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Original Scientific Paper

DO THE GUIDELINES GUIDE THE BELGRADE EMERGENCY MEDICAL SERVICE PHYSICIANS THROUGH THE MANAGEMENT OF ACUTE ST-ELEVATION MYOCARDIAL INFARCTION?

Goran Čolaković[1], Slađana Anđelić[1], Snežana Bogunović[1] and Nataša Čolaković[2]

[1]Emergency Medical Services, Belgrade, Serbia;
[2]Department of Oncologic Surgery, Bežanijska kosa University Medical Center, Belgrade, Serbia

SUMMARY – The aim of the study was to assess whether current guidelines for diagnosis and treatment of acute ST-elevation myocardial infarction (STEMI) in daily clinical practice are adequately applied in the Belgrade Emergency Medical Service (EMS). A retrospective research included 2,982 STEMI patients who were cared for by EMS teams. Therapy consisting of morphine, oxygen, nitroglycerin and aspirin (MONA) was applied. Dual antiaggregation therapy (aspirin 325 mg + ticagrelor 180 mg or clopidogrel 600 mg) was administered to patients with primary percutaneous coronary intervention (PCI) indicated. With electrocardiographic monitoring included, the patients were transported directly to PCI unit with announcement of the arrival. Response times I-V were measured. There was an increasing trend in the number of STEMI patients. A rapid increase in the use of dual antiaggregation therapy (MONA and clopidogrel or MONA and ticagrelor) was reported from year to year, as well as a dramatic increase in the use of ticagrelor compared to clopidogrel. The time from receiving the call to the arrival on the scene was 13.72 minutes, and the time from receiving the call to hospital arrival was 52.83 minutes. Our physicians care for STEMI patients in accordance with the current international and local recommendations.

Key words: *Guidelines, Acute myocardial infarction, ST elevation, Emergency medical care*

Introduction

Coronary heart disease (CHD) is the leading cause of mortality worldwide; it is growing and takes on a form of a pandemic that does not respect any boundaries[1]. There is considerable articles that a sedentary lifestyle and obesity increase the risk of CHD[2,3]. There is probably no medical field where there are so many data derived from large, well-performed randomized studies than diagnosis and treatment of patients with acute coronary syndrome (ACS)[4]. Moreover, in no other branch of medicine have the latest technological inventions and the entire organization of treatment been put into service of disease management as in the treatment of acute myocardial infarction with ST-elevation (STEMI).

Guidelines for diagnosis and treatment of ACS are established on the principles of good clinical practice and on evidence-based medicine. This enables formation of a unique diagnostic and therapeutic approach to patients across the country, ensures the equality of all patients, i.e., the possibility of receiving the same treatment regardless of the health care facility in which the patient is treated. In addition, in the present overwhelming number of information,

Correspondence to: *Prof. Slađana Anđelić, MD, PhD*, Franse d`Eperea 5, 11000 Belgrade, Serbia
E-mail: novizivot94@gmail.com

it is often a problem to a medical practitioner to choose the right option, so guidelines should provide a source of security of the right choice and the most appropriate procedure in the given circumstances. These types of national guidelines have been present in a number of developed countries since 1994[1]. In Serbia, the history of good clinical practice guidelines started in 2003/2004, together with the introduction of the principles of the health care system reform[5]. The Ministry of Health of the Republic of Serbia started writing the guidelines with an intention to create a modern health care system in which patients will be treated equally and in the currently most effective way, and they did it in order to standardize diagnostic and therapeutic procedures.

Every five years, when new knowledge and results of large randomized studies are summarized, new recommendations are published. In 2017, the European Society of Cardiology and the American College of Cardiology/American Heart Association published comprehensive guidelines for the diagnosis and treatment of ACS with and without ST elevation[6]. This guide is not only a significant guidepost in the treatment of ACS patients, but also a form of continuous medical education. A STEMI network has been established in Serbia, which includes coordination of medical emergency services and cardiologic teams in practical implementation of current recommendations.

