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Brief Report

Colchicine: A New Dawn for Preventing Complications After Heart Attack? Unveiling its Network Pharmacology and the COLD-MI Trial

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ABSTRACT

Acute myocardial infarction, or heart attack, remains a significant cause of morbidity and mortality globally. Despite substantial advancements in acute management, the residual risk of recurrent coronary events, including myocardial infarction, stroke, and heart failure, poses a substantial challenge. This persistent threat underscores the imperative for ongoing research into novel therapeutic strategies to improve patient outcomes. The recently published COLD-MI trial results has generated significant interest by highlighting the potential of colchicine, a readily available and inexpensive medication, in preventing complications after a heart attack. This report delves into the rationale behind the COLD-MI trial, scrutinizes its findings, and explores the implications in correlation with network pharmacology of colchicine for future clinical practice.

Keywords: Myocardial infarction, Ischemia, Cardiology, Cardiac Care.

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BACKGROUND

Acute Myocardial Infarction (AMI), commonly referred to as a heart attack, is a critical medical condition arising from a sudden blockage of blood flow to the heart muscle.[1,2] This blockage results in the death of heart tissue. It remains a leading cause of morbidity and mortality worldwide, imposing a substantial burden on healthcare systems and societies.[3,4] The global incidence of AMI is significant and varies across different regions. While there has been improvement in AMI rates due to optimal risk factor management and advancements in medical care, the disease burden and its consequences specially under comorbid conditions remains a cause for concern.[3,4] These concerns are further fortified with urban lifestyle, changing dietary habits, increased stress levels, and growing prevalence of risk factors such as smoking, hypertension, and diabetes. It is essential to note that the true global burden of AMI is likely underestimated due to variations in data collection and reporting systems across countries.

Biological response and healing post heart attack

Following a heart attack, the body undergoes a complex and gradual healing process. The heart, unable to regenerate damaged muscle cells, undergoes a process of repair and remodelling.[5-7] The immediate aftermath of a heart attack involves the death (necrosis and apoptosis) of heart muscle cells in the affected area.[8,9] The body initiates an inflammatory response to clear away dead tissue.[5,10,11] White blood cells are dispatched to the site of injury to clean up the debris. As the inflammation subsides, the heart begins to repair itself by forming scar tissue. This scar tissue replaces the damaged heart muscle. The endogenous regeneration of heart muscle is not universally observed, but does occur is some patients.[12-15] The heart may undergo changes in shape and size as the scar tissue/heart muscles forms (remodelling). The scar tissue is not as efficient as healthy heart muscle, which can lead to a weakened heart.[16-19] The electrical activity of the heart may be disrupted due to scar tissue, potentially leading to arrhythmias.[20,21] The healing process typically takes several weeks.[5,22-25] However, the heart continues to adapt and remodel for months, and even years, after a heart attack.

Several factors influence the healing process, including: Size of the heart attack (Larger heart attacks tend to have more extensive damage and a longer healing period). Prompt medical treatment (Early intervention can limit heart damage and improve the healing process). Overall heart health (Pre-existing heart conditions or other health issues can impact healing).[5,22-25] It's crucial to emphasize that while the heart can heal to a certain extent, it cannot fully regain its pre-injury state. Therefore, patients who have experienced a heart attack need ongoing care and lifestyle modifications to manage their heart health and reduce the risk of future complications. One such complication

