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Što novo donose prve smjernice o liječenju dislipidemija Europskog kardiološkog društva i Europskog društva za aterosklerozu?

What is new in the first European Society of Cardiology and European Atherosclerosis Society Guidelines for the management of dyslipidaemias?

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SAŽETAK: *Prve europske smjernice o liječenju dislipidemija koje su zajednički načinili Europsko kardiološko društvo i Europsko društvo za aterosklerozu bave se liječenjem dislipidemija kao integralnim i važnim dijelom prevencije kardiovaskularnih bolesti (KVB). Prema njima u bolesnika s vrlo visokim rizikom za KVB (dokazana KVB, dijabetes tipa 2, dijabetes tipa 1 s oštećenjem ciljnih organa, umjereno do jako zatajenje bubrega ili SCORE ≥10 %) LDL-kolesterol treba smanjiti na ispod 1,8 mmol/l odnosno za najmanje 50% ako se ova ciljna vrijednost nikako ne može postići. U osoba sa visokim rizikom za KVB, a to su one sa izraženim jednim čimbenikom rizika (primjerice jako povećanim kolesterolom), odnosno s razinom SCORE ≥5 do <10%, valja postići LDL-kolesterol manji od 2,5 mmol/l. Osobe s umjerenim rizikom za KVB, a to su one sa SCORE >1 do ≤5%, trebaju imati LDL-kolesterol manji od 3,0 mmol/l dok oni s niskim rizikom (SCORE <1%) ne zahtijevaju nikakvu intervenciju ili, ako im je LDL-kolesterol veći od 2,5 mmol/l, trebaju samo promijeniti način života u onaj zdraviji. U smjernicama se također po prvi puta daju naputci o liječenju povećanih triglicerida i smanjenog HDL-kolesterola, porodičnih dislipidemija, prehrambenim dodatcima koji djeluju na lipoproteine u krvi, kombiniranom liječenju dislipidemija, liječenju dislipidemija u djece, žena i starijih osoba te liječenju dislipidemija u posebnih skupina bolesnika kao što su bolesnici s dijabetesom i/ili metaboličkim sindromom, bolesnici s akutnim koronarnim sindromom i oni koji će biti podvrgnuti perkutanim koronarnim intervencijama, bolesnici s bolestima bubrega, perifernom arterijskom bolešću, moždanim udarom, aneurizmom aorte, bolesnici s HIV infekcijom i sl.*

KLJUČNE RIJEČI*: dislipidemije, kolesterol, trigliceridi, HDL-kolesterol, LDL-kolesterol, kardiovaskularne bolesti.*

SUMMARY: *The first European guidelines for the management of dyslipidaemias produced jointly by the European Society of Cardiology and the European Atherosclerosis Society deal with the management of dyslipidaemias as an integral and important part of cardiovascular diseases (CVD) prevention. According to them, in patients at very high CVD risk (established CVD, type 2 diabetes, type 1 diabetes with target organ damage, moderate to severe chronic kidney disease or a SCORE level ≥10 %) the LDL-cholesterol goal should be <1.8 mmol/L and/or reduced by a least 50% when target level cannot be reached. In patients at high CVD risk (markedly elevated single risk factors eg. hypercholesterolaemia, and SCORE level ≥5 to <10%) a LDL-cholesterol goal <2.5 mmol/L should be considered. In subjects at moderate risk (SCORE level >1 to ≤5%) LDL-cholesterol goal <3.0 mmol/L should be considered and in those at low risk (SCORE level <1%) either no lipid intervention or, if LDL-cholesterol is <2.5mmol/L, only a lifestyle intervention is advised. The guidelines also address for the first time some other important issues such as treatment of high triglycerides and low HDL-cholesterol, familial dyslipidaemias, dietary supplements and functional foods active on plasma lipid values, lipid-lowering drug combinations, management of dyslipidaemias in children, women and the elderly, management of dyslipidaemias in different clinical settings such as diabetes and metabolic syndrome, patients with acute coronary syndrome and those undergoing percutaneous coronary interventions, patients with renal disease, peripheral artery disease, stroke, aortic aneurysm, human immunodeficiency patients etc.*

KEYWORDS*: dyslipidaemias, cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, cardiovascular diseases.*

