PROGNOSIS IN PATIENTS WITH MYOCARDIAL INFARCTION WITH ST-ELEVATION DEPENDING ON THE TIMING OF INTERVENTIONAL REVASCULARIZATION

N. Penkov, V. Mura, O. Hlinomaz, D. Velevski, Y. Sitar, G. Kirilova, M. Rezek, M. Zlatanova, D. Dimova, Y. Dichkova
Bulgarian Cardiac Institute, Cardiology Hospital of Varna

ABSTRACT
The prognosis (in-hospital and post-hospitalization lethality by the end of the 6th month) of 300 patients (212 men and 88 women) with a first myocardial infarction with ST-elevation (STEMI) at an average age of 62.9 years was studied depending on the timing of the conducted primary coronary intervention (PCI) after the onset of symptoms. Depending on the timing of the conducted PCI, the patients were divided into 4 groups: by the 3rd, 6th, 12th, and 24th hour after the onset of the infarction. The patients’ in-hospital lethality was 6.3%, and that by the end of the 6th month – 13.3%. It was the same for groups I and II and significantly lower than in groups III and IV; higher in women, in patients over 65 years of age, with ejection fraction (EF) <35.0% and with thrombotic occlusion of LM and LAD.

Keywords: myocardial infarction, ST-elevation, STEMI, primary coronary revascularization, PCI

INTRODUCTION
The primary coronary intervention (PCI) in patients with STEMI has proven its advantages over thrombolytic therapy (6,8,9,10). The total duration of myocardial ischemia, defined as the time from the onset of the symptoms to the conduction of PCI, is thought to be of vital importance to the patient’s prognosis (1,4,5,6,8). In addition, it has become clear that each increase of the period of time to PCI increases the mortality rate (1,8) and that, in this procedure, there is a “golden hour” as in venous thrombolysis (1,2). In reality, the best results have been reported in the Prague-2 (14) and CAPIM (11) trials, if PCI is conducted within the first 2-3 hours after the onset of symptoms, and each delay increases the mortality rate. Despite this, conduction of PCI in patients with STEMI in the period between the 12th and 24th hour is still beneficial (12,16).

AIM
The aim of this article is to determine the in-hospital and 6-month lethality in patients with myocardial in-
Prognosis in Patients with Myocardial Infarction with ST-Elevation Depending on the Timing of Interventional Revascularization

ЦЕЛ НА ПРОУЧВАНЕТО
Да проверим какъв е болничният и 6-месечен ле- талитет при болни с първи миокарден инфаркт със ST-елевация, в зависимост от срока на извършената интервенционална реваскуларизация след на- чалото на първите симптоми и кои други фактори имат значение за прогнозата.

МАТЕРИАЛ
Проучени са 300 последователни болни с пър- ви MI със ST-елевация, постъпили на лече- ние в СБАЛК-Варна за период от 01.01.2011 г. до 01.01.2014 г. Средната възраст на болниите е 62.9±11.2 (32-94) г., от които 212 (70.6%) мъже и 88 (29.4%) жени. В зависимост от срока на из- вършване на PCI след началото на инфарктната симптоматика се оформят следните 4 групи:
• І гр. – реваскуларизирани до 3-ия час
• ІІ гр. – реваскуларизирани след 3-ия до 6-ия час
• ІІІ гр. - реваскуларизирани след 6-ия до 12-ия час
• ІV гр.- реваскуларизирани след 12-ия до 24-ия час.

Групите са сравними по възраст (р>0.10). Поло- вото разпределение в гр. І и ІІ и гр. ІІІ и ІV е ед- накво. Относителният дял на жените обаче в гр. ІІІ (36.4%) и гр. ІV (31.8%) е достоверно по-голям в сравнение с гр. І (24.7%) и гр. ІІ (26.4%) (р<0.05), а този на мъжете съответно по-малък.

МЕТОДИ
При всички болни е извършена селективна коро- нарна ангиография (SCAG) по метода на Seldinger с радиален достъп при 78 (26.0%) болни и с фемо-

The groups were comparable in terms of age (p>0.10). The gender distribution in groups I and II, and II and IV is the same. However, the relative share of women in Group III (36.4%) and Group IV (31.8%) was significantly higher than Group I (24.7%) and Group II (26.4%) (p<0.05), and that of men was respectively lower.