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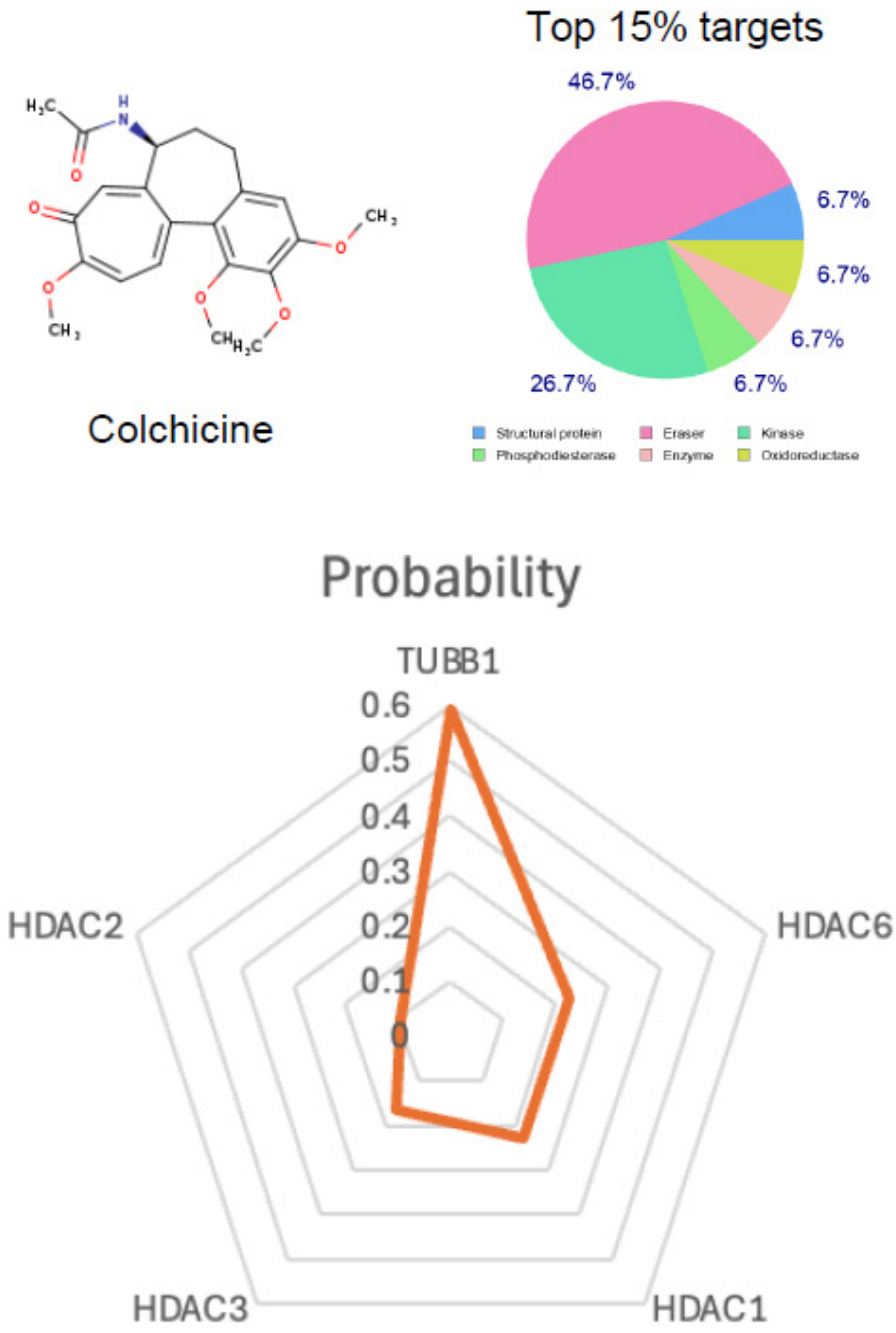

Figure 1: Target profile of colchicine. Chemical structure of colchicine along its major target categories is shown in the top panel. The major target categories of colchicine in humans were eraser's (47% of the top 15% targets) and kinases (27% of the top 15% targets). Bottom panel shows the probability of interaction with the top 5 targets of colchicine identified in the Swiss target prediction database (the gene codes of the targets are mentioned in the figure).

commonly observed is an undesirable phenomenon known as sympathetic denervation.[26-28] This refers to the damage or loss of nerves that regulate heart function and blood pressure. Sympathetic denervation disrupts the delicate balance of the autonomic nervous system, leading to an overactive sympathetic state characterized by increased heart rate, blood pressure, and inflammation. This heightened sympathetic activity is associated with an increased risk of adverse cardiovascular events including progressing towards heart failure.[26,29]

Synopsis of the COLD-MI trial and colchicine pharmacology

The recently published COLD-MI trial[26,29-32] aimed to investigate whether colchicine could mitigate the detrimental effects of sympathetic denervation after a heart attack, thereby reducing

