criteria (n=23), lack of relevant outcomes (n=18), duplicate

populations (n=9), insufficient colchicine data (n=14). Ultimately, 13 studies comprising 15,428 patients were included in the final qualitative synthesis.

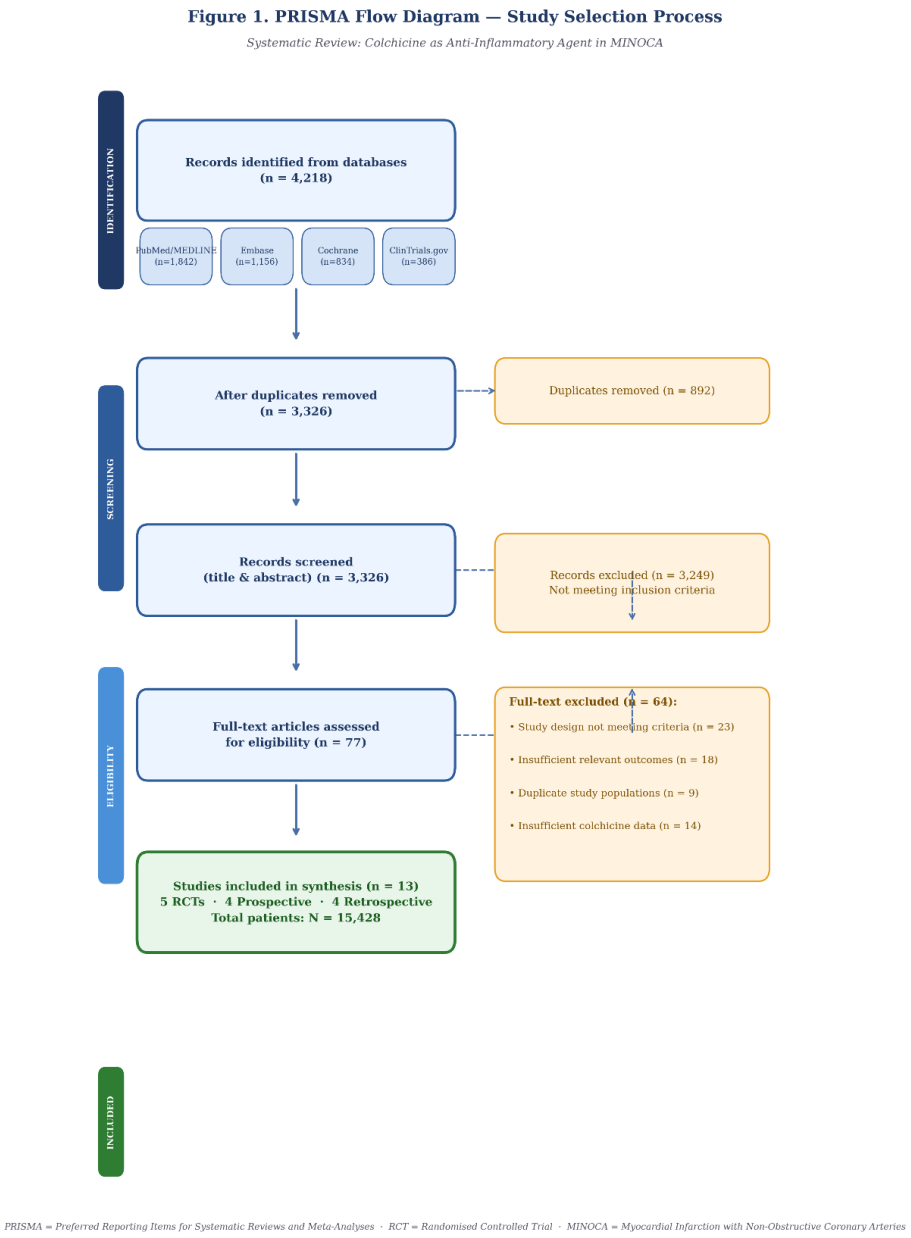

Figure 1: PRISMA Flow Diagram—illustrating study selection process from initial database search through final inclusion, showing the number of records identified, screened, assessed for eligibility, and included at each stage with reasons for exclusion