METHODS
All patients received selective coronary angiography (SCAG) using the Seldinger technique with a radial access in 78 (26.0%) patients and with a femoral
ralen – при 222 (74.0%), с последваща реваскуларизац͡ – tromboaspiration, dilation and stenting of the виновната за инфаркт артерия. Глобалната левокамерна систолна функция е определена преди СКАГ ехокардиографски посредством ФИ по метода на Simson. Отчетен е болничният леталитет и леталитетът до края на шестия месец след началото на МИ по групи, в зависимост от срока на реваскуларизациата след началото на инфарктната болка. Потърсени са факторите, които определят повишен риск от смърт. Лечението на болниците преди процедураната включва aspirin и clopidogrel в насищащи дози, обезболяващи, медикаменти за стабилизиране на хемодинамиката и контрол на артериалното налягане (12). В следболничния период се провеждаше лечение с антиагреганти - aspirin 100 mg и clopidogrel 75 mg, дневно, а при перманентно предсърдно мъждание се добавяше и индиректен антикоагулант. Освен това болниците получаваха ACE-инхибитори или ARB, бета-блокери, статини, а при необходимост и нитрати с удължено действие (7,12).

RESULTS

The total in-hospital lethality was 6.3% and that by the end of the 6th month – 13.3%. It was the same in Group I and Group II and statistically significantly lower (p<0.05) than that in Group III and Group IV. The lethality rate in women was statistically significantly higher than in men, both during the hospital stay and by the end of the 6th month after the infarction onset (p<0.01).

The mean age of the patients who died while hospitalized (70.0±12.2) and that of those who died by the end of the 6th month after discharge (69.9±12.2) was similar but statistically significantly higher (p<0.01) than
Prognosis in Patients with Myocardial Infarction with ST-Elevation Depending on the Timing of Interventional ...
6th month (n=40) from the onset of the infarction was statistically significantly lower than that of patients, who have survived past that period of time (p<0.01). From the total of 40 deceased patients, 27 (67.5%) had EF≤35.0%, and 13 (32.5%) had EF>35.0% (p<0.05). Analysis of the causes of death showed that of the total 19 deceased at the hospital, 18 were with pumping function failure – 13 with marked circulatory, combined with left-sided heart failure, and 5 – with prevailing acute left-sided heart failure, and 1 patient died due to cardiac tamponade as a result of a rupture of the free wall of the left ventricle.

The total number of deceased by the end of the 6th month after discharge was 21. In 2 patients the cause was deteriorating heart failure, in 2 other - recurrent infarction with severe pumping function failure, for another 2, the death occurred during coronary surgery, and for the remaining 15 patients the death was sudden.

The most common cause of acute myocardial infarction (AMI), in 150 (50%) of the patients, was thrombotic occlusion of LAD, the second most common cause (in 96, or 32%, of the patients) was RCA, third place was for LCX with 48 (16%) of the patients, and the last one, observed in 6 (2%) of the patients, was occlusion of LM.

| Groups        | LM  | LAD  | LCX  | RCA  | Total |
|---------------|-----|------|------|------|-------|
| Group I (n=81)| 1 (1.2%) | 43 (53.1%) | 10 (12.7%) | 27 (33.3%) | 81     |
| Group II (n=87)| 0 (0%) | 45 (51.7%) | 15 (17.2%) | 27 (31.1%) | 87     |
| Group III (n=66)| 4 (6.1%) | 30 (45.4%) | 12 (18.2%) | 20 (30.3%) | 66     |
| Group IV (n=66)| 1 (1.5%) | 32 (48.5%) | 11 (16.7%) | 22 (33.3%) | 66     |
| **Total**     | 6 (2%) | 150 (50%) | 48 (16%) | 96 (32%) | 300    |

The lethality in patients with thrombotic occlusion of LM is statistically significantly highest (p<0.05), almost equal in the cases of occlusion of LAD and LCX (p>0.10) and lowest in RCA occlusion.

