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Colchicine Effect on Atrial Fibrillation Onset Prevention Depending on Non-High-Density Lipoprotein Cholesterol

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Abstract

Introduction. Atrial fibrillation (AF) is a common cardiac arrhythmia associated with increased morbidity and mortality, particularly in patients with chronic coronary artery disease (CAD). The anti-inflammatory properties of colchicine have been studied in cardiovascular disease, suggesting a potential role in the prevention of AF.
Purpose. To investigate the efficacy of colchicine in preventing the occurrence of AF in relation to non-high-density lipoprotein (non-HDL) cholesterol levels.
Materials and methods. This prospective study enrolled 224 CAD patients identified as high-risk for AF development using the FIND-AF algorithm. Patients were stratified into two groups based on their non-HDL cholesterol levels: group A (114 patients, ≥130 mg/dL) and group B (110 patients, <130 mg/dL). In a sub-analysis, group C included 102 patients with non-HDL levels ≥130 mg/dL, and group D included 122 patients with non-HDL <130 mg/dL. Within each group, patients were further randomized into subgroups receiving low-dose colchicine (0.5 mg/day) or no colchicine: group C1 (48 patients) and group C2 (56 patients) in group C, and group D1 (56 patients) receiving colchicine or group D2 (56 patients) without colchicine in group D. The primary endpoint was the incidence of AF episodes (>30 seconds) over a 6-month period. Statistical analysis was conducted using IBM SPSS version 21, with a significance level set at $p<0.05$.
Results. In the general cohort of patients, the colchicine group A demonstrated no reduction in AF compared to the control group B with 24 (21.04%) versus 28 (25.45%), respectively; p=0.871. In the sub-analysis among patients with high non-HDL cholesterol levels (group C), group C1 exhibited a significantly lower rate of AF onset compared to group C2 (9 patients, 37.54% vs. 15 patients, 62.52%, respectively; p=0.026). Conversely, in patients with low non-HDL cholesterol levels (group D), there was no significant difference in AF onset between group D1 and D2 (9 patients, 13.06% vs. 9 patients, 16.04%, respectively; p=0.781).
Conclusion. This study highlights the differential effect of colchicine on AF prevention in CAD patients based on their non-HDL cholesterol levels. Colchicine appears to be

more effective in preventing AF onset in patients with elevated non-HDL cholesterol levels (≥130 mg/dL) compared to those with lower levels. These findings underscore the importance of considering lipid profiles when assessing colchicine's effectiveness in AF prevention among CAD patients.
Keywords: colchicine, atrial fibrillation, chronic coronary artery disease, non-high-density lipoprotein cholesterol, risk of onset atrial fibrillation

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Влияние колхицина на профилактику возникновения фибрилляций предсердий в зависимости от уровня холестерина липопротеинов невысокой плотности

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Резюме

Введение. Фибрилляция предсердий (ФП) – распространенная сердечная аритмия, являющаяся причиной повышенной заболеваемости и смертности, особенно среди пациентов с хронической ишемической болезнью сердца (ИБС). Противовоспалительные свойства колхицина были изучены при сердечно-сосудистых заболеваниях, что предполагает его потенциальную роль в профилактике ФП.
Цель. Исследовать эффективность колхицина в профилактике возникновения ФП в зависимости от уровня холестерина липопротеинов невысокой плотности (не-ЛПВП).
Материалы и методы. В проспективное исследование было включено 224 пациента с ИБС и высоким риском развития ФП. Отбор проводили с использованием алгоритма FIND-AF. Пациенты были распределены по двум группам в зависимости от уровня холестерина не-ЛПВП: группа A – 114 пациентов (≥130 мг/дл) и группа B – 110 пациентов (<130 мг/дл). В ходе дополнительных исследований (субанализа) 102 пациента с уровнем не-ЛПВП ≥130 мг/дл были включены в группу C, а 122 пациента с уровнем не-ЛПВП <130 мг/дл – в группу D. Пациенты групп C и D в последующем были случайным образом распределены по подгруппам: C1 – 48 пациентов, получавших низкую дозу (0,5 мг/день) колхицина, и C2 – 54 пациента, не получавших колхицин, а также D1 – 56 пациентов с колхицином и D2 – 56 пациентов без колхицина.

