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Submission date: 27-Mar-2026 11:27AM (UTC+0100)
Submission ID: 2914587498
File name: 1023406690185248768.docx (74.4K)
Word count: 4298
Character count: 27621

Therapeutic Inertia and Lipid-Lowering Treatment Modification after Acute Coronary Syndrome: A Longitudinal Real-World Study Using a Lagged Decision–Outcome Design

Abstract

Background: Intensive low-density lipoprotein cholesterol (LDL-C) lowering after acute coronary syndrome (ACS) is recommended to reduce cardiovascular risk, but real-world attainment of LDL-C targets remains suboptimal. Therapeutic inertia and varying lipid-lowering strategies may contribute to this gap, but their longitudinal impact is not well characterized.

Methods: In this retrospective longitudinal study, ACS patients with repeated follow-up visits (6–54 months) were evaluated. Lipid-lowering treatment strategies were categorized as no change/discontinuation, combination therapy, dose up-titration, or switching/intensification. A lagged decision–outcome design linked treatment strategies at Visit T_n to LDL-C target attainment at T_{n+1}. Generalized estimating equations and mixed-effects logistic regression models were used to assess associations with subsequent LDL-C target attainment using the 2016 guideline (<1.8 mmol/L). For sensitivity analyses, the 2023 guideline was applied (<1.4 mmol/L).

Results: A total of 1,731 ACS patients were included, with follow-up visits at 6–54 months. Combination therapy was the most frequently used strategy, followed by dose up-titration and switching/intensification. Notably, 10–15% of visits had no treatment adjustment. Treatment modification was significantly associated with improved LDL-C target attainment. Combination therapy showed the strongest effect (OR 0.25, 95% CI: 0.21–0.30), followed by dose up-titration (OR 0.48, 95% CI: 0.40–0.58) and switching/intensification (OR 0.71, 95% CI: 0.59–0.86). Therapeutic inertia was linked to more than double the risk of persistent LDL-C non-attainment (OR 2.46, 95%

CI: 2.09–2.90).

Conclusions: In ACS patients, lipid-lowering treatment modification, particularly combination therapy, was associated with improved LDL-C target attainment, whereas therapeutic inertia was detrimental. Proactive treatment adjustment is crucial for improving secondary prevention in real-world practice.

Keywords: Acute coronary syndrome; Cholesterol, LDL; Lipid-lowering therapy; Secondary prevention; Therapeutic inertia

Introduction

Acute coronary syndrome (ACS) remains a leading cause of morbidity and mortality worldwide and represents a critical manifestation of atherosclerotic cardiovascular disease driven by coronary plaque rupture and thrombosis [1]. ACS encompasses unstable angina, non–ST elevation myocardial infarction, and ST-elevation myocardial infarction, and its pathogenesis implicates lipid-rich plaque instability and systemic atherogenic risk factors.

Low-density lipoprotein cholesterol (LDL-C) is a well-established causal risk factor for atherosclerotic cardiovascular disease (ASCVD). Randomized clinical trials such as the Scandinavian Simvastatin Survival Study (4S) [2], MIRACL [3], PROVE-IT TIMI-22 [4], and TNT [5] have consistently demonstrated that more intensive LDL-C lowering reduces recurrent cardiovascular events and mortality in patients with established ASCVD, including ACS. However, despite robust evidence supporting aggressive LDL-C reduction, achieving guideline-recommended LDL-C targets in real-world practice remains suboptimal [6].

In current international guidelines, early and intensive LDL-C lowering for secondary prevention after ACS is strongly recommended. In the 2016 Chinese guidelines for lipid management, a target LDL-C of <1.8 mmol/L is recommended for very-high-risk patients, such as those with ACS [7], while an even more stringent target of <1.4 mmol/L with at least a 50% reduction from baseline for such high-risk populations is advocated in the 2023 Chinese guidelines. Additionally, in the 2019 ESC/EAS guidelines, a target LDL-C of <1.4 mmol/L (or ≥50% reduction from

baseline) for very-high-risk patients is emphasized, which serves as an important reference in our study [8]. These recommendations embody the principle that "lower LDL-C is better" for reducing recurrent ASCVD risk.

This study is part of what is known as implementation science, which explores the gap between evidence-based guidelines and their actual implementation in clinical practice. Research in this field has shown that it takes about 17 years for evidence from clinical trials to be widely adopted in routine clinical practice on average. This time lag underscores the importance of studies that seek to understand and address barriers to implementing guideline-directed lipid management in real-world settings.

