Uvodnik Editorial

Intervencijsko liječenje akutnog infarkta miokarda u Hrvatskoj

Interventional treatment of acute myocardial infarction in Croatia

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Infarkt miokarda sa ST-elevacijom

Posljednjih desetak godina potpuno je jasno da je primarna perkutana koronarna intervencija (pPCI) superiorna metoda liječenja akutnog infarkta miokarda sa ST-elevacijom (STEMI) u odnosu na medikamentozno liječenje, uključujući i ono fibrinolizom, smanjujući kratkoročnu smrtnost, nefatalne reinfarkte, moždane udare, no i poboljšavajući dugoročne rezultate te snižavajući troškove liječenja.[1-7] Da bi pPCI bila superiorna u odnosu na trombolizu, potrebno je zadovoljiti dva uvjeta: iskustvo operatera i centra u kojemu se provodi intervencijsko kardiološko liječenje te zadani vremenski okvir (intervencija unutar 12 sati od početka bolova te unutar 90 minuta od prvoga javljanja u zdravstvenu ustanovu) u kojem se takvo liječenje provodi.[8,9]

Prateći znanstvena saznanja u međunarodnoj kardiološkoj javnosti i gotovo istodobno s njima hrvatski kardiolozi osnivaju prve centre intervencijskog liječenja, a 2000. godine i permanentnu službu liječenja pPCI u akutnoj fazi STEMI za bolesnike zaprimljene u hitnu službu tih bolnica. Postojeći centri 2005. započinju se postupno organizirati u Hrvatsku mrežu pPCI preuzimajući odgovornost za bolesnike transportirane iz okolnih županijskih bolnica u akutnoj fazi STEMI pokrivajući do danas gotovo sve dijelove Republike Hrvatske (**Slika 1**).

The ST-segment elevation myocardial infarction

During the last ten years it has become obvious that primary percutaneous coronary intervention (pPCI) is the superior method of treatment of acute ST-segment elevation myocardial infarction (STEMI) in comparison to the medicamentous treatment, including the one by fibrinolysis, reducing short-term mortality, nonfatal re-infarction, strokes, improving long-term results and lowering treatment costs.[1-7] In order to make pPCI superior compared to thrombolysis, it is necessary to satisfy the two conditions: operator's experience and the experience of the center performing interventional cardiac treatment and a given time schedule (intervention within 12 hours from the onset of chest pains and within 90 minutes from the first contact to the medical institution) where such treatment is carried out.[8,9]

Keeping up with the scientific knowledge in the international cardiac publicity and almost at the same time when they founded interventional treatment centers, the Croatian cardiologists founded the first interventional treatment centers and in 2000 permanent pPCI treatment service for the acute phase STEMI for the patients admitted to the emergency department of such hospitals. The existing centers in 2005 began to be gradually organized in the Croatian pPCI Network taking responsibility for patients transported from the surrounding county hospitals in the acute phase of STEMI, covering up to now almost all parts of the Republic of Croatia (**Figure 1**).

Figure 1. *Croatian Primary Percutaneous Coronary Intervention Network.*

Rezultati prve faze ove mreže (između 2005. i 2007. god.) međunarodno su prepoznati te unatoč nižem bruto nacionalnom dohotku u odnosu na zemlje s kojima se uspoređuje, sa 400-600 hitnih intervencija na milijun stanovnika i pokrivenošću 75% populacije mrežom naša zemlja se svrstava među zemlje s najbolje organiziranim liječenjem akutnog STEMI u Europi, a time i u svijetu (**Slika 2**). Dosezi Hrvatske mreže pPCI uvelike se zasnivaju na entuzijazmu svih sudionika koji su uključene u ovaj vid zbrinjavanja bolesnika te njihove trajne edukacije koju provodi Radna skupina za akutni koronarni sindrom Hrvatskog kardiološkog društva. Rezultati su evidentni i kroz statističke pokazatelje Hrvatskog zavoda za javno zdravstvo koji upućuju da je smrtnost kardiovaskularnih bolesti u Hrvatskoj u proteklih pet godina, dakle od osnivanja mreže, smanjena sa 53% na 49% , što je najvećim dijelom posljedica smanjene smrtnosti od akutnog infarkta miokarda. Rezultati Hrvatske mreže pPCI, osim što se mogu pronaći u najpoznatijim američkim i europskim kardiološkim časopisima, izrijekom su od inozemnih stručnjaka na EuroPCR kongresu 2011. god. u Parizu navedeni kao primjer dobre organizacije i raspodjele sredstava za intervencijsku kardiologiju.[10-15]