Первичной контрольной точкой являлась частота эпизодов ФП (≥30 секунд) в течение 6 месяцев. Статистический анализ проводили с использованием IBM SPSS версии 21 с уровнем значимости p<0,05.

Результаты. В общей когорте пациентов в группе колхицина (A) не выявлено снижения частоты ФП по сравнению с контрольной группой (B): 24 (21,04%) и 28 (25,45%) соответственно, p=0,871. По результатам дополнительных исследований среди пациентов с высоким уровнем холестерина не-ЛПВП группа C1 продемонстрировала значительно более низкую частоту возникновения ФП по сравнению с группой C2: 9 (37,54%) и 15 (62,52%) соответственно, p=0,026. В противоположность этому у пациентов с низким уровнем холестерина не-ЛПВП не было выявлено значительной разницы в возникновении ФП между группами D1 и D2: 9 (13,06%) и 9 (16,04%) соответственно, p=0,781.

Заключение. Результаты исследования свидетельствуют о дифференциальном эффекте колхицина в профилактике ФП у пациентов с ИБС в зависимости от уровня холестерина не-ЛПВП. По всей видимости, колхицин повышает эффективность профилактики возникновения ФП у пациентов с повышенным уровнем холестерина не-ЛПВП (≥130 мг/дл) по сравнению с пациентами с более низким уровнем холестерина не-ЛПВП. Полученные результаты подчеркивают важность учета липидных профилей при оценке эффективности колхицина в профилактике ФП среди пациентов с ИБС.

Ключевые слова: колхицин, фибрилляция предсердий, хроническая коронарная болезнь, холестерин липопротеинов невысокой плотности, риск возникновения фибрилляций предсердий

■ INTRODUCTION

Atrial fibrillation (AF), a common cardiac arrhythmia, often complicates the clinical course of patients with coronary diseases [1]. New onset of atrial fibrillation aggravates the condition of patients with multiple diseases [2]. It worsens their quality of life and increases the incidence of stroke and mortality [3]. The questions for effective prevention strategies to mitigate the recurrence of AF in this patient population has led researchers to explore novel approaches [4]. Among these, colchicine, a medication historically used to treat gout and familial Mediterranean fever, has emerged as a promising candidate due to its anti-inflammatory properties [5].

Colchicine is one of the oldest remedies still in use today. It is derived from the bulb-like corms of the Colchicum autumnale plant, also known as autumn crocus. Its history as an herbal remedy for joint pain goes back at least to the 1500 BCE Egyptian manuscript, the Ebers Papyrus [6].

In June 2023, the U.S. FDA approved a low-dose colchicine regimen for the prevention of heart attacks in adult patients with multiple risk factors for cardiovascular disease. As an anti-inflammatory drug, a dose of 0.5mg/d reduces the rates of cardiovascular events by 25% to 30% in patients with coronary atherosclerosis. The drug is most effective in combination therapy with lipid-lowering and other anti-inflammatory medications [7].

Colchicine is effective for prevention of atrial fibrillation after cardiac surgery [8]. Potential applications for the anti-inflammatory effect of colchicine have been studied

with regard to atherosclerosis and chronic coronary disease (e.g., stable ischemic heart disease). In people with recent myocardial infarction (recent heart attack), it has been found to reduce risk of future cardiovascular events. Its clinical use may grow to include this indication [9].

More recently, colchicine has also shown therapeutic efficacy in alleviating cardiovascular complications of COVID-19. COLCOT and LoDoCo2 are two milestone clinical trials that confirm the curative effect of long-term administration of colchicine in reducing the incidence of cardiovascular events in patients with coronary artery disease [10].

Coronary artery disease is a significant risk factor for the development of atrial fibrillation [11]. Experimental studies have elucidated mechanisms by which atrial ischemia, particularly induced by right coronary artery (RCA) stenosis, can promote AF triggers and foster the development of an electro-anatomical substrate conducive to AF [12]. The interplay between inflammatory activation and oxidative stress creates a pathway that fosters atrial electrical and structural remodeling, leading to various complications, including atrial ectopy, interstitial fibrosis, and arrhythmias [13] Understanding these mechanisms is crucial for developing targeted therapeutic interventions.

Colchicine's potential as a drug that modulates microtubule polymerization adds another layer to its therapeutic profile. While the precise mechanism underlying colchicine's antifibrotic effects remains somewhat elusive, its efficacy has been corroborated in various experimental models [14]. Notably, studies have demonstrated that colchicine can prevent AF in animal models, such as rats, by inhibiting atrial fibrosis [15].

