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Editorial

Suboptimal management of dyslipidemia in everyday clinical practice: Alarming signals from real-world data

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In 2019, the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) published their new guidelines for the management of dyslipidemia by revising their previous 2016 version [1]. In this time, compelling data showed that lower low-density lipoprotein cholesterol (LDL-c) levels (<70 mg/dl) with the addition of ezetimibe or/and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors on top of statin at a maximum tolerated dose were associated with a further reduction in cardiovascular risk in very-high risk individuals. Indeed, ESC/EAS 2019 guidelines recommended a goal of at least a half reduction from baseline LDL-c level, along with LDL-c <55 mg/dl in very-high risk patients (atherosclerotic cardiovascular disease, SCORE ≥ 10%, diabetes mellitus and target-organ damage, severe chronic kidney disease, familial hypercholesterolemia). Furthermore, if the LDL-c goal is not accomplished, a drug combination of statin with ezetimibe or/and PCSK9 inhibitor is recommended [1]. Albeit, this recommendation stands well-documented, real-world data showed that even the previous LDL-c goal (<70 mg/dl) was achieved in only a minority of these patients [2].

In this issue of the IJC, De Luca et al. reported relevant outcomes from the STable Coronary Artery Diseases RegisTry (START) study [3]. They conducted a cross-sectional analysis of the baseline characteristics from this nation-wide Italian registry, in order to assess the use of lipid-lowering agents and achievement of adequate LDL-c control in very-high risk patients, based on current and previous ESC/EAS guidelines, as well as to estimate how many of them may be eligible for PCSK9 inhibitor therapy [3]. In total, 4751 very-high risk patients (age 67.6 years; female 19.2%) were included in the analysis from March 2016 to February 2017. Approximately 80, 76, 33, 14, 12, and 10% had hypertension, dyslipidemia, diabetes mellitus, heart failure, chronic kidney disease, and peripheral artery disease, respectively. Moreover, approximately 39 and 6% of them experienced myocardial infarction and cerebrovascular event, respectively; while, 83.5% of participants underwent coronary revascularization. Regarding the lipid profile, the mean total cholesterol, LDL-c, and triglyceride levels were 127.1, 62.4, and 101.2 mg/dl, respectively.

Overall, 94.1% of the very-high risk participants used statins, with atorvastatin being the most common agent, followed by simvastatin and rosuvastatin [3]. A low dose of statin was prescribed in approximately 13%, whereas 54.1% were treated with a high dose of statin (atorvastatin ≥40 mg/d, rosuvastatin ≥20 mg/d). Combination lipid-lowering therapy of a high dose of statin and ezetimibe accounted for around the disappointing 5%. Of great interest, it was observed that based on the active ESC/EAS 2016 guidelines only 58% of the very-high risk participants had an adequate management of LDL-c (≥70 mg/dl). Further analysis showed that 3.2% of study patients had efficient LDL-c management, and 9.4% were eligible for PCSK9 inhibitor therapy, based on the ESC/EAS 2019 guidelines. However, acquisition of data took place long before the release of the current ESC/EAS guidelines.

The study by De Luca et al. poses a thoughtful insight in the management of dyslipidemia in a large sample of very-high risk patients from everyday clinical practice in Italy [3]. In specific, it was demonstrated that approximately 42% of the very-high risk participants had insufficient management of dyslipidemia (LDL-c <70 mg/dl), based on the active ESC/EAS 2016 guidelines. This might be ascribed to the large proportion of participant not receiving a high dose of statin and the tiny number of participants treated with combination therapy. However, the findings of the study should be carefully interpreted through the inherent limitations of registries. Especially, the ESC/ESH 2019 guidelines related outcomes carry additional limitations and should be cautiously interpreted.

This study demonstrates another alarming sign in terms of dyslipidemia management in real-world very-high risk patients. Accumulating data from Europe and other continents showed a poor management of dyslipidemia in high and very-high risk patients with potentially detrimental health consequences [3–9]. In a huge retrospective cohort of more than 350,000 high-risk Korean patients, it was found that more than half of participants with documented atherosclerotic cardiovascular disease failed to achieve a LDL-c level< 70 mg/dl [7]. In Europe, the cross-sectional EUROASPIRE IV study conducted in 24 European countries showed that 8 out of 10 high-risk participants had LDL-c ≥70 mg/dl [8]. In addition, the SURF clinical audit including 79 centers

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(11 countries) unveiled that an LDL-c target of <70 mg/dl was achieved by only 15, 33, and 35% of Asian, European, and Middle Eastern high-risk patients, respectively [9].

Altogether, real-world data notes that the majority of very-high and high risk individuals do not attain the LDL-c goal, jeopardizing a major adverse cardiovascular event. Several factors such as physicians' inertia, beware of allegedly and pragmatic side effects of statins and their dose-dependent risk, poor-adherence to pharmacotherapy, patients' unwillingness, and other might be implicated. Nevertheless, a clinically relevant aspect emerges after the well-established ESC/EAS 2019 recommendation to reduce the LDL-c goal <55 mg/dl in very-high risk patients [1]. Such low LDL-c levels seem clinically challenging to be achieved, even with the combination of statin and ezetimibe; hence, PCSK9 inhibitor might be indicated in many cases [2]. Indeed, data from SWEDEHED registry including more than 25,000 Swedish patients with recent myocardial infarction, simulated the impact of expanded lipid-lowering therapy on attainment of the LDL-c target as recommended by the current ESC/EAS 2019 guidelines [10]. Using the Monte Carlo model, it was estimated that approximately 20% of patients on high-intensity statin achieved a LDL-c <55 mg/dl along with half a reduction in LDL-c level, which increased up to 49% with the addition of ezetimibe. Of great interest, when use of PCSK9 inhibitors was simulated in eligible participants (50.6%), approximately 90% attained the LDL-c target. However, with respect to limited resources in healthcare systems, especially after the COVID-19 pandemic, the cost-effectiveness of this approach in a population-based level is rather warranted [2].

