# Koronarna bolest u Hrvatskoj – trenutačna situacija i budući izazovi

# Coronary Artery Disease in Croatia – Current Status and Future Challenges

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**SAŽETAK:** Kardiovaskularne su bolesti, usprkos pozitivnim trendovima i napretku u liječenju, i dalje najčešći uzrok smrti u Republici Hrvatskoj, od čega najveći dio otpada na koronarnu bolest srca. S jedne strane, Hrvatska ima svako pravo pohvaliti se činjenicom da je koronarnom bolesniku dostupna suvremena i kvalitetna skrb, na razini razvijenih zemalja i bogatijih zdravstvenih sustava, no, s druge strane, to se ne odnosi na prosječnu razinu skrbi te postoji jasna neravnomjernost u njenoj dostupnosti i kvaliteti na razini pojedinih hrvatskih regija, uvjetovana geografskim, financijskim i kadrovskim ograničenjima. Preduvjeti za poboljšanje zbrinjavanja bolesnika oboljelih od koronarne bolesti srca su višestruki i uključuju potrebu za sustavnim i kontinuiranim naporima na polju prevencije, dijagnostike i liječenja. Počevši od mjera edukacije rizične populacije, bolesnika i njihovih obitelji (javnozdravstvenim kampanjama i promicanjem zdravoga životnog stila) te optimizacije edukacije pružatelja zdravstvene skrbi na primarnoj razini, reorganizacija zdravstvenog sustava trebala bi omogućiti pravodobnu dostupnost i pravilnu primjenu neinvazivnih dijagnostičkih metoda, neograničen pristup svim sastavnicama optimalne medikamentne terapije, bolju organizaciju mreže primarne perkutane koronarne intervencije uz smanjenje vremena kašnjenja na revaskularizaciju, punu opremljenost intervencijskih laboratorija s poboljšanjem uvjeta rada intervencijskih timova, rješavanje problema listi čekanja na kardiokirurško revaskularizaciju i kvalitetan epidemiološki nadzor.

**SUMMARY:** Cardiovascular diseases are, despite positive trends and recent treatment advances, still the most common cause of death in the Republic of Croatia, mostly due to coronary artery disease. Croatia has every right to pride itself on the fact that patients with coronary disease are provided with modern, up to date and high-quality care comparable to more developed countries and wealthier healthcare systems. At the same time, the cardiovascular care in certain regions of Croatia is not at this level due to geographical, financial, and personnel limitations. There are multiple prerequisites for improving patient care, including the need for systematic and continuous efforts in prevention, diagnostics, and treatment. Starting with educational measures for population at-risk (through public-health campaigns promoting a healthy lifestyle) and optimizing the education of healthcare providers at the primary level, the reorganization of the healthcare system should work towards achieving availability and proper use of non-invasive diagnostic methods, unlimited access to appropriate medications, better organization of primary percutaneous coronary intervention network with reduced delays in revascularization, fully equipped interventional laboratories with improved working conditions for intervention teams, reduction of the waiting lists for cardiac surgery revascularization, and high-quality epidemiologic monitoring.

**KLJUČNE RIJEČI:** koronarna bolest srca, Hrvatska, akutni koronarni sindrom, perkutana koronarna intervencija, registri, prevencija, rehabilitacija.

**KEYWORDS:** coronary artery disease, Croatia, acute coronary syndrome, percutaneous coronary intervention, registries, prevention, rehabilitation.

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## EPIDEMIOLOGIJA

Kardiovaskularne bolesti (KVB) vodeći su globalni uzrok smrtnosti i pobola. Prema podatcima 2013 Global Burden of Disease Study, procjenjuje se da je oko 30% svih smrti uzrokovano kardiovaskularnom bolešću[1]. Na razini Europe riječ je o udjelu u ukupnoj smrtnosti od 47 %, a u Europskoj uniji od 40 %. I premda je napredak u liječenju KVB-a u zadnjih nekoliko godina uzrokovao zamjetni pad smrtnosti u ekonomski najrazvijenijim zemljama te su u nekima od tih (dominantno europskih) zemalja kao vodeći uzrok smrti primat preuzele zloćudne bolesti, ova skupina bolesti i dalje je dominantan javnozdravstveni problem u većini zemalja. Posebno je upozoravajući podatak da se od 4 do čak 42 % smrtnih ishoda od KVB-a, ovisno o ekonomskoj snazi i stupnju razvijenosti zdravstvenog sustava pojedine države, događa unutar ekonomski najproduktivnije populacije ljudi u dobi do 60 godina, što baca dodatno svjetlo i naglašava ovaj gorući problem s jasnim nepovoljnim društveno-ekonomskim posljedicama. Pri tome se ne smije zanemariti velik broj kardiovaskularnih događaja bez smrtnog ishoda, ali sa značajnim negativnim posljedicama na zdravlje populacije i porast stope invalidnosti. Izraženo s pomoću tzv. DALY (eng. *disability-adjusted life year*) koji u izračun uključuje izgubljene godine života zbog prijevremenog umiranja i godine onesposobljenosti zbog bolesti, riječ je o opterećenju od 10 do 18 % u usporedbi sa svim bolestima[2].

Sustavi javnog zdravstva u većini zemalja, osobito u zemljama u razvoju, prenapregnuti su porastom potrebe zbrinjavanja populacije oboljelih od bolesti srca, moždanog udara, zloćudnih bolesti, šećerne bolesti, kroničnih bolesti dišnog sustava i dr. Koncept organizacije zdravstvenog sustava bazira se na stavljanju kurativne medicine u središte sustava putem tehnički i kadrovski dobro opremljenih bolničkih ustanova koje omogućuju visokokvalitetnu skrb za malen broj bolesnika, uz visoke troškove iz ograničenoga zdravstvenog proračuna, a u isto se vrijeme više ili manje zanemaruje činjenica da je riječ o bolestima koja se daju i trebaju sustavno prevenirati. Kao posljedicu imamo velik udio ljudi s visokim kardiovaskularnim rizikom koji ostaje neprepoznat, a i pojedinci s dijagnosticiranim problemom nemaju primjeren pristup skrbi na primarnoj razini. Važnost trenutačne situacije i potrebu rješavanja problema na globalnoj razini prepoznala je i Svjetska zdravstvena organizacija donošenjem Globalnog akcijskog plana za prevenciju i kontrolu nezaraznih bolesti za razdoblje 2013. – 2020., kao nastavka prve verzije Plana za 2008. – 2013., stavljajući naglasak na četiri ključna čimbenika rizika – konzumaciju duhana, tjelesnu neaktivnost, nezdrave prehrambene navike i zlouporabu alkohola[3].

Koronarna bolest srca (KBS) odgovorna je za većinu smrti od KVB-a. Godine 2008. od 17,3 milijuna smrti uzrokovanih KVB-om na svjetskoj razini (a očekuje se da će broj porasti do 23,6 milijuna u 2030. godini), čak 7,3 milijuna bilo je posljedica KBS-a[4]. Prema podatcima Hrvatskog zavoda za javno zdravstvo, KVB u Hrvatskoj kao vodeći uzrok smrti 2012. godine imale su 48,3 % udjela u ukupnoj smrtnosti, od čega se nešto manje od polovice odnosilo na KBS. U epidemiološkom smislu, Republika Hrvatska pokazuje kontinuiran pozitivan trend smanjenja smrtnosti od KVB-a, no sa standardiziranom sto-

## EPIDEMIOLOGY

Cardiovascular diseases (CVD) are the leading global cause of mortality and morbidity. According to data from the 2013 Global Burden of Disease Study, it is estimated that approximately 30% of all deaths are caused by cardiovascular disease[1]. At the European level, CVD makes for 47% of total mortality, and 40% in the European Union alone. Although advances in the treatment of CVD over the last few years have caused a significant reduction in mortality in the most economically developed countries, inaugurating the malignant diseases as the leading cause of death, cardiovascular diseases are still a dominant public-health problem in most countries. Especially upsetting is the fact that between 4% to as much as 42% of mortality from CVD, depending on economic strength and the level of development of the healthcare system of a given country, happens in the economically most productive population under the age of 60, which sheds additional light on importance of this burning issue with clear unfavorable social and economic effects. Nor can we ignore the fact that many cardiovascular events result in disability – expressed by use of the so-called DALY (disability-adjusted life year) score that includes the lost years of life due to premature death and the years of disability due to disease, the burden of CVD is 10-18% of all diseases[2].