This finding opens ways for further research into its applications in human subjects.

We identified six studies on post-cardiac surgical patients, three on postpulmonary vein isolation (PVI)/ablation patients, and two on coronary artery disease [16].

In patients who underwent cardiac surgery, we found that colchicine is beneficial against postoperative atrial fibrillation (POAF) a p-value of 0.0001. We also found that in patients who underwent PVI/ablation, colchicine is beneficial in decreasing AF recurrence over three months with p-value of 0.0032 and over 12 months follow-up with p-value of 0.0008.

Our meta-analysis showed that in patients with coronary artery disease, colchicine had no significant benefit in decreasing the incidence of atrial fibrillation (AF). In the COLCOT trial conducted by Tardif et al. (2019) [17], the effect of colchicine was neutral in post-myocardial infarction patients, with a hazard ratio (HR) of 0.93 (0.59–1.46) and a p-value of 0.754. Similarly, in the LoDoCo2 trial conducted by Nidorf et al. (2020) [18], the effect of colchicine was also neutral regarding the new onset or first recurrence of atrial fibrillation or atrial flutter, with a hazard ratio (HR) of 0.86 (0.69–1.06) and a p-value of 0.16. We would like to highlight that in these trials, the ability of colchicine to prevent the occurrence of atrial fibrillation (AF) was not evaluated in relation to non-HDL cholesterol levels. Moreover, these trials did not consider the ability of colchicine to prevent AF in relation to non-high-density lipoprotein (non-HDL) cholesterol levels. Non-HDL cholesterol is calculated by subtracting high-density lipoprotein (HDL, or "good") cholesterol from total cholesterol [19], thus including all atherogenic lipoproteins. According to new guidelines on dyslipidemia, non-HDL cholesterol is considered an important predictor of worse prognoses and outcomes in patients with coronary diseases [20].

From this study, we conclude that colchicine may be beneficial for decreasing the incidence of AF in post-cardiac surgery patients and post-PVI/ablation patients. However, it may not reduce the incidence of AF in patients with coronary artery disease [21].

■ PURPOSE OF THE STUDY

This study aims to evaluate the efficacy of colchicine in preventing the onset of AF, particularly focusing on how this effect may vary according to levels of specifically non-high-density lipoprotein (non-HDL) cholesterol. Understanding the relationship between lipid profiles and the effectiveness of colchicine could provide valuable insights for tailoring preventive strategies in CAD patients.

■ MATERIALS AND METHODS

From 286 patient in 2022–2023 year, from several clinics, a total 214 patients with a high risk of developing AF by the FIND-AF algorithm [22] underwent randomization, from several clinics. 114 pt – were assigned to the colchicine and 110 pt, in non-colchicine group. The general and randomized patients basic characteristics is shown on table.

Basic characteristics of the Patients enrolled in the trail

Feature	Overall (no=224)	Colchicine Group A (no=114)	No Colchicine Group B (no=110)	P value
Epidemiological background				
Age (M±SD), years	62.0±6.0	62.0±5.9	62.1±6.0	1.00
Male, no. (%)	158 (71)	84 (74)	75 (69)	0.46
BMI, M (1Q; 3Q), kg/m^2	26.0 (24.0–28.5)	26.0 (24.0–28.5)	26.0 (24.0–28.8)	0.86
Smoking, no. (%)	80 (36)	42 (36)	38(36)	0.95
Hypertension, no. (%)	85 (38)	43 (38)	42 (38)	0.92
Diabetes, no. (%)	58 (26)	30 (26)	28(26)	0.89
Heart failure, no. (%)	54 (24)	30 (26)	24 (23)	0.61
Valvular heart disease, no. (%)	24 (11)	12(12)	10 (9)	0.55
Prior coronary revascularization, no. (%)	44 (20)	22 (21)	24(22)	0.96
Non-HDL cholsterol, M (1Q; 3Q), mg/dl	129(120–180)	128 (102-190)	126 (98–185)	0.95
LV ejection fraction, M (1Q; 3Q), %	52 (45–60)	53 (45–60)	52 (45–60)	0.87
LA diameter, (M±SD), mm	43.5±3.2	43.5±3.2	43.6±3.1	0.76
Treatment				
Beta-blocker, no. (%)	80 (36)	43 (38)	37 (34)	0.55
ACEi/ARB, no. (%)	129 (54)	64 (56)	65 (53)	0.70
CCB, no. (%)	92 (41)	47 (41)	45 (41)	0.95
Aspirin, no. (%)	220 (98)	112 (98)	108 (98)	0,97
Statin, no. (%)	89(37)	44 (36)	45 (39)	0.75

