

Almanah 2014.: stabilna koronarna bolest srca

Almanac 2014: stable coronary artery disease

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SAŽETAK: Stabilna koronarna bolest karakterizirana je tranzitornim anginoznim tegobama kao posljedice reverzibilnog i relativnog nesklada u opskrbi miokarda oksigeniranom krvi prema potrebama u trenucima tjelesnog napora, emocionalnog ili drugog stresa, no može se javiti i u mirovanju. Kronična ishemijska bolest srca čini značajan izazov u globalnom zbrinjavanju kardiovaskularnih bolesti. U općoj populaciji ima očekivanu prevalenciju od 1 do 4%, odnosno ona je nekoliko puta češća od akutnog koronarnog sindroma. U preglednom radu prikazane su osnove kliničke dijagnostike i liječenja stabilne koronarne bolesti srca u našoj sredini te u okviru recentnih smjernica Europskog kardiološkog društva.

KLJUČNE RIJEČI: koronarna bolest srca, dijagnoza, liječenje, smjernice.

SUMMARY: Stable coronary artery disease is characterized by transient angina symptoms as a result of reversible and relative inequality of myocardial oxygenated blood supply as per needs at the moments of physical exertion, emotional or other stress, but it can also occur at rest. Chronic ischemic heart disease poses a significant challenge in the global management of cardiovascular diseases. In the general population, it shows expected prevalence of 1-4%, that is several times more common than acute coronary syndromes. The review article shows the basics of clinical diagnosis and treatment of stable coronary artery disease in the Republic of Croatia and within the scope of the recent guidelines of the European Society of Cardiology.

KEYWORDS: coronary artery disease, diagnosis, treatment, guidelines.

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Uvod

Kardiovaskularne bolesti predstavljaju jedan od najvažnijih javnozdravstvenih problema današnjice u Republici Hrvatskoj¹. Radi se o najčešćim kroničnim bolestima, uz značajnu prevalenciju u općoj populaciji. Navedena grupa odgovorna je za oko polovinu ukupne godišnje smrtnosti. Epidemiološki podaci pokazuju varijabilnost, koja se može tumačiti starenjem populacije, opadanjem broja ukupne populacije, dugoročno negativnim socioekonomskim trendovima, nivou i kontinuitetu preventivnih aktivnosti te djelatnosti zdravstvenog sektora. Značajni pomoci u sustavnom smislu pratili su razvoj aktivnosti oko primarne prevencije, dominantno institucionalnog u domovima zdravlja te mreži akutne skrbi u bolnicama. Vjerojatno najznačajniji organizacijski doseg predstavlja stvaranje prve mreže ranog zbrinjavanja akutnog infarkta miokarda, odnosno tzv. mreže primarnih perkutanih koronarnih intervencija (PCI-mreža)². Također se u zadnjih nekoliko godina u Republici Hrvatskoj razvila djelatnost kardiokirurških centara, koji ukupno djeluju u okviru pet kliničkih bolnica te jedne specijalne bolnice. Osobito se mora naglasiti djelatnost Hrvatskog kardiološkog društva te pridruženih društava koje su također poduzimale brojne javnozdravstvene mjere i sveobuhvatne principe aktivnosti u liječenju i kroničnom zbrinjavanju kardiovaskularnih bolesti. Konkordantno s razvojem kardiologije u Republici Hrvatskoj razvija-

Introduction

Cardiovascular diseases represent one of the most important public health problems of nowadays in Croatia¹. These are commonly chronic diseases, with significant prevalence in the general population. The aforementioned group is accountable for about a half of the total annual mortality. Epidemiological data shows variability, which can be interpreted by aging of the population, by a decline in the number of the total population, the long-term negative socioeconomic trends, the level and continuity of prevention activities and the activities of the health sector. Significant progress in organizational terms was in line with the development of the activities relating to primary prevention, predominantly institutional development in the community health centers and a network of acute care in hospitals. The most significant organizational success was probably the establishment of the first network of early management of acute myocardial infarction, that is, the network of primary percutaneous coronary interventions (PCI-network)². In the last few years the activity of cardiac surgery centers has developed in Croatia, being active in the 5 university hospitals and one specialty hospital in total. We must specifically stress the activity of the Croatian Cardiac Society and affiliated associations that have also undertaken a number of public health measures and comprehensive principles of activities in the treatment