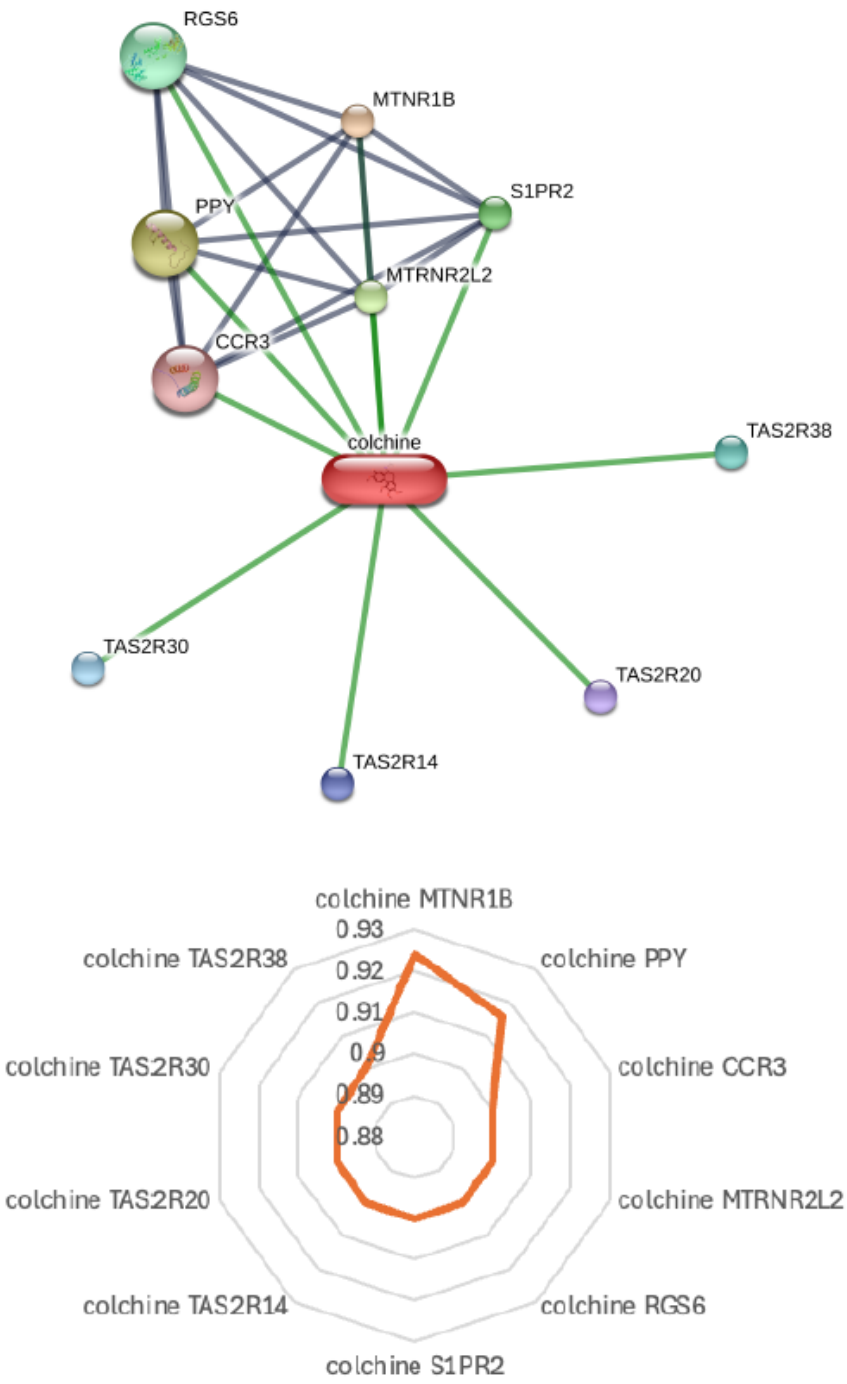

Figure 2: Target networks of colchicine. Top panel shows the top ten target networks of colchicine in humans identified in the STITCH database. Bottom panel shows the interaction scores of colchicine with each of its target network (the targets are represented by their gene code). The highest interaction score was observed for MTNR1B and PPY.