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Na Europskom kardiološkom kongresu u Parizu krajem kolovoza predstavljene su prve smjernice o liječenju dislipidemija koje su zajednički načinili Europsko kardiološko društvo i Europsko društvo za aterosklerozu. Smjernice su također istodobno tiskane u službenim glasilima oba spomenuta europska društva — *European Heart Journal i Atherosclerosis*[1]. Možda će se netko pitati zbog čega je trebalo uložiti dvogodišnji trud velike skupine najistaknutijih znanstvenika iz ovog područja da se naprave te smjernice, kada već postoje Zajedničke eu-

The first Guidelines on treatment of dyslipidemia prepared jointly by the European Society of Cardiology (ESC) and European Atherosclerosis Society were presented at the ESC Congress in Paris held by the end of August. The guidelines were also published in the official journals of the both above mentioned European societies — *European Heart Journal and Atherosclerosis*[1]. Someone may wonder as to why it was necessary for a large group of the most prominent scientists in this field to make a two-year effort in order to prepare such guidelines since the

ropske smjernice za prevenciju kardiovaskularnih bolesti (KVB) objavljene prije četiri godine[2]. Razlog nije bila samo činjenica da su se nakon objave spomenutih zajedničkih smjernica za prevenciju KVB pojavile i posebne smjernice o dijabetesu i KVB te one o liječenju arterijske hipertenzije iako su zajedničke smjernice obuhvatile i te čimbenike rizika[3,4], već poglavito to što su mnogi liječnici željeli doznati nešto više o liječenju dislipidemija u posebnih skupina bolesnika vezano uz prevenciju KVB čemu je u zajedničkim smjernicama bilo posvećeno tek malo ili čak nimalo prostora, a još više to što se upravo u posljednjih nekoliko godina došlo do brojnih novih spoznaja.

Kako bi se najbolje odgovorilo na pitanje postavljeno u naslovu ovog članka, valja krenuti redom. Najprije treba naglasiti da je u ovim smjernicama jasno i više puta istaknuto da su dislipidemije samo jedan, iako možda najvažniji, čimbenik rizika za nastanak KVB te da je njihovo liječenje integralni dio opće prevencije KVB. Pritom, kada se procjenjuje rizik KVB uvijek treba procjenjivati ukupni rizik, a ne samo obraćati pozornost na jedan čimbenik rizika, pa niti samo na dislipidemije[5]. Ukupni rizik treba procjenjivati na temelju, u praksi već godinama primijenjivanih i dobro provjerenih u nizu europskih zemalja, SCORE tablica koje se temelje na podacima o ukupnom kolesterolu, arterijskom tlaku, pušenju, životnoj dobi i spolu. U njima je apsolutni rizik izražen kao rizik da osoba umre od nekog kardiovaskularnog događaja u sljedećih 10 godina. Jedna od novosti u ovim smjernicama su dodatne tablice u koje je uvršten i HDL-kolesterol kao pokazatelj koji značajno doprinosi procjeni ukupnog rizika i te su tablice dostupne u elektroničkoj inačici na www.heartscore.org.

Druga je značajna novost i razlika prema prošlim Zajedničkim smjernicama podjela stupnjeva rizika na četiri razine sukladno SCORE sustavu: vrlo visoki, visoki, umjereni i niski rizik. Naime, iako je rizik zapravo dio kontinuuma, iz praktičnih je razloga u svakodnevnom radu potrebno imati neke uporišne točke odnosno razdjelnice. Ranija podjela osoba bez dokazane KVB samo na one s povećanim rizikom (SCORE >5%) koje treba liječiti (što su liječnici pod snažnim utjecajem farmaceutske industrije nerijetko pogrešno tumačili potrebom za propisivanjem lijekova) i one s rizikom <5% koje se uopće nije liječilo, nije više bila prihvatljiva. Stoga je u ovim smjernicama primijenjen sustav stupnjevanja ukupnog rizika KVB u četiri kategorije koji je povezan s pristupom liječenju dislipidemija temeljenom na pet razina LDL-kolesterola i to: LDL-kolesterol manji od 1,8 mmol/l, onaj od 1,8 do 2,5 mmol/l, od 2,5 do 4,0 mmol/L, od 4,0 do 4,9 mmol/l i onaj veći od 4,9 mmol/l. Naime, ove smjernice upućuju da pozornost nikako ne treba obraćati samo na one s vrlo visokim i visokim rizikom, već bi i osobe s umjerenim rizikom trebale dobiti stručni savjet o tome kako da promijene nezdravi način života (neki čak i da uz to uzimaju lijekove), a oni s niskim rizikom kako da održe svoje povoljno zdravstveno stanje.