The aim of our work was to evaluate whether the guidelines for diagnosis and treatment of STEMI in daily clinical practice are applied in the Emergency Medical Service (EMS) in Belgrade.

Patients and Methods

Belgrade EMS physicians are always well familiar with the current guidelines for diagnosis and treatment of STEMI. This is achieved by translating the guidelines into Serbian language immediately after their publication, by numerous lectures and courses organized by cardiologic experts from Belgrade, as well as by participating in congresses and symposia having STEMI as one of the sessions. In 2017, the EMS Education Center issued a set of professional and methodological instructions with ACS prehospital care algorithms, which was given to each physician in this institution (Fig. 1).

All Belgrade EMS teams are equipped with electrocardiographs (ECGs) and defibrillators, glucometers and pulse oximeters. In case of suspected ACS, physicians take an ECG reading. It is an obligation of every EMS physician to hand in the completed forms of medical calls and ECG reading duplicates at the end of their shift for all interventions performed that day. At the end of the month, the Committee for Internal Professional Quality Assurance in EMS analyzes medical reports for all patients with prehospital diagnosis of ACS.

A retrospective study included 8,843 patients with ACS who received intervention by Belgrade EMS teams in the period between January 1, 2014 and December 31, 2017. STEMI patients were selected from this cohort. The diagnosis of STEMI was based on history data, physical examination, and ECG findings (elevation of the ST segment or its equivalent). STEMI patients were administered a combination of MONA therapy (morphine 3 to 5 mg IV, maximum 8-10 mg IV; oxygen 100% 3-5 L/min through a nasal catheter (only in hypoxemic patients, not as a routine) with SaO2 (arterial oxygen saturation) <95 (until 2017), i.e., <90% (since 2017); nitroglycerin: aerosol spray 1 to 2 times or 1 tablet sublingually 0.3-0.4 mg, repeated dose up to 3 times at intervals of 5-10 minutes; aspirin 300-500 mg to chew). Due to the proximity to catheterization unit, EMS physicians do not use prehospital thrombolysis. If the EMS physician estimated that the primary percutaneous coronary intervention (PPCI) could be performed within 120 minutes from the 0 time, direct patient transfer to the catheterization unit was indicated, with ECG and vital paremeters monitored. It is the obligation of the physician to announce arrival of a STEMI patient. Dual antiaggregation therapy (aspirin 325 mg + ticagrelor 180 mg or clopidogrel 600 mg) was administered during transport. Clopidogrel was administered only when ticagrelor was unavailable or contraindicated. Patients were transported to ambulance on cardiac chairs or stretchers. Inside the ambulance, the patients were positioned on a stretcher with a raised headboard. All medicines were administered exclusively intravenously (i.v.) or *per os*.

At the same time, response times (RT) were measured as follows: RT I – the interval between call receipt and assignment to a medical team; RT II – the interval between call receipt and arrival on the scene; RT III – the interval between arrival on the scene and delivery to the hospital; RT IV – the interval between call asignment to a medical team and delivery of the