ju se dva stacionarna i jedan ambulanti centar za rehabilitaciju kardiovaskularnih bolesnika. U novije vrijeme, unatoč suboptimalnim resursima zdravstvenog sustava postiže se dodatne uspjehe zahvaljujući dostupnosti i povećanju primjene suvremenih metoda neinvazivne dijagnostike, između ostalog u vidu primjene višeslojne kompjutorizirane tomografije srca i krvnih žila (MSCT koronarografija), kao i magnetske rezonancije srca. Nadalje, većim izborom dostupnosti testova opterećenja, također se približavamo standardu poboljšane individualizacije dijagnostičkog pristupa i kasnijeg terapijskog zbrinjavanja sindroma grudne boli u odnosu na očekivanu vjerojatnost priležće koronarne bolesti srca (KBS)³.

Stabilna koronarna bolest srca

Značajan izazov u zbrinjavanju kardiovaskularnih bolesti predstavlja kronična ishemijska bolest srca koja u općoj populaciji ima očekivanu prevalenciju od 1 do 4%, odnosno ona je nekoliko puta veća od akutnog koronarnog sindroma⁴. Stabilna KBS karakterizirana je tranzitornim anginoznim tegobama kao posljedice reverzibilnog nesklada u opskrbi miokarda oksigeniranom krvi prema potrebama u trenucima tjelesnog napora, emocionalnog ili drugog stresa, no može se javiti i u mirovanju⁵.

Dijagnostička obrada stabilne koronarne bolesti srca

Osnovne pretrage u prvoj liniji dijagnostičke obrade stabilne KBS čine: elektrokardiogram (EKG) u mirovanju, standardne laboratorijske nalaze, po potrebi telemetrijsko praćenje EKG ili holter EKG, ultrazvuk srca i ovisno o indikaciji rendgensku sumacijsku snimku torakalnih organa. U slučaju da pomoću standardnog transtorakalnog ehokardiografskog pregleda i uz primjenu kontrasta zbog suboptimalne tehničke dostupnosti nismo u mogućnosti učiniti dobru procjenu srčanih struktura, funkcije ili segmentalnih poremećaja kontraktiliteta, može se učiniti slikovnu dijagnostiku primjenom magnetske rezonancije (MR srca)⁶.

Temeljem kliničke prosudbe potrebno je učiniti Bayesovu analizu (statistička vjerojatnost) odnosa predtestne vjerojatnosti (PTV) prisutnosti KBS, o čemu u potpunosti ovisi tijek budućih dijagnostičko-terapijskih intervencija. Glavni čimbenici koje se pri tom uzima u obzir su: dob, spol i karakteristike simptoma, uz standardnu obradu izraženosti čimbenika kardiovaskularnog rizika. U slučaju obrade osoba s nižim ili umjerenim omjerom PTV prisutnosti KBS osobito se povoljna čini dijagnostika primjenom MSCT koronarografije koja ima dobru negativnu prediktivnu vrijednost (optimalnije za isključenje bolesti), a prednost joj u navedenim okolnostima čini obrada mladih osoba s očekivanim nižim udjelom kalcijske u koronarnim arterijama.

U **Tablici 1** prikazani su osnovni dijagnostički testovi za procjenu koronarne bolesti srca.

Dodatna obrada osoba s nižom PTV prisutnosti KBS (<15%) uključuje dijagnostiku nekoronarnih uzroka sindroma grudne boli. U slučaju ponavljanih tegoba, uz pojavu anginoznih tegoba u mirovanju vrijedi u obzir uzeti mogućnost vazospastičke angine⁵. Kod ispitanika s intermedijarnom PTV prisutnosti KBS (15-85%) potrebna je dodatna obrada primjenom dostupne neinvazivne dijagnostike. Za slučaj da se

and management of chronic cardiovascular diseases. Concordantly with the development of cardiology in the Republic of Croatia, there are two in-patient centers and one out-patient center for the rehabilitation of cardiovascular patients that have been established. In recent times, despite suboptimal resources of the health system, additional success was achieved owing to the availability and increased use of modern methods of non-invasive diagnostics, in the form of using cardiac and blood vessel multi-slice computed tomography (MSCT coronary angiography) and magnetic resonance imaging of the heart. Furthermore, a greater diversity of available diagnostic tests has also resulted in our getting closer to the standard of improved individualization of a diagnostic approach and subsequent therapeutic management of chest pain syndrome compared to the expected probability of the underlying coronary artery disease (CAD)³.