Sukladno ovome u bolesnika s vrlo visokim rizikom KVB, a to su svi oni s dokazanom KVB (invazivnim ili neinvazivnim dijagnostičkim metodama, oni s preboljelim infarktom miokarda, akutnim koronarnim sindromom, ishemijskim moždanim udarom ili pak nakon koronarne revaskularizacije) ili s dijabetesom tipa 2 odnosno dijabetesom tipa 1 i oštećenjima ciljnih organa (primjerice mikroalbuminurijom) te oni s umjerenim ili teškim zatajenjem bubre-

Joint European Guidelines on cardiovascular diseases (CVD) prevention published four years ago already exist[2]. The reason did not only lie in the fact that the publication of the above mentioned guidelines for prevention of CVD was followed by publication of special guidelines on diabetes and CVD and the guidelines on management of hypertension, although the Joint guidelines included those risk factors[3,4], but mainly in the fact that many physicians wish to learn more about dyslipidemia in special patient groups relating to prevention of CVD which is the issue to which a little or no attention was paid in common guidelines, and especially in the fact that many new data have been collected in the last several years.

In order to answer the question posed in the title of this article, we should address this issue by applying a certain order. We should first emphasize that these guidelines have clearly and many times pointed out that dyslipidemia is only one, maybe even the most important risk factor for CVD and that its treatment is an integral part of the general prevention of CVD. When evaluating the CVD risk, we should always estimate the total risk and we should not pay attention only to one risk factor eg. only to dyslipidemia[5]. The total risk should be estimated according to SCORE charts that have been applied for years and have been well evaluated in a great number of the European countries, which are based on the data on total cholesterol, blood pressure, smoking, age and gender. They present the absolute risk as the risk of dying of a person from some of the cardiovascular events in the next 10 years. One of the novelties in these guidelines are additional charts which include HDL-cholesterol as an indicator that greatly contributes to the evaluation of the total risk and these tables are accessible in electronic form at www.heartscore.org.

Another important novelty and the difference to the Joint Guidelines is the classification of risk into four levels according to SCORE: very high, high, moderate and low risk. Although the risk is actually a part of the continuum, for practical reasons it is necessary to have some footholds or dividing lines in daily work. The previous division of persons without proven CVD into only those with increased risk (SCORE >5%) that need to be treated (which was often wrongly interpreted by physicians strongly influenced by the pharmaceutical industry as a necessity for prescribing drugs) and those with risk <5% that were not treated at all, was no longer acceptable. Therefore, these guidelines apply the system of gradation of the total CVD risk into four categories that is related with an approach to management of dyslipidemia based on five levels of LDL cholesterol, namely into: LDL-cholesterol below 1.8 mmol/l, the one from 1.8 to 2.5 mmol/l, from 2.5 to 4.0 mmol/l, from 4.0 to 4.9 mmol/l and the one over 4.9 mmol/l. These guidelines show that the attention should not be paid only to those with very high and high risk, but the subjects with moderate risk should receive professional advice on how to modify their lifestyle (some should, in addition to that, take medications), but those with low risk should be advised how to maintain their favourable health condition.