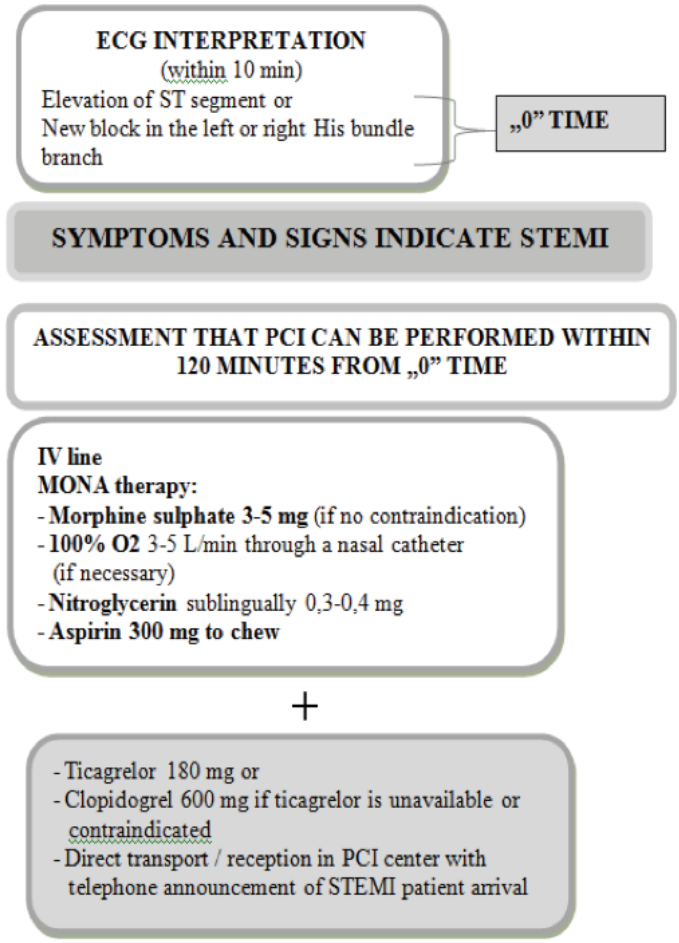

Fig. 1. Prehospital STEMI care.

ECG = electrocardiogram; STEMI = myocardial infarction with ST-elevation; PCI = percutaneous coronary intervention; MONA = morphine, oxygen, nitroglycerin and aspirin

patient to the hospital; and RT V – the interval between call receipt and delivery of the patient to the hospital.

Ethics

The study was approved by the Ethics Committee of the Municipal Institution for Emergency Medical Services (Decision No. 9631/18).

Statistics

Standard descriptive statistical methods (mean and standard deviation) were used in processing the results and appropriate statistical tests were applied depending on the type (Student's t test, χ^2-test). Data were processed using the EZR computer program, and results are shown in tables and figures. A p value of less than 0.01 was considered significant.

Results

In the period surveyed, EMS physicians set prehospital diagnoses of ACS in 8,843 cases, among which 2,982 STEMI patients were identified, of which 1,894 (63.50%) male and 1,088 (36.50%) female. The mean age of STEMI patients was 65.10±13.42 (20.82; 94.41). There was a statistical age difference between women (69.30±13.08 (32.30; 93.86)) and men (62.67±13.02 (20.82; 94.41)). Figure 2 shows the total number of ACS diagnoses with participation of STEMI by age.

There was a declining trend in ACS and an increase in STEMI patients. Figure 3 shows the number of ACS and STEMI patients by month in the period from January 2014 to December 2017.

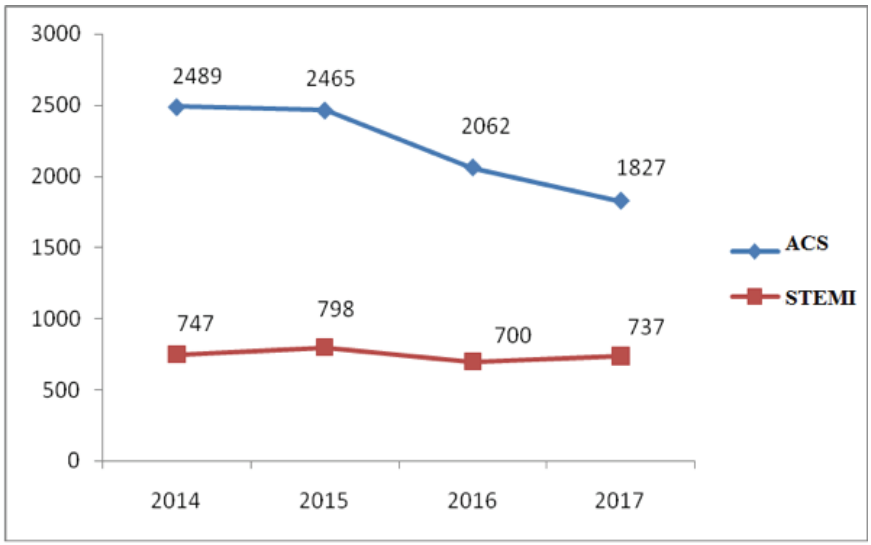

Fig. 2. The ratio between ACS and STEMI 2014–2017.