The insufficient management of dyslipidemia in everyday clinical practice poses a meaningful healthcare aspect and might result in detrimental cardiovascular outcomes. Relevant scientific authorities need to investigate this problem in depth and take action to improve the management of dyslipidemia. Future well-designed randomized controlled trials will elucidate whether a LDL-c goal <55 mg/dl is feasible without the use of PCSK9 inhibitors, overcoming the high cost of new therapies.

Older lipid guidelines needed a 10-year period to be implemented by the majority of physicians in clinical practice. Let's hope that the new guidelines will START to be implemented much earlier.

References

[1] Task Force Members, ESC Committee for Practice Guidelines (CPG), ESC National Cardiac Societies, ESC/EAS guidelines for the Management of Dyslipidaemias: lipid modification to reduce cardiovascular risk, Atherosclerosis. 290 (2019) (2019) 140–205, https://doi.org/10.1016/j.atherosclerosis.2019.08.014.

[2] Dykun, I., Mahabadi, A.A., Rassaf, T. A clinical perspective on the 2019 ESC/EAS guidelines for the management of dyslipidaemias: PCSK-9 inhibitors for all? Eur. Heart J., (2020), ehaa005. doi: https://doi.org/10.1093/eurheartj/ehaa005

[3] L. De Luca, M. Arca, P.L. Temporelli, J. Meessen, C. Riccio, P. Bonomo, A.R. Colavita, D. Gabrielli, M.M. Gulizia, F. Colivicchi, the START Investigators, Current lipid lowering treatment and attainment of LDL targets recommended by ESC/EAS Guidelines in very high-risk patients with established atherosclerotic cardiovascular disease: insights from the START registry, Int. J. Cardiol. (2020) (In press).

[4] L. Annemans, J. Azuri, K. Al-Rasadi, I. Al-Zakwani, V. Daclin, F. Mercier, N. Danchin, Healthcare resource utilization in patients on lipid-lowering therapies outside Western Europe and North America: findings of the cross-sectional observational International ChoLesterol management Practice Study (ICLPS), Lipids Health Dis. 19 (2020) 64, https://doi.org/10.1186/s12944-020-01235-5 (Online ahead of print).

[5] A. Tahkola, P. Korhonen, H. Kautiainen, T. Niiranen, P. Mäntyselkä, Lifetime risk assessment in cholesterol management among hypertensive patients: observational cross-sectional study based on electronic health record data, BMC Fam. Pract. 21 (2020) 62, https://doi.org/10.1186/s12875-020-01138-5.

[6] S. Kim, S. Han, P.P. Rane, Y. Qian, Z. Zhao, H.S. Suh, Achievement of the low-density lipoprotein cholesterol goal among patients with dyslipidemia in South Korea, PLoS One 15 (2020) e0228472, https://doi.org/10.1371/journal.pone.0228472.

[7] Y.S. Yang, B.R. Yang, M.S. Kim, Y. Hwang, S.H. Choi, Low-density lipoprotein cholesterol goal attainment rates in high-risk patients with cardiovascular diseases and diabetes mellitus in Korea: a retrospective cohort study, Lipids Health Dis. 19 (2020) 5, https://doi.org/10.1186/s12944-019-1158-5.

[8] Kotseva, K., Wood, D., De Bacquer, D., De Backer, G., Rydén, L., Jennings, C., Gyberg, V., Amouyel, P., Bruthans, J., Castro Conde, A., Cífková, R., Deckers, J.W., De Sutter, J., Dilic, M., Dolzhenko, M., Erglis, A., Fras, Z., Gaita, D., Gotcheva, N., Goudevenos, J., Heuschmann, P., Laucevicius, A., Lehto, S., Lovic, D., Miličić, D., Moore, D., Nicolaides, E., Oganov, R., Pajak, A., Pogosova, N., Reiner, Z., Stagmo, M., Störk, S., Tokgözoğlu, L., Vulic, D; EUROASPIRE Investigators. EUROASPIRE IV: a European society of cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. Eur. J. Prev. Cardiol., 23 (2016), pp. 636–648. doi: https://doi.org/10.1177/2047487315569401

[9] M. Zhao, M.T. Cooney, K. Klipstein-Grobusch, I. Vaartjes, D. De Bacquer, J. De Sutter, Ž. Reiner, E. Prescott, P. Faggiano, D. Vanuzzo, H. AlFaleh, I.B. Menown, D. Gait, N. Posogova, W.H. Sheu, D. Zhao, H. Zuo, D.E. Grobbee, I.M. Graham, Simplifying the audit of risk factor recording and control: a report from an international study in 11 countries, Eur. J. Prev. Cardiol. 23 (2016) 1202–1210, https://doi.org/10.1177/2047487316647827.

[10] Allahyari, A., Jernberg, T., Hagström, E., Leosdottir, M., Lundman, P., Ueda, P. Application of the 2019 ESC/EAS dyslipidaemia guidelines to nationwide data of patients with a recent myocardial infarction: a simulation study. Eur. Heart J., (2020), ehaa034. doi: https://doi.org/10.1093/eurheartj/ehaa034. (Online ahead of print).