The results of the first phase of this network (between 2005 and 2007) have been internationally recognized, and despite the lower gross national income compared to the other countries, having 400-600 emergency interventions per million of the population and covering 75% of the population by the network, our country is among the countries with the best-organized treatment of acute STEMI in Europe and in the world as well (**Figure 2**). The results of the Croatian pPCI Network are largely based on the enthusiasm of all participants involved in this kind of management of patients and their continuous education conducted by the Working Group for Acute Coronary Syndrome of the Croatian Cardiac Society. The results are evident through the statistical indicators of the Croatian National Institute of Public Health indicating that the mortality of cardiovascular diseases in Croatia in the last five years, that is, since the establishment of the network, has been reduced from 53% to 49% which is mainly the consequence of reduced mortality from acute myocardial infarction. The results of the Croatian pPCI Network, apart from being published in the prestigious American and European cardiology journals, have been specifically highlighted by foreign experts at the 2011 EuroPCR Congress in Paris as an example of good organization and allocation of funds for the interventional cardiology.[10-15]

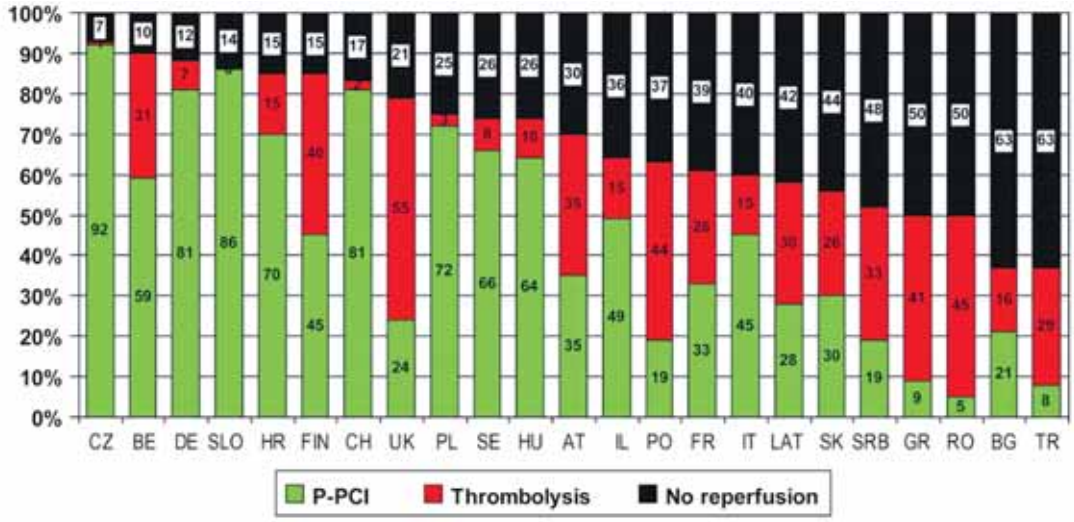

Figure 2. *Hospitalized STEMI treatment in Europe (data from national registries or surveys). 100%, all hospitalized STEMI patients in each given country; green colour, STEMI patients treated by primary PCI; red colour, STEMI patients treated by thrombolysis; black colour, STEMI patients not treated with any reperfusion.*

Countries abbreviations: CZ, Czech Republic; SLO, Slovenia; DE, Germany; CH, Switzerland; PL, Poland; HR, Croatia; SE, Sweden; HU, Hungary; BE, Belgium; IL, Israel; IT, Italy; FIN, Finland; AT, Austria; FR, France; SK, Slovakia; LAT, Latvia; UK, United Kingdom; BG, Bulgaria; PO, Portugal; SRB, Serbia; GR, Greece; TR, Turkey; RO, Romania.

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Rezultati druge faze razvoja Hrvatske mreže pPCI (2008. i 2009. godine) ukazuju da se broj centara koji redovito sudjeluju u liječenju akutnog infarkta miokarda popeo na deset (Klinički bolnički centar "Sestre milosrdnice", Klinički bolnički centar Zagreb, Klinička bolnica Dubrava, Klinički bolnički centar Rijeka, Klinički bolnički centar Split, Specijalna bolnica Magdalena, Klinička bolnica Sveti Duh, Klinički bolnički centar Osijek, Opća bolnica Zadar, Opća bolnica Slavonski Brod) te da se broj bolesnika s akutnim STEMI liječenih pPCI više nego podvostručio u odnosu na isto vremensko razdoblje prve faze. Nadalje, prati se tendencija pogoršanja rizičnog profila bolesnika liječenih u drugoj fazi koji su više dobi (60 nasuprot 61 go-