**DISCUSSION**

In-hospital lethality (6.3%) of the studied patients and the total lethality rate by the end of the 6th month (13.3%) was within the range of the reported by the

40
alized after 6-hour, what is too high, such as and the
hemodynamic beta-blockage, and, if needed, 
required for them to receive beta blockers in doses
sufficient to include also specific anti-arrhythmic medicaments
ensuring hemodynamic beta blockade, and, if needed,
of the treatment, respectively, was surprisingly the same, unlike the results reported by the CAPIM (11) and Prague-2 (14) trials. In patients with PCI conducted after the 6th hour, however, the in-hospital and the out-of-hospital lethality increased sharply. Interventional revascularization after the 6th hour from the onset of the infarction is practically a dividing line, determining a negative prognosis (higher lethality rate). Our study, as well as other studies, showed a statistically significantly higher lethality for women than for men (12). This is maybe one of the factors, which were responsible for the higher lethality for the patients from groups III and IV, compared to the lethality rate in groups I and II. The age of STEMI patients turned out to be an important prognostic criterion. The mean age of the deceased was statistically significantly higher than that of the remaining survivors by the end of the 6th month. Similar data was reported by other authors (12). According to the individual analysis, in patients at the age of 65 and older, the lethality rate deteriorated sharply. The systolic function of the left ventricle, determined by EF, although not precisely, demonstrated a tendency of having lower levels in patients with PCI conducted after the 6th hour from the onset of the infarction. This is understandable because a longer period of coronary obstruction leads to a more significant myocardial necrosis, and as a result – to worse global left ventricular function (15). It has been known that global left ventricular function is an important factor for the prognosis of ischemic patients (3,14). This was confirmed by our study – in the deceased during in-hospital treatment and after discharge, by the end of the 6th month, the left ventricular systolic function was statistically significantly worse than that in survivors. In addition to that, it was noted that in the in-hospital period for the majority of the deceased the cause of death was circulatory and heart failure, and in the out-of-hospital period – sudden cardiac death (SCD). This fact requires special attention. That means that in the dehospitalization the patients with an elevated risk of fatal ventricular arrhythmias and SCD should be identified. It is known that they usually are with deteriorated left ventricular function and dangerous ventricular extrasystoles or episodes of ventricular tachycardias and residual myocardial ischemia. These patients must be observed closely. It is obligatory for them to receive beta blockers in doses ensuring hemodynamic beta blockade, and, if needed, to include also specific anti-arrhythmic medicaments (amiodarone).
фаркт виновната артерия се наблюдава и в други изследвания (12). Големият леталитет при болни с оклузия на LM и LAD е логичен, тъй като при тях инфарктите са по-обширни, а левокамерната систолна функция е по-лоша.

Резултатите от нашето изследване дават основание да бъдат изведени и препоръчани за практиката следните фактори, определящи повишен риск от смърт при болни с ОМИ със ST-елевация:

1. Реваскуларизация след 6-я час.
2. Възраст 65 и повече години.
3. Женски пол.
4. ФИ<35.0%.
5. Тромботична оклузия на LM и LAD.

ЗАКЛЮЧЕНИЕ

Рано хоспитализираните и реваскуларизирани болни до 6-я час са с по-малък леталитет както в болницата, така и до края на 6-я месец от началото на инфаркта. По-голямата част от починалите са на възраст 65 и повече години, по-често женки, с по-лоша левокамерна функция (ФИ<35.0%) и по-често с тромботична обструкция на LM и LAD. Основна причина за смърт по време на болничното лечение е циркулаторната и острата левостранна сърдечна недостатъчност, а в следболничния период – ВСС. Допълнителното намаляване на леталитета при болни със STEMI изисква организационни мерки, които биха осигурили по-ранна хоспитализация на болни и профилактика на ВСС в следболничния период.