Stable coronary artery disease

A significant challenge in the management of cardiovascular disease is a chronic ischemic heart disease that in the general population has an expected prevalence of 1-4%, and it is several times greater than the acute coronary syndrome⁴. Stable CAD is characterized by transient angina problems as a result of reversible inequality of myocardial oxygenated blood supply as per needs at the moments of physical exertion, emotional or other stress, but it can also occur at rest⁵.

Diagnostic evaluation of stable coronary artery disease

The basic tests in the first line diagnostic evaluation of stable CAD include: electrocardiogram (ECG) at rest, standard laboratory values, telemetric monitoring ECG or Holter ECG if necessary, echocardiography, and depending on the indication, chest X-ray. In case technical difficulties occur due to suboptimal transthoracic echocardiographic analysis of cardiac structures, function or segmental contractility disorders by applying a standard transthoracic echocardiographic examination and by using the contrast due to suboptimal technical availability, imaging diagnostics can be done by using magnetic imaging resonance (cardiac MRI)⁶.

Based on clinical judgment, it is necessary to do a Bayesian analysis (statistical probability) of a relationship of pretest probability (PTP) of presence of CAD, which is entirely dependent on the progress of the future diagnostic and therapeutic interventions. The main factors to be taken into consideration are: age, gender, symptom characteristics, along with the standard treatment of pronounced cardiovascular risk factors. In case of treatment of persons with lower or moderate ratio of PTP of CAD, the diagnostics by using MSCT coronary angiography seems to be particularly beneficial, due to an excellent negative predictive value (more optimal for excluding the disease), whereas the treatment of young people with an expected lower proportion of calcium in the coronary arteries makes it more beneficial in the given circumstances.

Table 1 shows basic diagnostic tests for the evaluation of coronary artery disease.

Additional treatment of persons with lower PTP of CAD (<15%) include the diagnostics of non-coronary causes of chest pain syndromes. In the case of recurring problems along with the occurrence of angina pain at rest, it is worth considering the possibility of vasospastic angina⁵. In pa-

Table 1. Common diagnostic tests for diagnosing the presence of coronary artery disease (modified from European Society of Cardiology 2013 guidelines⁵).

Diagnostic test	Sensitivity (%)	Specificity (%)
Exercise electrocardiogram	45-50	85-90
Exercise stress echocardiography	80-85	80-85
Exercise stress SPECT	73-92	63-87
Dobutamine stress echocardiography	79-83	82-86
Dobutamine stress MRI	79-88	81-91
Vasodilator stress echocardiography	72-79	92-95
Vasodilator stress SPECT	90-91	75-84
Vasodilator stress MRI	67-94	61-85
Coronary computerized tomography	95-99	64-83
Vasodilator stress PET	81-97	74-91

SPECT = single photon emission computerized tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

radi o visokom stupnju PTV prisutnosti KBS (>85%), uz kliničke simptome koji jasno odgovaraju anginoznim dodatna testiranja neinvazivnom dijagnostikom nisu nužno potrebna te se bolesnika može uputiti na invazivnu koronarografiju⁵. U potonjem navedenom slučaju primjena dodatnih neinvazivnih dijagnostika očekivano ne dovodi do preciznijeg odgovora o prisutnosti KBS, no u slučaju procijenjene kliničke opravdanosti primjena dodatnih testova pomaže u dodatnoj diferencijaciji rizika pojave glavnih neželjenih kardiovaskularnih događaja.

U pogledu ispitanika s intermedijarnim stupnjem PTV prisutnosti KBS primjena MSCT za procjenu kalcifikata koronarnih arterija prema Agastonu, kada su iznosi kalcija >400 dovodi do značajnog povećanja udjela pozitivnih nalaza (lažno i stvarno pozitivnih). Obrada MSCT-kalcijским scoringom može se tada dijelom i smatrati pouzdanim ekvivalentom konvencionalnih stres testova, no odluka o daljoj obradi, odnosno invazivnoj koronarografiji u smislu žurnosti obrade donosi se temeljem ostalih karakteristika kliničke procjene⁷.