Notes: no. (%) – number of patients and percentage; M±SD – mean and standard deviation; M (1Q; 3Q) – median with interquartile range; ACEi – angiotensin converting enzyme inhibitor; ARB – angiotensin receptor blocker, AF – atrial fibrillation; BMI – Body mass index; CCB – calcium channel blocker; CRP – C reactive protein; LA – left atrium; LV – left ventricle.

Exclusion Criteria

Exclusion criteria were: age older than 80 years, active inflammatory or infectious disease or malignancy, known autoimmune diseases, corticosteroid or other immunosuppressive or immunomodulatory therapy, moderate or severe hepatic impairment, severe renal failure (estimated glomerular filtration rate <30 ml/min per 1.73 m^2), and inability or unwillingness to adhere to standard treatment or to provide consent. The protocol was approved by the clinic's review boards. All patients provided informed consent.

Study Design and Setting

In a randomized controlled trial, we assigned patients with chronic coronary disease to receive 0.5 mg of colchicine once daily or to not receive colchicine. The diagnosis of coronary artery disease was confirmed by previous coronary events (myocardial infarction, stenting procedures, CABG operations) after a physical stress test and 24-hour Holter monitoring. The primary endpoint was the new onset of atrial fibrillation lasting ≥30 seconds over a 6-month period, diagnosed clinically, by ECG, and through 24-hour Holter monitoring.Study treatments and adverse event monitoring

Monitoring of adverse events focused on gastrointestinal manifestations (mainly diarrhea), hepatotoxicity, myelotoxicity, myotoxicity, and alopecia. To monitor potential subclinical organ toxicity, complete blood counts and standard biochemical analyses (glucose, urea, creatinine, liver enzymes, creatinine kinase, lactate dehydrogenase) were performed after 4 weeks after starting Colchicine treatment.

Follow-up for AF Onset

The duration of the follow-up was 6 months, starting from the day the patient first received a Colchicine tablet. The main outcome measure was the onset of atrial fibrillation (AF).

Patients were followed up with visits on a monthly basis in dedicated outpatient clinics. Any of the following was considered to indicate AF onset: symptomatic AF (AF of any duration identified in symptom-triggered electrocardiograms at any time during the study), AF of any duration recorded in electrocardiograms obtained during patient visits, and AF of at least 30 seconds' duration in 24-hour ambulatory electrocardiogram recordings (Holter) performed monthly (each patient had 6 Holter recordings during the 6-month study period). Patients who missed more than one visit, more than one Holter recording, or both were excluded from the analysis to avoid underdetection of AF onset.

Statistical Analysis

Data were analyzed using IBM SPSS version 21. A p-value of <0.05 was considered statistically significant. Continuous variables were expressed as means ± standard deviation and were compared using the t-test if their distribution did not deviate significantly from normality; otherwise, nonparametric tests (the Wilcoxon and Mann – Whitney U tests) were used. Categorical variables were expressed as percentages and counts and were compared using the chi-square test. Kaplan-Meier analysis was performed to assess recurrence-free survival, and the log-rank test was used for comparisons between groups.

To achieve a rapid effect with Colchicine, we focused on a category of patients at high risk for developing atrial fibrillation. There are several algorithms for predicting the onset of atrial fibrillation, including the GARFIELD-AF Risk Calculator [23], the AFTRACK

calculator [24], and the BASIC-AF risk score [25]. However, we selected the "FIND AF" algorithm because it effectively identifies patients with a high likelihood of developing atrial fibrillation within a short period of six months.

A machine learning algorithm, Future Innovations in Novel Detection of Atrial Fibrillation (FIND-AF), was developed to predict incident AF within 6 months using data from primary care electronic health records (EHRs). It could be used to guide AF screening [22]. To assess the clinical impact of using FIND-AF compared to other risk prediction scores, we calculated the net reclassification index at a 0.4% AF risk threshold (the average 6-month incidence rate in the cohort) and conducted a decision curve analysis.