ACS = acute coronary syndrome; STEMI = myocardial infarction with ST-elevation

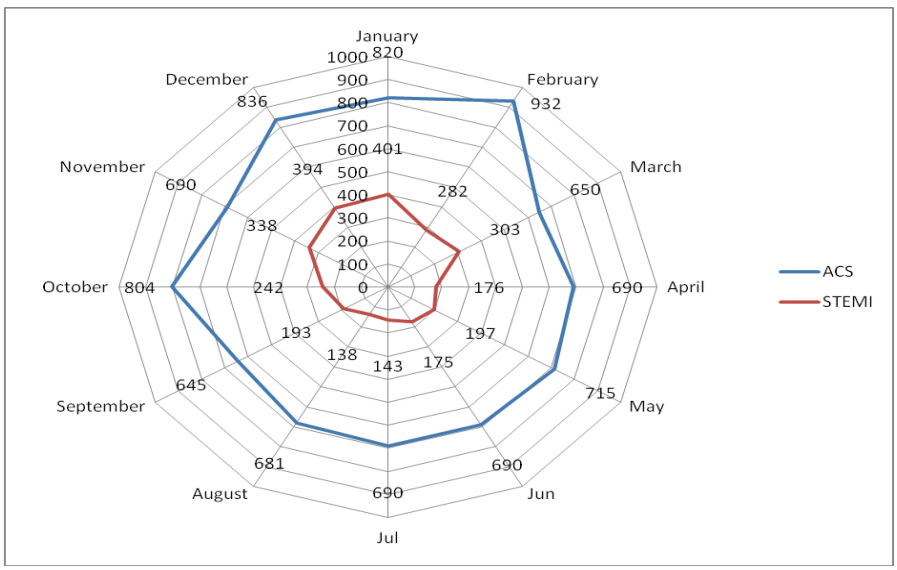

Fig. 3. Number of ACS and STEMI patients by month in the period from January 2014 to December 2017.

ACS = acute coronary syndrome; STEMI = myocardial infarction with ST-elevation

Initial MONA therapy was administered to 445 (59.71%) STEMI patients in 2014, 429 (53.76%) patients in 2015, 289 (41.29%) patients in 2016, and 221 (29.99%) patients in 2017.

When it comes to antiaggregation therapy, besides aspirin, in 2014 EMS physicians had only clopidogrel (Plavix) at their disposal, and since 2015 they have also included ticagrelor. Dual antiplatelet

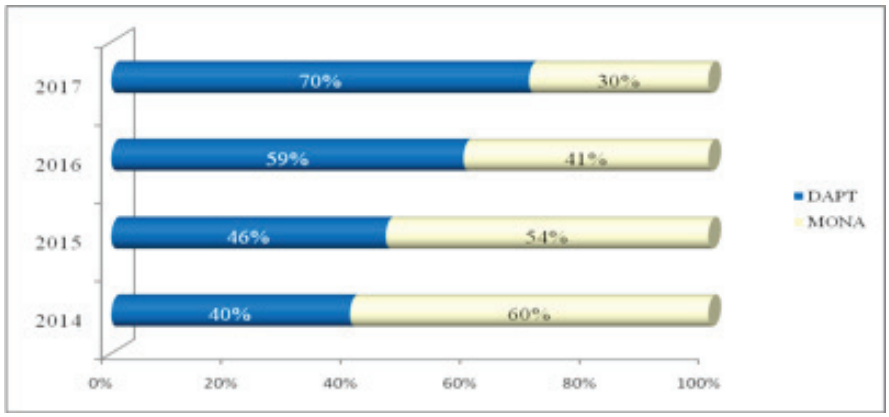

Fig. 4. The use of MONA and DAPT therapy in STEMI 2014–2017.