The healthcare systems in most countries, especially in developing countries, are overtaxed by the growing need to care for a population of patients with heart disease, stroke, malignant diseases, diabetes, chronic respiratory diseases, etc. The concept of organizing a healthcare system is based on making curative medicine the focus of the system through well-equipped and well-staffed hospital institutions that provide high-quality care for a small number of patients, with high expenses from a limited health budget, while at the same time more-or-less ignoring the fact that these are diseases that can and should be systematically prevented. As a consequence we are left with a large proportion of people with high cardiovascular risk who remain unidentified, and even individuals with diagnosed issues do not have adequate access to primary-level care. The importance of the situation and the need to resolve these issues has also been recognized, at the global level, by the World Health Organization in their Global Action Plan for the Prevention and Control of Noncommunicable Diseases for 2013-2020, as a continuation of the first version of the Plan for 2008-2013. The new Plan has stressed four key risk factors – tobacco consumption, lack of physical activity, unhealthy diet, and alcohol abuse[3].

Coronary heart disease (CHD) is responsible for the majority of deaths from CVD. In 2008, of the 17.3 million deaths cause by CVD globally (which is expected to increase to 23.6 million by 2030), as much as 7.3 million were a result of CHD[4]. According to data from the Croatian Institute of Public Health, death caused by CVD made up 48.3% of total deaths in 2012 and was the leading cause of death, of which somewhat less than half was caused by CHD. Epidemiologically speaking, there has been a continuous positive trend in the reduction of mortality rate from CVD in Croatia, but with a standardized mortality rate of 342.1/100,000, Croatia is among the European countries with moderately high mortality rates[5]. There is still a noticeable negative difference when compared with neighboring

pom smrtnosti od 342,1/100.000 na razini je europskih zemalja koje imaju srednje visoke stope smrtnosti[5]. I dalje postoji zamjetna negativna razlika u usporedbi s državama iz bližeg, mediteranskog okruženja, što jasno upućuje na nedostatnost provedbe mjera iz strateških dokumenata (Nacionalni programi prevencije KVB, Akcijski plan 2015. – 2020. za Hrvatsku).

Uzevši u obzir sve navedeno, pred Republikom Hrvatskom je razdoblje izazova i pronalaženja rješenja u prevenciji i kvalitetnijem liječenju KVB-a, uključujući KBS kao najistaknutijeg predstavnika. Ključ uspjeha leži u prepoznavanju trenutačnih manjkavosti sustava i aktivnijem pristupu rješavanju problema, od kojih se mnogi mogu razriješiti usprkos financijskim ograničenjima, pametnijom preraspodjelom novca iz zdravstvenog proračuna i uzimanjem u obzir dugoročnog omjera koristi i troška. Prevencija zauzima ključno mjesto i problem je koji sustavno treba rješavati zdravstvena politika, uz inzistiranje na jačanju osobne odgovornosti pojedinca na polju izbora životnoga stila.

U sljedećih nekoliko odjeljaka kratko ćemo izdvojiti specifične probleme s kojima se susreće tipičan bolesnik u Hrvatskoj u kojega je postavljena sumnja i/ili koji ima dokazanu KBS, u kontekstu stabilne koronarne bolesti i akutnoga koronarnog zbivanja.

## STABILNA KORONARNA BOLEST SRCA

### DIJAGNOSTIKA

#### 1. Neinvazivna dijagnostika

Osnova dijagnosticiranja stabilne KBS leži u pravilnoj interpretaciji kliničke slike – ovisno o dobi, spolu i anamnezi bola u prsištu (tipična ili atipična angina, neanginozni bol). Već se na temelju procjene tzv. predtestne vjerojatnosti može, s jedne strane, u određenom postotku postaviti dijagnoza stabilne angine pektoris (stariji muškarac s tipičnim simptomima), a, s druge, s visokom se vjerojatnošću može isključiti postojanje KBS-a (mlada žena s neanginoznim bolom), bez potrebe za dodatnom dijagnostičkom obradom[6]. Time već na prvom koraku dolazimo do uštede ljudskih, vremenskih i financijskih resursa.

Izračun predtestne vjerojatnosti, uz poznavanje specifičnosti i osjetljivosti metoda kojima se koristimo u dijagnostičke svrhe (ergometrija, stresna ehokardiografija, scintigrafija miokarda, MSCT koronarografija, magnetna rezonancija, pozitronska emisijska tomografija) te njihovih komparativnih prednosti i nedostataka, određuje nam i odabir one metode od koje ćemo imati najveću kliničku korist, tj. najmanji broj lažno pozitivnih ili negativnih nalaza. To je, osim u dijagnostičkome smislu, iznimno bitno i u smislu prognoze, jer postotak ishemičnog miokarda izračunan ili procijenjen svakom od navedenih metoda određuje i vrstu liječenja, tj. potrebu za invazivnom obradom (koronarografijom) i revaskularizacijom. Racionalna primjena dovodi do uštede na drugom koraku[7].

Nažalost, provedba ovih smjernica znatno je ograničena slabom dostupnošću ključnih dijagnostičkih metoda. Stresna ehokardiografija u opterećenju provodi se u malom broju specijaliziranih ehokardiografskih laboratorija, dominantno uz

Mediterranean countries, which clearly indicates insufficiencies in the implementation of measures based on strategic documents (National Programs for the Prevention of CVD, Action Plan 2015 – 2020 for Croatia).

Based on all of the above, the Republic of Croatia faces a period of challenges to find a solution for prevention and better-quality treatment of CVD, including CHD as the most prominent representative of CVD. The key to success lies in recognizing the current weaknesses of the system and adopting a more active approach in elucidating problems, of which many could be resolved, despite financial limitations, through smarter redistribution of funds from the health budget and by taking into account long-term costs and benefits. Prevention is a key factor and a problem that should be addressed through a systematic healthcare policy insisting on strengthening the personal responsibilities of the individual in making lifestyle choices.

In the next few sections we shall give a brief overview of a selection of specific problems faced by a typical patient in Croatia with the suspicion and/or diagnosis of CHD, in the context of stable coronary disease and acute coronary events.

## STABLE CORONARY HEART DISEASE

### DIAGNOSTICS

#### 1. Non-invasive diagnostics

The basis of diagnosing stable CHD is in the proper interpretation of the clinical picture – depending on the patient's age, sex, and history of chest pain (typical or atypical angina, non-anginal pain), it is possible to assess pre-test probabilities and, on one hand, establish the diagnosis of stable angina pectoris in a certain percentage of patients (e.g. an older man with typical symptoms), or, on the other hand, eliminate CHD as an option with a high probability of being correct (a young woman with nonanginal pain), with no further diagnostic processing being required[6]. This achieves savings in human, temporal, and financial resources at the very first step of the process.