■ RESULTS

In the general cohort of patients, the Colchicine group (A) showed no reduction in AF onset compared to the control group (B), with 24 (21.04%) versus 28 (25.45%), respectively, p=0.871 (Fig. 1).

To understand the antiarrhythmic effect of colchicine based on non-HDL levels, we performed a sub-analysis. In this sub-analysis, Group C included 102 patients with non-HDL levels ≥130 mg/dl, while Group D included 122 patients with non-HDL levels <130 mg/dl. The groups did not differ significantly in terms of baseline comorbidities, CPR, and age. The primary endpoint was the incidence of AF episodes lasting >30 seconds during a 6-month period, with a p-value <0.05 considered statistically significant.

Group C – patients with non-HDL cholesterol levels ≥130 mg/dl – was further divided into Group C1, which included 48 patients receiving colchicine, and Group C2, which included 54 patients not receiving colchicine. The groups did not differ significantly in terms of baseline comorbidities, CPR, and age. AF onset occurred in 9 (37.5%) patients in Group C1 and 15 (62.5%) patients in Group C2, respectively (p=0.026). Thus, in the group with high non-HDL cholesterol levels, there was a reduction in AF onset (Fig. 2).

Group D – patients with non-HDL cholesterol <130 mg/dl were divided into group D1, which included 56 patients receiving Colchicine, and group D2, which included 56 patients not receiving Colchicine. The groups didn't differ significantly in terms of baseline significant comorbidities, CRP, and age. In group D, there was no reduction in AF

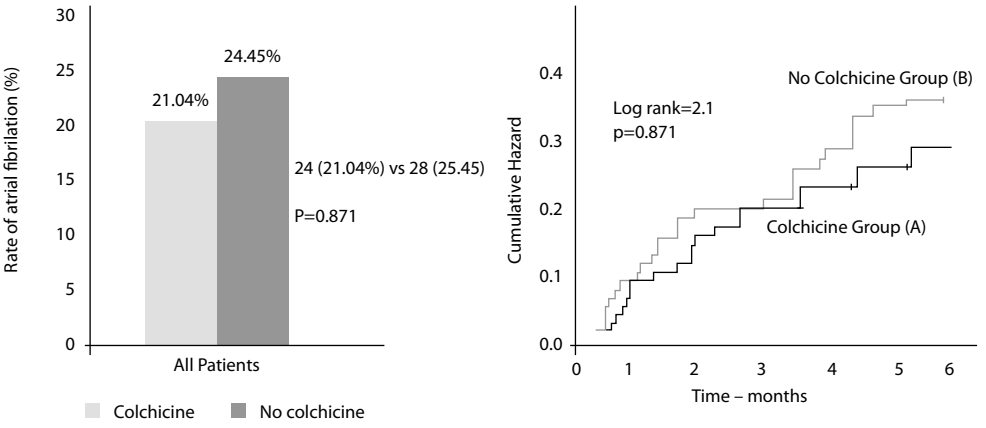

Fig. 1. Rate of AF onset depending on administering Colchicine 0.5 mg daily

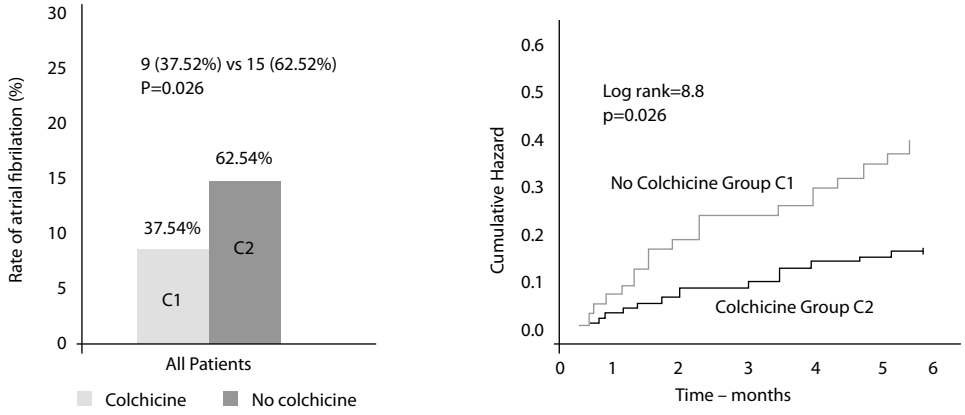

Fig. 2. Rate of AF in patients with non-HDL cholesterol ≥130 mg/dl depending on administering Colchicine 0.5 mg daily

