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PERSPECTIVE

How a Plant-Based Diet and Ultra-Low LDL Levels Can Reverse Atherosclerosis and Prevent Restenosis: A Breakthrough in Heart Health

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Abstract

Low-Density Lipoprotein Cholesterol (LDL-C) remains a key target in preventing and treating cardiovascular disease. Recent data and expert consensus increasingly support aggressive LDL-C lowering strategies, with emerging evidence suggesting that levels below 30 mg/dL (ultralow/ UL) may provide significant clinical benefits, including atherosclerosis regression and reduced rates of restenosis post-intervention.

At our cardiology centre at Bethsaida Hospital in Indonesia, directed by Prof. Dasaad Mulijono, we have successfully implemented a comprehensive approach that combines a Plant-Based Diet (PBD) with high-intensity lipid-lowering therapy (excluding PCSK9 inhibitors) to achieve sustained UL-LDL-C in patients with Coronary Artery Disease (CAD). This strategy has resulted in a restenosis rate of approximately 2%, compared to rates as high as 10-20% in other centres. Furthermore, Computed Tomography Coronary Angiography (CTCA), angiographic, and clinical follow-up data suggest signs of halted or regressed atherosclerotic progression.

These findings support the hypothesis that integrating a PBD with intensive lipid management may represent an effective and sustainable model for secondary prevention in high-risk cardiovascular populations. Future guidelines may consider more aggressive LDL-C targets and lifestyle-based interventions to optimize patient outcomes.

Introduction

LDL-C, commonly referred to as "bad cholesterol," plays a significant role in the development of atherosclerosis and subsequent cardiovascular events, including restenosis. While the importance of LDL-C reduction is universally acknowledged, the extent to which it should be lowered remains debatable. This article examines the rationale for targeting UL-LDL-C to regress atherosclerosis and prevent restenosis [1-5], comparing current guidelines with expert opinions and emerging clinical evidence.

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Differing Guidelines: American College of Cardiology (ACC) compared with European Society of Cardiology (ESC)

The ACC and ESC have both updated their LDL-C target recommendations over the years, yet key differences remain:

- **1993:** The NCEP ATP II recommended an LDL-C level of less than 130 mg/dL for high-risk patients, while some experts suggested a less than 100 mg/dL [6].
- **2000 & 2004:** NCEP ATP III introduced less than 100 mg/dL for high-risk patients and less than 70 mg/dL for very high-risk individuals [7].
- **2016:** The ESC guidelines recommended LDL-C levels of less than 70 mg/dL for patients at very high risk [8].
- **2019 & 2021:** The ESC lowered targets to less than 55 mg/dL for individuals at very high risk and less than 40 mg/dL for those with extreme cases [9,10].
- **2022:** The ACC remained more conservative, retaining an LDL-C target of less than 70 mg/dL for patients at very high risk [6,11].

These discrepancies highlight the ACC's relatively cautious approach compared to the ESC's more aggressive stance [12], reflecting a growing body of research supporting lower LDL-C targets to achieve better cardiovascular outcomes. Please refer to table 1.

UL-LDL-C: The expert perspective

Renowned cardiologists, including Eugene Braunwald and Eric Topol, advocate for an UL-LDL-C [13-15], citing accumulating clinical evidence that demonstrates the benefits of aggressive lipid lowering. Several landmark studies indicate that reducing LDL-C to ultra-low levels significantly decreases the incidence of cardiovascular events, supporting the principle that "lower is better." This approach is further validated by trials involving PCSK9 inhibitors and high-intensity statin therapy [16,17], demonstrating superior cardiovascular outcomes with LDL-C reductions that are well below current guideline recommendations. Numerous studies have shown that UL-LDL-C levels are safe for long-term health outcomes [17-21].

Table 1: Comparison between ACC and ESC guidelines for LDL-C levels for secondary CAD prevention.

Year	LDL-C mg/dL [ACC]	LDL-C mg/dL[ESC]
1990	<100 - 130	<135 - 160
2000	<70 - 100	<100 - 115
2010	<70 - 100	<70
2020	<55 - 70	<40 - 55
2025	<55 - 70	<40 - 55

Why target for UL-LDL-C?

- **Atherosclerosis regression:** Achieving an UL-LDL-C has been linked to plaque stabilization and even regression of atherosclerosis, thereby reducing the risk of acute coronary events [1,2,20-28].
- **Restenosis prevention:** Patients undergoing Percutaneous Coronary Interventions (PCIs) benefit from UL-LDL-C levels, which minimize the risk of restenosis and improve long-term outcomes [3-5].
- **Historical trends:** Over the years, LDL-C targets have progressively decreased, with each reduction correlating with improved cardiovascular protection. The transition from 130 mg/dL to 70 mg/dL has been validated, and a level of less than 30 mg/dL may be the next logical step [21].
- **Real-time expert insights:** While guidelines take years to adapt, leading experts analyze emerging data promptly, often predicting future guideline shifts well in advance [13-15].
- **Tailored risk management:** High-risk individuals may require more aggressive LDL-C reduction than current guidelines recommend, underscoring the need for individualized treatment strategies.

Impact of a PBD and intensive lipid-lowering therapy

Our cardiology centre at Bethsaida Hospital, Indonesia, has successfully implemented a comprehensive strategy integrating a PBD with intensive lipid-lowering therapy to achieve UL-LDL-C levels.

Plant-based nutrition: A diet rich in whole grains, legumes, fruits, and vegetables has been shown to significantly reduce LDL-C levels while enhancing endothelial function.

High-intensity statin therapy: Optimizing statin therapy, in combination with ezetimibe, has proven highly effective in achieving UL-LDL-C levels. Notably, most patients have successfully attained that level with good tolerability.

In Indonesia, the use of PCSK9 inhibitors remains limited due to their high cost and the lack of coverage by private insurance.

Our clinical experience suggests that this regimen reduces the risk of restenosis, resulting in a 2% rate instead of the 10-20% experienced in other centres following percutaneous coronary intervention. It also promotes the regression of atherosclerosis, ultimately leading to improved patient outcomes [29-31]. Furthermore, the therapy has demonstrated a favourable safety and tolerability profile.

Conclusion

The ongoing debate over optimal LDL-C targets continues to evolve, with growing support for more aggressive reductions. While ACC and ESC guidelines have progressively lowered LDL-C thresholds, experts such as Braunwald and Topol advocate for an even more aggressive target of less than 30 mg/dL, citing emerging evidence of superior cardiovascular protection. PBDs and intensive lipid-lowering therapy reinforces the feasibility and benefits of achieving these UL-LDL-C levels.

Future guidelines may align with expert recommendations as research continues to validate the advantages of extreme LDL-C lowering. In the meantime, clinicians should integrate evidence-based guidelines with expert insights to optimize cardiovascular risk management, emphasizing proactive measures to slow the progression of atherosclerosis and prevent restenosis.

Throughout history, the medical community has often been slow to adopt expert opinions, prioritizing rigorous studies before incorporating new insights into clinical guidelines. While this cautious approach aims to ensure patient safety, it also has significant drawbacks. Many patients who could have benefited from early interventions to prevent atherosclerosis and restenosis are left vulnerable to recurrent stenosis and adverse cardiac events while awaiting the formal validation and implementation of these advancements.

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D.M.; Conceptualization, writing, review, and editing.

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