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THE IMPACT OF TARGETED LDL CHOLESTEROL CONTROL ON ANGINA SYMPTOMS AND LONG-TERM PROGNOSIS IN PATIENTS WITH ISCHEMIC HEART DISEASE: A LITERATURE REVIEW

Qobilov Dostonbek Rustamovich
Master's student at Tashkent State Medical University
Maksudova Malika Khamdamjanovna
Associate Professor, Candidate of Medical Sciences, Department of Hospital Therapy, Nephrology and Hemodialysis, Faculty No. 2 of Tashkent State Medical University
Jabborov Ozimboy Otakhonovich
Professor of Faculty No. 2 and the Department of Hospital Therapy, Nephrology, and Hemodialysis at Tashkent State Medical University

Abstract: Ischemic heart disease (IHD) remains one of the major manifestations of atherosclerotic cardiovascular disease and is associated with recurrent angina, myocardial infarction, coronary revascularization, heart failure, and cardiovascular mortality. Low-density lipoprotein cholesterol (LDL-C) plays a central causal role in the development and progression of atherosclerotic cardiovascular disease. Therefore, targeted reduction of LDL-C represents a fundamental component of secondary prevention in patients with IHD. The aim of this literature review was to evaluate the relationship between achieving LDL-C treatment targets, angina symptoms, and long-term cardiovascular prognosis in patients with IHD. Published randomized clinical trials, meta-analyses, and international clinical guidelines concerning LDL-C lowering were reviewed. Evidence indicates that more intensive LDL-C reduction is associated with a significant decrease in major cardiovascular events. Meta-analytic data demonstrate that each 1 mmol/L reduction in LDL-C is associated with approximately a 20–22% reduction in major vascular events [1, 2]. Clinical trials such as TNT and PROVE-IT TIMI 22 further demonstrated the benefits of intensive statin therapy [3, 4]. Additional LDL-C reduction with ezetimibe or PCSK9 inhibitors may provide further cardiovascular benefit in patients who remain above target despite maximally tolerated statin therapy [5, 6]. Although LDL-C lowering primarily improves long-term prognosis rather than providing an immediate anti-anginal effect, sustained lipid control may contribute to stabilization and regression of atherosclerotic plaques and consequently reduce recurrent ischemic events.

Keywords: ischemic heart disease, coronary artery disease, LDL cholesterol, low-density lipoprotein, angina pectoris, lipid-lowering therapy, statins, cardiovascular prognosis, secondary prevention, atherosclerosis.

Introduction

Ischemic heart disease is a major clinical manifestation of atherosclerotic cardiovascular disease and remains an important cause of morbidity and mortality worldwide. Patients with established coronary artery disease are considered to be at high or very high cardiovascular risk and require comprehensive secondary prevention aimed at reducing recurrent ischemic events and improving long-term prognosis. Contemporary management of chronic coronary syndromes therefore includes lifestyle modification, control of blood pressure and diabetes, antithrombotic treatment when indicated, and intensive lipid-lowering therapy [7].

Among modifiable cardiovascular risk factors, low-density lipoprotein cholesterol (LDL-C) has a particularly important role. Genetic, epidemiological, and clinical evidence supports a causal

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relationship between cumulative LDL-C exposure and atherosclerotic cardiovascular disease [8]. Prolonged exposure to elevated LDL-C contributes to cholesterol accumulation within the arterial wall, promotes atherosclerotic plaque development, and increases the probability of plaque rupture and subsequent coronary thrombosis. Consequently, lowering LDL-C is not simply a means of improving a laboratory parameter but a strategy directed toward reducing the underlying atherosclerotic burden.

The concept of targeted LDL-C reduction has evolved considerably during the last two decades. Earlier treatment strategies focused on achieving LDL-C values below approximately 2.6 mmol/L (100 mg/dL) in patients with coronary disease. Contemporary European recommendations advocate substantially lower targets for patients at very high cardiovascular risk. The 2019 ESC/EAS guideline recommends an LDL-C reduction of at least 50% from baseline together with an LDL-C target below 1.4 mmol/L (55 mg/dL) for very-high-risk patients [9]. This approach is supported by evidence demonstrating that progressively lower LDL-C concentrations are associated with fewer cardiovascular events without an identified threshold below which the cardiovascular benefit disappears [9].

