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# 2019 ESC/EAS GUIDELINES FOR DYSLIPIDAEMIA – WHAT'S NEW?

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***Abstract***

*The European Society of Cardiology and the European Atherosclerotic Society are recommending in the 2019 guideline for dyslipidemia the best management strategies for an individual patient with a given condition.*

*The guideline recommends the use of new tests to help identify high-risk patients. These include both coronary artery calcium imaging and biomarker tests.*

*Modifications have also been made to the risk stratification categories, so that patients with atherosclerotic artery disease, diabetes mellitus with target organ damage, familial hypercholesterolaemia and severe chronic kidney disease are all included in very-high risk patients.*

*The new ESC/EAS guideline for dyslipidemia management compared with the 2016 version include more intensive reduction of LDL-c across CV risk categories. If the goals are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended. An important message of the new guideline is that until this moment there are no known adverse effects of very low LDL-c concentrations.*

***Keywords:*** *dyslipidemia, cardiovascular risk, European Society of Cardiology, European Atherosclerotic Society, guidelines, statin, ezetimibe.*

***Abstract***

*Societatea Europeană de Cardiologie și Societatea Europeană pentru Ateroscleroză recomandă, în ghidul din 2019 pentru dislipidemie, cele mai bune strategii de management pentru un pacient cu o afecțiune dată. Ghidul recomandă utilizarea de teste noi pentru identificarea pacienților cu risc crescut. Acestea includ atât evaluarea imagistică a depunerilor coronariene de calciu, cât și utilizarea biomarkerilor.*

*S-au făcut, de asemenea, modificări în ceea ce privește stratificarea riscului, astfel încât pacienții cu boală aterosclerotică, diabet zaharat, leziuni ale organelor țintă, hipercolesterolemie familială și boală renală cronică severă se încadrează în categoria cu risc foarte crescut.*

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*În comparație cu versiunea din 2016, noul ghid pentru managementul dislipidemiei recomandă o reducere mai intensă a LDL-c pentru toate categoriile de risc cardiovascular. Dacă obiectivele nu sunt atinse cu doza maximă tolerată de statină, se recomandă asocierea cu ezetimibe. Un mesaj important al este că, până în acest moment, nu se cunosc efecte adverse ale concentrațiilor foarte mici de LDL-c.*

***Cuvinte cheie:*** *dislipidemie, risc cardiovascular, statine, ezetimibe.*

The European Society of Cardiology (ESC) and the European Atherosclerotic Society (EAS) are recommending in the 2019 guideline for dyslipidemia the best management strategies for an individual patient with a given condition[1].

The previous ESC/EAS dyslipidemia guideline were published in August 2016[2]. In the mean time new evidence has confirmed that the key initiating event in atherogenesis is the retention of low-density lipoprotein cholesterol (LDL-c) and other cholesterol-rich apolipoprotein (Apo) B containing lipoproteins within the arterial wall. Several recent clinical trials have shown that the addition of either ezetimibe or anti-proprotein convertase subtilisin/kexin type 9 (PCSK9) monoclonal antibodies (mAbs) to statin therapy provides a further reduction in atherosclerotic cardiovascular disease (ASCVD) risk, which is directly and positively correlated with the incrementally achieved absolute LDL-C reduction. A life time approach to cardiovascular disease (CVD) risk should be also considered. This means that people of all ages should be encouraged to adopt or sustain a healthy lifestyle.

In apparently healthy persons, CVD risk is most frequently the result of multiple, integrating risk factors. This is the basis of total CV risk estimation and management. SCORE (Systematic COronaryRisk Evaluation) is a risk estimation system which can assist in making logical management decisions and may help to avoid both under- and overtreatment[1].

The guideline recommends for the first time the use of new test to help identify high-risk patients.

These include both coronary artery calcium (CAC) imaging and biomarker tests.CAC score assessment with CT may be helpful in reaching decisions about treatment in people who are at moderate risk of ASCVD. Also, the assessment of arterial (carotid or femoral) plaque burden on ultrasonography

may also be informative in these circumstances.

Modifications have been made to the risk stratification categories so that patients with atherosclerotic artery disease (ASCVD), diabetes mellitus (DM) with target organ damage, familial hypercholesterolaemia (FH) and severe chronic kidney disease (CKD) are all included in very-high risk patients. Also, patients with acute coronary syndrome (ACS) are now considered to be at very high risk of recurrent events.

Lp(a) measurement should be considered at least once in each adult person's lifetime to identify those with high inherited Lp(a) levels >180mg/dL(>430nmol/L) who may have a lifetime risk of ASCVD equivalent to the risk associated with heterozygous familial hypercholesterolemia.

Apo B may be a better measure of an individual's exposure to atherosclerotic lipoproteins. ApoB analysis is recommended for risk assessment, particularly in people with high triglycerides (TG), diabetes mellitus (DM), obesity or metabolic syndrome or very low LDL-c. It can be used as alternative to LDL-c, as the primary measurement for screening, diagnosis and management. ApoB may be preferred over non-HDL-c in the category of patients mentioned before.