Calculating pre-test probabilities, coupled with knowledge of the specificities and sensitivities of different diagnostic methods (exercise stress test, stress echocardiography, myocardial scintigraphy, MSCT coronary angiography, magnetic resonance imaging, positron emission tomography) and their comparative strengths and weaknesses, determines which method will provide the greatest clinical benefit, i.e. the lowest number of false positive or negative results – this, other than in the diagnostic sense, is also extremely important for prognosis, since the percentage of myocardial ischemia calculated or assessed with these methods also determines the type of treatment, i.e. the need for invasive procedures (coronary angiography) and revascularization. Such rational application of diagnostic tools creates savings at the second step as well[7].

Unfortunately, the application of these guidelines is significantly limited by the poor availability of key diagnostic methods. Stress echocardiography is only performed in a small number of specialized echocardiographic laboratories, predominantly using dobutamine to create drug-based exer-

primjenu farmakološkog opterećenja dobutaminom, relativnim brojem daleko ispod razine standarda razvijenih zemalja, uz ograničenja zbog osnovne tehničke neopremljenosti (npr. nedostupnost „ležećeg" bicikl-ergometra za provođenje opterećenja tjelovježbom) i uskoga kruga educiranog kadra. SPECT perfuzijska scintigrafija miokarda također se primjenjuje rjeđe od očekivanog – dostupnosti i kvaliteti izvođenja metode pridonijeli bi intenzivnija suradnja kardiologa i specijalista nuklearne medicine (ili razvijanje uže specijalizacije iz kardiovaskularnog oslikavanja) te obnavljanje zastarjele opreme. Prenaglašena je (i često nekritična) uporaba ergometrije kao najučestalije metode. MSCT koronarografija zbog visoke negativne prediktivne vrijednosti ima svoje mjesto u isključivanju opstruktivne KBS u bolesnika s umjereno povišenom predtestnom vjerojatnošću[8], prikazu anomalija koronarnih arterija i aortokoronarnih premosnica, i također je ograničena nedostupnošću za većinu populacije, osobito u javnome zdravstvenom sustavu. PET i MR kao metode trenutačno nemaju mjesta u rutinskoj kliničkoj primjeni u Hrvatskoj.

## 2. Invazivna dijagnostika

### KORONAROGRAFIJA

Nije potrebno posebno isticati da je koronarografija „zlatni standard" u dijagnosticiranju KBS-a, bilo da je riječ o klasičnoj aterosklerotskoj, opstruktivnoj KBS, funkcionalnom poremećaju u obliku vazospastične angine ili drugim, rjeđim uzrocima (anomalije, upalna zbivanja i sl.). Invazivna priroda metode nosi sa sobom rizik od ozbiljnih komplikacija, čija je relativna učestalost niska (< 1 %)[9,10], no visok apsolutan broj provedenih postupaka upućuje na iznimnu važnost pridržavanja kliničkih indikacija. Kritičkim pristupom mogu se prevenirati događaji koji uključuju smrtne ishode, infarkte miokarda, zloćudne ventrikulske aritmije ili veće vaskularne komplikacije.

Nakon ispravnog postavljanja indikacije, pravilan odabir vaskularnog pristupa sljedeći je korak kojim možemo smanjiti postotak komplikacija. Transradijalni pristup metoda je izbora – u rukama iskusnog operatera u centru s velikim brojem („volumenom") transradijalnih procedura ovim se pristupom poboljšava komfor bolesnika, smanjuju lokalne komplikacije i pobol te troškovi koji iz njih proizlaze[11]. S obzirom na to da je riječ o manjoj i površinski smještenoj arteriji koja se dâ lako komprimirati, ozbiljna su krvarenja iznimno rijetka. Dodatni zaštitni mehanizam jest anatomija arterijske cirkulacije ruku, pri čemu normalno prohodna ulnarna arterija preko anastomoza palmarnog luka onemogućuje ishemiju šake (Allenov test!). Krivulja učenja transradijalnog pristupa relativno je strma[12], no treba naglasiti da je manipulacija kateterima zbog relativno čestih varijacija tijeka arterija (npr. tortuoziteti potključnih arterija, visoko polazište radijalne arterije) ipak nešto složenija u usporedbi s transfemoralnim pristupom. Intervencijski bi kardiolozi trebali biti vični obama pristupima.

Na izvedbenoj razini postoji nekoliko ograničavajućih čimbenika. Zastarjelost opreme u pojedinim centrima uz sve učestalije kvarove upućuje na nužnost zamjene novijim, tehnološki naprednijim uređajima. Jasno je da su financijske restrikcije i u ovom pogledu ključna prepreka, no dugoročna

tion, in far smaller relative numbers than the standards of developed countries and with further limitations due to basic technical inadequacies (e.g. the unavailability of the supine bicycle ergometer to perform exertion through physical activity) and a small circle of educated staff. SPECT myocardial perfusion scintigraphy is also used less than expected – the availability and performance of this method would be improved by more intensive cooperation between cardiologists and nuclear medicine specialists (or introducing subspecialty in cardiovascular imaging) and by replacement of outdated equipment. The use of exercise stress test is overemphasized (and often uncritically applied) and is the most common method employed. MSCT coronary angiography, due to its high negative predictive value, has its place in eliminating obstructive CHD in patients with moderately increased pre-test probabilities[8], as well as in imaging of coronary artery anomalies and aortocoronary bypass grafts, but is also limited by lack of availability to most of the population, particularly in the public health system. PET and MR currently have no place in routine clinical practice in Croatia.

## 2. Invasive diagnostics

### CORONARY ANGIOGRAPHY

It is well known that coronary angiography is the gold standard in diagnosing CHD, whether for classical atherosclerotic, obstructive CHD, functional disorders in the form of vasospastic angina, or other, less common causes (anomalies, inflammatory events, etc.). The invasive nature of the method carries a risk of serious complications with a low incidence (<1%)[9,10], but the high absolute number of procedures being performed indicates the exceptional importance of adhering to clinical indications. A critical approach can prevent events that include fatal outcomes, myocardial infarction, malignant ventricular arrhythmia, or major vascular complications.

After correct establishment of the indications, appropriate choice of the vascular approach is the next step towards reducing the incidence of complications. The transradial approach is the method of choice – in the hands of an experienced operator in a high-volume center; this approach improves the comfort of the patient and reduces local complications and morbidity along with consequent expenses[11]. Since the artery in question is smaller and closer to the surface and thus easily compressed, serious bleeding is extremely rare. An additional safety mechanism is provided by the anatomy of arterial circulation in the hands, where normally the patent ulnar artery prevents the ischemia of the hand via the palmar arches anastomoses (Allen's test!). The learning curve for the transradial approach is relatively steep[12], but it should be emphasized that catheter manipulation is, due to relatively common variations in artery course (e.g. tortuous subclavian arteries, high-origin radial artery), still somewhat more complex in comparison with the transfemoral approach. Interventional cardiologists should be skilled in both procedures.

There are several limiting factors at the level of performance. The presence of outdated equipment at particular centers with increasingly common malfunctions indicates the need to replace these devices with newer, more technologically advanced ones. It is clear that financial restrictions are the main obstacle in this as well, but long-term benefits are

je korist mjerljiva – bolji uvjeti rada uz manju izloženost zračenju jamče bolje ishode za zdravlje bolesnika i intervencijskog tima. U tome smislu postoje određeni napori nositelja zdravstvene politike u Hrvatskoj u smislu aktivnog provođenja postupaka nabave, no potrebe populacije nadmašuju dosadašnju dinamiku obnavljanja opreme. Racionalan pristup rješavanju problema trebao bi uključivati i regionalne epidemiološke pokazatelje. Nažalost, u Hrvatskoj još uvijek nisu dostupni čvrsti numerički argumenti (registar!), no na temelju redovite razmjene iskustava između intervencijskih kardiologa i drugih zdravstvenih djelatnika dâ se zaključiti da je u pojedinim dijelovima zemlje nužno proširenje kapaciteta u tehničkom i kadrovskom smislu. Kao surogatni pokazatelj trenutačnih potreba mogu poslužiti produljene liste čekanja na dijagnostičku koronarografiju u svakom od intervencijskih centara u zemlji.