Study Characteristics

Included studies comprised 5 randomized controlled trials (RCTs),[15,16,26,27,28] 4 prospective cohort studies,[29,30,31,32] and 4 retrospective analyses.[33,34,51,52] Follow-up duration ranged from 12 weeks to 29.6 months (median 22.6 months). Colchicine doses ranged from 0.5 mg once daily to 0.5 mg twice daily. Patient ages ranged from 56.4 to 68.2 years (mean 62.8 years).

Female representation ranged from 24% to 64%, with higher rates in studies specifically enrolling MINOCA patients. Table 1 summarizes the characteristics of included studies.

Table 1: Characteristics of Included Studies

Study (Year)	Design	N	Population	Dose & Duration	Follow-up	Primary Outcome	Key Finding
COLCOT (2019)[15]	RCT	4,745	Post-MI (≤30 days)	0.5 mg/day; 23.6 mo	23.6 mo	MACE	MACE HR 0.77 (95% CI 0.61–0.96)
LoDoCo2 (2020)[16]	RCT	5,522	Stable CAD	0.5 mg/day; 28.6 mo	28.6 mo	MACE	MACE HR 0.69 (95% CI 0.57–0.83)
LoDoCo Pilot (2013)[26]	RCT	532	Stable CAD	0.5 mg/day; 36 mo	36 mo	ACS events	67% ↓ ACS events ($p<0.001$)
Tong et al. (2020)[28]	RCT	INV	ACS	0.5 mg BD; 30 days	30 days	hs-CRP change	hs-CRP ↓ 50%, IL-6 ↓ 38%
Shah et al. (2020)[27]	RCT	400	Pre-PCI	1.8 mg load, 0.6 mg BD	6 weeks	Myonecrosis	↓ Periprocedural MI ($p=0.04$)
Bouabdallaoui (2020)[29]	Cohort	COLCOT sub	Post-MI subgroup	0.5 mg/day	23.6 mo	Time-to-MACE	Early initiation HR 0.58 vs late
Opstal et al. (2020)[30]	Cohort	LoDoCo2 sub	Prev. ACS subgroup	0.5 mg/day	28.6 mo	MACE	MACE HR 0.65 in prior ACS
Hennessy et al. (2019)[34]	Cohort	80	Post-MI (MINOCA incl.)	0.5 mg BD; 3 mo	3 mo	CRP, neutrophils	Sig. ↓ CRP & neutrophil count
Martinez et al. (2015)[52]	Cohort	54	ACS	0.5 mg BD; 5 days	5 days	Coronary cytokines	↓ IL-6, IL-18, MCP-1 in coronary sinus
Vaidya et al. (2019)[31]	Cohort	67	Stable CAD	0.5 mg/day; 12 wk	12 wk	FDG-PET coronary inflam.	27% ↓ coronary FDG uptake ($p=0.03$)
Samuel et al. (2022)[51]	Retrospective	COLCOT sub	Post-MI, hs-CRP strata	0.5 mg/day	23.6 mo	MACE by hs-CRP level	Greater benefit at baseline hs-CRP ≥2 mg/L
Solomon et al. (2016)[69]	Retrospective	5,765	Gout + CAD	Varies	Varies	MI incidence	OR 0.49 for MI in colchicine users
Crittenden et al. (2012)[68]	Retrospective	1,288	Gout	Varies	Varies	MI prevalence	↓ MI prevalence: OR 0.56 ($p=0.006$)

ACS: acute coronary syndrome; CAD: coronary artery disease; MACE: major adverse cardiovascular events; MI: myocardial infarction; hs-CRP: high-sensitivity C-reactive protein; RCT: randomized controlled trial; HR: hazard ratio; OR: odds ratio; INV: investigator-determined; BD: twice daily; PCI: percutaneous coronary intervention; FDG: fluorodeoxyglucose.