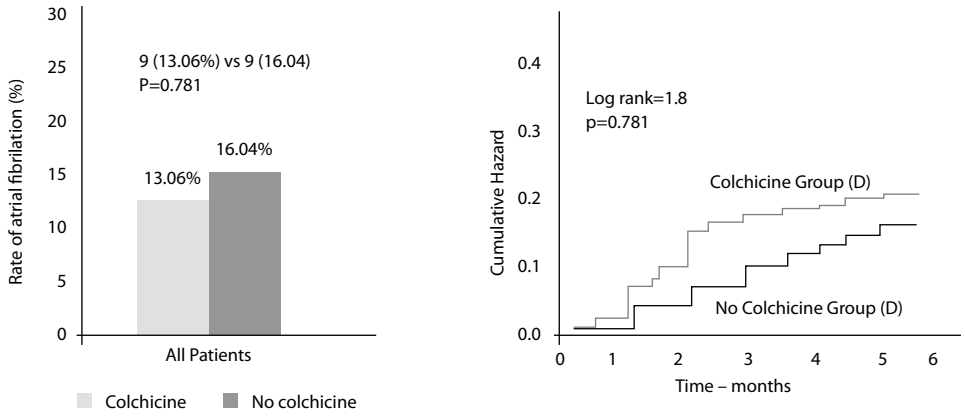

Fig. 3. Rate of atrial fibrillation in patients with non-HDL cholesterol <130 mg/dl depending on administering Colchicine 0.5 mg daily

incidence: 9 (13.06%) with Colchicine versus 9 (16.04%) without Colchicine, respectively, p=0.781. Therefore, Colchicine didn't help patients with non-HDL cholesterol <130 mg/dl in preventing AF onset (Fig. 3).

■ DISSCUSION

In this study, we specifically selected a contingent of patients where it would be easy to test the effect of colchicine for the prophylactic treatment of atrial fibrillation (AF). In the general group of patients with chronic coronary disease, colchicine, as in previous studies, didn't show a reduction in the risk of AF onset. Colchicine had an effect on reducing the risk of AF onset only in patients with high non-HDL cholesterol levels. This effect of colchicine on this group can be explained by the fact that these patients had a higher inflammatory status of coronary vessels, making the anti-inflammatory effect of colchicine more pronounced.

There is limited specific research on the relationship between cholesterol profiles and the action of colchicine in preventing AF onset. However, we can discuss the potential implications of cholesterol profiles on the effectiveness of colchicine in AF prevention based on known mechanisms of action.

Cholesterol plays a crucial role in the development of atherosclerosis and cardiovascular disease. High levels of non-HDL cholesterol, often referred to as "bad" cholesterol, are associated with an increased risk of cardiovascular events, including AF. It is well-established that inflammation and oxidative stress, which are influenced by cholesterol levels, play a role in the pathogenesis of AF [26].

Colchicine, as mentioned earlier, exerts its effects partially through its anti-inflammatory properties. By reducing inflammation, colchicine may help prevent the electrical and structural remodeling that can lead to AF [27]. Therefore, individuals with dyslipidemia and high cholesterol levels may benefit from the anti-inflammatory effects of colchicine in preventing AF onset.

Additionally, high cholesterol levels can contribute to endothelial dysfunction and promote a pro-thrombotic state, which are also risk factors for AF development. Colchicine's ability to modulate these pathways may be particularly beneficial in individuals with unfavorable cholesterol profiles.

However, it is essential to note that individual responses to colchicine may vary based on multiple factors, including genetic predisposition, comorbidities, and concomitant medications. The interplay between cholesterol profiles and the action of colchicine in AF prevention is complex and likely influenced by various factors beyond cholesterol levels alone.

Further research is needed to explore the potential interaction between cholesterol profiles and the effectiveness of colchicine in preventing AF onset. Clinical trials that specifically investigate the impact of cholesterol levels on the response to colchicine in AF prevention could provide valuable insights into personalized treatment approaches for individuals at risk of developing AF.