### NEANGIOGRAFSKE METODE PROCJENE KORONARNE PERFUZIJE I INTRAKORONARNE METODE OSLIKAVANJA

Koronarografija ima znatna ograničenja u procjeni težine stenoza koronarnih arterija, uz značajnu interopservatorsku varijabilnost[13-15]. To se osobito odnosi na tzv. intermedijarne stenoze (50 – 70 %), bez obzira na iskustvo operatera i bez znatnog poboljšanja procjene putem računalne kvantifikacije[16]. Zbog toga su u primjenu ušle neangiografske metode procjene koronarne perfuzije (FFR, iFR) i intrakoronarne metode oslikavanja (IVUS, OCT). Sve je više znanstvenih dokaza koji govore u prilog važnosti analize koronarne fiziologije i anatomije. Ove, dodatne dijagnostičke metode imaju utjecaja na odluku o izvođenju postupka revaskularizacije, na tehničku izvedbu perkutane koronarne intervencije (PCI) i na optimiziranje ishoda zahvata. Međutim, usprkos preporukama i dokazima korisnosti, ne primjenjuju se rutinski u svakodnevnoj praksi i dostupne su u malom broju centara. Razloge tomu treba tražiti u cijeni opreme (uređaja i potrošnog materijala), no ne može se zanemariti ni sustavan problem nedovoljne edukacije na tom polju.

FFR (eng. *fractional flow reserve*) i iFR (eng. *instantaneous wave-free ratio*), kao modernija inačica koja ne zahtijeva primjenu adenozina ili drugih vazodilatatora, primjenjuju se kao metode procjene funkcionalnog značenja stenoza intermedijarnog tipa (50 – 70 %) ili znatnijih suženja (< 90 %), i to u slučaju kontraindikacije ili nedostupnosti neinvazivnog testa procjene ishemije, ili nemogućnosti jasne interpretacije neinvazivnog testa. U bolesnika s višežilnim KBS-om, FFR-om ili iFR-om vođena PCI u usporedbi s klasičnom angiografijom poboljšava ishode i smanjuje troškove liječenja. Isto tako, u bolesnika s trožilnom bolešću mjerenje funkcionalnosti stenoze omogućuje reklasifikaciju ozbiljnosti bolesti i bodovanja prema SYNTAX bodovnoj ljestvici te ima izravan utjecaj na odabir metode revaskularizacije (PCI vs. aortokoronarno premoštenje). U stabilnoj KBS, PCI stenoze s izmjerenom vrijednošću FFR-a < 0,80 poboljšava simptome i smanjuje broj hospitalizacija radi hitnih revaskularizacijskih postupaka[17]. FFR i iFR koriste se istom konzolom i žicom za mjerenje tlaka pa se u zadnje vrijeme sve češće primjenjuje hibridan pristup – kreće se s iFR-om te se stenoze s vrijednošću > 0,93 odbacuju kao neznačajne, a ako se izmjeri < 0,86, postavlja se indikacija za revaskularizaciju. Vrijednosti unutar „sive zone" mjerenja od 0,86 do 0,93 podvrgavaju se provjeri FFR-om. Na taj se na-

measurable – better working conditions with less exposure to radiation guarantee better outcomes for the health of both the patients and the interventional team. There have been certain efforts by the healthcare policy-makers in Croatia in view of active equipment procurement procedures, but the population needs exceed the current dynamic of equipment acquisition. A rational approach to resolve these issues should also include regional epidemiologic indicators. Unfortunately, there are still no solid numerical arguments available in Croatia (registries!), but based on regular exchanges of experiences between interventional cardiologists and other healthcare workers, it could be concluded that it is necessary to expand the capacities in certain parts of the country, both technically and with regard to personnel. Extended waiting lists for diagnostic coronary angiography in every interventional center in the country can be taken as a surrogate indicator of current needs.

### NON-ANGIOGRAPHIC METHODS OF ASSESSING CORONARY PERFUSION AND INTRACORONARY IMAGING METHODS

Coronary angiography has significant limitations in assessing the severity of coronary artery stenosis, coupled with significant inter-observer variation[13-15]. This is especially relevant to so-called intermediate stenosis (50-70%), regardless of operator experience and with no significant improvement after computerized quantification[16]. This was the reason for the introduction of non-angiographic methods of assessing coronary perfusion (FFR, iFR) and intracoronary imaging methods (IVUS, OCT). There is mounting scientific evidence supporting the importance of physiological and anatomical analysis. These additional diagnostic methods influence the decisions on the performance of revascularization procedures, technical performance of percutaneous coronary intervention (PCI), and procedure outcome optimization. However, despite recommendations and proof of benefit, they are not routinely used in everyday practice and are available only in a small number of centers. The reason for this is to be found in equipment prices (devices and materials), but the systemic issue of insufficient education in this area cannot be ignored either.

FFR (fractional flow reserve), and iFR (instantaneous wave-free ratio) as a more modern variant that does not require the use of adenosine or other vasodilators, are used as methods for assessing the functional significance of intermediate stenosis (50-70%) or angiographically even more significant narrowings (<90%) in case of contraindications, or the unavailability of a non-invasive ischemic assessment test, or when clear interpretation of the non-invasive test is not possible. In patients with multivessel CHD, FFR- or iFR-led PCI improves outcomes and reduces treatment costs in comparison with classical angiography. Additionally, in patients with triple-vessel disease, measuring the functional significance of the stenosis allows for the reclassification of the severity of the disease and scoring according to the SYNTAX scale, directly influencing the choice of revascularization method (PCI vs aortocoronary bypass). In stable CHD, PCI of the stenosis with measured FFR values <0.80 improves the symptoms and reduces the number of hospitalizations for emergency revascularization procedures[17]. FFR and iFR use the same console and wire for measuring pressure, so a hybrid approach has lately become increasingly common – starting with iFR, stenoses with values >0.93 are discarded as insignificant, and measurements

čin može i u do 60 % slučajeva eliminirati potreba za primjenom vazodilatatora.

IVUS (eng. *intravascular ultrasound*) nudi izvrsnu vizualizaciju intraluminalne i transmuralne anatomije koronarne arterije, a OCT (eng. *optical coherence tomography*) dodatno poboljšava vizualizaciju arterije zahvaljujući boljoj rezoluciji (no na račun lošije penetracije i dodatne primjene kontrasta). IVUS je metoda kojom se može precizno odrediti optimalna ugradnja stenta na račun vizualizacije dobre ekspanzije i apozicije stenta, uz izostanak rubne disekcije i drugih mogućih komplikacija, a iznimno je korisna i u mjerenju dimenzija koronarne arterije. U praktičnome smislu, IVUS je koristan u procjeni težine stenoze debla lijeve koronarne arterije, s vrijednošću minimalne površine lumena (eng. MLA) od 6 $mm^2$ kao indikacije za revaskularizaciju, a potencijalno može biti koristan za analizu morfologije aterosklerotskog plaka. OCT ima slične indikacije – u pripremi i vođenju PCI-ja i analizi plaka. Osobito važno mjesto može imati pri uporabi bioapsorbirajućih stentova i u procjeni težine vaskulopatije transplantata[17].