Early combination therapy—such as high-intensity statin plus ezetimibe—has shown superior LDL-C reductions and cardiovascular outcomes compared with statin monotherapy in ACS populations, as demonstrated in the IMPROVE-IT trial [9]. PCSK9 inhibitors such as alirocumab and evolocumab further expand therapeutic options. ODYSSEY OUTCOMES and FOURIER show reductions in major adverse cardiovascular events among high-risk patients [10][11].

Despite guideline recommendations and proven pharmacologic efficacy, treatment gaps persist in routine care. Observational studies indicate that a substantial proportion of ACS patients, who are typically diagnosed during hospitalization, do not receive high-intensity statins at discharge; and adherence declines over time, and intensification of lipid-lowering therapy is infrequent even when LDL-C remains above targets [6][12]. These gaps are partly attributed to therapeutic inertia—failure to escalate therapy appropriately—which has been associated with poorer long-term

outcomes after ACS [13].

Therapeutic inertia in lipid management has significant clinical implications. Failure to intensify treatment in response to unmet LDL-C goals may contribute to persistent residual risk [14]. Although individual trials and cohort studies have documented LDL-C reductions with intensification strategies, comprehensive longitudinal analyses linking treatment strategies to subsequent LDL-C target attainment over time are scarce in real-world settings.

To address this gap, in the present study, a longitudinal real-world design with lagged decision–outcome pairs was used to evaluate whether lipid-lowering treatment modification at one follow-up visit was associated with improved LDL-C target attainment at the subsequent visit after ACS. It was hypothesized that treatment intensification would be associated with improved subsequent target attainment, whereas therapeutic inertia would be associated with persistent LDL-C non-attainment. The novel contribution of this study is linking real-world treatment decisions to subsequent lipid outcomes over repeated follow-up visits.

Methods

Study Design and Data Source

This study was a single-center, retrospective, observational study conducted at Shanghai Fifth People's Hospital, Fudan University, a Grade-A tertiary public hospital located in Shanghai, China, from January 2018 to January 2024. The institution is affiliated with Fudan University and serves as a teaching hospital that provides comprehensive medical services across various specialties, including cardiology and cardiovascular care. It manages a large volume of emergency and inpatient cases annually, reflecting typical urban tertiary clinical practice in China. The hospital is actively involved in medical education and research, integrating clinical care with academic activities.

The institutional database used in this study routinely collects detailed clinical, laboratory, and follow-up data for patients after hospital discharge, enabling longitudinal analysis. Given the retrospective nature of the study, informed consent was waived. However, all data were anonymized prior to analysis to ensure patient confidentiality. The study was conducted in accordance with the principles of the Declaration of Helsinki, and the institutional ethics committee approved the waiver of informed consent, ensuring that all personal information was securely handled and kept confidential throughout the study.

Study Population and Follow-Up Schedule

Patients hospitalized with a diagnosis of ACS and with available LDL-C measurements during follow-up were eligible for inclusion. The inclusion criteria

were as follows: 1. Age ≥18; 2. Hospitalized with a diagnosis of ACS (unstable angina, non-ST elevation myocardial infarction, or ST-elevation myocardial infarction), with complete inpatient medical records; 3. Initiated or continued lipid-lowering therapy (e.g., statins) at discharge, with detailed prescription records; 4. Completed at least one follow-up visit with available LDL-C measurement; 5. Data completeness for constructing lagged decision–outcome pairs for analysis.

Exclusion criteria included: 1. No baseline LDL-C measurement data; 2. No lipid-lowering therapy prescribed at discharge; 3. Missing LDL-C data during follow-up or inability to form decision–outcome pairs; 4. Severe hepatic or renal dysfunction, or other serious diseases affecting lipid metabolism (e.g., acute hepatitis and end-stage renal disease); 5. Loss to follow-up or withdrawal from the study, leading to insufficient follow-up data.

Patients were followed longitudinally after discharge at predefined time points: 6, 12, 18, 24, 30, 36, 42, 48, and 54 months (denoted as T1–T9). Follow-up visits with available LDL-C measurements were included in the analysis. Visits without LDL-C data or subsequent follow-up visits were excluded from analyses requiring lagged outcome assessment. The study flow and derivation of the analytic dataset are illustrated in Figure 1.