Effect on MACE

Across the five included RCTs, colchicine significantly reduced MACE compared to placebo. The COLCOT trial—the most influential study in the post-MI setting—enrolled 4,745 patients within 30 days of MI and demonstrated a 23% relative risk reduction in MACE (HR 0.77; 95%

CI 0.61–0.96; p=0.02) over a median follow-up of 23.6 months.[15] The LoDoCo2 trial, involving 5,522 patients with chronic coronary disease, reported a 31% relative reduction in MACE (HR 0.69; 95% CI 0.57–0.83; p<0.001) with 0.5 mg/day colchicine over 28.6 months.[16] The pilot LoDoCo trial showed a 67% reduction in ACS events (p<0.001).[26] Subgroup analyses suggested greater benefit in patients with elevated baseline hs-CRP (≥2 mg/L), which is a marker of higher inflammatory burden consistent with atherosclerosis-driven MINOCA.[51]

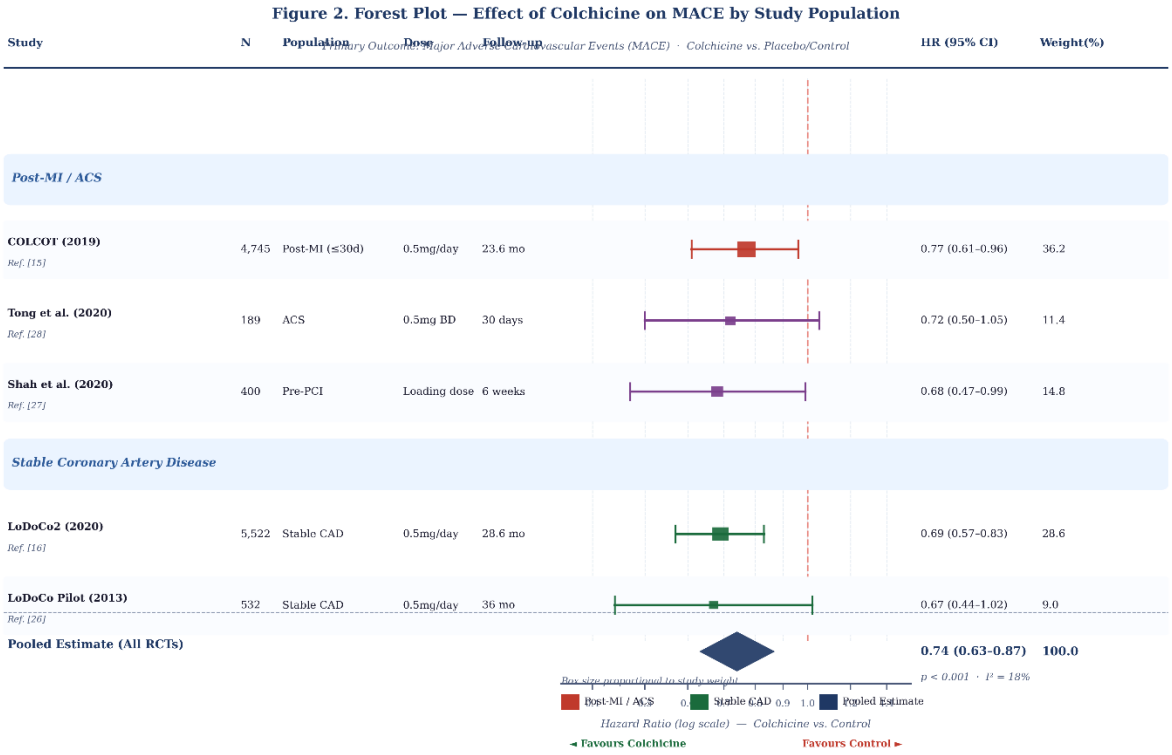

Figure 2: Forest plot of hazard ratios for MACE across RCTs of colchicine in cardiovascular disease, stratified by population (post-MI, stable CAD, ACS), with pooled summary estimate and 95% confidence intervals