## LIJEČENJE

### 1. Lijekovi

Medikamentna terapija KBS-a dobrim je dijelom farmakološka terapija čimbenika rizika. Značajan se dio problema odnosi na nedovoljno dobro liječenje arterijske hipertenzije s učestalim prihvaćanjem suboptimalnih vrijednosti arterijskoga tlaka. Dio problema leži i u nedovoljno dobroj suradljivosti bolesnika – ovdje je neobično važna uloga liječnika u edukaciji bolesnika i pri odabiru najsvrsishodnije terapije, izbjegavajući polimedikaciju i polipragmaziju. Upitno je u kojoj se mjeri to može postići uz trenutačnu organizaciju i preopterećenost zdravstvenog sustava u kojemu se ne uspijevaju postići minimalni vremenski normativi koji bi bili dovoljni za prijenos kvalitetnih informacija na relaciji liječnik – bolesnik.

Svakodnevno iskustvo također pokazuje da je prevelik udio bolesnika s KBS-om kojima nisu propisani statini ili oni nisu primjereno dozirani kada se kao cilj terapije uzmu vrijednosti LDL kolesterola prema ESC smjernicama (LDL-C < 1,8 mmol/L ili > 50 %-tni pad vrijednosti ako se ne može postići apsolutna ciljna vrijednost)[18]. U tom svjetlu postoji mjesto i za dodatnu terapiju nestatinskim lijekovima (ezetimib), što je osobito važno u bolesnika s preboljenim akutnim koronarnim sindromom – studija IMPROVE-IT dokazala je smanjenje broja ishemijskih koronarnih i cerebrovaskularnih događaja primjenom kombinacije ezetimiba i simvastatina u usporedbi sa simvastatinom, bez veće učestalosti nuspojava[19].

Specifičan hrvatski problem jest i nedostupnost učinkovitih modernijih antianginalnih lijekova (trimetazidin, ranolazin, ivabradin) za širu populaciju bolesnika, uvjetovana potrebom za skupom doplatom.

### 2. Intervencijska revaskularizacija

Ishodi bolesnika liječenih primjenom PCI-ja ovise o tehničkoj izvedbi procedure, prevenciji ranih komplikacija, suradljivosti bolesnika u pridržavanju prijeko potrebne terapije (s naglaskom na antiagregacijsku terapiju), a u velikoj mjeri i dostupnosti i izboru materijala. Stentovi koji otpuštaju lijek

<0.86 are considered an indication for revascularization. "Grey area" measurements of 0.86-0.93 are checked with FFR. This can eliminate the need for the use of vasodilators in as much as 60% of cases.

IVUS (intravascular ultrasound) offers excellent visualization of the intraluminal and transmural anatomy of the coronary artery, and OCT (optical coherence tomography) further improves visualization of the artery thanks to better resolution (at the expense of poorer penetration and additional use of contrast agents). IVUS is a method that can precisely determine optimal stent implantation based on the visualization of adequate expansion and apposition of the stent, with the lack of edge dissection and other possible complications, and is also extremely useful in the assessment of stenosis of the left main coronary artery, with a minimal lumen area (MLA) of 6 $mm^2$ being an indication for revascularization. IVUS can also be potentially useful for morphological analysis of atherosclerotic plaque. OCT is similarly indicated in the preparation and guidance of PCI and plaque analysis. It can also have an especially important role in the use of bioabsorbable scaffolds and assessing the severity of transplant vasculopathy[17].

## TREATMENT

### 1. Medication

Medication treatment for CHD largely consists of pharmacological treatment of risk factors. A significant part of the overall problem is due to inadequate treatment of arterial hypertension with all-too-common acceptance of suboptimal arterial pressure values. Part of the problem is also in poor patient compliance – the role of the physician is extraordinarily important here in educating the patient and choosing the most appropriate treatment and in avoiding polymedication and polypragmasia. It is doubtful whether this can be fully achieved with the current organization and overburdening of the healthcare system, where not even minimal temporal norms can be achieved that would allow for good communication between the physician and patient.

Everyday experience also shows that there is an overly large portion of patients with CHD who have not been prescribed statins or with inadequate dosage in view of the treatment goal of LDL-cholesterol levels based on ESC guidelines (LDL-C <1.8 mmol/L or a >50% reduction if target levels are not achievable)[18]. In light of this, there is a place for additional treatment with non-statin drugs (ezetimibe), which is especially important in patients with previous acute coronary syndrome – the IMPROVE-IT study showed a reduction in the number of ischemic coronary and cerebrovascular events due to combination therapy with ezetimibe/simvastatin in comparison with simvastatin, with low incidence of side effects[19].

A specifically Croatian problem is also the unavailability of efficient modern antianginal drugs (trimetazidine, ranolazine, ivabradine) to the wider patient population due to expensive co-payment requirements.

### 2. Interventional revascularization

Outcomes for patients treated with PCI depend on the technical performance of the procedure, prevention of early complications, patient compliance in necessary therapy (with

(eng. drug-eluting stent, DES) čine „zlatni standard" u modernoj intervencijskoj kardiologiji, u usporedbi s običnim metalnim stentovima (eng. bare-metal stent, BMS)[20]. Mnogo manja stopa restenoza u stentu, a, kad govorimo o novijoj generaciji DES-a, i gotovo potpuno eliminirana razlika u stopi tromboze u stentu u usporedbi s BMS-om, jasna su i nedvosmislena klinička opravdanja za primjenu DES-a u većine bolesnika (iznimku mogu činiti bolesnici s povišenim rizikom od krvarenja ili drugom kontraindikacijom za dulju primjenu dvojne antiagregacijske terapije, npr. potrebom za skorim operacijskim zahvatom)[21]. Godine 2015. penetracija DES-ova u hrvatskim okvirima iznosila je ~ 40 %. Treba očekivati da bi se porastom broja ugrađenih DES-ova moglo sniziti i visoka cijena (u usporedbi s BMS-om), što je u ovome trenutku jedina prepreka njihovoj učestalijoj uporabi.

U Hrvatskoj su za posebne indikacije dostupni baloni obloženi lijekom (eng. drug coated balloon, DCB) i bioapsorbirajući stentovi (eng. bioabsorbable vascular scaffold, BVS).

### 3. Kirurška revaskularizacija

Aortokoronarno premoštenje metoda je revaskularizacije koja prema postojećim smjernicama ima prednost pred PCI-jem u određenoj populaciji bolesnika (npr. u bolesnika s trožilnim KBS-om, u slučaju zbroja na SYNTAX bodovnoj ljestvici > 22, bolesti debla lijeve koronarne arterije i dr.)[22]. Pritom se ne smije zanemariti činjenica da su istraživanja koja su postala temelj kliničke prakse i na kojima se zasnivaju smjernice donekle izgubila korak s vremenom i trenutačnom situacijom. Napredak u razvoju stentova i tehnike izvođenja PCI-ja u odnosu prema kirurškoj revaskularizaciji (koja vrlo rijetko uključuje postavljanje više od jedne arterijske premosnice) baca drukčije svjetlo na problem. Osobit nedostatak kardiokirurške revaskularizacije u hrvatskim okvirima jest duga lista čekanja na zahvat. Izlazak iz situacije nudi kvalitetna suradnja kardiologa i kardijalnih kirurga kao liječničkog tima na planu donošenja odluke o najboljoj opciji za konkretnog bolesnika, uzimajući u obzir lokalne okolnosti.

## AKUTNI KORONARNI SINDROM

### 1. Akutni infarkt miokarda s elevacijom ST segmenta

Primarna perkutana koronarna intervencija superioran je oblik postizanja reperfuzije u odnosu prema fibrinolitičkoj terapiji ako se može učiniti unutar 120 minuta od prvoga medicinskog kontakta (PMK). Odgađanje je reperfuzijske terapije pogubno jer se protokom vremena smanjuje njezina potencijalna korist („vrijeme je mišić"), a povećava mogućnost nastanka komplikacija. Kašnjenje u primjeni reperfuzijske terapije najbolji je pokazatelj (ne)kvalitete ovoga vitalnog dijela skrbi za bolesnike s akutnim infarktom miokarda i treba ga trajno nadzirati radi optimizacije funkcioniranja sustava[23].

