Achieving the unachievable: How to optimize lipid-lowering therapy in survivors of acute myocardial infarction

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Related article
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The causal role of elevated levels of low-density lipoprotein cholesterol (LDL-C) in the development and progression of atherosclerotic cardiovascular disease (ASCVD) is well-established [1]. Pharmacological treatment with statins, ezetimibe, and, more recently, proprotein convertase subtilisin/kexin type 9 serine protease (PCSK9) inhibitors or bempedoic acid to lower LDL-C and other apolipoproteins is, therefore, crucial to reducing the risk of ASCVD. The most recent European guidelines for lipid management [2] and cardiovascular disease (CVD) prevention [3] strongly recommend an LDL-C treatment target of <1.4 mmol/l with a ≥50% reduction from baseline in patients at very high risk. This includes patients with established ASCVD, diagnosed either by imaging or by clinical criteria such as patients who have survived a myocardial infarction (MI). The reduction in ASCVD risk has been shown to be proportional to absolute LDL-C reduction [4], and recent studies indicate that LDL-C reduction to as low as 0.5 mmol/l is both safe and beneficial even in the long term [5].

Despite such strong evidence and clear recommendations, the implementation of lipid-lowering treatment in daily clinical practice is rather poor. As an example, real-world data on dyslipidemia treatment among MI survivors show that more than 75% failed to meet the LDL-C treatment target recommended at that time [6–8].

Against this background, Nowowiejska-Wiewióra and colleagues are to be praised for their initiative to assess the effect of lipid-lowering after MI in a new treatment program implemented in clinical practice [9]. The "Managed Care for Acute Myocardial Infarction Survivors" (MACAMIS) program was implemented in Poland to improve the quality of medical care during the first 12 months post-MI through a comprehensive follow-up schedule. The program consists of four treatment modules: I) hospitalization and acute intervention, II) cardiac rehabilitation, III) implantation of a cardiac electronic device where indicated, and IV) 12 months of specialized ambulatory cardiac care [10]. Indeed, participation in cardiac rehabilitation following MI is strongly recommended [3], and the effect of participating in the 12-month nationwide MACAMIS program has been already shown [10]. Similarly, the beneficial effect on LDL-C target achievement has been demonstrated in a German registry study with significantly higher use of both high-dose atorvastatin and ezetimibe among post-MI patients who attended an in-patient program [11].

In the current study including almost 1500 patients, the realities of what can be achieved become clearly visible: in line with previous real-world data, only approximately 20% achieved the LDL-C target of <1.4 mmol/l at 12 months follow-up [9]. In accordance with data from the international DA-VINCI, NORCOR, and EUROSPIRE studies, the patients were frequently prescribed suboptimal doses of lipid-lowering treatment [6–8]. In fact, fewer than 20% were receiving combination