Diarrhea, the major gastro-intestinal (GI) side effect of colchicine, occurred in only three patients receiving colchicine, including one patient who required treatment discontinuation. This low rate of GI intolerance is in line with the results of other trials using a similar dose.

A few limitations must be discussed. There was no continuous cardiac rhythm monitoring between monthly 24-hour Holter monitoring. Thus, asymptomatic episodes of AF may have been missed, leading to underestimation of the true incidence of AF onset. However, missed episodes were likely to have occurred equally in both groups, and thus, the overall conclusion of the trial would not have been affected.

While the relationship between cholesterol profiles and the action of colchicine in preventing AF onset is not well-established, it is plausible that individuals with dyslipidemia and high cholesterol levels may benefit from colchicine's anti-inflammatory effects in reducing the risk of AF. Healthcare providers should consider a holistic approach to patient care, taking into account individual risk factors and tailoring treatment strategies accordingly.

■ CONCLUSIONS

Colchicine treatment in patients with chronic coronary artery disease is associated with lower AF incidence rates only in patients with high non-HDL levels ≥130 mg/dl. Therefore, for chronic coronary disease with high non-HDL cholesterol ≥130 mg/dl, it is advisable to add low-dose colchicine (0.5 mg daily) to statin therapy. There is a need for further research to identify and confirm the benefits of colchicine against AF in patients with chronic coronary artery disease.