Definition of LDL-C Targets

LDL-C target attainment was defined according to contemporary guideline recommendations. For the primary analysis, in the 2016 Chinese guidelines, it is recommended that the LDL-C target for secondary prevention should be applied

(LDL-C<1.8 mmol/L) [15]. Sensitivity analyses were conducted using the more stringent 2023 Chinese guidelines, in which a target LDL-C of <1.4 mmol/L with at least a 50% reduction from baseline is recommended for high-risk patients [16]. These thresholds reflect evolving clinical standards for lipid management and were used to assess the impact of lipid-lowering strategies over time.

Definition of Lipid-Lowering Treatment Strategies

At each follow-up visit, lipid-lowering treatment strategies were classified based on physician prescriptions recorded at that visit. Treatment strategies were categorized into four mutually exclusive groups:

1. No change or discontinuation: no adjustment to lipid-lowering therapy or treatment cessation;
2. Combination therapy: addition of a non-statin lipid-lowering agent (e.g., ezetimibe or a PCSK9 inhibitor) to statin therapy;
3. Dose up-titration: increase in the dose of the existing statin regimen;
4. Switch or intensification: switching to a more potent statin or intensifying therapy through alternative regimens.

In this study, up-titration specifically refers to increasing the dosage of the same statin, while intensification refers to changing the treatment to a more potent statin or combining statins with non-statin agents to achieve more aggressive lipid-lowering.

If a patient transitioned from no statin therapy to a basic statin prescription, this would generally be classified as dose up-titration (if a statin was added without the inclusion of a non-statin agent) or combination therapy (if a non-statin agent was added

alongside the statin). Although this transition might appear as "switching" or "intensifying," it mainly reflects the initiation of lipid-lowering therapy and is thus classified under dose up-titration.

All treatment strategies, except for "no change," required a modification in the prescription, ensuring an active effort to manage lipid levels more effectively.

Definition of Therapeutic Inertia:

Therapeutic inertia refers to the failure to appropriately escalate or adjust treatment in response to unmet clinical goals, such as not achieving target LDL-C levels. In the context of lipid-lowering therapy, therapeutic inertia occurs when healthcare providers do not intensify or modify the prescribed treatment despite patients' failure to reach recommended LDL-C targets, leading to persistent lipid control inadequacy and increased cardiovascular risk.

Lagged Decision–Outcome Pair Construction

To assess the temporal association between treatment decisions and subsequent lipid control, a lagged decision–outcome design was used. This design is a longitudinal analytical method that links treatment decisions at one visit (T_n) to outcomes at the subsequent visit (T_{n+1}), creating decision–outcome pairs.

Lagged decision–outcome design is a novel approach that allows for the evaluation of the causal effect of treatment decisions on subsequent outcomes, while preserving the natural temporal sequence of exposure (treatment decision) and outcome (lipid control). This approach is especially valuable in clinical research where treatment decisions and their effects occur over time and need to be assessed in a sequential

manner.

In this study, treatment strategies (e.g., no change, dose titration, combination therapy, or intensification) made at Visit T_n were linked to LDL-C outcomes at Visit T_{n+1}. By using this design, it was possible to assess whether the treatment strategies used at T_n influenced LDL-C target attainment at T_{n+1}, thus evaluating the effectiveness of different lipid-lowering strategies.

Only visits with available LDL-C measurements at both T_n and T_{n+1} were included in the lagged analyses. This ensures that the analysis focuses on visits where both treatment decisions and outcomes were appropriately recorded, allowing for a clear and valid assessment of treatment effects.

Covariates

Baseline and time-invariant covariates included age, sex, and comorbidities such as hypertension and diabetes mellitus. Baseline lipid parameters included LDL-C, total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C). Current LDL-C levels and target attainment status at Visit T_n were also included as covariates in regression models to account for disease severity at the time of treatment decision. The frequency and distribution of these covariates are provided in Table 1.

Handling of Missing Data

Missing data were addressed using multiple imputation by chained equations. Five imputed datasets were generated under the assumption of missing at random. The imputation model included all variables used in the analyses. Patient identifiers were

excluded from the imputation process and were not used as predictors. Imputed datasets were pooled for subsequent analyses.

Statistical Analysis

All data processing and statistical analyses were conducted using R (Version 4.4.0). Multiple imputation was performed using the mice package. Generalized estimating equations (GEE) and mixed-effects models were fitted using appropriate R packages for longitudinal and clustered data analysis. Baseline characteristics were summarized at the patient level using means and standard deviations for continuous variables and counts with percentages for categorical variables. The distribution of lipid-lowering treatment strategies across follow-up visits was summarized descriptively.

The association between treatment strategies and LDL-C target attainment at the subsequent visit was assessed using GEE with a logit link function to account for repeated measurements in patients. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported, using the no change or discontinuation strategy as the reference category.