The clinical importance of LDL-C control is particularly relevant in patients with angina pectoris. Recurrent angina reflects myocardial ischemia and may substantially impair physical activity, psychological well-being, and quality of life. Although lipid-lowering treatment is not primarily an immediate anti-anginal intervention, long-term LDL-C reduction may influence the structural stability of coronary plaques and thereby reduce the risk of acute coronary events. Therefore, the relationship between achieving LDL-C targets, angina symptoms, and long-term cardiovascular outcomes deserves systematic consideration.

Aim of the review. The aim of this literature review was to analyze available evidence regarding the influence of targeted LDL-C control on angina symptoms and long-term cardiovascular prognosis in patients with ischemic heart disease.

This study was designed as a narrative literature review. Scientific publications concerning LDL-C, lipid-lowering treatment, ischemic heart disease, angina pectoris, and cardiovascular outcomes were reviewed. Particular attention was given to randomized controlled trials, large-scale meta-analyses, consensus statements, and international clinical practice guidelines.

The literature search focused on studies evaluating the association between the degree of LDL-C reduction and cardiovascular outcomes in patients with established coronary artery disease. Major areas of interest included intensive versus moderate statin therapy, achievement of lower LDL-C concentrations, addition of ezetimibe to statin treatment, PCSK9 inhibition, and the relationship between lipid control and recurrent ischemic events.

The reviewed evidence included landmark trials such as PROVE-IT TIMI 22, TNT, IMPROVE-IT, FOURIER, and ODYSSEY OUTCOMES, as well as major meta-analyses conducted by the Cholesterol Treatment Trialists' Collaboration [1, 3–6]. Current European recommendations concerning lipid targets and management of chronic coronary syndromes were also considered [7, 9].

The principal outcomes considered in the review were changes in LDL-C concentration, recurrent angina or ischemic symptoms, myocardial infarction, coronary revascularization, stroke, hospitalization for unstable angina, and cardiovascular mortality.

LDL-C as a causal factor in ischemic heart disease. The evidence supporting the causal role of LDL-C in atherosclerotic cardiovascular disease is extensive. Ference et al. analyzed genetic, epidemiological, Mendelian randomization, and randomized clinical trial evidence and concluded that LDL exposure is causally related to the development of atherosclerotic cardiovascular disease [8].

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Importantly, both the duration and magnitude of LDL-C exposure appear to influence cardiovascular risk.

This relationship provides a strong biological rationale for intensive LDL-C reduction in patients with established IHD. LDL particles penetrate the arterial wall and contribute to lipid accumulation, inflammatory activation, and atherosclerotic plaque formation. Persistent LDL-C exposure can therefore contribute to progression of coronary artery disease, whereas substantial LDL-C reduction can reduce the probability of future cardiovascular events [8].

The clinical importance of lowering LDL-C was demonstrated in the large meta-analysis conducted by the Cholesterol Treatment Trialists' Collaboration. Analysis of 26 randomized trials involving approximately 170,000 participants showed that more intensive statin therapy produced an additional 15% reduction in major vascular events compared with less intensive treatment. The analysis also demonstrated significant reductions in coronary death or non-fatal myocardial infarction, coronary revascularization, and ischemic stroke [1]. These findings established the dose-dependent relationship between LDL-C reduction and cardiovascular risk reduction.

Target LDL-C levels in patients with IHD. The concept of "lower is better" has become increasingly important in lipid management. Current European recommendations classify patients with established atherosclerotic cardiovascular disease as very-high-risk patients and recommend both a substantial percentage reduction and an absolute LDL-C target [9]. For very-high-risk patients, an LDL-C reduction of at least 50% from baseline and a target below 1.4 mmol/L (55 mg/dL) are recommended [9].

This target is particularly relevant to patients with established IHD because their residual cardiovascular risk remains substantial even when conventional risk factors are controlled. The 2024 ESC guideline for chronic coronary syndromes emphasizes comprehensive long-term management of patients with confirmed chronic coronary syndromes, including aggressive modification of cardiovascular risk factors [7].

The achievement of an LDL-C target should therefore be viewed as a dynamic therapeutic objective rather than a single laboratory measurement. Treatment intensity may need to be adjusted according to baseline LDL-C, treatment response, adherence, tolerance, and overall cardiovascular risk.

Intensive statin therapy and long-term prognosis. Statins remain the cornerstone of LDL-C-lowering therapy. Their clinical benefit extends beyond the numerical reduction in cholesterol because lowering LDL-C reduces the probability of major atherosclerotic cardiovascular events.