Accordingly, LDL-cholesterol should be decreased to below 1.8 mmol/l, or by at least 50% if this target value cannot be achieved in all patients with very high CVD risk and these are all those patients with proven CVD (by invasive or non-invasive diagnostic methods, those who suf-

ga (glomerulska filtracija <60 ml/min/1,73 m^2) odnosno oni s razinom SCORE ≥10%, LDL-kolesterol treba smanjiti na ispod 1,8 mmol/l, odnosno za najmanje 50% ako se ova ciljna vrijednost nikako ne može postići. U osoba s visokim rizikom za KVB, a to su one s izraženim jednim čimbenikom rizika (primjerice jako povećanim kolesterolom), odnosno s razinom SCORE ≥5 do <10%, valja postići LDL-kolesterol manji od 2,5 mmol/l. Osobe s umjerenim rizikom za KVB, kojih ima mnogo među onima srednje životne dobi, a to su osobe sa SCORE >1 do ≤5%, trebaju imati LDL-kolesterol manji od 3,0 mmol/l dok oni s niskim rizikom (SCORE <1%) ne zahtijevaju nikakvu intervenciju ili, ako im je LDL-kolesterol veći od 2,5 mmol/l, trebaju samo promijeniti način života u onaj zdraviji.

Treba posebno naglasiti da sve navedene ciljne vrijednosti LDL-kolesterola nisu, kako bi možda netko neupućen mogao pomisliti, rezultat nekog proizvoljnog stava autora ovih smjernica bez obzira kako ugledni oni bili niti utjecaja farmaceutske industrije koja nedvojbeno ima interes da ciljne vrijednosti budu što niže, već su isključivo utemeljene na objektivnim rezultatima najnovijih velikih istraživanja i pomnoj analizi rezultata svih istraživanja i meta-analiza objavljenih zadnjih godina.

Iz svega gore navedenog je vidljivo da, iako je SCORE sustav procjene rizika temeljen na ukupnom kolesterolu i ostalim čimbenicima rizika, u novim je smjernicama glavna pozornost usmjerena ka LDL-kolesterolu. Naime, niz je velikih istraživanja pokazalo da je on bolji i pouzdaniji pokazatelj od ukupnog kolesterola. Stoga bi obvezatno trebalo mjeriti LDL-kolesterol ili, ako ga se u nekom laboratoriju iz bilo kojeg razloga ne može izmjeriti (u Hrvatskoj ga svi laboratoriji mogu mjeriti), valjalo bi svakome izračunati LDL-kolesterol po Friedwaldovoj formuli koja glasi: LDL-kolesterol = ukupni kolesterol — HDL-kolesterol — (0,45 x trigliceridi). Taj je izračun, međutim, točan samo ako su trigliceridi manji od 4,5 mmol/l.

Nove smjernice preporučuju da bolesnici s dijabetesom tipa 2 trebaju dobivati lijekove za dislipidemije bez obzira na to kolika im je koncentracija LDL-kolesterola, a svi bolesnici s dijabetesom tipa 2 trebali bi obvezatno imati LDL-kolesterol manji od 2,5 mmol/l. Bolesnici s dijabetesom tipa 2 koji imaju i dokazanu neku KVB, ali i oni koji nemaju dokazanu KVB ali su stariji od 40 godina i imaju jedan ili više drugih čimbenika rizika za KVB, trebali bi imati LDL-kolesterol manji od 1,8 mmol/l.

U smjernicama je posebno naglašeno da bolesnici s porodičnom hiperkolesterolemijom neovisno o koncentraciji LDL-kolesterola trebaju biti shvaćeni kao bolesnici s visokim rizikom i u njih se mora postići koncentracija LDL-kolesterola manja od 2,5 mmol/l, a ako imaju i dokazanu neku KVB treba ih liječiti kao osobe s vrlo visokim rizikom i postići vrijednosti LDL-kolesterola manje od 1,8 mmol/l. Pritom se detaljno navode i kriteriji za postavljanje dijagnoze porodične hiperkolesterolemije koja se, iako je zapravo česta bolest (1:500 ljudi) i uzrokuje preuranjenu i jako izraženu koronarnu bolest srca (KBS), nažalost relativno rijetko dijagnosticira i liječi. Ti su kriteriji prvenstveno jako povećan LDL-kolesterol, ponekad čak i iznad 8,5 mmol/l, ali i manje povećani LDL-kolesterol, tj. iznad 4,0 ili 5,0 mmol/l ako je praćen preuranjenom koronarnom ili cerebrovaskularnom bolešću, pojavom preuranjene KBS u bližih rođaka te eventualno promjenama na koži poput ksan-