The results of the second phase of development of Croatian pPCI Network (2008 and 2009) indicate that the number of centers that regularly participate in the treatment of acute myocardial infarction has risen to ten (University Hospital Centre Sestre Milosrdnice, University Hospital Centre Zagreb, Clinical Hospital Dubrava, University Hospital Centre Rijeka, University Hospital Cente Split, Specialized Hospital Magdalena, Clinical Hospital Sveti Duh, University Hospital Centre Osijek, General Hospital Zadar, General Hospital Slavonski Brod) and that the number of patients with acute STEMI treated from pPCI has more than doubled compared to the same period of the first phase. Furthermore, we monitor the tendency of ag-

dina), češće zahvaćenog debla lijeve koronarne arterije (0,7 nasuprot 1,6%) i češće u kardiogenom šoku (6,7 nasuprot 7,9%). Organizacijskim naporima na sve tri razine zdravstvene zaštite skraćeno je vrijeme od dolaska u prvu zdravstvenu ustanovu do postizanja reperfuzije (door-to-balloon time, 109 nasuprot 91 minuta), no produljeno je vrijeme od početka simptoma do dolaska u prvu zdravstvenu ustanovu (symptom onset-to-door time, 130 nasuprot 180 minuta) i zbog toga i totalno ishemijsko vrijeme (symptom onset-to-balloon time, 265 nasuprot 285 minuta). Navedene činjenice, ali i uključivanje novih centara nižeg volumena u mrežu što je dokazala statistička subanaliza, dovelo je do toga da su rezultati liječenja u drugoj fazi jednaki ili lošiji od onih iz prve faze: postproceduralni optimalni TIMI 3 protok (87,1 nasuprot 81,8%), unutarbolnička smrtnost (4,4% u obje faze), šestmjesečna smrtnost (1,2 nasuprot 2,2%), postinfarktna angina pektoris (12,1 nasuprot 21,4%) te ostali veliki neželjeni kardiovaskularni događaji (MACE, 6,4 nasuprot 21,7%).

Dok pogoršanje rizičnog profila bolesnika liječenih pPCI u drugoj fazi ne predstavlja njen korak unazad, obzirom da je ova vrsta liječenja upravo najkorisnija takvim bolesnicima, produljenje vremena do dolaska u prvu zdravstvenu ustanovu zahtjeva javnozdravstvene akcije, uključujući i kontinuiranu medijsku kampanju. Nadalje, povećanjem volumena i iskustva novouključenih intervencijskih centara očekuje se i poboljšanje njihovih i ukupnih rezultata Hrvatske mreže pPCI.

Infarkt miokarda bez ST-elevacije

Nakon što je u prošlom desetljeću težište međunarodne kardiološke javnosti bilo stavljeno na STEMI što je rezultiralo značajnim poboljšanjem u njegovu, osobito intervencijskom, lječenju, početkom ovoga destljeća u žarište interesa dolazi infarkt miokarda bez ST-elevacije (NSTEMI) kao sve učestaliji entitet u svakodnevnoj kliničkoj praksi čija se smrtnost već nakon godinu dana izjednačava s onom akutnog STEMI. U takvom ozračju je prije dva mjeseca Europsko kardiološko društvo objavilo najnovije smjernice za liječenje akutnog koronarnog sindroma bez ST-elevacije[16] u kojima se ponovno naglašava da rana invazivna strategija u ovih bolesnika reducira ishemiju miokarda, stopu reinfarkta miokarda i kardiovaskularni mortalitet na srednji i duži rok u ovih bolesnika.

U znanstvenoj literaturi još uvijek nema podataka o rezultatima liječenja NSTEMI mreža na regionalnoj ili nacionalnoj razini. U sklopu proučavanja druge faze (2008. i 2009.) Hrvatske mreže pPCI sakupljeni su i podaci pet centara iz svih dijelova Hrvatske (KBC Sestre milosrdnice, KB Dubrava, KBC Split, SB Magdalena, OB Slavonski Brod) o liječenju NSTEMI unutar 72 sata od početka bolova i uspoređeni s rezultatima liječenja STEMI. Unutar NSTEMI skupine bilo je manje transportiranih bolesnika (25,5 nasuprot 35,6%) i onih u kardiogenom šoku (3,6 nasuprot 8,8%), a više onih sa zahvaćenom prednjom stijenkom lijeve klijetke (49,5 nasuprot 44,4%), stenozom debla lijeve koronarne arterije (3,5 nasuprot 1,4%) i arterije cirkuflekse (23,0 nasuprot 14,6%). Neovisno o dulja sva tri ishemijska vremena, niži postotak kardiogenog šoka u bolesnika s NSTEMI rezultirao je i nižim unutarbolničkim mortalitetom (1,8 nasuprot 4,9%). Transportirani NSTEMI bolesnici u odnogravation of risk profile of patients treated in the second phase that are of higher age (60 vs. 61) with more frequently affected left main trunk coronary artery (0.7 vs. 1.6%) and more frequently in cardiogenic shock (6.7 vs. 7.9%). Organizational efforts at all three levels of healthcare has seen reduced door-to-balloon time (109 vs. 91 minutes), but the symptom onset-to-door time (130 vs. 180 minutes), and consequently the total ischemic time (symptom onset-to-balloon time, 265 versus 285 minutes) has been extended. These facts, but also inclusion of new low-volume centers in the network as proved by statistical subanalysis, have led to the fact that the results of treatment in the second phase are the same or worse than those obtained in the first phase: the optimal post-procedural TIMI 3 flow (87.1 vs. 81.8%), inhospital mortality (4.4% in both phases), six-month mortality (1.2 vs. 2.2%), post-infarction angina pectoris (12.1 vs. 21.4%) and other major adverse cardiovascular events (MACE, 6.4 vs. 21.7%).