MONA therapy = morphine, oxygen, nitroglycerin, aspirin; DAPT = dual antiplatelet therapy

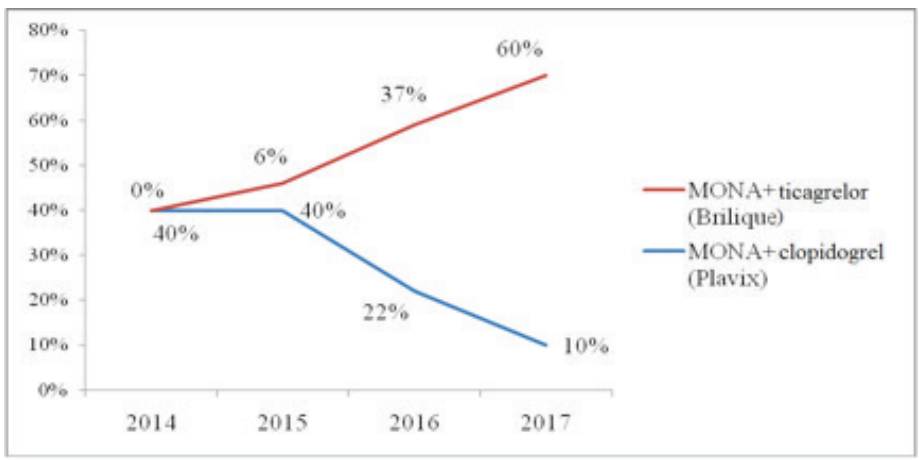

Fig. 5. The use of clopidogrel and ticagrelor 2014–2017.

MONA therapy = morphine, oxygen, nitroglycerin, aspirin

therapy (DAPT) was applied as follows by study years: in 2014, aspirin and clopidogrel were given to 301 (40.29%) patients; in 2015, aspirin and clopidogrel were given to 322 (40.35%), and aspirin and ticagrelor to 47 (5.89%) patients. In 2016, 155 (22.14%) STEMI patients received aspirin + clopidogrel, while 256 (36.57%) patients received aspirin + ticagrelor. In 2017, 71 (9.63%) patients were given aspirin + clopidogrel, and 445 (60.38%) aspirin and ticagrelor. Other STEMI patients did not receive dual antiaggregation therapy (Fig. 4). Physicians stated the following reasons for that: the patient had already taken these medicines before as they were included in regular therapy, the patient had disturbance of consciousness, ST elevation was insufficient, there were contraindications for the use or it was the physician's personal decision. Figure 4 shows rapid increase in the use of dual antiaggregation therapy by years. Figure 5 shows drastic increase in the use of ticagrelor compared to clopidogrel by years.

Patients were transported to ambulances on cardiac chairs or stretchers. Inside the ambulance, patients

Table 1. Emergency Medical Service response times

Interval	$\bar{x}$ ± SD	Median (Q_1; Q_3)
Interval between call receipt and assignment to a medical team	7.94±10.40	3.92 (1.38; 9.85)
Interval between call receipt and arrival on the scene	11.16±7.19	9.80 (6.22; 14.88)
Interval between arrival on the scene and delivery to hospital	36.06±13.02	35.00 (29.00; 2.00)
Interval between call asignment and delivery to hospital	46.86±15.99	46.24 (37.22; 6.33)
Interval between call receipt and delivery to hospital	54.80±19.88	52.83 (42.24; 66.08)

SD = standard deviation

were positioned on a stretcher with a raised headboard. During transport, patients received constant ECG and vital parameter monitoring. They were transported directly to an on-duty PCI center with announcement of arrival. Response times of EMS for this group of patients are shown in Table 1.