Stres testovi primjenom tjelesnog opterećenja predstavljaju metodu prvog izbora u dijagnostičkoj obradi, jednostavno zbog veće reprezentativnosti patofizioloških promjena u kontroliranom testiranju koje su bliske naporima u svakodnevnom životu. Nadalje, primjena tjelesnog opterećenja donosi nam vrijedne kliničke podatke poput objektivnije procjene stupnja podnošenja tjelesnih napora, dinamiku vrijednosti arterijskog tlaka i pulsa, uz monitoriranje elektrokardiografskih promjena. Primjena farmakoloških oblika stresa osobito je pogodna za dodatnu obradu već poznatih segmentalnih poremećaja kontraktiliteta miokarda, ili kod osoba koji ne mogu uspješno izvesti test uz primjenu tjelesnog opterećenja.

Dobutaminski stres test pokazao se osobito korisnim za izazivanje nesklada u opskrbi i potrebama miokarda za kisikom. Osobito su velike mogućnosti otkrivanja segmentalnih ispada u kontraktilitetu nakon primjene dobutamina, u smislu detekcije vijabilnosti / omamljenosti miokarda na MR srca⁸. Važno je napomenuti da je sigurnosni profil primjene dobutaminskog stresa podjednak kod MR srca i ehokardiografije⁹. Primjena vazodilatatorskih testova poput adenozi- na, odnosno tzv. "MRI-perfuzije" značajno se češće koristi u kliničkoj praksi, uz zadovoljavajući sigurnosni profil i dobar stupanj dijagnostičke točnosti, podjednak SPECT i PET testiranjima¹⁰. Ukoliko se za procjenu ispada perfuzije primjenjuju kvalitativne metode analize protoka, dijagnostička toč-

lients with intermediate PTP of CAD (15-85%) additional treatment by using the available non-invasive diagnostics is required. In case that a high degree of PTP of CAD (>85%) along with clinical symptoms that clearly resembles angina chest pain, additional tests by noninvasive diagnostics are not necessarily taken, and a patient may well be referred for invasive coronary angiography⁵. In the latter case, the application of additional noninvasive diagnostics does not, as expected, lead to a more precise answer about the presence of CAD, but if it is clinically justified, the application of additional tests helps in additional differentiation of risks for occurrence of major adverse cardiovascular events.

Regarding the subjects with intermediate degree of PTV of CAD, the use of MSCT to evaluate coronary artery calcification based on Agaston score, when the amounts of calcium >400 leads to a significant increase in the proportion of positive results (falsely and truly positive ones). The evaluation based on MSCT-calcium scoring can then partly be considered to be a reliable equivalent to conventional stress tests, but the decision on further treatment or invasive coronary angiography in terms of the urgency of the treatment is to be made on the basis of other characteristics of the clinical evaluation⁷.

Stress tests by using the physical stress represent the first choice method in the diagnostic evaluation, simply because of the greater representativeness of pathophysiological changes in the controlled environment that are as close to the everyday life stress. Furthermore, the use of physical stress brings us valuable clinical data such as objective evaluation of a degree of endurance of physical stress, dynamics of blood pressure and pulse, accompanied by the monitoring of changes in the ECG. The application of pharmacological stress types is particularly suited for additional evaluation of already known segmental myocardial contractility disorders, or in patients who are unable to successfully perform the test with physical load.

Dobutamine stress test is established as particularly useful for inducing of mismatch of myocardial oxygen supply and myocardial oxygen demands. There are particularly great possibilities of identifying segmental deficits in the contractility after the administration of dobutamine, in terms of detection of viability/numbness of myocardium to MRI⁸. It is important to note that the safety profile of the application of dobutamine stress is equal in MRI and echocardiography⁹. The vasodilator tests such as adenosine, or the so-called

nost MR srca odgovara približno invazivnoj koronarografiji uz primjenu frakcione analize protoka/rezerve (FFR)¹¹.