Sensitivity analyses were performed using mixed-effects logistic regression models with random intercepts for individual patients to further account for intra-patient correlation. Additional sensitivity analyses were conducted using the 2023 LDL-C target threshold.

Therapeutic inertia was further evaluated in a binary analysis comparing no treatment adjustment versus any treatment modification strategy. A two-sided *P* value<0.05 was considered statistically significant.

Results

Study Population and Analytical Framework

The study flow is illustrated in Figure 1. Patients with ACS were identified from a single-center database and followed longitudinally after discharge at predefined intervals (T1–T9, corresponding to 6–54 months). Visits with available LDL-C measurements were included, and those failing to achieve guideline-recommended LDL-C targets were identified.

To evaluate the clinical impact of lipid-lowering treatment decisions, lagged decision–outcome pairs were constructed by linking treatment strategies at Visit Tn to LDL-C outcomes at the subsequent visit (T_{n+1}). These paired observations constituted the analytic dataset for the main analysis using the 2016 LDL-C target and sensitivity analyses applying the 2023 target.

Baseline Characteristics

Baseline characteristics of the study population at the patient level are summarized in Table 1. The total cohort consisted of 1,731 patients with ACS. The mean age was 63.3±12.2. A majority of the patients were male (74.9%) and the remaining 25.1% were female.

The mean Body Mass Index (BMI) was 25.3±3.4kg/m², indicating that the population was generally overweight. Hypertension was present in 55.3% of patients, and 27.8% had a history of diabetes mellitus. Additionally, 36.1% of the patients were smokers at the time of baseline assessment, while 18.0% had a history of prior PCI.

At baseline, the mean LDL-C level was 2.77±1.00 mmol/L, which was substantially

higher than the recommended targets for secondary prevention. The mean total cholesterol was 4.64±0.88 mmol/L, and the mean HDL-C was 1.04±0.37 mmol/L, which is relatively low and indicative of a higher cardiovascular risk. Triglycerides had a mean value of 1.99±4.20 mmol/L, with a significant spread as indicated by the large standard deviation, suggesting variability in triglyceride levels in the cohort.

During the follow-up period, LDL-C levels decreased to a mean of 1.91±0.71 mmol/L, but they remained above the recommended targets. This indicates that many patients failed to meet guideline-recommended targets despite some lowering of LDL-C levels.

Regarding treatment, 56.7% of patients were prescribed high-intensity statin therapy, while 18.9% were prescribed a combination of statin and ezetimibe. These treatment regimens reflect a high proportion of patients receiving more intensive lipid-lowering therapies.

Distribution of Lipid-Lowering Treatment Strategies during Follow-up

The lagged analysis cohort included all 1,731 patients in the study cohort. Among these patients, the number of visits with LDL-C non-attainment varied across follow-up time points, as shown in Supplementary Table S1. Across all follow-up time points, combination therapy was the most frequently adopted strategy, accounting for approximately 35–40% of non-attainment visits. Dose up-titration was used in 26–36% of visits, while switching or intensifying therapy accounted for 16–22%.

Notably, no treatment adjustment or treatment discontinuation (“no change/stop”)

occurred in approximately 10–15% of visits with LDL-C non-attainment throughout follow-up. The relative distribution of treatment strategies remained largely stable over time, indicating persistent clinical practice patterns during long-term secondary prevention.

Association between Treatment Strategies and Subsequent LDL-C Target Attainment (2016 Target)

The associations between lipid-lowering treatment strategies and LDL-C target attainment at the subsequent visit were evaluated using GEE. Sensitivity analyses were performed using mixed-effects logistic regression models. Results are summarized in Table 2.

Compared with no treatment adjustment or discontinuation, all treatment modification strategies were significantly associated with a lower likelihood of non-attainment of LDL-C targets at the subsequent visit. Combination therapy showed the strongest association (GEE odds ratio [OR] 0.25, 95% confidence interval [CI] 0.21–0.30), followed by dose up-titration (OR 0.48, 95% CI 0.40–0.58) and switching or intensification strategies (OR 0.71, 95% CI 0.59–0.86). These associations were highly consistent in mixed-effects models accounting for intra-patient clustering.

Therapeutic Inertia and Risk of Persistent LDL-C Non-attainment

Supplementary Table S2 shows the distribution of lipid-lowering treatment strategies at all follow-up visits. At each time point, the most frequently adopted strategy was combination therapy, followed by dose up-titration and switch/intensification. The proportion of visits with no change or stop in therapy remained relatively stable over

time, ranging from approximately 15% to 18%. This suggests that therapeutic inertia persisted across the study period. A notable portion of patients did not receive the necessary adjustments to their lipid-lowering treatment.