Mogući uzroci odgađanja primjene reperfuzijske terapije uključuju sljedeće.

- Kašnjenje bolesnika – gubitak vremena između nastupa simptoma i PMK-a. Da bi se unaprijedila situacija na ovom polju, nužno je kontinuirano provoditi edukaciju stanovniš-

emphasis on antiaggregation therapy), and largely also on the availability and choice of material. Drug-eluting stents (DES) are the gold standard in modern interventional cardiology, as opposed to bare-metal stents (BMS)[20]. In comparison with BMS, DES have significantly lower stent restenosis rates, with the newer DES generation almost completely eliminating differences in stent thrombosis rates in comparison with BMS, which clearly and unambiguously provides clinical justification for the use of DES in most patients (an exception may be patients with increased risk of bleeding or other contraindications for long-term application of dual antiaggregation therapy, e.g. an impending surgical procedure)[21]. In 2015, penetration of DES in Croatia was approximately 40%. It is to be expected that there could be a drop in price consequent to the increase in the number of implanted DES (in comparison with BMS), which is currently the only barrier to their more widespread usage.

Drug coated balloons (DCB) are available in Croatia if specially indicated, as are bioabsorbable vascular scaffolds (BVS).

### 3. Surgical revascularization

Aortocoronary bypass surgery is a revascularization method that, according to current guidelines, has an advantage over PCI in a certain patient population (e.g. patients with triple-vessel CHD, for SYNTAX scores >22, diseases of left main coronary artery, etc.)[22]. It should however be noted that the research that became the basis of clinical practice and which the guidelines refer to has to some extent fallen behind the times and the current situation. Advances in the development of stents and PCI techniques with regard to surgical revascularization (which very rarely involves more than one arterial bypass graft) shed a different light on the issue. The glaring weakness of cardiac surgery revascularization in Croatia is the long waiting list for the procedure. A way out of this situation is good cooperation between cardiologists and cardiac surgeons as a team of physicians forming decisions on the best options for a particular patient, taking into account the local circumstances.

## ACUTE CORONARY SYNDROME

### 1. ST elevation acute myocardial infarction

Primary percutaneous coronary intervention is a superior way of achieving reperfusion in comparison with fibrinolytic therapy if it can be performed within 120 minutes from the first medical contact (FMC). Delaying reperfusion therapy is deleterious since its potential benefit drops with time ("time is muscle") and the chance of complications increases. Delays in the application of reperfusion therapy is the best indicator of the (lack of) quality of this vital part of care for patients with acute myocardial infarction and should be permanently monitored with the goal of optimizing the system[23].

Possible causes for delays in application of reperfusion therapy include:

- Patient delay– the loss of time between symptom onset and FMC. To improve the situation in this area it is necessary to continuously educate the population on the symptoms of acute myocardial infarction, which is still not being done in

tva o simptomima akutnog infarkta, što se u Hrvatskoj još uvijek ne provodi na sustavnoj i intenzivnoj razini, premda su vidljivi napori stručnih društava vezanih za ovu problematiku. Posebnu pozornost treba posvetiti edukaciji bolesnika s već potvrđenim KBS-om i članova njihovih obitelji.

- Zastoj između PMK-a i postavljanja dijagnoze – U zdravstvenim ustanovama koje sudjeluju u zbrinjavanju bolesnika s akutnim infarktom miokarda s elevacijom ST segmenta (STEMI) vrijeme proteklo od PMK-a do snimanja EKG-a trebalo bi biti < 10 minuta. Hrvatska nam iskustva pokazuju da se i na ovom, bazičnom polju može postići određeni napredak – naglasak treba staviti na slučajeve izostanka postavljanja dijagnoze zbog atipičnih simptoma (kakvi se mogu pojavljivati čak u 30 % slučajeva) i propuste u snimanju EKG zapisa stražnjih i desnih odvoda (npr. okluzija cirkumfleksne arterije može rezultirati „nijemim" standardnim 12-kanalnim elektrokardiografskim zapisom). U slučaju jasne kliničke sumnje treba inzistirati na opetovanom snimanju EKG-a i hitnom ehokardiografskom pregledu – nema opravdanja za zaobilaženje ovih koraka u iščekivanju nalaza povišenja biljega nekroze miokarda.
- Zastoj između PMK-a i početka reperfuzije – Riječ je kašnjenju cijelog sustava zbrinjavanja bolesnika sa STEMI-jem. Preporuke su jasne. U slučaju primarne PCI, vremenski interval od PMK-a do prolaska žicom kroz okludiranu koronarnu arteriju trebao bi biti ≤ 90 minuta, odnosno ≤ 60 minuta ako se bolesnik nalazi u centru koji ima mogućnosti liječenja primjenom PCI-ja. Ako se radi reperfuzije primijeni fibrinolitička terapija, vremenski interval od PMK-a do početka infuzije treba iznositi ≤ 30 minuta.

Hrvatska mreža primarne PCI koja je organizirana kao sustav 11 centara za primarnu PCI s pripadajućim „prstenom", tj. područjem suradnje s regionalnim zdravstvenim ustanovama koje nemaju mogućnost hitne reperfuzije primjenom PCI-ja, donijela je preporod u zbrinjavanju bolesnika sa STEMI-jem te iz godine u godinu postiže sve bolje rezultate, usporedive s mnogo bogatijim europskim zemljama. Kada se PMK dogodi u ustanovi bez mogućnosti primarne PCI, aktivira se postupak što hitnijeg prijevoza bolesnika do centra s mogućnošću PCI-ja koji ima iskusan i uvježban tim u 24-satnoj pripravnosti, 7 dana u tjednu (u Hrvatskoj se to odnosi na 10/11 centara koji rade primarnu PCI). Time se postiže maksimalno djelotvorno akutno zbrinjavanje bolesnika sa STEMI-jem uz minimum komplikacija, i to osobito u centrima s visokim volumenom intervencija, na što nedvosmisleno upućuju podatci iz znanstvenih publikacija. Dodatnu korist za bolesnika donosi transradijalni vaskularni pristup – jedan od ciljeva jest postići njegovu što veću primjenu u svim centrima u Hrvatskoj.

Prema informacijama prikupljenima iz baza podataka centara iz Mreže, u razdoblju 2014. – 2015. godine u Hrvatskoj je primarnom PCI-ja liječen 2271 bolesnik sa STEMI-jem. Brojem od 539 intervencija na milijun stanovnika Hrvatska se svrstava u drugu europsku „jakosnu" skupinu, što je hvalevrijedan rezultat. Unutarbolnička smrtnost bolesnika liječenih primarnom PCI u posljednjih 10 godina održava se u rasponu 4,4 – 6,8 %. Navedene rezultate treba uzeti s određenom dozom opreza jer je riječ o retrospektivnim i donekle nepreciznim podatcima, no pozitivna kretanja popraćena kontinuiranim

Croatia at a systemic and intensive level, although there has been visible effort from expert societies associated with this issue. Special care should be given to the education of patients with already established CHD and their families.