the risk of future complications. Colchicine, a natural alkaloid derived from the autumn crocus (Colchicum autumnale), has a rich history dating back to its FDA approval in 1961.[33,34] Traditionally employed for the acute management of gout flares[35] and as a prophylactic treatment for familial Mediterranean fever,[36,37] the therapeutic spectrum of colchicine has expanded considerably. Contemporary clinical practice also leverages its anti-inflammatory properties for the prevention of major cardiovascular events.[30,38-41] Furthermore, ongoing research delves into its potential in managing a diverse array of inflammatory and fibrotic conditions.[42,43] Recent research suggests colchicine possesses anti-inflammatory properties and may modulate the activity of the autonomic nervous system.[30-32,44] Colchicine exerts its anti-inflammatory effects through multiple mechanisms. By

inhibiting microtubule polymerization,[45] it disrupts key cellular processes in neutrophils and monocytes, including activation, migration, and degranulation.[46-48] This interference with the cytoskeleton also prevents the assembly of the inflammasome complex, a critical mediator of inflammation.[49] Consequently, colchicine reduces the production of inflammatory cytokines such as interleukin-1β.[33,50] Additionally, the drug attenuates neutrophil adhesion and reactive oxygen species generation. These combined actions contribute to colchicine's efficacy in managing gout and potentially preventing cardiovascular events.

The COLD-MI trial was a multicenter, randomized, double-blind, placebo-controlled trial that enrolled over 4,400 patients hospitalized for a heart attack.[30-32] Participants were randomly assigned to receive either colchicine or a placebo for one year, alongside standard heart attack treatment. The primary endpoint of the study was myocardial sympathetic denervation assessed at six months via 123I-metaiodobenzylguanidine scintigraphy (123I-MIBG SPECT) imaging. Secondary endpoints encompassed clinical outcomes such as survival and revascularization rates, as well as imaging parameters including planar 123I-MIBG Heart-to-Mediastinum (H/M) ratio and Left Ventricular Ejection Fraction (LVEF) by echocardiography. Additionally, we evaluated arrhythmic burden through electrocardiographic analysis and heart rate variability assessment.

The trial yielded intriguing results.[30-32] Compared to the placebo group, patients receiving colchicine (1 mg colchicine tablet, one per day for 30 days, initiated within 48 hr after revascularization) experienced a statistically significant reduction in the primary endpoint. Patients who took colchicine were less likely to experience myocardial sympathetic denervation (damage to the heart's nerve supply) compared to those who didn't.[30-32] Pharmacometrics suggested a ~58% relative risk reduction preferentially in the non-infarcted zones than the infarcted zones, signifying a noteworthy potential benefit. However, it is essential to note that the odd ratio reported was an unadjusted analysis, meaning other factors that could influence the results (like age, other medications, severity of heart attack) haven't been accounted for. Hence further analysis with adjustments for these factors will be essential to assess the true effect of colchicine. The benefits in secondary outcomes were evident on H/M ratio, suggesting a potential protective effect of colchicine on myocardial sympathetic innervation, with no therapeutic influence on the extent of heart damage (necrosis), overall heart function (LVEF), heart rhythm, heart rate variability, or major clinical events. In addition to the benefits observed, colchicine was associated with more gastrointestinal side effects[51-54] compared to the control group.

Network Pharmacology of Colchicine

In lieu of these new findings from COLD-MI trial, an objective assessment of colchicine's network pharmacology[55-59] is essential to understand if colchicine can be a beacon of hope or is a glimmer in the dark. Although colchicine is previously reported to be well-tolerated, the significant incidence of gastrointestinal side effects is a cause for concern. While the study showed a positive effect on the H/M ratio, suggesting potential benefits for myocardial sympathetic innervation,[30-32] the overall long-term impact on patient outcomes is not clear-cut. The protection for the heart's sympathetic innervation offered by colchicine could potentially also have long-term implications (beyond 6 months) for heart health, and further research will be needed to confirm this. It will also be essential to understand the mechanism of action/s by which colchicine exerts its protective effects on sympathetic innervation. Further research is needed to elucidate whether the observed benefits stem from its anti-inflammatory properties, direct modulation of the autonomic nervous system, or a combination of both or a completely new mechanism/s. The screening in Swiss target prediction site[56-61] for human specific targets of colchicine indicated Histone deacetylase's (1, 2, 3 and 6) to be their major targets followed by kinases (Figure 1). The interaction probability (0.6) of colchicine with tubulin beta-1 chain was the highest, and showed similar degree of interactions with all types of histone deacetylase's (Figure 1). The screening of colchicine networks in STITCH database revealed six general targets (MTNR1B, PPY, CCR3, MTRNR2L2, RGS6, and S1PR2) and four taste receptor specific targets (TAS2R14, TAS2R20, TAS2R30, and TAS2R38) (Figure 2), all with high network scores (>0.9). The highest network score of colchicine was observed for melatonin receptor 1B (MTNR1B, 0.93) and pancreatic polypeptide (PPY, 0.92). Considering these targets of colchicine the observation of significant gastrointestinal side effects among patients are not surprising.[30-32,49,62] The MT-RNR2-like 2 (MTRNR2L2) is known to be neuroprotective factor and possibly may have a role in the reduced myocardial sympathetic denervation following colchicine treatment. In addition to these targets of Colchicine, Chemokine (C-C motif) receptor 3 (CCR3), Sphingosine 1-Phosphate Receptor 2 (S1PR2) and Regulator of G-protein Signalling 6 (RGS6) through their influence on myeloid progenitors are likely to be responsible for beneficial effects of colchicine post AMI.