In a complementary binary analysis, therapeutic inertia was independently associated with a substantially increased risk of failing to achieve LDL-C targets at the subsequent visit. As shown in Supplementary Table S3, therapeutic inertia was associated with more than a twofold higher risk of persistent LDL-C non-attainment in both GEE (OR 2.46, 95% CI 2.09–2.90) and mixed-effects logistic regression models (OR 2.52, 95% CI 2.13–2.98).

Sensitivity Analyses Using the 2023 LDL-C Target

When applying the more stringent 2023 LDL-C target (<1.4 mmol/L), a greater proportion of visits were classified as LDL-C non-attainment, accompanied by an increased prevalence of therapeutic inertia (Supplementary Table S2).

Despite the stricter threshold, the associations between treatment strategies and subsequent LDL-C target attainment remained directionally and statistically consistent. As shown in Supplementary Table S4, combination therapy continued to demonstrate the strongest association with LDL-C non-attainment (OR 0.32, 95% CI 0.28–0.37), followed by dose up-titration (OR 0.55, 95% CI 0.47–0.64) and switching or intensification strategies (OR 0.78, 95% CI 0.67–0.90).

Summary of Findings

Collectively, these results indicate that treatment modification strategies were commonly used in real-world practice but therapeutic inertia persisted in a substantial

proportion of visits with LDL-C non-attainment. Treatment modification—particularly combination therapy—was consistently associated with improved LDL-C target attainment across analytic approaches and guideline thresholds.

Discussion

Principal Findings

In this retrospective longitudinal study of patients with ACS, real-world lipid-lowering treatment strategies were comprehensively evaluated during long-term follow-up and their association with subsequent LDL-C target attainment was examined. Using a lagged decision–outcome design, treatment modification strategies were found to be consistently associated with improved LDL-C goal attainment compared with no treatment adjustment or discontinuation. These findings were robust across multiple modeling approaches and LDL-C target definitions.

Treatment Strategies and Real-World Practice Patterns

A key finding of this study is the persistent heterogeneity in lipid-lowering treatment strategies over time. Combination therapy was the most frequently adopted strategy across follow-up visits, while therapeutic inertia—defined as no change or treatment discontinuation—remained common throughout long-term follow-up. Notably, the proportion of patients receiving no treatment adjustment did not decrease substantially over time, despite repeated opportunities for intensification.

These findings highlight a critical gap between guideline recommendations and real-world clinical practice. In contemporary guidelines, early and sustained LDL-C reduction in very-high-risk populations such as ACS patients is emphasized; however, our results suggest that treatment inertia persists even during prolonged follow-up periods, potentially limiting the achievement of optimal lipid control [17]. Although several studies have been conducted on lipid-lowering treatment strategies globally,

there are relatively fewer studies specifically focusing on ACS patients in China. This study provides real-world data from a single-center cohort in China to offer further insights into the impact of therapeutic inertia on LDL-C management, and contributes to the understanding of guideline implementation in Chinese clinical practice [18, 19]. While all the challenges in this field may not be fully addressed in this study, it provides valuable perspectives on the role of therapeutic inertia and its implications [20].

Effectiveness of Treatment Modification Strategies

Using GEE to account for repeated measurements in patients, all three intensification strategies were shown to be associated with significantly higher odds of subsequent LDL-C target attainment compared with no treatment adjustment. Among these strategies, combination therapy showed the strongest association with LDL-C goal attainment, followed by statin dose up-titration and treatment switching or intensification. These findings are consistent with the results of major clinical trials, including IMPROVE-IT, which demonstrated the benefits of adding ezetimibe to statin therapy in patients with ACS, and FOURIER, which showed the effectiveness of PCSK9 inhibitors in achieving LDL-C targets [13, 20–22].

These associations remained consistent in sensitivity analyses using mixed-effects logistic regression models and when applying the more stringent 2023 LDL-C target threshold. The robustness of these results across various modeling approaches reinforces the clinical relevance of intensification strategies, especially combination therapy, in achieving optimal lipid control. This suggests that combination therapy

should be considered early in the treatment course for high-risk ACS patients, particularly those who fail to achieve LDL-C targets with statin monotherapy.