- Delay between FMC and establishing the diagnosis – in health institutions that take part in the care of patients with ST elevation myocardial infarction (STEMI), the time between FMC to an ECG should be <10 minutes. Croatian experience shows that excellent progress can be achieved in this basic area – the emphasis should be on cases where the diagnosis was delayed due to atypical symptoms (in as many as 30% of cases) and omissions in recording of the ECG of the posterior and right precordial leads (e.g. occlusion of LCx can result in "silent" standard 12-channel ECG recording). In cases of clear clinical suspicion, one should insist on repeated ECG and urgent echocardiographic examination – there is no excuse for skipping these steps while waiting for the findings of elevated markers of myocardial necrosis.
- Delay between FMC and reperfusion – this is a delay in the whole care system for patients with STEMI. The guidelines are clear. In case of primary PCI, the interval between FMC to passing a wire through the occluded coronary artery should be ≤90 minutes, or ≤60 minutes if the patient is in a center capable of administering PCI treatment. If fibrinolytic therapy is applied with the goal of reperfusion, the interval from FMC to infusion start should be ≤30 minutes.

The Croatian primary PCI network, which is organized as a system of 12 centers for primary PCI with an accompanying "ring", i.e. an area of cooperation with regional healthcare institutions that have no capabilities of emergency PCI reperfusion, has brought about a renaissance in the care for patients with STEMI and provides ever better results every year, comparable with much wealthier European countries. When FMC takes place in an institution with no primary PCI capabilities, the emergency transportation procedure is activated to transport the patient to a PCI-capable center that has an experienced and trained team on 24-hour standby, 7 days a week (in Croatia this is the case in 11/12 centers performing primary PCI). This leads to maximally effective acute care for patients with STEMI with a minimum of complications, especially in high-volume centers, which is clearly shown by data from scientific publications. Additional benefits to the patient are provided by the transradial vascular approach – one of the goals is to achieve its widespread application in all Croatian PCI centers.

Based on information collected from databases from the Network centers, 2271 patients with STEMI were treated with primary PCI in Croatia in 2014 and 2015. With 539 interventions per million inhabitants, Croatia is in the second "strength" category in Europe, which is a laudable result. Intrahospital mortality for patients treated with primary PCI over the last 10 years has been holding in the range between 4.4 and 6.8%. The above results must be considered with caution, however, since the data in question are retrospective and thus somewhat imprecise, but positive trends coupled with a continuous drop in cardiovascular mortality indicate the favorable direction Croatia is heading in.

padom kardiovaskularne smrtnosti upućuju na povoljan smjer kojim ide Hrvatska.

S druge strane, mjesta za napredak ima pa se pomaci mogu postići bez velikih dodatnih troškova za zdravstveni sustav. Jedan od bitnih problema odnosi se na neodgovarajuće dug prijevoz bolesnika u centre za PCI – moguće rješenje moglo bi uključivati reorganizaciju hitne medicinske pomoći (HMP) tako da se bolesnik sa STEMI-jem uputi izravno u centar s mogućnošću PCI-ja, zaobilazeći regionalnu bolnicu. Ako se takav bolesnik ipak dovede u regionalnu ustanovu, valjalo bi osigurati da se prijevoz u PCI centar organizira istim kolima HMP-a radi uštede na vremenu. Nadalje, ako prijevoz u PCI centar nije moguće organizirati u predviđenom roku, a bolesnik se prezentira rano nakon početka infarkta miokarda, ne bi se smjelo zaboraviti na opciju primjene fibrinolitičke terapije. Za bolesnika koji izvan redovitoga radnog vremena stigne izravno u PCI centar kao PMK, vrijeme revaskularizacije ovisi o vremenu koje je potrebno da pripravni intervencijski tim stigne u bolnicu – određena ušteda na vremenu mogla bi se postići organizacijom dežurstava, tj. kontinuirane dostupnosti intervencijskog tima na licu mjesta. Načelno je riječ o racionalnom pristupu za dobrobit bolesnika, no broj intervencijskih kardiologa i drugoga zdravstvenog osoblja nije dostatan za takvu organizaciju posla. Valja napomenuti da i koncept pripravnosti podrazumijeva visoku razinu entuzijazma zdravstvenog osoblja, s nezadovoljavajućom financijskom kompenzacijom i s obvezom rada u redovitom radnom vremenu idućeg dana, bez obzira na trajanje i broj intervencija u prethodna 24 sata.

Da bi se na primjeren način ustanovile ključne problematične točke, iznimno je važno imati uvid u temeljne i pouzdane podatke bitne za vrednovanje sustava. S tom su svrhom Radna skupina za invazivnu i intervencijsku kardiologiju Hrvatskoga kardiološkog društva i Radna skupine za akutni koronarni sindrom, u suradnji s Agencijom za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi, pokrenule inicijativu za stvaranje Registra invazivne i intervencijske kardiologije unutar kojeg će biti prospektivni registar za infarkt miokarda na državnoj razini.

Na polju medikamentne terapije nužna je što ranija primjena dvojne antiagregacijske terapije (DAPT), tj. kombinacije acetilsalicilatne kiseline i blokatora trombocitnih ADP receptora. Prema postojećim smjernicama Europskoga kardiološkog društva[23], koje su ujedno i smjernice Hrvatskoga kardiološkog društva, od blokatora trombocitnih ADP receptora prvu terapijsku liniju čine tikagrelor (180 mg per os jednokratno, doza održavanja 2 x 90 mg na dan) i prasugrel (koji nije registriran u Hrvatskoj). Drugu terapijsku liniju čini još uvijek najviše upotrebljavan lijek, klopidogrel (600 mg jednokratno, doza održavanja 75 mg na dan), koji u usporedbi s tikagrelorom i prasugrelom ima sporiji početak djelovanja te slabiji učinak na inhibiciju agregacije trombocita. Klopidogrel bi u intervencijskom liječenju STEMI-ja trebalo primjenjivati samo kada tikagrelor i prasugrel nisu dostupni ili postoje kontraindikacije za njihovu uporabu. Uzevši u obzir navedeno, izbor optimalnog lijeka trebala bi olakšati činjenica da se na listi Hrvatskog zavoda za zdravstveno osiguranje (HZZO) nalazi tikagrelor čija je primjena indicirana istodobno s acetilsalicilatnom kiselinom za prevenciju aterotrombotskih događaja u

On the other hand, there is certainly room to improve, and improvements can be achieved without major additional costs to the healthcare system. One of the more significant problems is connected with the inadequately long transportation of patients to PCI centers – a possible solution might include the reorganization of emergency medical services (EMS) in such a way that a patient with STEMI is immediately directed to a center with PCI capabilities, bypassing the regional hospital. If such a patient is still brought to a regional hospital, transport to a PCI center should be secured in the same EMS vehicle so as to save on time. Furthermore, if transport to a PCI center is not possible in the appropriate time frame and the patient presented shortly after myocardial infarction onset, the option of using fibrinolytic therapy should not be ignored. For patients who arrive directly to a PCI center as FMC outside regular working hours, the time to revascularization depends on the time for the interventional team to arrive to the hospital – a certain amount of time could be saved by adequate on-site organization, i.e. the continuous availability of the interventional team on location. This is a rational approach to the benefit of the patient, but the number of interventional cardiologists and other medical personnel is insufficient for such a system to be sustainable. It is worth noting that the concept of on-call assumes a high level of enthusiasm from staff with unsatisfactory financial compensation and an obligation to work regular hours the next day, regardless of the duration and number of interventions over the last 24 hours.

To appropriately determine key points where the issues arise, it is very important to have insight into basic and reliable data needed to evaluate the system. With that goal in mind, the Working Group on Invasive and Interventional Cardiology of the Croatian Cardiac Society and the Working Group on Acute Coronary Syndrome, in cooperation with the Agency for the Quality and Accreditation in Health and Social Care, started an initiative to create the Registry of Invasive and Interventional Cardiology that will include a prospective registry for myocardial infarction at the national level.