The Treating to New Targets (TNT) trial provides important evidence for intensive LDL-C reduction in patients with stable coronary disease. In this study, 10,001 patients with clinically evident coronary heart disease were randomized to receive either 10 mg or 80 mg of atorvastatin daily. The mean LDL-C concentrations achieved were approximately 2.6 mmol/L and 2.0 mmol/L, respectively. Intensive therapy was associated with a 22% relative reduction in the incidence of major cardiovascular events [3]. These findings demonstrated that achieving LDL-C concentrations below traditional treatment thresholds could provide additional clinical benefit in patients with stable coronary disease.

The PROVE-IT TIMI 22 trial similarly demonstrated the benefit of intensive lipid lowering following acute coronary syndrome. Patients receiving high-intensity atorvastatin therapy experienced better cardiovascular outcomes than those receiving standard-dose pravastatin therapy [4]. Together, these studies provided important evidence that treatment intensity and the magnitude of LDL-C reduction are clinically relevant determinants of prognosis.

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LDL-C reduction and angina symptoms. The relationship between LDL-C control and angina symptoms is more complex than the relationship between LDL-C and major cardiovascular events. Angina is directly influenced by the degree of myocardial ischemia, coronary stenosis, myocardial oxygen demand, endothelial function, and the presence of vasomotor abnormalities. Consequently, lipid-lowering therapy should not be considered a substitute for established anti-anginal treatments such as beta-blockers, calcium-channel blockers, nitrates, or other appropriate therapies.

Nevertheless, LDL-C reduction may have an indirect beneficial effect on ischemic symptoms through stabilization of coronary plaques and modification of the atherosclerotic process. Progressive reduction of atherosclerotic lipid burden may limit further plaque growth and decrease the probability of plaque disruption. Thus, the long-term effect of LDL-C control may be reflected not necessarily by immediate disappearance of angina but by a lower frequency of recurrent ischemic events and reduced need for coronary intervention.

The clinical significance of this distinction is important. A patient may report symptomatic improvement because of anti-anginal treatment while continuing to have substantial residual atherosclerotic risk if LDL-C remains above the recommended target. Conversely, a patient with well-controlled symptoms may still benefit substantially from further LDL-C reduction. Therefore, symptom control and lipid control should be regarded as complementary rather than interchangeable components of IHD management.

Additional LDL-C lowering with ezetimibe. For patients who do not achieve recommended LDL-C targets despite maximally tolerated statin therapy, combination therapy provides an important therapeutic option. The IMPROVE-IT trial evaluated the addition of ezetimibe to simvastatin in 18,144 patients following acute coronary syndrome. The combination produced greater LDL-C reduction than statin monotherapy and resulted in a modest but statistically significant reduction in cardiovascular events [5].

These findings support the principle that the clinical benefit is associated with the magnitude of LDL-C lowering itself rather than being restricted to a particular pharmacological class. The results are consistent with the concept that patients with established IHD who remain above their LDL-C target may obtain additional cardiovascular protection through further LDL-C reduction.

PCSK9 inhibitors and achievement of very low LDL-C levels. PCSK9 inhibitors have expanded the therapeutic possibilities for patients with persistent LDL-C elevation despite intensive statin therapy. In the FOURIER trial, evolocumab produced a substantial reduction in LDL-C and significantly reduced the risk of major cardiovascular outcomes in patients with established atherosclerotic cardiovascular disease receiving statin therapy [6].

Similarly, the ODYSSEY OUTCOMES trial demonstrated that alirocumab reduced cardiovascular events among patients who had experienced an acute coronary syndrome and were receiving intensive or maximally tolerated statin therapy [10]. These findings are particularly relevant for patients who cannot achieve their LDL-C target with statin therapy alone.

The results of PCSK9 inhibitor trials also support the safety and effectiveness of achieving very low LDL-C concentrations in appropriately selected high-risk patients. Consequently, treatment strategies have progressively shifted from simply prescribing a statin toward a target-oriented approach in which therapy is intensified until the desired LDL-C reduction is achieved.

LDL-C control and long-term cardiovascular prognosis. The strongest evidence for targeted LDL-C control concerns long-term cardiovascular prognosis. Reduction of LDL-C is consistently

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associated with lower rates of myocardial infarction, coronary revascularization, ischemic stroke, and other major vascular events [1, 3–6].

The relationship is also biologically plausible because atherosclerotic plaque formation is a cumulative process. The longer an individual is exposed to elevated LDL-C, the greater the cumulative atherosclerotic burden. Therefore, sustained LDL-C reduction may be more clinically important than a temporary decrease in cholesterol concentration.