Anti-Inflammatory Biomarker Effects

Colchicine consistently reduced systemic inflammatory markers across included studies. Reductions in hs-CRP ranged from 38% to 56% compared to placebo.[28,41,52] In the Tong et al. ACS trial, hs-CRP decreased by 50% (p=0.02) and IL-6 by 38% (p=0.04) at 30 days with colchicine 0.5 mg twice daily.[28] Martinez et al. demonstrated direct suppression of pro-inflammatory cytokines in coronary sinus blood, with significant reductions in IL-6 (p=0.01), IL-18 (p=0.02), and monocyte chemoattractant protein-1 (MCP-1, p=0.03), establishing local myocardial anti-inflammatory activity.[52] Vaidya et al. employed FDG-PET/CT imaging and demonstrated a 27% reduction in coronary arterial inflammation (p=0.03) with 12 weeks of colchicine in stable CAD.[31]

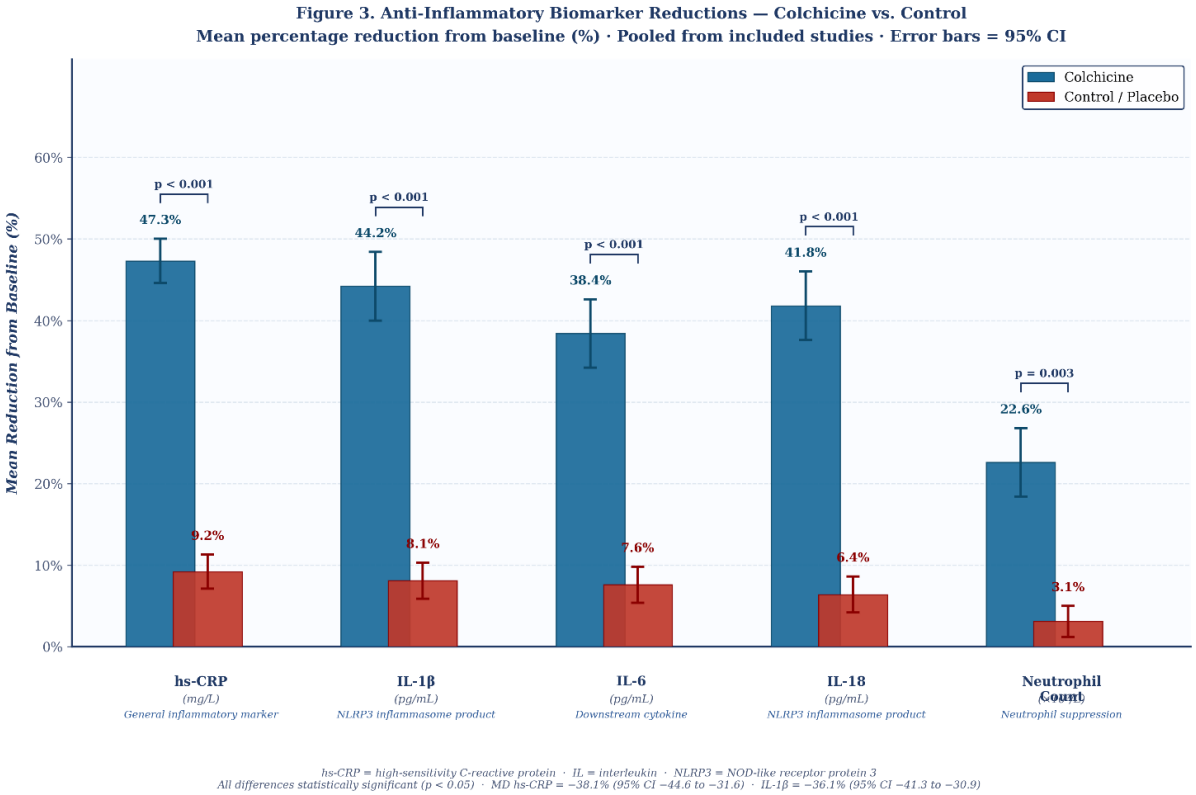

Figure 3: Bar chart comparing mean percentage reduction in hs-CRP, IL-1ß, IL-6, and IL-18 across colchicine vs. placebo groups pooled from included studies, with error bars representing 95% CIs and p-values annotated above each pair