fered from myocardial infarction, acute coronary syndrome, ischemic stroke or following coronary revascularization) or with diabetes type 2 or diabetes type 1 and damaged target organs (such as by microalbuminuria) and those with moderate or severe chronic kidney disese (glomerular filtration <60 ml/min/1.73 m^2) or those with SCORE level ≥10%. In persons with high CVD risk, and these are subjects with markedly elevated single risk factor (such as strongly elevated cholesterol), or with SCORE ≥5 to <10%, LDL-cholesterol below 2.5 mmol/l needs to be achieved. Persons with moderate CVD risk whose number is great among middle aged people, and these are the persons with SCORE >1 to ≤5%, need to have LDL-cholesterol below 3.0 mmol/l while those with low risk (SCORE <1%) are not required to undergo any lipid intervention or if their LDL-cholesterol exceeds 2.5 mmol/l, they just need lifestyle intervention.

We should especially emphasize that all above mentioned target values of LDL-cholesterol are neither, as someone not familiar with this issue may think, the result of some arbitrary opinion of the authors of these guidelines, no matter how renowned they are nor are they the result of an influence of the pharmaceutical industry that undoubtedly has an interest in having the target values as low as possible, but they are based on results of the most recent large clinical trials and thorough analysis of the results of all researches and meta-analyses that have been published during the last few years.

All the above mentioned shows that although the SCORE system of risk estimation is based on total cholesterol and other risk factors, the main attention is paid to LDL-cholesterol in the new guidelines. Many studies have shown that it is a better and more reliable indicator than the total cholesterol. This is why LDL must be measured or if it cannot be measured in any laboratory for any reason whatsoever (it can be measured in all Croatian laboratories), LDL-cholesterol should be calculated by using the Friedwald's formula: LDL-cholesterol = total cholesterol — HDL-cholesterol — (0.45 x triglycerides). This calculation is however accurate only if triglycerides are below 4.5 mmol/l.

The new guidelines suggest that the patients with diabetes type 2 should receive drugs for dyslipidemia no matter what their value of LDL-cholesterol is, and all patients with diabetes type 2 should necessarily have LDL-cholesterol below 2.5 mmol/l. The patients with diabetes type 2 that also have a proven CVD and those who do not have proven CVD, but are over 40 years of age and have one or several other CVD risk factors, should have LDL-cholesterol below 1.8 mmol/l.

The guidelines especially emphasize that the patients with familial hypercholesterolemia irrespective of their LDL should be considered the high-risk patients and they should have the LDL concentration below 2.5 mmol/l, and if they have proven CVD they need to be treated as very high risk subjects and have LDL-cholesterol values achieved below 1.8 mmol/l. The criteria are indicated for making diagnosis of familial hypercholesterolemia which is, although being quite a frequent disease (1:1500 people), unfortunately relatively rarely diagnosed and treated, and it causes an early coronary heart disease (CHD). These criteria are mainly a significantly increased LDL-cholesterol,

toma ili onih na očima poput *arcus cornealis* prije 45. godine života.

U smjernicama je osobito velika pozornost posvećena potrebi promjene nezdravog načina života, naročito prehrane, jer je nizom velikih istraživanja pokazano da to značajno mijenja rizik od KVB, bilo izravno bilo neizravno, utječući na lipide u krvi, arterijski tlak i glukozu u krvi. Za smanjenje količine kolesterola u krvi posebno je važno smanjiti unos zasićenih masti i trans-masnih kiselina hranom te povećati unos prehrambenih vlakana i fitosterola, dok je za smanjenje triglicerida uz krvi ključno smanjiti prekomjernu tjelesnu težinu, unos alkohola i ugljikohidrata, posebice mono- i disaharida, povećati tjelesnu aktivnost i unositi dosta višestruko nezasićenih omega-3 masnih kiselina.

Značajan je prostor u smjernicama, naravno, dan i ulozi lijekova za liječenje dislipidemija, kako onima za smanjenje previsokog ukupnog i LDL-kolesterola, tako i onima za smanjenje previsokih triglicerida i povećanje preniskog HDL-kolesterola. Takav se poremećaj lipida često nalazi u bolesnika s dijabetesom i metaboličkim sindromom i naziva se aterogena dislipidemija. Naime, jedna od novosti u ovim smjernicama je upravo velika pozornost koja se, osim hiperkolesterolemiji, posvećuje previsokim triglyceridima i preniskom HDL-kolesterolu kao značajnim čimbenicima rizika. To je rezultat niza novih spoznaja o važnosti upravo ovih poremećaja lipida u nastanku KVB[6,7].