CONCLUSION

The COLD-MI trial represents a pivotal advancement in our understanding of post-myocardial infarction care. The demonstration of colchicine's efficacy in reducing recurrent cardiovascular events offers a promising therapeutic avenue. However, this is merely the beginning of a new chapter in heart disease management. To fully realize the potential of colchicine, several areas warrant further investigation. Refining risk stratification will be essential to identify patients who may derive the greatest benefit from this medication. Exploring synergistic interactions with other established therapies could lead to even more robust prevention strategies. Additionally, a

comprehensive cost-effectiveness analysis is needed to evaluate the economic implications of colchicine integration into routine care. While the results of the COLD-MI trial are encouraging, it is imperative to conduct long-term studies to assess the sustained benefits and safety profile of colchicine. Delving deeper into the underlying mechanisms of action will provide valuable insights for developing novel therapeutic approaches. Ultimately, the goal is to translate these findings into improved patient outcomes. By carefully considering the data and conducting rigorous research, we can optimize the use of colchicine and other preventive strategies to reduce the burden of heart disease.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

123I-MIBG SPECT: 123I-metaiodobenzylguanidine scintigraphy; **AMI:** Acute Myocardial Infarction; **CCR3:** Chemokine (C-C motif) receptor 3; **COLD-MI:** Colchicine to Prevent Sympathetic Denervation after an Acute Myocardial Infarction; **H/M:** Heart-to-Mediastinum; **HDAC1:** Histone deacetylase 1; **HDAC2:** Histone deacetylase 2; **HDAC3:** Histone deacetylase 3; **HDAC6:** Histone deacetylase 6; **LVEF:** Left Ventricular Ejection Fraction; **MTNR1B:** Melatonin receptor type 1B; **MTRNR2L2:** Humanin-like 2; **PPY:** Pancreatic polypeptide prohormone; **RGS6:** Regulator of G-protein signaling 6; **S1PR2:** Sphingosine 1-phosphate receptor 2; **TAS2R14:** Taste receptor, type 2, member 14; **TAS2R20:** Taste receptor, type 2, member 20' **TAS2R30:** Taste receptor, type 2, member 30; **TAS2R38:** Taste receptor, type 2, member 38; **TUBB1:** Tubulin beta-1 chain.