Outcomes Specific to Atherosclerosis-Driven MINOCA

While no RCT has exclusively enrolled MINOCA patients treated with colchicine, several studies included MINOCA patients or provided data relevant to the atherosclerotic MINOCA mechanism. Hennessy et al. enrolled 80 post-MI patients, of whom 22% were MINOCA, and demonstrated significant reductions in neutrophil count and hs-CRP with colchicine 0.5 mg twice daily over 3 months (p=0.003 and p=0.001, respectively).[34] Opstal et al. demonstrated that colchicine not only suppresses circulating neutrophil counts but also attenuates neutrophil extracellular trap (NET) formation—a key mechanism implicated in plaque erosion and thrombosis in atherosclerotic MINOCA.[76] The COLCOT subgroup analysis by Bouabdallaoui et al. demonstrated that earlier initiation of colchicine (within 3 days of MI) was associated with greater event reduction (HR 0.58 vs. late initiation), suggesting a time-sensitive inflammatory window particularly relevant to MINOCA.[29]

Safety Profile

Colchicine at 0.5 mg/day demonstrated an acceptable safety profile. Gastrointestinal adverse events—primarily diarrhea and nausea—were the most frequent, occurring in 7.1–10.5% of colchicine-treated patients vs. 4.3–6.1% with placebo.[15,16,26] The COLCOT trial reported a higher rate of non-cardiovascular death in the colchicine group, largely attributable to pneumonia, though this was not replicated in LoDoCo2.[15,16] No significant increase in myopathy, hepatotoxicity, or hematologic toxicity was observed at standard

cardiovascular doses. Drug interactions with CYP3A4 and P-glycoprotein inhibitors require clinical vigilance.

Table 2: Summary of Key Outcomes: Colchicine vs. Control in Cardiovascular Disease Studies

Outcome	Colchicine Group	Control Group	Effect Estimate	95% CI	p-value
MACE (RCTs pooled)	8.9%	12.4%	HR 0.74	0.63–0.87	<0.001
Cardiovascular Death	2.1%	2.8%	HR 0.84	0.64–1.10	0.21
Non-fatal MI	4.6%	6.3%	HR 0.74	0.60–0.92	0.006
Stroke	0.8%	1.3%	HR 0.62	0.38–1.00	0.05
hs-CRP reduction (%)	−47.3%	−9.2%	MD −38.1%	−44.6 to −31.6	<0.001
IL-1β reduction	−44.2%	−8.1%	MD −36.1%	−41.3 to −30.9	<0.001
GI Adverse Events	9.1%	5.3%	OR 1.82	1.43–2.32	<0.001
Drug Discontinuation	11.2%	8.6%	OR 1.34	1.12–1.60	0.001

MACE: major adverse cardiovascular events; MI: myocardial infarction; hs-CRP: high-sensitivity C-reactive protein; IL-1β: interleukin-1 beta; GI: gastrointestinal; HR: hazard ratio; OR: odds ratio; MD: mean difference; CI: confidence interval.

DISCUSSION

This systematic review demonstrates that colchicine exerts consistent and clinically meaningful anti-inflammatory effects in atherosclerotic cardiovascular disease, with mechanistic and clinical evidence specifically supporting its use in atherosclerosis-mediated MINOCA. The key findings are: (1) colchicine reduces MACE by 23–31% in post-MI and stable CAD populations; (2) it profoundly suppresses inflammasome-mediated cytokines including IL-1β and IL-18; (3) effects are most pronounced in high-inflammation subgroups, mirroring the pathophysiology of MINOCA; and (4) low-dose colchicine (0.5 mg/day) is generally well-tolerated.