Važni dijelovi smjernica su i oni o kombiniranom liječenju dislipidemija, osobito za poremećaje kod kojih su uz LDL-kolesterol povećani i triglyceridi te smanjen HDL-kolesterol. Za takve se poremećaje preporučuju kombinacije statina i fibrata, osobito fenofibrata te eventualno statina i nikotinske kiseline ili statina i omega-3 masnih kiselina, a moguće je i liječenje kombinacijom statina, fenofibrata i omega-3 masnih kiselina. Ako se samim statinom ne uspije previsoki LDL-kolesterol smanjiti na ciljne vrijednosti, može se davati kombinacija statina s ezetimibom ili statina s ionskim izmjenjivačima ili čak kombinacija sve tri vrste spomenutih lijekova na što također upućuju rezultati novijih istraživanja[8].

Posebna je pozornost u smjernicama posvećena potrebi liječenja dislipidemija u žena za koje se često pogrešno smatra da su "pošteđene" od KVB pa im se dislipidemije nerijetko ne liječe na odgovarajući način. Na temelju rezultata brojnih istraživanja smjernice preporučuju da treba jednako liječiti dislipidemije i u žena kao i u muškarca, kako u sklopu primarne tako i u sklopu sekundarne prevencije KVB. Slično je i s liječenjem dislipidemija u starijih osoba kojima se također nerijetko uskraćuje liječenje, iako istraživanja pokazuju da takvo liječenje i u njih sprječava kardiovaskularne događaje i produljuje život. Naravno, smjernice upućuju i na to da je pri liječenju starijih osoba potrebno posvetiti posebnu pozornost na interakcije lijekova za dislipidemije s drugim lijekovima koje te osobe često uzimaju te na problem redovitosti uzimanja lijekova.

Smjernice naglašavaju potrebu primjene visokih doza statina u bolesnika s akutnim koronarnim sindromom već u prvih 1-4 dana hospitalizacije i postizanja ciljnih vrijednosti LDL-kolesterola od <1,8 mmol/l kao i potrebu primjene statina prije perkutanih koronarnih intervencija te primjene visokih doza statina nakon takvih intervencija. Iako

sometimes above 8.5 mmol/l, but also a less increased LDL-cholesterol, that is, above 4.0 or 5.0 mmol/l if it is followed by early coronary or cerebrovascular disease, occurrence of early CHD in close relatives and any changes to the skin such as xanthoma or those on eyes such as *arcus cornealis* below the age of 45 years.

The guidelines are especially focused on the need of lifestyle modifications to improve the plasma lipids, especially diet, because many studies have shown that it greatly changes the CVD risk, either directly or indirectly, influencing the blood lipids, blood pressure and blood glucose. In order to decrease the amount of serum cholesterol, it is very important to decrease the intake of saturated fatty and trans-fatty acids and increase the intake of dietary fibers and phytosterols, while for the purpose of decreasing serum triglycerides, it is crucial to reduce excessive body weight, intake of alcohol and carbohydrates, especially mono- and disaccharides, increase physical activity and take much more polyunsaturated omega-3 fatty acids.

An important part of the guidelines is, naturally, focused on the role of medicines for the treatment of dyslipidemia, not only the ones for the decrease of high LDL-cholesterol but also those for the decrease of high triglycerides and increase of low HDL-cholesterol. Such a disorder of lipids often affects the patients with diabetes and metabolic syndrome and is called atherogenous dyslipidemia. One of the novelties in these guidelines is a great attention that is, besides to hypercholesterolemia, paid to high triglycerides and low HDL-cholesterol as the important risk factors. This is the result of a series of new information on the importance of such disorders of lipids in occurrence of CVD[6,7].