Procjena vijabilnosti miokarda pomoću MR srca pruža morfološke detalje visoke rezolucije, uključujući i funkcionalnu procjenu lijeve klijetke u svega 30-ak minuta oslikavanja. Princip oslikavanja gadolinijem temelji se na većoj brzini ispiranja gadolinija iz normalnog miokarda naspram onog zamijenjenog fibrozom ili ožiljkom. Na tim osnovama odgođeno oslikavanje, 5 do 20 minuta nakon ubrizgavanja kontrastnog sredstva, jasno će prikazati fibrozu ili ožiljak. U kliničkim ispitivanjima na ljudima, MR srca uz primjenu gadolinija kao kontrastnog sredstva je predstavljena kao precizna metoda određivanja vijabilnosti miokarda u kojoj je oporavak funkcije miokarda nakon koronarne prenosnice predstavljen kao referentni standard. U 52 bolesnika koji su bili podvrgnuti koronarnoj revaskularizaciji, uočena je bolja regionalna funkcija u 82% segmenata u kojih nije ustanovljena preoperativna imbibicija kontrastom, u 64% segmenata s 1% do 25% zahvaćenosti miokarda, a svega 37% u segmentima s 26% do 50% zahvaćenosti miokarda.¹²

Meta analizom ranijih studija primjena MSCT koronarografije u dijagnostici KBS pokazuje visoke stope senzitivnosti (98-99%) i negativne prediktivnu vrijednost (99-100%), no uz nešto manju specifičnost (82-89%) i pozitivnu prediktivnu vrijednost (91-93%)¹³. Na drugoj strani, veća multicentrična studija na bolesnicima s poznatom KBS, ranijim perkutanim koronarnim intervencijama i preboljelim infarktom, dijagnostička točnost je nešto niža (senzitivnost 85%, specifičnost 90%)¹⁴. Tahikardija, aritmije i povećan udio kalcifikata koronarnih arterija zbog mineralnih artefakata otežavaju analizu MSCT koronarografije te smanjuju dijagnostičku točnost¹⁵.

Procjena dugoročnog kliničkog rizika stabilne koronarne bolesti srca

Procjena dugoročnog kliničkog rizika stabilne KBS uključuje analizu većeg broja čimbenika iz sfere kliničkog pregleda i obrade čimbenika rizika, relevantnih ranijih anamnestičkih podataka te nalaza aktualne dijagnostičke obrade uz podrazumijevanje primjene kliničkog zbrinjavanja u skladu s važećim smjernicama kliničke prakse, odnosno medicine utemeljene na dokazima. Posljednje smjernice Europskog kardiološkog društva (ESC) iz 2013. godine podrazumijevaju visok klinički rizik, odnosno opravdanost za dodatnom invazivnom obradom, uz pružanje mogućnosti adekvatnog oblika revaskularizacijskog liječenja (gdje je to moguće) za bolesnika s očekivanom stopom jednogodišnjih komplikacija i velikih neželjenih događaja od $\geq 3\%$ ⁵.

Dijagnostičko-terapijsko kliničko pitanje, odnosno obrada stope rizika uključuje kliničku reevaluaciju, procjenu rizika temeljem istisne frakcije lijeve klijetke, odgovora na stres testiranje i morfološkog nalaza koronarnih arterija. U **Tablici 2** prikazane su stope rizika, temeljem dijagnostičke obrade, prema važećim smjernicama ESC.

"MRI-perfusion" are significantly more commonly used in clinical practice, with a satisfactory safety profile and a sufficient degree of diagnostic accuracy, equaling to SPECT and PET tests¹⁰. If qualitative methods of flow analysis are applied for the evaluation of perfusion deficit, the diagnostic accuracy of MRI approximately corresponds to invasive coronary angiography accompanied by using fractional flow reserve (FFR) analysis¹¹.

The evaluation of myocardial viability by using MRI provides high-resolution morphological details, including functional evaluation of the left ventricle in only 30 minutes of imaging. The principle of gadolinium-based imaging is based on a delayed wash out of gadolinium from normal myocardium compared to the one replaced by fibrosis a scar. A delayed imaging from 5 to 20 minutes after the injection of a contrast agent will clearly show fibrosis or a scar. In clinical trials on human subjects, cardiac MRI accompanied by the use of gadolinium as a contrast agent is introduced as an accurate method of identifying myocardial viability where the recovery of the myocardial function after coronary artery bypass surgery is presented as a reference standard. In 52 patients who underwent coronary revascularization, we observed a better regional function in 82% of segments in whom preoperative imbibition by the contrast agent was not established, in 64% of segments where myocardium was affected from 1% to 25%, and only 37% in segments where myocardium was affected from 26% to 50%.¹²