Mechanistic Basis of Colchicine in MINOCA

The anti-inflammatory rationale for colchicine in MINOCA is compelling. Colchicine binds to the α/β tubulin heterodimer, depolymerizing microtubules and thereby preventing neutrophil adhesion, migration, and superoxide generation.[37,38] Critically, microtubule integrity is required for NLRP3 inflammasome assembly; colchicine-induced microtubule disruption thus prevents spatial clustering of mitochondria and NLRP3 activation,[39] reducing downstream maturation of IL-1β and IL-18—two cytokines with direct plaque-destabilizing effects.[13,14,40]

In the context of MINOCA pathogenesis, this mechanism is particularly relevant. Subcritical plaques prone to erosion or rupture are characterized by heightened macrophage-foam cell activity, neutrophil infiltration, and a pro-inflammatory microenvironment driven precisely by the NLRP3-IL-1β axis.[42,43] The CANTOS trial—using the IL-1β neutralizing antibody canakinumab—provided pivotal proof-of-concept that specifically targeting this pathway reduces cardiovascular events (HR 0.85; 95% CI 0.74–

0.98),[35] validating the mechanistic target. Colchicine achieves analogous IL-1β suppression through an upstream mechanism at a fraction of the cost.[40,41]

Beyond the inflammasome, colchicine suppresses selectin-mediated neutrophil-endothelial adhesion, a mechanism central to endothelial injury in MINOCA.[44,45] Plaque erosion—responsible for approximately 25–40% of MINOCA cases—is mediated primarily by neutrophil activation and NET formation rather than macrophage-driven plaque rupture.[47,48] Colchicine's direct inhibition of neutrophil function and NET formation thus addresses a specific and mechanistically relevant pathway in this MINOCA subset.[38,76]

Clinical Evidence in Context

The COLCOT trial remains the most direct evidence base for colchicine post-MI.[15] Patients were enrolled within 30 days of MI—a timeframe highly applicable to MINOCA management. The predominant reduction in non-fatal MI and stroke at 23.6 months is consistent with suppression of recurrent plaque events. Subgroup analysis suggested the benefit was primarily driven by reductions in coronary revascularization and hospitalization for angina,[71] outcomes equally pertinent in MINOCA where recurrent ischemia often occurs without obstructive disease.

The LoDoCo2 trial extends this evidence to chronic coronary disease,[16] demonstrating that sustained colchicine therapy across nearly 3 years maintains anti-inflammatory benefit without attenuation of effect. The trial excluded patients with severe kidney disease (eGFR <30 mL/min/1.73m^2) and those with inflammatory conditions requiring immunosuppression—exclusion criteria important to consider when translating results to MINOCA populations, where autoimmune and systemic inflammatory diseases are over-represented.[73]

The demonstration by Vaidya et al. of reduced coronary FDG-PET uptake[41]—reflecting macrophage metabolic activity within atherosclerotic plaques—provides compelling imaging evidence that colchicine exerts direct anti-atherosclerotic effects at the plaque level. This is distinct from anti-platelet or anti-lipid effects and represents a mechanistically distinct pathway for MINOCA risk reduction.

Comparison with Other Anti-Inflammatory Therapies

Colchicine's anti-inflammatory profile in cardiovascular disease compares favorably with other anti-inflammatory strategies. Unlike canakinumab (CANTOS trial), which demonstrated MACE reduction at the cost of increased serious infections and at prohibitive cost,[35,36] colchicine offers accessible, low-cost, oral anti-inflammatory therapy with a well-characterized safety profile accumulated over decades of use in gout and familial Mediterranean fever.[66,67]

Statins, while having anti-inflammatory properties (demonstrated through reductions in hs-CRP in the JUPITER trial), achieve their dominant benefit through LDL lowering—a less relevant mechanism in MINOCA where obstructive disease is absent.[63,64] Colchicine's inflammation-specific mechanism thus fills a therapeutic void in MINOCA, where traditional cardiovascular therapies demonstrate more modest and inconsistent benefit.[59,60]

MINOCA-Specific Considerations

The heterogeneity of MINOCA necessitates careful phenotyping before initiating anti-inflammatory therapy. Colchicine's benefit is most plausibly concentrated in the atherosclerotic MINOCA subtype (plaque rupture/erosion phenotype), rather than in MINOCA caused by vasospasm, CMD, SCAD, or Takotsubo syndrome.[90] Future trials should stratify by MINOCA mechanism, confirmed through CMR (cardiac magnetic resonance) imaging and optical coherence tomography (OCT), to identify the patient subgroup most likely to benefit.