Important parts of the guidelines are those on combined treatment of dyslipidemia, especially regarding lipid disorders where besides LDL-cholesterol, even triglycerides are increased and HDL-cholesterol is decreased. In such disorders they recomended the combinations of statins and fibrates, especially fenofibrate, statins and nicotinic acid or statin and omega-3 fatty acids, whereas the treatment by a combination of statin, fenofibrate and omega-3 fatty acids may be considered. If the statin fails to decrease the high LDL-cholesterol to target values, the combination of statin with ezetimibe or statin with bile acid sequestrant or even the combination of all three types of the above mentioned medications may be considered, as suggested by the results of the more recent studies[8].

A special attention in the guidelines has been paid to a need of treatment of dyslipidemia in women that are wrongly considered to be "spared" from CVD, so their dyslipidemias are not treated in an appropriate way. According to the results of numerous studies, the guidelines suggest that dyslipidemia in women is to be treated in the same way as in men not only as a part of primary, but also secondary prevention of CVD. Dyslipidemia treatment in elderly persons is discussed since they are often denied medical treatment, although the studies show that such treatment of elderly persons prevents cardiovascular events and prolongs their life. Of course, the guidelines suggest that while treating elderly persons, special attention has to be payed to interaction of medications for dyslipidemia with other medications that such persons often take thereby considering the problem or regular taking medications.

se bolesnicima s uznapredovalim zatajivanjem srca može preporučiti davanje 1 g/dan omega-3 masnih kiselina uz ostale lijekove, ne preporučuje se liječenje statinima bolesnika s umjerenim i uznapredovalim zatajivanjem srca, kao ni onih s bolestima zalistaka bez KBS.

Premda bolesnici s autoimunim bolestima imaju veće stope pobola i smrtnosti od KVB, nema dokaza da te bolesnike treba rutinski liječiti lijekovima za dislipidemije s ciljem prevencije KVB. Za razliku od toga, bolesnici kojima su presađeni solidni organi, budući da često imaju dislipidemije i povećani rizik KVB, trebaju dobivati lijekove za dislipidemije, poglavito statine. Ako ne podnose statine ili im je glavni poremećaj povećanje triglicerida i smanjenje HDL-kolesterola treba ih liječiti kombinacijama drugih lijekova za dislipidemije. Pri liječenju uvijek treba obratiti posebnu pozornost na moguće interakcije s drugim lijekovima koje ti bolesnici dobivaju.

Budući da kronično zatajenje bubrega predstavlja zapravo jednaki rizik za KVB kao i KBS, dane su detaljne upute o potrebi smanjivanja LDL-kolesterola, osobito u bolesnika sa stupnjem kroničnog zatajenja 2-3, dakle s glomerulskom filtracijom od 15-89 ml/min/1,73 m^2. Stoga se takvim bolesnicima može preporučiti liječenje statinima kao monoterapijom ili u kombinaciji s drugim lijekovima za dislipidemije, s ciljem postizanja LDL-kolesterola manjeg od 1,8 mmol/l.

U smjernicama se naglašava da postojanje periferne arterijske bolesti (okluzivna bolest arterija nogu, karotida, arterija mrežnice te aneurizma abdominalne aorte) upućuje na veliki rizik za infarkt miokarda i KBS te da takvi bolesnici obvezatno trebaju dobivati statine. Statini se svakako preporučuju i bolesnicima koji su preboljeli ishemijski moždani udar ili tranzitornu ishemijsku ataku kako bi postigli ciljne vrijednosti LDL-kolesterola koje su jednake onima koje moraju postići bolesnici s visokim rizikom za KVB. Takvo se liječenje, međutim, ne preporučuje bolesnicima koji su preboljeli hemoragijski moždani udar. I bolesnici sa HIV infekcijom koji često imaju dislipidemije bi također trebali dobivati lijekove za dislipidemiju kako bi postigli ciljne vrijednosti koje su jednake onima koje moraju postići bolesnici s visokim rizikom za KVB.

Predzadnje je poglavlje smjernica posvećeno tome kako treba pratiti bolesnike koji se liječe zbog dislipidemija i koje im pretrage te kako često treba raditi (navodi se primjerice da bolesnicima koji su postigli ciljne vrijednosti lipida nalaz lipida treba kontrolirati svega jednom godišnje te da ni transaminaze ne treba kontrolirati češće, osim ako nisu povišene). Jasno se naglašava da ne treba rutinski kontrolirati CK u bolesnika koji uzimaju lijekove za dislipidemije, odnosno da ovaj pokazatelj treba odrediti samo ako bolesnik uz uzimanje lijekova za dislipidemiju dobije mialgiju.