■ REFERENCES

1. Weng LC, Preis SR, Hulme OL, et al. Genetic Predisposition, Clinical Risk Factor Burden, and Lifetime Risk of Atrial Fibrillation. *Circulation.* 2018;137:1027–1038.
2. Naser N, Dilic M, Durak A, et al. The Impact of Risk Factors and Comorbidities on The Incidence of Atrial Fibrillation. *Mater Sociomed.* 2017 Dec;29(4):231–236. doi: 10.5455/msm.2017.29.231-236
3. Townsend N, Wilson L, Bhatnagar P, et al. Cardiovascular diseases in Europe: epidemiological update 2016. *European Heart Journal.* 2016;37:3232–45.
4. Van Wagoner DR, Piccini JP, Albert CM, et al. Progress toward the prevention and treatment of atrial fibrillation: A summary of the Heart Rhythm Society Research Forum on the Treatment and Prevention of Atrial Fibrillation, Washington, DC, December 9–10, 2013. *Heart Rhythm.* 2015 Jan;12(1):e5–e29. doi: 10.1016/j.hrthm.2014.11.011
5. El Hasbani G., Jawad A., Uthman I. Update on the management of colchicine resistant Familial Mediterranean Fever (FMF). *Orphanet J Rare Dis.* 2019;14:224. https://doi.org/10.1186/s13023-019-1201-7
6. Dasgeb B, Kornreich D, McGuinn K, et al. Colchicine: an ancient drug with novel applications. *Br J Dermatol.* 2018 Feb;178(2):350–356. doi: 10.1111/bjd.15896
7. Samuel M, Tardif JC, Bouabdallaoui N, et al. Colchicine for Secondary Prevention of Cardiovascular Disease: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Can J Cardiol.* 2021;37:776–785.
8. Shvartz V, Le T, Kryukov Y, et al. Colchicine for Prevention of Atrial Fibrillation after Cardiac Surgery in the Early Postoperative Period. *J Clin Med.* 2022 Mar 3;11(5):1387. doi: 10.3390/jcm11051387
9. Nawabi AQ, Hassan W, Chen L, et al. Is Colchicine a New Game-Changer in Patients With Acute Coronary Syndrome? *Cureus.* 2022 Mar 5;14(3):e22874. doi: 10.7759/cureus.22874
10. Nadia Bouabdallaoui, Lucie Blondeau, Jean-Claude Tardif. Lessons from COLCOT and LoDoCo2: colchicine for secondary prevention in coronary artery disease. *European Heart Journal*, 2021;42(28):2800–2801. Available at: https://doi.org/10.1093/eurheartj/ehab020
11. Michniewicz E, Mlodawska E, Lopatowska P, et al. Patients with atrial fibrillation and coronary artery disease – Double trouble. *Adv Med Sci.* 2018;63(1):30–35.
12. Kornej J, Henger S, Seewöster T, et al. Prevalence of atrial fibrillation dependent on coronary artery status: Insights from the LIFE-Heart Study. *Clin Cardiol.* 2020 Dec;43(12):1616–1623. doi: 10.1002/clc.23490
13. Gutierrez A, Van Wagoner DR. Oxidant and Inflammatory Mechanisms and Targeted Therapy in Atrial Fibrillation: An Update. *J Cardiovasc Pharmacol.* 2015 Dec;66(6):523–9. doi: 10.1097/FJC.0000000000000313
14. Clare GC, Troughton RW. Management of constrictive pericarditis in the 21st century. *Curr. Treat. Options Cardiovasc Med.* 2007;9(6):436–442. 10.1007/s11936-007-0038-x
15. Rennard SI, Bitterman PB, Ozaki T, et al. Colchicine suppresses the release of fibroblast growth factors from alveolar macrophages in vitro. The basis of a possible therapeutic approach ot the fibrotic disorders. *Am. Rev. Respir. Dis.* 1988;137(1):181–185. 10.1164/ajrccm/137.1.18
16. Kommu S, Arepally S. The Effect of Colchicine on Atrial Fibrillation: A Systematic Review and Meta-Analysis. *Cureus.* 2023 Feb 17;15(2):e35120. doi: 10.7759/cureus.35120
17. Jean-Claude Tardif, Simon Kouz, David D. Waters. Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction. November 16, 2019. *N Engl J Med.* 2019;381:2497–2505. doi: 10.1056/NEJMoa1912388
18. Nidorf SM, Fiolet ATL, Mosterd A, et al. Colchicine in patients with chronic coronary disease. *N Engl J Med.* 2020;383:1838–47. doi: 10.1056/NEJMoa2021372
19. Castelli WP. The New HDL Cholesterol Guidelines. *The American Journal of Cardiology.* 1988;61(6):5B–10B.
20. Pirillo A, Casula M, Catapano AL. European guidelines for the treatment of dyslipidaemias: New concepts and future challenges. *Pharmacol Res.* 2023 Oct;196:106936. doi: 10.1016/j.phrs.2023.106936
21. Zhan Y, Yue H, Zhao X, et al. Colchicine in atrial fibrillation: are old trees in bloom? *Front Physiol.* 2023 Oct 17;14:1260774. doi: 10.3389/fphys.2023.1260774
22. Nadarajah R, Wu J, Frangi AF, et al. Predicting patient-level new-onset Atrial fibrillation from population-based nationwide electronic health records: protocol of FIND-AF for developing a precision medicine prediction model using artificial intelligence. *BMJ Open.* 2021;11:e052887. doi: 10.1136/bmjopen-2021-052887
23. Fox KAA, Virdone S, Pieper KS, Bassand JP, et al. GARFIELD-AF Investigators. GARFIELD-AF risk score for mortality, stroke, and bleeding within 2 years in patients with atrial fibrillation. *Eur Heart J Qual Care Clin Outcomes.* 2022 Mar 2;8(2):214–227. doi: 10.1093/ehjqcco/qcab028
24. Bisbal F, Abugattas JP, Trotta O, et al. Personalized assessment of the cumulative complication risk of the atrial fibrillation ablation track: The AF-TRACK calculator. *Heart Rhythm O2.* 2022 Aug 9;3(6Part A):656–664. doi: 10.1016/j.hroo.2022.07.013
25. Yavelov IS. Prevention of cardiovascular events in patients with stable coronary artery disease: myocardial revascularization or pharmacological treatment? *Cardiovascular Therapy and Prevention.* 2021;20(3):2888. (In Russ.). Available at: https://doi.org/10.15829/1728-8800-2021-2888
26. Pinho-Gomes AC, Reilly S, Brandes RP, Casadei B. Targeting inflammation and oxidative stress in atrial fibrillation: role of 3-hydroxy-3-methylglutaryl-coenzyme a reductase inhibition with statins. *Antioxid Redox Signal.* 2014 Mar 10;20(8):1268–85. doi: 10.1089/ars.2013.5542
27. Melgari D, Barbier C, Dilanian G, et al. Microtubule polymerization state and clathrin-dependent internalization regulate dynamics of cardiac potassium channel Microtubule and clathrin control of K V 1. 5 channel. *J Mol Cell Cardiol* [Internet] 2020;144(April):127–39. Available at: https://doi.org/10.1016/j.yjmcc.2020.05.004