Therapeutic Inertia as a Key Barrier to Optimal Lipid Control

An important contribution of this study is the explicit evaluation of therapeutic inertia. When treatment strategies were dichotomized into no intensification versus any intensification, therapeutic inertia was independently associated with a substantially lower likelihood of subsequent LDL-C target attainment. This finding underscores therapeutic inertia as a major modifiable barrier to effective secondary prevention in ACS patients.

Importantly, this association persisted after adjustment for baseline lipid levels and comorbidities, suggesting that inertia cannot be fully explained by patient characteristics alone. Instead, it likely reflects system-level and physician-related factors, including risk perception, therapeutic hesitation, and limited adoption of combination therapy in routine practice [7]. Addressing therapeutic inertia is crucial for improving lipid management in high-risk cardiovascular populations, and interventions targeting clinician education, decision support tools, and structured follow-up protocols may help to reduce inertia and improve outcomes [14] .

Moreover, the impact of therapeutic inertia goes beyond simple treatment delay. It may also be linked to long-term suboptimal outcomes, as patients with persistent LDL-C non-attainment may remain at higher risk for recurrent cardiovascular events, even in the absence of other modifiable risk factors [23]. Therefore, reducing

therapeutic inertia not only helps to achieve short-term lipid goals but may also play a key role in the reduction of the long-term burden of cardiovascular disease.

Methodological Strengths and Novelty

Several methodological aspects distinguish this study from prior observational analyses. First, the lagged decision–outcome design explicitly preserves the temporal relationship between treatment decisions and subsequent lipid outcomes, thus strengthening causal inference in a non-randomized setting. Second, in the use of repeated-measures models, intra-patient correlation is accounted for and the longitudinal nature of the data is leveraged. Third, robustness was demonstrated through multiple sensitivity analyses, including alternative modeling frameworks and guideline thresholds. These methodological strengths add to the validity and applicability of the findings.

Moreover, rather than focusing solely on LDL-C levels, in this study, clinical decision-making processes and their downstream consequences are emphasized. By linking specific treatment strategies to subsequent goal attainment, our findings provide actionable insights into how real-world treatment patterns may be optimized to improve secondary prevention efforts and reduce cardiovascular risk.

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Clinical Implications

The results of this study have important clinical implications. The findings suggest that early and proactive treatment modification—particularly the use of combination therapy—may substantially improve LDL-C target attainment in ACS patients. On the contrary, persistent therapeutic inertia may undermine long-term secondary

prevention efforts, even in patients with repeated follow-up opportunities. These observations support guideline recommendations in which early combination therapy is advocated and highlight the need for implementation strategies to reduce therapeutic inertia in routine care. Interventions targeting clinician awareness, decision support tools, and structured follow-up protocols may help to bridge the gap between evidence-based recommendations and real-world practice.

In addition to Chinese and American guideline contexts discussed above, a 2025 focused update of the 2019 ESC/EAS dyslipidemia guidelines highlights the importance of early and intensive LDL-C lowering after ACS and the role of combination therapy when targets are not met with high-intensity statins alone. The update also reinforces the use of modern CV risk stratification tools (e.g., SCORE2/SCORE2-OP) to inform treatment decisions. These recommendations corroborate the present findings that proactive intensification, particularly combination therapy, is critical for closing the gap between guideline-recommended targets and real-world attainment.

Strengths and Limitations

Strengths

This study has several strengths. First, the lagged decision–outcome design preserved the temporal ordering between treatment decisions and subsequent LDL-C outcomes. Second, repeated follow-up assessments allowed evaluation of longitudinal treatment patterns in routine clinical practice. Third, the analysis addressed a clinically important but underexplored problem, i.e. therapeutic inertia after ACS.

Limitations

Several limitations should also be acknowledged. First, as a single-center retrospective analysis, residual confounding and selection bias cannot be entirely excluded. Second, information on medication adherence was not available, and treatment strategies were inferred from prescription records. Third, clinical outcomes such as recurrent cardiovascular events were not evaluated, limiting conclusions to surrogate lipid endpoints. Additionally, the generalizability of these findings may be limited by the single-center nature of the study and the potential for regional or institutional variations in practice.

Conclusions

In patients with acute coronary syndrome, failure to intensify lipid-lowering therapy after LDL-C non-attainment may represent a modifiable gap in care. Lipid-lowering treatment modification was associated with improved subsequent LDL-C target attainment during follow-up, whereas therapeutic inertia was associated with persistent non-attainment. These findings support more structured post-discharge lipid monitoring and earlier treatment escalation to improve secondary prevention in routine clinical practice.

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