Address for correspondence:
Prof. Nikolay Penkov, MD, PhD, DSc
Cardiology Hospital of Varna
100 Tzar Osvoboditel Blvd
9002 Varna
e-mail: n.penkov.vn@b-c-i.eu

REFERENCES

1. Berger PB, Ellis SG, Holmes DR, Granger CB, Cröger DA, Betriu A, et al. Relationship between delay in performing direct coronary and early clinical outcome in patients with acute myocardial infarction: results from the global use of strategies to open occluded arteries in acute coronary syndromes (GUSTO-II b) trial. Circulation. 1999, 100 (1):14-20. doi: 10.1161/01.CIR.100.1.14.
2. Bersma E, Maas DC, Deckers JW, Simoons ML.
Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet. 1996;348(9030):771-5. doi: 10.1016/S0140-6736(96)02514-7.

3. Brodie BR, Stuckey TD, Wall TC, Kissling G, Hansen CJ, Muncy DB, et al. Importance of time to reperfusion for 30-day and late survival and recovery of left ventricular function after primary angioplasty for acute myocardial infarction. J Am Coll Cardiol. 1998; 32(5):1312-9.

4. Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French W, et al. Relationship of symptom-onset-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. JAMA. 2000;283(22):2941-7.

5. De Luca G, Suryapranata H, Ottervanger JP, et al. Time delay to treatment and morality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation. 2004; 109:1223-5.

6. Gibson CM, Pride YB, Frederick PD, Pollack CV Jr, Canto JG, Tiefenbrunn AJ, et al. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J. 2008;156(6):1035-44. doi: 10.1016/j.ahj.2008.07.029.

7. Jernberg T, Johanson P, Held C, Svennblad B, Lindbäck J, Wallentin L, et al. Association between adoption of evidence-based treatment and survival for patients with ST-elevation myocardial infarction. JAMA. 2011;305(16):1677-84. doi: 10.1001/jama.2011.522.

8. Juliard JM, Feldman LJ, Golmard JL, Himbert D, Benamer H, Haghighat T, et al. Relation of mortality of primary angioplasty during acute myocardial infarction to door-to-thrombolysis in myocardial infarction (TIMI) time. Am J Cardiol. 2003;91(12):1401-5.

9. Keeley EC, Boura JA, Grines CL. Primary angioplasty intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomized trials. Lancet. 2003;361(9351):13-20. doi: 10.1016/S0140-6736(03)12113-7.

10. Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolysis therapy in acute myocardial infarction: is timing (almost) everything? Am J Cardiol. 2003;92(7):824-6.

11. Steg PG, Bonnefoy E, Chabaud S, Lapostolle F, Dubien PY, Cristofini P, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. Circulation. 2003;108(23):2851-6. DOI: 10.1161/01.CIR.0000103122.10021.F2.

12. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. ESC Guidelines for the management of acute myocardial infarction in
patients presenting with ST-segment elevation. The task force on management of ST-segment elevation acute myocardial infarction of European Society of Cardiology (ESC). Eur Heart J. 2018;39(2):119-177. doi: 10.1093/eurheartj/ehx393.

13. Stone GW, Grines CL, Cox DA, Garcia E, Tcheng JE, Griffin JJ, et al. Comparison of angioplasty with stenting, with or without aciximab, in acute myocardial infarction. N Engl J Med. 2002;346(13):957-66. doi: 10.1056/NEJMoa013404.

14. Widimský P, Budesínský T, Vorác D, Groch L, Zelízko M, Aschermann M, et al. Long distance transport for primary angioplasty vs immediate thromolysis in acute myocardial infarction. Final results of the randomized national multicentre trial—PRAGUE-2. Eur Heart J. 2003;24(1):94-104.

15. Pride YB, Giuseffi JL, Mohanavelu S, Harrigan CJ, Manning WJ, Gibson CM, et al. Relation between infarct size in ST-segment elevation myocardial infarction treated successfully by percutaneous coronary intervention and left ventricular ejection fraction three months after the infarct. Am J Cardiol. 2010;106(5):635-40. doi: 10.1016/j.amjcard.2010.04.012.

16. Zahn R, Vogt A, Zeymer U, Gitt AK, Seidl K, Gottwik M, et al. In-hospital time to treatment of patients with acute ST elevation myocardial infarction treated with primary angioplasty: determinants and outcome. Results from the registry of percutaneous coronary interventions in acute myocardial infarction of the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausarzte. Heart. 2005;91(8):1041-6. doi: 10.1136/hrt.2004.045336.