While the aggravation of the risk profile of patients treated by pPCI in the second phase does not represent a step backwards since this kind of treatment is the most beneficial for such patients, an extension of time until the arrival in the first medical institution requires public health actions, including continuous media campaign. Furthermore, an increase in the volume and experience of newly integrated interventional centers is to result in an improvement of their and total results and the Croatian pPCI Network.

The non ST-segment elevation myocardial infarction

After the emphasis during the last decade was placed on STEMI by the international cardiology experts, which resulted in significant improvement in its, in particular, interventional treatment, at the beginning of this decade non ST-segment elevation myocardial infarction (NSTEMI) has been emphasized as an increasingly common entity in daily clinical practice whose death rate was only after one year equal to that of acute STEMI. In such an environment, two months ago the European Society of Cardiology published the latest guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation[16] which re-emphasize that the early invasive strategy reduces myocardial ischemia, the rate of myocardial re-infarction and medium and longer term cardiovascular mortality in these patients.

In the scientific literature there is still no data on the treatment outcomes for NSTEMI network at the regional or national level. Within the study of the second phase (2008 and 2009) of the Croatian pPCI Network, the data was collected from the five centers from all parts of Croatia (University Hospital Centre Sestre Milosrdnice, Clinical Hospital Dubrava, University Hospital Centre Split, Specialized Hospital Magdalena, General Hospital Slavonski Brod) about the treatment of NSTEMI within 72 hours from the onset of chest pains and compared with the results of treatment of STEMI. Within the NSTEMI group there were fewer transported patients (25.5 vs. 35.6%) and those in cardiogenic shock (3.6 vs. 8.8%) and a greater number of those with affected anterior wall of left ventricle (49.5 vs. 44. 4%), stenosis of the left main trunk coronary artery (3.5 vs. 1.4%) and left circumflex artery (23.0 versus 14.6%).

su na direktno zaprimljene u PCI centre češće su liječeni PCI tijekom dana (92,9 nasuprot 76,2%) bez ijednog transportiranog bolesnika s kardiogenim šokom u istraživanom periodu (0 nasuprot 5,6%) s posljedično nižim unutarbolničkim mortalitetom (0 nasuprot 2,7%) te šestmjesečnim postotkom MACE (6,9 nasuprot 20,6%).

U svezi s početkom NSTEMI mreže u Republici Hrvatskoj može se zaključiti da se javljaju isti problemi kao u početku STEMI mreže: nizak postotak NSTEMI bolesnika liječenih ranom PCI, osobito onih u kardiogenom šoku i tijekom noćnih sati. Ti su nedostaci naročito izraženi u transportiranih bolesnika.

Na tragu spomenutih rezultata, ali i porasta interesa za NSTEMI u međunarodnim kardiološkim krugovima Radna skupina za akutni koronarni sindrom Hrvatskog kardiološkog društva organizira 30. studenoga 2011. god. u Zagrebu skup "Suvremeno liječenje NSTEMI" na kojem se očekuje prikaz najnovijih rezultata liječenja ovoga entiteta, ali i STEMI u svim dijelovima Hrvatske.

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Regardless of extended all three ischemic times, a lower percentage of cardiogenic shock in patients with NSTEMI has resulted in lower inhospital mortality (1.8 vs. 4.9%). Transported NSTEMI patients as compared to the directly admitted patients in PCI centers were often treated by PCI during the day (92.9 vs. 76.2%) without any transported patient with cardiogenic shock in the analysed period (0 vs. 5.6%) with consequently lower inhospital mortality (0 vs. 2.7%) and six-month percentage of MACE (6.9 vs. 20.6%).

With the beginning of NSTEMI network in the Republic of Croatia, we may conclude that the same problems occur as at the beginning of the STEMI network: a low percentage of NSTEMI patients treated by early PCI, particularly of those patients in cardiogenic shock and during the night hours. These shortcomings are especially pronounced in transported patients.

Based on these results, but also due to a growing interest in NSTEMI in international cardiology literature, the Working Group for Acute Coronary Syndrome of the Croatian Cardiac Society organized on 30 November 2011 in Zagreb the Symposium "Modern treatment of NSTEMI" at which we expect to see the latest results of treatment of this entity and STEMI in all parts of the Croatia.

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