Discussion

Recently, it has been demonstrated that pre-hospital emergency care reduces in-hospital mortality in patients admitted with ACS[7]. Good recommendations for ACS are the main mechanism for enhancing health care and improving outcomes in STEMI patients. The current guidelines address the first hours after the onset of symptoms. Out-of-hospital management and initial therapy may vary according to local capabilities, resources and regulations. Clinical pathway protocols are strongly recommended and must be available for emergency teams working in the prehospital setting. In addition to European protocols, Belgrade EMS physicians have their own internal protocols for the management of ACS. While epidemiological analyses show that women make up about 30% of STEMI population at the global level, in our study that percentage was 36%[8]. A seven-year study on 27,993 STEMI subjects in Finland found, the same as we did, that women with STEMI were significantly older than men ($p<0.0001$)[9].

When ACS is suspected, a 12-channel ECG record should be made and interpreted as soon as possible after the first medical contact to facilitate early diagnosis, triage and therapy[10]. Using pre-hospital 12-lead ECG, the time from hospital admission to initiating reperfusion therapy is reduced by 10 to 60 min. This is associated with shorter times to reperfusion and improved patient survival in both patients with PCI and those undergoing fibrinolysis[11]. The STEMI diagnosis is set at the moment of recorded elevation of the ST segment (or its equivalent) on the ECG, and precisely that moment, regardless of the time of the onset of patient's distress, represents the zero time from which the countdown begins, unlike the previous STEMI guide where the zero time represented the moment of the first medical contact[4]. In recent years, based on the results of a number of European studies such as ours, there has been a declining trend of STEMI[12]. Pre-hospital STEMI diagnosis, as in our study, is based on the symptoms consistent with myocardial ischemia (i.e., persistent chest pain) and signs (i.e., 12-lead ECG). There is no evidence to support the use of troponin point-of-care testing in isolation as a primary test in the pre-hospital setting to evaluate patients with symptoms suspicious of cardiac ischemia[13].

Initial therapy, both in the old and new guidelines, is MONA therapy, which was applied to our patients. The only difference compared to the 2012 recommendations is that the oxygen saturation limit (SaO2), in cases when oxygen is to be applied, has been changed from 95% to 90%. Although the application of fibrinolytics found its place in STEMI recommendations, after the STREAM study, the Belgrade EMS has no longer been using fibrinolytic tenecteplase (TNK-tPA) due to the proximity of PCI centers. PPCI is the preferred reperfusion strategy in patients with STEMI within 12 hours of symptom onset (time 0), provided it can be performed expeditiously (i.e., 120 min from STEMI diagnosis) by an experienced team[14]. Both treatment strategies are well established and have been the subject

of large randomised multicenter trials over the last decades. Patients undergoing PPCI should receive DAPT, a combination of aspirin and a P2Y12 inhibitor. Aspirin is recommended indefinitely in all patients with STEMI[15]. The ISIS-2 study showed that the use of aspirin (160 mg) within 24 hours of STEMI reduced mortality by 23%, and reinfarction and ischemic stroke by 50%[16]. However, the use of monotherapy with aspirin did not lead to an expected improvement in the prognosis of patients with ACS.

Our physicians were increasingly using ticagrelor year after year as the recommended P2Y12 inhibitor of the first order of choice[17]. When ticagrelor was not available or was contraindicated, our physicians were using clopidogrel instead, in accordance with the CURRENT-OASIS trial[18].

The COMMIT study, which included over 45,000 patients with STEMI, demonstrated that a combined therapy of clopidogrel and aspirin significantly reduced the risk of death, non-fatal myocardial infarction or stroke compared to aspirin monotherapy[19]. As recommended, our patients were appropriately transferred to ambulance and during transport they were on continuous ECG montoring and monitoring of vital functions[5].