In a meta-analysis of of MSCT coronary angiography in the diagnostics of CAD shows a high rate of sensitivity (98-99%) and negative predictive value (99-100%), but with slightly lower specificity (82-89%) and positive predictive value (91-93%)¹³. A larger multi-centric study on patients with a history of CAD, previous percutaneous coronary interventions and previous myocardial infarction shows that the diagnostic accuracy is slightly lower (sensitivity 85%, specificity 90%)¹⁴. Tachycardia, arrhythmia and an increased frequency of calcification of the coronary arteries due to mineral artifacts make the performance of the analysis of MSCT coronary angiography more difficult and reduce diagnostic accuracy¹⁵.

Evaluation of long-term clinical risk of stable coronary artery disease

The evaluation of the long-term clinical risk of stable CAD involves an analysis of a large number of factors in the field of clinical examination and processing of risk factors, relevant previous history data and findings of the current diagnostic workup assuming the application of the clinical management in accordance with applicable clinical practice guidelines or evidence-based medicine. The latest guidelines of the European Society of Cardiology (ESC) of 2013 suggest a high clinical risk, or the justification for additional invasive workup, accompanied by providing an adequate form of revascularization treatment (where possible) for patients with an expected rate of annual complications and major adverse events of $\geq 3\%$ ⁵.

Diagnostic and therapeutic clinical question or evaluation of risk rate involves clinical re-evaluation, risk assessment based on the left ventricular ejection fraction, the response to stress test and morphological findings of coronary arteries. **Table 2** shows the risk level, based on the diagnostic workup, according to the applicable ESC guidelines.

Table 2. Definitions of risk by different testing modalities according to the European Society of Cardiology 2013 guidelines⁵.

Exercise stress electrocardiogram	High risk	Cardiovascular mortality $\geq 3\%$ /year
	Intermediate risk	Cardiovascular mortality $\leq 1-3\%$ /year
	Low risk	Cardiovascular mortality $< 1\%$ /year
Ischaemia imaging	High risk	Area of ischaemia $> 10\%$ ($> 10\%$ SPECT; $> 2/16$ segments MRI; > 3 dobutamine-induced dysfunctional segments; > 3 dysfunctional segments by stress echocardiography)
	Intermediate risk	Area of ischaemia 1-10% and any ischaemia less than high risk by MRI or stress echocardiography
	Low risk	No ischaemia
Multislice computed tomography coronary angiography	High risk	Significant lesions of high risk category (three-vessel disease with proximal stenoses, left-main and proximal stenosis of left anterior descendent artery)
	Intermediate risk	Significant lesion(s) in large and proximal coronary artery(ies) but not high risk category.
	Low risk	Normal coronary artery or plaques only.

Adapted from ESC 2013 guidelines⁵

Mikrovaskularna angina

Primarna mikrovaskularna bolest klinički se prezentira kao tipične ponavljajuće anginozne tegobe. Navedeni entitet češće se javlja uz šećernu bolest, hipertrofičnu kardiomiopatiju ili aortnu stenozu te se podrazumijeva pod sekundarnom mikrovaskularnom bolesti, za razliku od stabilne KBS. Dugogodišnja arterijska hipertenzija također ponekad dovodi do pojave grudne boli uz uredan morfološki nalaz epikardijalnih koronarnih arterija, no iz ranijih istraživanja poznati su slučajevi koronarografski utvrdene smanjene koronarne pričuve (FFR), čak i u uvjetima bez značajnije hipertrofije lijeve klijetke. Nasuprot tome, uz hipertenzivnu hipertrofiju lijeve klijetke dolazi do hipertrofije kardiomiocita, umnažanja veziva, kao i perivaskularnih promjena u intramuralnom toku koronarne cirkulacije uz poremećaje dijasistolčke funkcije¹⁶.

Dodatna obrada potrebna je kada su slikovne ili EKG metode stres testiranja postavile sumnju na KBS, no nalaz koronarografije je isključio fiksnu ili dinamičku koronarnu stenozu u epikardijalnom tijeku koronarnih arterija¹⁷.

Dijagnostika, obrada i prognostički čimbenici vazospastičke angine, koja također suštinski ne spada u oblike stabilne KBS prikazani su u odgovarajućim smjernicama ESC.