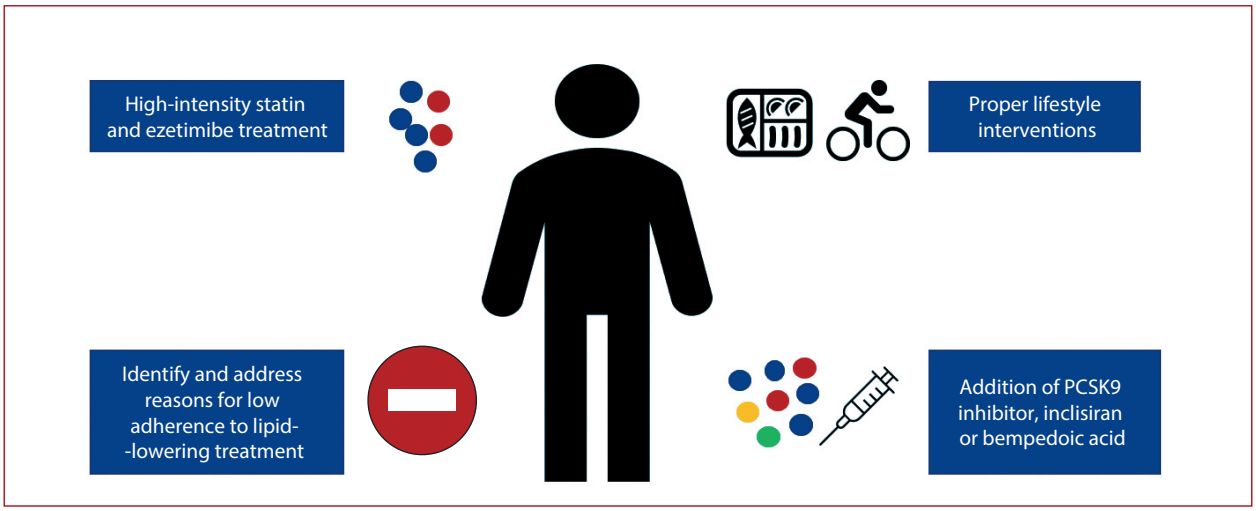

Figure 1. Factors potentially improving LDL-C target achievement in post-MI programs

Abbreviations: LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCSK9, proprotein convertase subtilisin/kexin type 9

therapy. In this sense, the present study confirms previous findings that there is great potential to optimize targeted LDL-C lowering therapy. For example, the small number of patients on ezetimibe in this study (18%) is noteworthy, given their participation in this treatment program. Further, it is estimated that about 50% of ASCVD patients will need a PCSK9-inhibitor or another LDL-C lowering agent (e.g., bempedoic acid) on top of their high-intensity statin and ezetimibe to achieve this LDL-C goal [12]. In general, as shown in recent studies on PCSK9 inhibition, one will need to both increase the dose and add combination therapy to improve prognosis [13].

What are the reasons why a significant proportion of patients do not achieve guideline-recommended LDL-C reduction despite intensive statin treatment? The answer is complex and comprises both patient factors (e.g., low drug adherence or treatment discontinuation), healthcare personnel factors (e.g., clinical inertia), or simply remaining high residual risk despite being on such therapy due to individual (genetic and non-genetic) differences in drug metabolism [14]. For example, the most common reason among patients in whom statin treatment was withdrawn during the 12-month program was patients' reluctance to continue therapy triggered by perceived statin side effects. This also corresponds to previous findings that failure to reach LDL-C targets was associated with low statin dose, low adherence, and statin-specific side effects [7].

As pointed out before, for high-risk patients in whom statin therapy alone is insufficient, add-on treatment with non-statin medications, i.e., ezetimibe and PCSK9-inhibitors, is both a recommended and valuable option. Another societal aspect is barriers to access to PCSK9-inhibitors. These barriers need to be appropriately identified and characterized so approaches to overcome those barriers can be developed. This will include reducing the clinical and economic burden for patients who are likely to benefit from PCSK9 inhibition and will likely result in more cost-effective policies [15].

What is then the major lesson learned from the work by Nowowiejska-Wiewióra et al. [9] who indirectly point to the need to further optimize the LDL-C therapy program? Figure 1 highlights four of the proposed actionable items which might further improve the great potential of the MACAMIS program in achieving a better LDL-C target.

Those items include:

Prescriptions should aim at the highest tolerated dosages of high-intensity statins together with ezetimibe. In clinical practice, rosuvastatin turns out to be slightly more efficient than atorvastatin [2].

Physicians should systematically check patient compliance to lipid-lowering treatment since poor adherence is a prevalent challenge shown to carry a poor prognosis. A part of this action plan entails physicians addressing patient skepticism such as a general disbelief in medications or a mindset expecting side effects irrespective of the type of medication (e.g., the nocebo phenomenon) [1, 2].

A comprehensive implementation of lifestyle interventions including both physical activity and dietary measures as recommended in the current European Society of Cardiology Guidelines on CVD prevention [3].

A further push to increase prescriptions of PCSK9-inhibitors on top of high-intensity high-dose statins and ezetimibe, or, where appropriate, bempedoic acid.

Taken together, the present findings presented by Nowowiejska-Wiewióra and colleagues [9] will continue to have great importance for clinical practice in Poland. They help maintain a continuous focus on strategies to improve the prognosis of post-MI patients by relentlessly exploring the opportunities for potential improvements in secondary prevention, of which LDL-C lowering is one of the most important pillars.

Article information

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