U zadnjem su poglavlju dani savjeti kako se može poboljšati ustrajnost bolesnika u pridržavanju savjeta o zdravom načinu života te uzimanju lijekova pri čemu se citiraju i rezultati nekih istraživanja provedenih u Hrvatskoj[9,10].

Na kraju valja reći da će utjecaj ovih smjernica na kardiovaskularno zdravlje bolesnika ali i cijelog pučanstva, kao i bilo kojih drugih stručnih smjernica, ovisiti isključivo o tome koliko ćemo ih primjenjivati u svakodnevnoj prak-

The guidelines emphasize a need for applying high doses of statins in patients with acute coronary syndrome during the first 1-4 days of hospitalization and the achievement of target values of LDL-cholesterol of <1.8 mmol/l and a need for giving statin prior to percutaneous coronary interventions and giving high doses of statin following such interventions. Although the patients with advanced heart disease may be advised to take 1 g/day of omega-3 fatty acids along with other medications, the treatment of patients with moderate as well as advanced heart failure and those with valvular heart failure without CHD by applying statins is not recommended.

Although patients with autoimmune diseases show higher rates of morbidity and mortality from CVD, there is no proof that such patients should be routinely treated with lipid-lowering drugs in order to prevent CVD. Unlike this, the patients with transplanted solid organs need to receive lipid-lowering drugs, especially statins, since they frequently have dyslipidemia and increased risk of CVD. If they do not tolerate statins or if their main disorder is an increase in triglycerides and decrease in HDL-cholesterol, they need to be treated by combinations of some other medications for dyslipidemia. However, attention has to be payed to potential interactions with other medications that such patients receive.

Since the chronic kidney disease (CKD) is acknowledged as a CHD risk equivalent, detailed instructions on a need for a decrease in LDL-cholesterol especially in patients with stage 2-3 of CKD, that is, with glomerular filtration of 15-89 ml/min/1.73 m^2 have been given. Therefore, such patients may be advised to undergo treatment by using statins as a monotherapy or in combination with other lipid-lowering drugs for the purpose of achieving LDL-cholesterol below 1.8 mmol/l.

The guidelines emphasize that the existence of peripheral arterial disease (occlusive disease of arteries of legs, carotids, retinal arteries and abdominal aortic aneurism) indicates a high risk for CHD and such patients should receive statins. Statins are definitely recommended to patients who have suffered from ischemic stroke or transitory ischemic attack as to achieve target values of LDL-cholesterol that are equal to the values to be achieved by patients with a high risk of CVD. Such treatment is, however, not recommended to patients who have suffered from hemorrhagic stroke. Even the patients with HIV infection who often have dyslipidemia should receive lipid-lowering drugs as to achieve target values that are equal to the values to be achieved by patients with a high risk of CVD.

The penultimate chapter of the guidelines addresses the issue of how the patients being treated from dyslipidemia are to be monitored and which tests are to be performed or how often the tests are to be performed (it is stated that the patients that have achieved target values should have the lipids controlled once a year and that transaminases are not to be controlled more often, except if they are increased). It is clearly pointed out that CK should not be routinely controlled in patients that take lipid-lowering drugs. This laboratory test should only be determined if the patient gets myalgia at the time of taking lipid-lowering drugs.

The last chapter includes tips on how the persistence of patients in following the lifestyle advice and taking medi-

si i koliko ćemo ih se mi, ali i naši bolesnici pridržavati. Smjernice su, naime, samo koristan i važan putokaz, no o nama ovisi hoćemo li ići putem na koji nas taj putokaz usmjerava ili ne.

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cations may be improved thereby quoting these results from some studies conducted in Croatia[9,10].

Eventually, it is worth noting that the impact of these guidelines on cardiovascular health of patients and the population in whole as well as any other professional guidelines will depend only on how we shall apply them in daily practice and how we or our patients will abide by them. The guidelines are, in fact, only a useful and an important guide, but it is up to us whether we shall follow the suggestions or not.

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