The new ESC/EAS guideline for dyslipidemia management compared with the 2016 version include more intensive reduction of LDL-c across CV risk categories. For both primary and secondary prevention in very high-risk patients, a LDL-c reduction of ≥50% from baseline and a LDL-c goal of <1.4mmol/L (<55mg/dL) are recommended (IA). For patients with atherosclerotic artery disease (ASCVD) who experience a second vascular event within 2 years and not necessarily the same type as the first event, while taking maximally tolerated statin therapy, a LDL-c goal of < 1mmol/L (<40 mg/dL) may be considered (IIbB). For patients at high riskan reduction of LDL-c of ≥50% from baseline and an LDL-c goal of <1.8 mmol/L (<70 mg/dL) are recommended (IA). At high-risk are people with markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-c >4.9 mmol/L (>190 mg/dL) or BP ≥180/100 mmHg; patients with heterozygous familial hypercholesterolemia (FH) without other major risk factors; patients with diabetes mellitus (DM) without target organ damage, with DM duration ≥10 years or another additional risk factors; moderate chronic kidney disease - CKD (eGFR 30-59 mL/min/1.73 $m^2$); a calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.

An important message of the new guideline is that until this moment there are no known adverse effects of very low LDL-c concentrations.

The expected clinical benefit of pharmacological treatment to lower the LDL-c level depends on the intensity of therapy, the baseline LDL-c level and the estimated risk of ASCVD. It is recommended that a high-intensity statin therapy be prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk (IA). If the goals are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended (IB). Ezetimibe inhibits intestinal uptake of dietary and biliary cholesterol at the level of the brush border of the intestine (by interacting with the Niemann-Pick C1-like protein 1 – NPC1L1), without affecting the absorption of fat-soluble nutrients. For secondary prevention patients at very high risk not achieving their goal on a maximum tolerated dose of statin and ezetimibe, a combination

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with a PCSK9 inhibitor is recommended (IA).

The ESC/EAS guideline emphasize the importance of combination treatment in high and very high-risk patients, first with ezetimibe, and then with a PCSK9 inhibitor to achieve the targets mentioned before.

CVD risk is increased when fasting TGs are >1.7 mmol/L (>150mg/dL), but the use of drugs to lower TG levels may only be considered in high-risk patients when TGs >2.3mmol/L (>200mg/dL) and cannot be lowered by lifestyle measures (IIB). The pharmacological treatment includes statins, fibrates, PCSK9 inhibitors and n-3 PUFAs.

Statin treatment is recommended and not just considered as the first drug of choice for reducing CVD risk in high-risk patients with hypertriglyceridaemia [TG>2.3mmol/L (200mg/dL)] (IB). In high and very-high risk patients with TG between 1.5 and 5.6 mmol/L (135-499mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2x2g daily) should be considered in combination with statins (IIaB).

The REDUCE-IT trial demonstrated that in statin-treated patients with high CV risk with fasting TG, high dose of icosapent ethyl, a highly purified and stable EPA (Eicosapentaenoic acid), significantly reduced the risk of ischaemic events, including CV death. In primary prevention patients who are at LDL-c goal with TG levels >2.3mmol/L (>200mg/dL), fenofibrate or bezafibrate may be considered in combination with statins (IIbB).

Placebo-controlled randomized trials showed very clearly that true statin intolerance is rare and that it's generally possible to institute some form of statin therapy by changing the statin or reducing the dose in the overwhelming majority of patients at risk of ASCVD.

New randomized trials support a strategy of intensification of LDL-c lowering therapy in ver-high risk patients with acute coronary syndrome - ACS (MI or instable angina). If the specified LDL-c treatment goals is not achieved after 4-6 weeks with the highest tolerated statin dose and ezetimibe, it is appropriate to add a PCSK9 inhibitor (IA).

Heterozygous familial hypercholesterolemia (FH) is a common codominant monogenic dyslipidemia causing premature CVD due to lifelong elevation of plasma levels of LDL-c. Cholesterol-lowering treatment should be initiated with high-intensity statin therapy, in most cases in combination with ezetimibe, as soon as possible after a diagnosis has been made.

Treatment of FH includes for primary prevention, for patients at very-high risk, an LDL-c reduction of ≥50% from baseline and an LDL-c goal of <1.4mmol/L (<55 mg/dL) should be considered (IIaC).If goals cannot be achieved, a drug combination is recommended (ezetimibe). In patients with

FH which are at very-high risk, if the treatment goal is not achieved on maximal tolerated statin dose plus ezetimibe, therapy with a PCSK9 inhibitor is recommended (IC).

A meta-analysis of randomized trials showed that the effects of statin therapy are determined by the absolute reduction in LDL-c as well as the baseline ASCVD risk and are independent of all known risk-factors, including age. Initiation of statin treatment for primary prevention in older people age >75 years may be considered, if they are at high risk or above (IIbB). Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients (IA). It's recommended that the statin to be started with a low dose if there is significant renal impairment and/or the potential for drug interactions, and then titrated upwards to achieve LDL-c treatment goals (IC).

***References***

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