Response times are key variables in pre-hospital care of STEMI patients. The median time interval from the call pick-up to PCI delivery was 52.83 minutes, which complied with the recommendations for reperfusion strategy. However, time targets for the maximum time from the first medical contact to the ECG and diagnosis, although not defined in the physician calls of Belgrade EMS, is certainly much longer than the recommended 10 minutes, since the median from the EMS call pick-up to reaching the patient was 13.72 minutes in total (3.92 minutes from the call receipt to assigning the call to the team +9.8 minutes from call assignment to reaching the site of intervention).

As peventing delay is crucial for patients with STEMI, especially at the pre-hospital level, other studies[20,21] state the reasons for a delay too. While anticipating concrete solutions to its reduction, we can only provide suggestions for the correction of current response times in our institution's medical report. We propose introducing new time response performances by dividing the time from reaching the intervention site to the delivery of the patient to the hospital into the following intervals: the time of the first medical contact, the time of the first ECG reading, the time of preparation for transport, the transportation time, the time of arrival at the hospital, and the time of patient delivery to the PCI center.

Accapting the good clinical practice guidelines for pre-hospital care of STEMI as the framework for everyday practice is the basis for further work on the development and implementation of clinical pathways, and will contribute to increasing the effectiveness of the health care system, to which all the system users are entitled. National guidelines to the good clinical practice do not have a binding character; it is left to the consciousness of every physician to apply what is currently regarded as the most effective diagnostic and therapeutic principle in the world in treating their patients. Our physicians are managing STEMI patients in a modern way in accordance with the current international and national recommendations.

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Sažetak

VODE LI SMJERNICE LIJEČNIKE BEOGRADSKE HITNE POMOĆI U ZBRINJAVANJU AKUTNOG INFARKTA MIOKARDA SA ST ELEVACIJOM?

G. Čolaković, S. Anđelić, S. Bogunović i *N. Čolaković*

Cilj ovoga rada bio je procijeniti primjenjuju li se aktualne smjernice za dijagnostiku i liječenje akutnog infarkta miokarda sa ST elevacijom (STEMI) primjereno u svakodnevnoj kliničkoj praksi u beogradskoj hitnoj medicinskoj pomoći (HMP). Retrospektivnim istraživanjem obuhvaćeno je 2.982 bolesnika sa STEMI kod kojih su intervenirali timovi HMP. Ordinirana je terapija MONA (morfin, kisik, nitroglicerin, aspirin). Dualna antiagregacijska terapija (aspirin 325 mg + tikagrelor 180 mg ili klopidogrel 600 mg) davana je bolesnicima kojima je indicirana primarna perkutana koronarna intervencija (PCI). Bolesnici su uz elektrokardiografsko praćenje transportirani izravno u jedinicu PCI uz prethodnu najavu. Mjerena su vremena reakcije I-V. Bolesnika sa STEMI je bilo 2982, više muškaraca nego žena (63,5% prema 36,5%), sa statistički značajnom razlikom (p<0,001) u dobi između žena (69,30±13,08) i muškaraca (62,67±13,02). Uočen je rastući trend bolesnika sa STEMI. Zabilježen je brz porast primjene dvojne antiagregacijske terapije (MONA i klopidogrel ili MONA i tikagrelor) iz godine u godinu, kao i drastičan porast primjene tikagrelora u odnosu na klopidogrel. Vrijeme od primitka poziva do stizanja ekipe na mjesto intervencije je iznosilo 13,72 min, a vrijeme od primitka poziva do predaje bolesnika u bolnicu 52,83 min. Naši liječnici liječe bolesnike sa STEMI u skladu s aktualnim svjetskim i domaćim preporukama.

Ključne riječi: *Smjernice; Akutni infarkt miokarda; ST elevacija; Hitna pomoć; Zbrinjavanje*