Zbrinjavanje stabilne koronarne bolesti srca

Moramo napomenuti da sveukupno zbrinjavanje ishemijske bolesti srca uključuje aktivnosti oko rane dijagnostike i prevencije te kontinuiranih sveobuhvatnih mjera koje moraju osigurati čim povoljniju podlogu u vidu kroničnog zbrinjavanja čimbenika rizika. U našoj državi i dalje je prisutna relativno velika zastupljenost pušenja, suboptimalne kontrole arterijske hipertenzije, dislipidemije i pretilosti te nepovoljan socioekonomski profil koji su bitan izazov u javnozdravstvenom smislu¹⁸.

U suštinskom smislu liječenje stabilne KBS u okrilju medicine utemeljene na dokazima podrazumijeva optimizaciju medikamentozne terapije kombiniranu s mjerama interven-

Microvascular angina

Primary microvascular disease clinically presents as a typical recurring angina symptoms. The above said disease commonly occurs with diabetes, hypertrophic cardiomyopathy or aortic stenosis, and is understood to be secondary microvascular disease, unlike the stable CAD. Long-term hypertension can sometimes lead to chest pain with normal morphology of epicardial coronary arteries, but the previous studies suggest the well-known case of determined reduced fractional flow reserve (FFR), even without significant left ventricular hypertrophy. Unlike this, hypertensive left ventricular hypertrophy is accompanied by hypertrophy of cardiomyocytes, proliferation of connective tissues, as well as perivascular changes in the intramural flow of coronary circulation with diastolic function disorders¹⁶.

Additional evaluation is required when the imaging or ECG stress test methods suggest CAD, but the result of coronary angiography has excluded fixed or dynamic coronary stenosis in the flow of epicardial coronary arteries¹⁷.

Diagnostics, treatment and prognostic factors of vasospastic angina, which also essentially is not considered as stable CAD are presented in the relevant ESC guidelines.

Management of stable coronary artery disease

We have to note that the overall management of ischemic heart disease includes the activities involving early diagnostics and prevention as well as continuous comprehensive measures which must provide a favorable base in the form of chronic risk factor management. In our country, a relatively high prevalence of smoking, suboptimal control of hypertension, dyslipidemia and obesity and adverse socioeconomic profile that are essential challenge in public health terms are still present¹⁸.

The treatment of stable CAD within the scope of evidence-based medicine basically involves the optimization of medical therapy combined with measures of intervention treat-

cijskog liječenja perkutanom koronarnim intervencijama i/ili kardiokirurškim zahvatima.

Medikamentozna terapija stabilne koronarne bolesti

Ciljevi medikamentozne terapije stabilne KBS podrazumijevaju:

1. kontrolu simptoma (angina)
2. prevenciju neželjenih kardiovaskularnih događaja
3. dobru kontrolu čimbenika kardiovaskularnog rizika.

U pogledu antiaterosklerotske terapije ciljevi liječenja uključuju stabilizaciju i regresiju poznatih plakova, smanjenje sistemske upalne reakcije blagog intenziteta i sprečavanje aterotrombotskih komplikacija. Optimalna medikamentozna terapija stabilne KBS uključuje više grupa lijekova poput: antitrombocitnih, inhibitora 3-hidroksi-3-metilglutarilkoenzim-A-reduktaze (statini), blokatore beta adrenergičkih receptora, nitrate, inhibitore enzima angiotenzinogenske konvertaze, kalcijске antagoniste te grupu novijih antiishemijskih lijekova poput ranolazina, trimetazidina i ivabradina¹⁹.

U pogledu općih terapijskih napomena važno je istaknuti da u okrilju dobre medicinske prakse liječenje stabilne KBS podrazumijeva primjenu barem 2 grupe lijekova (antiishemijsko i preventivno liječenje neželjenih kardiovaskularnih događaja), bolesnike kontinuirano treba podučavati o stanju bolesti, pridruženim rizicima te na svakoj kontroli učiniti procjenu pridržavanja terapije kao i terapijske učinkovitosti (rezistencija).