REFERENCES

1. Samsky MD, Morrow DA, Proudfoot AG, Hochman JS, Thiele H, Rao SV. Cardiogenic shock after acute myocardial infarction: a review. *Jama*. 2021;326:1840-50.
2. Gong FF, Vaitenas I, Malaisrie SC, Maganti K. Mechanical complications of acute myocardial infarction: a review. *JAMA cardiology*. 2021;6:341-9.
3. Milazzo V, Cosentino N, Genovese S, Campodonico J, Mazza M, De Metrio M, Marenzi G. Diabetes mellitus and acute myocardial infarction: impact on short and long-term mortality. *Diabetes: from Research to Clinical Practice*: *Volume 4*. 2021:153-69.
4. Damluji AA, Van Diepen S, Katz JN, Menon V, Tamis-Holland JE, Bakitas M, *et al.* Mechanical complications of acute myocardial infarction: a scientific statement from the American Heart Association. *Circulation*. 2021;144:e16-e35.
5. Matter MA, Paneni F, Libby P, Frantz S, Stähli BE, Templin C, *et al.* Inflammation in acute myocardial infarction: the good, the bad and the ugly. *European heart journal*. 2024;45:89-103.
6. Del Buono MG, Moroni F, Montone RA, Azzalini L, Sanna T, Abbate A. Ischemic cardiomyopathy and heart failure after acute myocardial infarction. *Current Cardiology Reports*. 2022;24:1505-15.
7. Berezin AE, Berezin AA. Adverse cardiac remodelling after acute myocardial infarction: old and new biomarkers. *Disease Markers*. 2020; 2020:1215802.
8. Nair R, Johnson M, Kravitz K, Huded C, Rajeswaran J, Anabila M, *et al.* Characteristics and outcomes of early recurrent myocardial infarction after acute myocardial infarction. *Journal of the American Heart Association*. 2021;10:e019270.
9. Duncan SE, Gao S, Sarhene M, Coffie JW, Linhua D, Bao X, *et al.* Macrophage activities in myocardial infarction and heart failure. *Cardiology Research and Practice*. 2020; 2020:4375127.
10. Paolisso P, Bergamaschi L, Santulli G, Gallinoro E, Cesaro A, Gragnano F, *et al.* Infarct size, inflammatory burden, and admission hyperglycemia in diabetic patients with acute myocardial infarction treated with SGLT2-inhibitors: a multicenter international registry. *Cardiovascular Diabetology*. 2022;21:77.
11. Mahtta D, Sudhakar D, Koneru S, Silva GV, Alam M, Virani SS, *et al.* Targeting inflammation after myocardial infarction. *Current Cardiology Reports*. 2020;22:1-10.
12. Tan Y, Wang L, Chen G, Liu W, Li Z, Wang Y, *et al.* Hyaluronate supports hESC-cardiomyocyte cell therapy for cardiac regeneration after acute myocardial infarction. *Cell Proliferation*. 2020;53:e12942.
13. Giacca M. Cardiac regeneration after myocardial infarction: an approachable goal. *Current cardiology reports*. 2020;22:122.
14. Hynes B, Kumar AH, O'Sullivan J, Klein Buneker C, Leblond A-L, Weiss S, *et al.* Potent endothelial progenitor cell-conditioned media-related anti-apoptotic, cardiotrophic, and pro-angiogenic effects post-myocardial infarction are mediated by insulin-like growth factor-1. *European heart journal*. 2013;34:782-789.
15. O'Sullivan JF, Leblond A-L, Kelly G, Kumar AH, Metharom P, Büneker CK, *et al.* Potent long-term cardioprotective effects of single low-dose insulin-like growth factor-1 treatment postmyocardial infarction. *Circulation: Cardiovascular Interventions*. 2011;4:327-35.
16. Brazile BL, Butler JR, Patnaik SS, Claude A, Prabhu R, Williams LN, *et al.* Biomechanical properties of acellular scar ECM during the acute to chronic stages of myocardial infarction. *Journal of the mechanical behavior of biomedical materials*. 2021;116:104342.
17. Aceves JL, López RV, Terán PM, Escobedo CM, Muciño MAM, Castillo GG, *et al.* Autologous CXCR4+ hematopoietic stem cells injected into the scar tissue of chronic myocardial infarction patients normalizes tissue contractility and perfusion. *Archives of Medical Research*. 2020;51:135-44.