For patients with IHD, this principle has direct implications for secondary prevention. Achieving and maintaining the recommended LDL-C target should be accompanied by continued monitoring of adherence and treatment response. Failure to reach the target should prompt evaluation of adherence, lifestyle factors, statin tolerance, secondary causes of dyslipidemia, and the potential need for combination therapy.

At the same time, it is important to recognize that cardiovascular prognosis is multifactorial. LDL-C control alone cannot eliminate the risk of recurrent coronary events. Smoking cessation, blood-pressure control, diabetes management, physical activity, healthy nutrition, appropriate antithrombotic treatment, and adherence to evidence-based anti-anginal and cardiovascular therapies remain essential components of comprehensive secondary prevention [7, 9].

Conclusion

The reviewed literature demonstrates that targeted LDL-C reduction is a central component of secondary prevention in patients with ischemic heart disease. LDL-C is causally involved in atherosclerotic cardiovascular disease, and greater reductions in LDL-C are consistently associated with lower risks of major cardiovascular events [1, 8].

Intensive statin therapy has been shown to improve cardiovascular outcomes in both stable coronary disease and acute coronary syndromes [3, 4]. In patients who remain above the recommended LDL-C target, addition of ezetimibe or a PCSK9 inhibitor can provide further LDL-C reduction and additional cardiovascular protection [5, 6, 10].

The effect of LDL-C control on angina symptoms should be interpreted differently from its effect on long-term prognosis. Lipid-lowering therapy is not primarily an immediate anti-anginal treatment; rather, its principal value lies in modifying the underlying atherosclerotic process, stabilizing plaques, and reducing the risk of future myocardial infarction, revascularization, stroke, and cardiovascular death. Therefore, symptom control should be combined with systematic achievement and maintenance of individualized LDL-C targets.

Overall, current evidence supports a target-oriented lipid management strategy in IHD, with intensive LDL-C reduction for patients at very high cardiovascular risk. The combination of high-intensity or maximally tolerated statin therapy with additional lipid-lowering agents when necessary provides an evidence-based approach for improving long-term cardiovascular prognosis.

References

1. Cholesterol Treatment Trialists' Collaboration; Baigent C., Blackwell L., Emberson J., et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials // The Lancet. — 2010. — Vol. 376, No. 9753. — P. 1670–1681. — DOI: 10.1016/S0140-6736(10)61350-5.
2. Cholesterol Treatment Trialists' Collaboration; Baigent C., Blackwell L., Emberson J., et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins // The Lancet. — 2005. — Vol. 366, No. 9493. — P. 1267–1278.

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3. LaRosa J.C., Grundy S.M., Waters D.D., et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease // New England Journal of Medicine. — 2005. — Vol. 352, No. 14. — P. 1425–1435. — DOI: 10.1056/NEJMoa050461.
4. Cannon C.P., Braunwald E., McCabe C.H., et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes // New England Journal of Medicine. — 2004. — Vol. 350, No. 15. — P. 1495–1504. — DOI: 10.1056/NEJMoa040583.
5. Cannon C.P., Blazing M.A., Giugliano R.P., et al. Ezetimibe added to statin therapy after acute coronary syndromes // New England Journal of Medicine. — 2015. — Vol. 372, No. 25. — P. 2387–2397. — DOI: 10.1056/NEJMoa1410489.
6. Sabatine M.S., Giugliano R.P., Keech A.C., et al. Evolocumab and clinical outcomes in patients with cardiovascular disease // New England Journal of Medicine. — 2017. — Vol. 376, No. 18. — P. 1713–1722. — DOI: 10.1056/NEJMoa1615664.
7. Vrints C., Andreotti F., Koskinas K.C., et al. 2024 ESC Guidelines for the management of chronic coronary syndromes // European Heart Journal. — 2024. — Vol. 45. — P. 3415–3537.
8. Ference B.A., Ginsberg H.N., Graham I., et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies: a consensus statement from the European Atherosclerosis Society Consensus Panel // European Heart Journal. — 2017. — Vol. 38, No. 32. — P. 2459–2472. — DOI: 10.1093/eurheartj/ehx144.
9. Mach F., Baigent C., Catapano A.L., et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk // European Heart Journal. — 2020. — Vol. 41, No. 1. — P. 111–188.
10. Schwartz G.G., Steg P.G., Szarek M., et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome // New England Journal of Medicine. — 2018. — Vol. 379, No. 22. — P. 2097–2107. — DOI: 10.1056/NEJMoa1801174.

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