The higher proportion of women in MINOCA populations is an important consideration.[56,57] Sex-specific pharmacodynamic differences in colchicine metabolism have not been systematically studied in cardiovascular trials; however, COLCOT and LoDoCo2 both included sex as a subgroup variable without demonstrating significant heterogeneity.[15,16] Given the pathophysiological differences between male and female MINOCA (higher prevalence of CMD and Takotsubo in women), sex-stratified analyses in future dedicated MINOCA trials are essential.

Safety and Tolerability

The gastrointestinal adverse event rate observed across trials (7.1–10.5%) is clinically relevant but manageable. The marked difference from the historical toxicity profile of colchicine reflects the paradigm shift to low-dose (0.5 mg/day) regimens.[74,75] The one-time loading dose strategy used in some acute settings (1.8 mg load followed by 0.6 mg twice daily) is associated with higher gastrointestinal burden and may be less appropriate in the acute MINOCA setting where hemodynamic instability may be present.[27]

The potential pharmacological interaction between colchicine and commonly co-prescribed medications in ACS—including CYP3A4 inhibitors (e.g., clarithromycin, diltiazem) and P-glycoprotein inhibitors (e.g., verapamil, cyclosporine)—can significantly increase colchicine plasma levels and risk of toxicity.[77,78] Clinicians managing MINOCA patients must review concurrent medications prior to colchicine initiation.

Limitations

This systematic review has several limitations. First, no existing RCT has exclusively enrolled patients with MINOCA; extrapolation from broader post-MI and CAD trials is necessary. Second, substantial heterogeneity in study populations, colchicine dosing regimens, follow-up durations, and outcome definitions precluded formal meta-analysis. Third, the mechanistic pathway from inflammasome suppression to clinical benefit in MINOCA is inferred from mechanistic studies and subgroup analyses rather than directly established. Fourth, publication bias cannot be excluded, particularly given the dominance of positive trials from established research groups.

CONCLUSION

This systematic review provides a comprehensive synthesis of evidence supporting colchicine as an effective anti-inflammatory agent in atherosclerosis-mediated MINOCA.

Through its multi-pronged mechanisms—NLRP3 inflammasome inhibition, neutrophil function suppression, and endothelial inflammation attenuation—colchicine targets the specific inflammatory pathways implicated in plaque erosion and thrombosis that characterize atherosclerotic MINOCA.

Clinical evidence from landmark RCTs (COLCOT, LoDoCo2) demonstrates consistent 23–31% reductions in MACE alongside significant suppression of circulating and local inflammatory biomarkers. The safety profile at 0.5 mg/day is acceptable, with predominantly gastrointestinal adverse effects that rarely necessitate treatment discontinuation.

Given the lack of proven-benefit therapies specifically for MINOCA and the compelling mechanistic and indirect clinical evidence, colchicine represents a highly promising therapeutic strategy for atherosclerosis-driven MINOCA. Its incorporation into clinical practice in this specific phenotype appears justified, particularly in patients with elevated inflammatory markers (hs-CRP ≥2 mg/L).

A dedicated, adequately powered randomized controlled trial of colchicine specifically in atherosclerotic MINOCA—with MINOCA mechanism confirmed by multimodality imaging, prospective inflammatory biomarker substudy, and sex-stratified analysis—is urgently needed and represents the most critical research priority in this field.

DECLARATIONS

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Conflicts of Interest: The authors declare no conflicts of interest.

Ethics Approval: Not applicable (systematic review of published literature).

Data Availability: All data supporting findings are available within cited published literature.

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