18. Messroghli DR, Niendorf T, Schulz-Menger J, Dietz R, Friedrich MG. T1 mapping in patients with acute myocardial infarction: myocardial infarction and scar. *Journal of Cardiovascular Magnetic Resonance*. 2003;5:353-9.
19. Uusimaa P, Risteli J, Niemelä M, Lumme J, Ikäheimo M, Jounela A, *et al.* Collagen scar formation after acute myocardial infarction: relationships to infarct size, left ventricular function, and coronary artery patency. *Circulation*. 1997;96:2565-72.
20. Cesaro A, Gragnano F, Paolisso P, Bergamaschi L, Gallinoro E, Sardu C, *et al.* In-hospital arrhythmic burden reduction in diabetic patients with acute myocardial infarction treated with SGLT2-inhibitors: Insights from the SGLT2-I AMI PROTECT study. *Frontiers in Cardiovascular Medicine*. 2022;9:1012220.
21. Vallabhajosyula S, Patlolla SH, Verghese D, Ya'Qoub L, Kumar V, Subramaniam AV, *et al.* Burden of arrhythmias in acute myocardial infarction complicated by cardiogenic shock. *The American journal of cardiology*. 2020;125:1774-81.
22. Chalise U, Becirovic-Agic M, Lindsey ML. The cardiac wound healing response to myocardial infarction. *WIREs mechanisms of disease*. 2023;15:e1584.
23. Dreyer RP, Pavlo AJ, Hersey D, Horne A, Dunn R, Norris CM, *et al.* "Is My Heart Healing?" A Meta-synthesis of Patients' Experiences After Acute Myocardial Infarction. *Journal of Cardiovascular Nursing*. 2021;36:517-30.
24. Reindl M, Tiller C, Holzknecht M, Lechner I, Hein N, Pamminger M, *et al.* Aortic Stiffness and Infarct Healing in Survivors of Acute ST-Segment-Elevation Myocardial Infarction. *Journal of the American Heart Association*. 2020;9:e014740.
25. Arai AE. Healing after myocardial infarction: a loosely defined process. In: American College of Cardiology Foundation Washington, DC; 2015:680-3.
26. Ziegler KA, Ahles A, Wille T, Kerler J, Ramanujam D, Engelhardt S. Local sympathetic denervation attenuates myocardial inflammation and improves cardiac function after myocardial infarction in mice. *Cardiovascular research*. 2018;114:291-9.
27. Joho S, Asanoi H, Takagawa J, Kameyama T, Hirai T, Nozawa T, *et al.* Cardiac sympathetic denervationmodulates the sympathoexcitatoryresponse to acute myocardial ischemia. *Journal of the American College of Cardiology*. 2002;39:436-42.
28. Hartikainen J, Kuikka J, Mäntysaari M, Länsimies E, Pyörälä K. Sympathetic reinnervation after acute myocardial infarction. *The American journal of cardiology*. 1996;77:5-9.
29. Ciarka A, Borne Pvd, Pathak A. Myocardial infarction, heart failure and sympathetic nervous system activity: new pharmacological approaches that affect neurohumoral activation. *Expert opinion on investigational drugs*. 2008;17:1315-30.
30. Huet F, Mariano-Goulart D, Aguilhon S, Delbaere Q, Lacampagne A, Fauconnier J, *et al.* Colchicine to prevent sympathetic denervation after acute myocardial infarction: the COLD-MI trial. *European Heart Journal*. 2024;45:725-7.
31. Huet F, Fauconnier J, Legall M, Sicard P, Lozza C, Lacampagne A, *et al.* Low-dose colchicine prevents sympathetic denervation after myocardial ischemia-reperfusion: a new potential protective mechanism. *Future Science OA*. 2021;7:FSO656.
32. Huet F, Delbaere Q, Aguilhon S, Dupasquier V, Delseny D, Gervasoni R, *et al.* Colchicine to prevent sympathetic denervation after an acute myocardial infarction: the COLD-MI trial protocol. *Medicina*. 2021;57:1047.
33. Imazio M, Andreis A, Brucato A, Adler Y, De Ferrari GM. Colchicine for acute and chronic coronary syndromes. *Heart*. 2020;106:1555-60.
34. Slobodnick A, Shah B, Pillinger MH, Krasnokutsky S. Colchicine: old and new. *The American journal of medicine*. 2015;128:461-70.