Uz statin, mandatna terapija sprečavanja neželjenih kardiovaskularnih događaja uključuje acetilsalicilatnu kiselinu, odnosno klopidoget u slučaju nepodnošenja acetilsalicilata. Iako su se noviji P2Y antagonisti prasugrel i tikagrelor u dosadašnjim studijama pokazali i terapijski učinkovitijim od klopidogeta, adekvatne studije primarno u pogledu stabilne KBS još nisu dostupne. Također vrijedi napomenuti, da primjena dvojne antitrombocitne terapije u okrilju stabilne koronarne ili aterosklerotske bolesti uz povišen kardiovaskularni rizik (studija CHARISMA) nije dovela do bolje prevencije velikih neželjenih kardiovaskularnih događaja, a izlaže bolesnika dodatnim rizicima komplikacija, odnosno krvarenja²⁰. Nasuprot tome, kod poznatih aterotrombotskih komplikacija i akutnog koronarnog sindroma primjena dvojne antiagregacijske terapije je vrijedna i korisna te opisana u nadležnim smjernicama.

Revaskularizacijsko liječenje

Revaskularizacijsko liječenje, kao što je ranije spomenuto, treba imati na umu kod bolesnika sa stabilnom KBS i očekivanom procijenjenom stopom rizika kardiovaskularnih događaja $\geq 3\%$ na godinu. Dodatna klinička reevaluacija preporuča se u intermedijarnim razredima rizika (≤ 1 do 3% /godina)⁵. Odluku o vremenu i opsegu optimalnog oblika revaskularizacijskog liječenja uputno je donijeti na stručnom konziliju koji uključuje intervencijskog kardiologa i kardijalnog kirurga te ostale subspecialnosti u okrilju kliničkog pitanja. Dodatne stratifikacije rizika opisane su u ranijem tekstu o dijagnostičkoj obradi te nadležnim smjernicama ESC.

ment by percutaneous coronary interventions and/or surgical interventions.

Medical therapy of stable coronary artery disease

The goals of medical therapy of stable CAD include:

1. the control of symptoms (angina)
2. prevention of adverse cardiovascular events
3. good control of cardiovascular risk factors.

Regarding the antiatherosclerotic therapy, the treatment goals include stabilization and regression of known plaques, reduction of systemic inflammatory response of mild intensity and prevention of atherothrombotic complications. Optimal medical therapy of stable coronary artery disease includes several groups of drugs such as: antiplatelet, 3-hydroxy-3-methylglutaryl-coenzyme-A reductase inhibitors (statins), beta adrenergic receptor antagonists, nitrates, angiotensin-converting enzyme inhibitors, calcium antagonists, and a group of new anti-ischemic drugs such as ranolazine, trimetazidine and ivabradine¹⁹.

Regarding general therapeutic notes, it is important to stress that within the scope of good medical practice, the treatment of stable CAD involves the administration of at least two groups of drugs (anti-ischemic and preventive treatment of adverse cardiovascular events). Besides, the patients should be continually studied as to the state of the disease, associated risks, and the evaluation of therapy compliance and the therapeutic efficacy (resistance) should be made at the time of every follow-up.

In addition to statin, the mandatory therapy for prevention of cardiovascular adverse events includes acetylsalicylic acid or clopidogrel in case of intolerance of acetylsalicylates. Although the more recent P2Y antagonists prasugrel and ticagrelor proved in the previous studies to be more therapeutically effective than clopidogrel, the relevant studies primarily in terms of stable CAD are not yet available. The use of dual antiplatelet therapy for stable coronary or atherosclerotic diseases with increased cardiovascular risk (CHARISMA study) did not result in better prevention of major adverse cardiovascular events, but it exposed patients to additional risks of complications, i.e. bleeding²⁰. On contrary, in case of atherothrombotic complications and acute coronary syndrome the use of dual antiplatelet therapy is beneficial and useful, and is described in the relevant guidelines.

Revascularization treatment

Revascularization treatment, as mentioned earlier, should be taken into consideration in patients with stable CAD and the expected estimated risk rate for cardiovascular events $\geq 3\%$ per year. Additional clinical re-evaluation is recommended in the intermediate risk classes (≤ 1 to 3% /year)⁵. The decision on the timing and extent of the optimal form of revascularization treatment is to be analyzed by multiprofessional teamwork involving intervention cardiologists, cardiac surgeons and other subspecialties with regard to the clinical issue. Additional risk stratifications have been described in the ESC relevant guidelines considering acute and post-acute care settings.

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