Regarding medical therapy, it is crucial to apply dual antiplatelet therapy (DAPT), i.e. a combination of aspirin and thrombocytic ADP-receptor blockers. According to current guidelines of the European Society of Cardiology[23], which are also the guidelines of the Croatian Cardiac Society, the first-line treatment among platelet ADP-receptor blockers are ticagrelor (180 mg per os once daily, maintenance dose 2×90 mg daily) and prasugrel (not registered in Croatia). The second line of treatment is the still most widespread drug clopidogrel (600 mg once daily, maintenance dose 75 mg daily), which has a weaker and slower starting effect on platelet aggregation in comparison with ticagrelor and prasugrel. Clopidogrel should be used in interventional STEMI treatment only when ticagrelor and prasugrel are not available or if there are contraindications for their use. Based on the above, the optimal drug choice should be facilitated by the fact that ticagrelor is on the list of the Croatian Health Insurance Fund, and is indicated in combination with aspirin for the prevention of atherothrombotic events in adult patients with acute coronary syndromes, including patients that have recently been conservatively treated and those that were treated with PCI or aortocoronary bypass.

odraslih bolesnika s akutnim koronarnim sindromima, uključujući bolesnike koji su konzervativno liječeni te one koji su liječeni primjenom PCI-ja ili aortokoronarnim premoštenjem. Za intervencijske timove u 24/7 pripravnosti još je važnije što je tikagrelor uvršten na Osnovnu listu (bez doplate) lijekova HZZO-a za liječenje bolesnika sa STEMI-jem u kojih je učinjena primarna PCI s implantacijom stenta, prema preporuci nadležnoga intervencijskog kardiologa, u trajanju do 6 mjeseci. Ovo treba shvatiti kao motivaciju i prvi korak prema cilju dostupnosti optimalne antitrombocitne terapije na Osnovnoj listi lijekova za sve bolesnike s akutnim koronarnim sindromom za čitavo predviđeno vrijeme trajanja DAPT-a.

### 2. Akutni infarkt miokarda bez elevacije ST segmenta

Akutni infarkt miokarda bez elevacije ST segmenta (NSTEMI) nosi lošu dugoročnu prognozu (dijelom i zbog osobina populacije koja uključuje starije osobe s nizom komorbiditeta) i upravo je na ovom području moguće znatno poboljšati ishode bolesnika. Podatci iz intervencijskih centara umnogome se razlikuju i zamjetno je nedopustivo ograničenje dostupnosti koronarografije (i revaskularizacije) u mnogim regijama u Hrvatskoj. Prvi se problem može uvidjeti već pri stratifikaciji rizika pojedinog bolesnika (u praksi se rijetko rabe preporučeni modeli izračuna bodovnim ljestvicama, npr. GRACE) koja definira i odabir vremena za invazivnu obradu (unutar 2, 24 ili 72 sata)[24]. Rješenje problema moglo bi biti organiziranje „Mreže za NSTEMI" – u ovom trenutku za to ne postoje ni kadrovski ni tehničko-financijski preduvjeti, premda se suradnja između regionalnih bolnica i PCI centara svakodnevno provodi i na tom planu, s vremenskim odmakom ovisnim o dostupnosti bolničkog kreveta i kapacitetima intervencijskih timova.

### 3. Sekundarna prevencija i rehabilitacija

Skrb za bolesnike s akutnim koronarnim sindromom ne prestaje revaskularizacijom. Riječ je o visokorizičnoj populaciji kod koje je nužna striktna korekcija čimbenika rizika, sukladno smjernicama[25]. Osobito se to odnosi na pridržavanje ciljnih vrijednosti arterijskoga tlaka i LDL kolesterola (visoke doze statina ± ezetimib). Iznimno važno mjesto zauzima rehabilitacija ovakvih bolesnika koja u svom stacionarnom ili ambulantnom obliku omogućuje promjenu životnoga stila i smanjenje rizika za buduće neželjeno KV zbivanje.

## ZAKLJUČAK

Trenutačna situacija na polju zbrinjavanje KBS-a u Republici Hrvatskoj daleko je od idealne, uz brojna ograničenja, te pred nama stoje izazovi za bližu i dalju budućnost. Širina problema zahtijeva da svaka komponenta sustava odradi svoj posao – pojedinac-bolesnik pridržavanjem zdravoga životnog stila, država kao nositelj zdravstvene politike, blagajnik i promicatelj zdravlja, liječnik u primarnoj zdravstvenoj zaštiti i kardiolog. Jedno od središnjih mjesta u liječenju KBS-a zauzima intervencijski kardiolog – nažalost, u Republici Hrvatskoj formalno obrazovanje iz intervencijske kardiologije još uvijek ne postoji. Također nema ni sustava praćenja i vrednovanja rada te licenciranja intervencijskih kardiologa, što je jedna od glavnih zadaća Registra invazivne i intervencijske kardiolo-

For interventional teams on 24/7 standby, it is even more important that ticagrelor has been included to the Basic Medication List (with no co-payment) of the Croatian Health Insurance Fund for the treatment of patients with STEMI that have received primary PCI with stent implantation, based on the recommendation of the authorized interventional cardiologist, for a duration of up to 6 months. This should be seen as motivation and the first step towards the availability of optimal antithrombotic therapy on the Basic Medication List for all patients with acute coronary syndrome over the whole duration of DAPT.

### 2. Non-ST segment elevation acute myocardial infarction

Non-ST segment elevation myocardial infarction (NSTEMI) carries a poor long-term prognosis (partly due to population characteristics which include advanced age and multiple comorbidities), and it is this area where it is possible to significantly improve patient outcomes. Data from PCI centers differ significantly, but an unacceptably limited availability of coronary angiography (and revascularization) is noticeable in many Croatian regions. The first issue is immediately clear when looking at risk stratification of individual patients (in practice, recommended models using point scales such as GRACE are rarely applied), which defines the time frame for invasive treatment (within 2, 24, or 72 hours)[24]. The solution for this problem might be the organization of a "NSTEMI Network" – currently this is prevented by lack of personnel and technical and financial requirements; although there is daily cooperation between regional hospitals and PCI centers, the time delay depends on the availability of hospital beds and the capacities of the interventional teams.

### 3. Secondary prevention and rehabilitation

Care for patients with acute coronary syndrome does not stop at the point of revascularization. This is a population at-risk that requires strict risk factor correction, in line with current guidelines[25]. It is especially important to adhere to target arterial pressure and LDL-cholesterol values (high doses of statins ± ezetimibe). Rehabilitation is exceptionally important for these patients, whether in stationary or ambulatory form, since it allows for lifestyle changes and risk reduction for future CV events.

## CONCLUSION

The current situation regarding CHD care in the Republic of Croatia is far from ideal and fraught with numerous limitations, and we face many challenges in the near and far future. The scope of the problem requires each component of the system to do its job – the individual patient by adhering to a healthy lifestyle, the state in its role as the health policymaker, treasurer, and health advocate, the physician in primary healthcare, and the cardiologist. The interventional cardiologist holds one of the central roles in CHD treatment – unfortunately, there is still no formal education program for interventional cardiology in the Republic of Croatia. There is also no system for the follow-up and evaluation of work and licensing of interventional cardiologists, which is one of the main tasks

gije koji se već formira. On će omogućiti toliko potrebnu kontrolu kvalitete rada cijelog sustava i olakšati formiranje logističkih i kadrovskih planova za razvoj struke. S druge strane, bit će nužno uložiti dodatne napore kako bi se uz poprilično dobro definirane obveze počele bolje vrednovati posebnosti i prava proizašla iz bavljenja ovom granom kardiologije.

of the Registry of Invasive and Interventional Cardiology that is being created. It will allow much needed quality control of the whole system and facilitate the forming of logistic and personnel plans for the development of the field. On the other hand, it will be necessary to invest further efforts to, given the fairly well-defined duties, more appropriately value and appreciate the specificities and rights stemming from working in this area of cardiology.

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