35. Robinson PC, Terkeltaub R, Pillinger MH, Shah B, Karalis V, Karatza E, *et al.* Consensus statement regarding the efficacy and safety of long-term low-dose colchicine in gout and cardiovascular disease. *The American journal of medicine*. 2022;135:32-8.
36. Özen S, Sag E, Ben-Chetrit E, Gattorno M, Gül A, Hashkes PJ, *et al.* Defining colchicine resistance/intolerance in patients with familial Mediterranean fever: a modified-Delphi consensus approach. *Rheumatology*. 2021;60:3799-3808.
37. Marko L, Shemer A, Lidar M, Grossman C, Druyan A, Livneh A, Kivity S. Anakinra for colchicine refractory familial Mediterranean fever: a cohort of 44 patients. *Rheumatology*. 2021;60:2878-83.
38. Razavi E, Ramezani A, Kazemi A, Attar A. Effect of Treatment with Colchicine after Acute Coronary Syndrome on Major Cardiovascular Events: A Systematic Review and Meta-Analysis of Clinical Trials. *Cardiovascular Therapeutics*. 2022; 2022:8317011.
39. Samuel M, Tardif J-C, Bouabdallaoui N, Khairy P, Dubé M-P, Blondeau L, *et al.* Colchicine for secondary prevention of cardiovascular disease: a systematic review and meta-analysis of randomized controlled trials. *Canadian Journal of Cardiology*. 2021;37:776-785.
40. Akrami M, Izadpanah P, Bazrafshan M, Hatamipour U, Nouraein N, Drissi HB, *et al.* Effects of colchicine on major adverse cardiac events in next 6-month period after acute coronary syndrome occurrence; a randomized placebo-control trial. *BMC cardiovascular disorders*. 2021;21:1-10.
41. Roubille F, Tardif J-C. Colchicine for secondary cardiovascular prevention in coronary disease. In: Am Heart Assoc; 2020:1901-4.
42. Landau D, Shukri N, Arazi E, Tobar A, Segev Y. Beneficiary effects of colchicine on inflammation and fibrosis in a mouse model of kidney injury. *Nephron*. 2023;147:693-700.
43. Yue H, Liang W, Zhan Y, Zhang Z, Qin X, Bian L, He K, Wu Z. Colchicine: emerging therapeutic effects on atrial fibrillation by alleviating myocardial fibrosis in a rat model. *Biomedicine & Pharmacotherapy*. 2022;154:113573.
44. Korkmaz C, Cansu DÜ, Cansu GB. A Hypothesis regarding neurosecretory inhibition of stress mediators by colchicine in preventing stress-induced familial Mediterranean fever attacks. *Frontiers in Immunology*. 2022;13:834769.
45. Forkosh E, Kenig A, Ilan Y. Introducing variability in targeting the microtubules: Review of current mechanisms and future directions in colchicine therapy. *Pharmacology Research & Perspectives*. 2020;8:e00616.
46. Weng J-H, Koch PD, Luan HH, Tu H-C, Shimada K, Ngan I, *et al.* Colchicine acts selectively in the liver to induce hepatokines that inhibit myeloid cell activation. *Nature metabolism*. 2021;3:513-22.
47. Vaidya K, Tucker B, Kurup R, Khandkar C, Pandzic E, Barraclough J, *et al* Colchicine inhibits neutrophil extracellular trap formation in patients with acute coronary syndrome after percutaneous coronary intervention. *Journal of the American Heart Association*. 2021;10:e018993.
48. Bettiol A, Becatti M, Silvestri E, Argento FR, Fini E, Mannucci A, *et al.* Neutrophil-mediated mechanisms of damage and *in vitro* protective effect of colchicine in non-vascular Behçet's syndrome. *Clinical & Experimental Immunology*. 2021;206:410-21.
49. Pappritz K, Lin J, El-Shafeey M, Fechner H, Kühl U, Alogna A, *et al.* Colchicine prevents disease progression in viral myocarditis via modulating the NLRP3 inflammasome in the cardiosplenic axis. *ESC heart failure*. 2022;9:925-41.
50. Guan J, Abudouaini H, Lin K, Yang K. Emerging insights into the role of IL-1 inhibitors and colchicine for inflammation control in type 2 diabetes. *Diabetology & Metabolic Syndrome*. 2024;16:140.
51. Mewton N, Roubille F, Bresson D, Prieur C, Bouleti C, Bochaton T, *et al.* Effect of colchicine on myocardial injury in acute myocardial infarction. *Circulation*. 2021;144:859-69.
52. Kofler T, Kurmann R, Lehnick D, Cioffi GM, Chandran S, Attinger-Toller A, *et al.* Colchicine in patients with coronary artery disease: a systematic review and meta-analysis of randomized trials. *Journal of the American Heart Association*. 2021;10:e021198.
53. Andreis A, Imazio M, Casula M, Avondo S, De Ferrari GM. Colchicine efficacy and safety for the treatment of cardiovascular diseases. *Internal and Emergency Medicine*. 2021;16:1691-700.

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