ПРОГНОЗА ПРИ БОЛНИ СЪС СЪРЦЕ-БЯЛ ДРОБ СЪС ST-ЕЛЕВАЦИЯ В ЗАВИСИМОСТ ОТ СРОКА НА ИНТЕРВЕНЦИОНАЛНАТА РЕВАСКУЛАРИЗАЦИЯ

Н. Пенков, В. Мура, О. Хлиномаз, Д. Велевски, Я. Ситар, Г. Кирилова, М. Резек, М. Златанова, Д. Димов, Й. Дичкова
Български кардиологичен институт, СБАЛК-Варна

РЕЗЮМЕ
Проверена е прогнозата (болнична и следболничния леталитет до края на 6-ия месец) при 300 болни (212 мъже и 88 жени) със ръкавица инфаркт със ST-елевация (STEMI) на средна възраст 62.9 год, в зависимост от срока на извършваната първична коронарна интервенция (PCI) след началото на симптомите. В зависимост от срока на извършваната PCI болниите са разделени на 4 групи: до 3-ия, до 6-ия, до 12-ия и до 24-ия час след началото на инфаркта. Болничният леталитет за всички болни е 6.3%, а до края на 6-ия месец – 13.3%; еднакъв при І-ва и ІІ-ра група и достоверно по-малък отколко при III-та и IV-та група, по-голям при жени, при болни над 65 г., с ФИ <35.0% и с тромботична оклузия на LM и LAD.

Ключови думи: миокарден инфаркт, ST-елевация, STEMI, първична коронарна интервенция, PCI

ВЪВЕДЕНИЕ
Първичната коронарна интервенция при болни със STEMI е доказала предимствата си в сравнение с тромболитичното лечение (6,8,9,10). Общата продължителност на миокардната исхемия, определена като време от началото на симптомите до извършване на първичната PCI, се смята, че е от съществено значение за прогнозата при болни (1,4,5,6,8). Освен това става ясно, че всяко увеличаване на времето до PCI увеличава смъртността (1,8) и че при тази процедура има „златен час”, както при венозната тромболиза (1,2). В действителност най-добри резултати са докладвани в проучванията Prague-2 (14) и CAPIM (11), при условие че PCI бъде реализирана в първите 2-3 часа след началото на симптомите, а всяко задържане след това увеличава смъртността. Въпреки това, извършването на PCI при болни със STEMI във времето между 12 и 24 час все още е от полза (12,16).

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-
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 извърше-
ната интервенционна реваскуларизация след на-
чалото на първите симптоми и кои други фактори
имат значение за прогнозата.

МАТЕРИАЛ
Проучени са 300 последователни болни с пър-
ви МИ със ST-елевация, постъпили на лече-
ние в СБАЛК-Варна за период от 01.01.2011 г.
do 01.01.2014 г. Средната възраст на болните 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-
vършване на PCI след началото на инфарктната
симптоматика се оформят следните 4 групи:
• І гр. – реваскуларизирани до 3-ия час
• ІІ гр. – раваскуларизирани 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
tози на мъжете съответно по-малък.

МЕТОДИ
При всички болни е извършена селективна коро-
нарна ангиография (СКАГ) по метода на Seldinger
c 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
рален – при 222 (74.0%), с последваща реваскулари-
зация – trombаспирация, дилатация и стентиране на
виновната за инфаркта артерия. Глобалната левокамерна систолна функция е определена преди СКАГ
ehокардиографски 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 реваскулариза-
цията след началото на инфарктната болка. Потвър-
сени са факторите, които определят повишен риск от смърт. Лечението на болните преди процедурата
включва aspirin и clopidogrel в насищащи дози, обез-
боляващи, медикаменти за стабилизиране на хемо-
dинамиката и контрол на артериалното налягане
(12). В следболничния период се провеждаше лече-
ние с антиагреганти - aspirin 100 mg, и clopidogrel 75
mg, дневно, а при перманентно предсърдно мъжде-
не се добавяше и индиректен антикоагулант. Освен
това болните получаваха ACE-инхибитори или
ARB, бета-блокери, статини, а при необходимост и
нитрати с удължено действие (7,12).

РЕЗУЛТАТИ
Общият болничен леталитет е 6.3%, а до края на
6-я месец - 13.3%, еднакъв в I-а и II-а група и дос-
tоверно по-малък (р<0.05), отколкото при III-а и
IV-а група. Леталитетът при жените както по време на бол-
ничното лечение, така и до края на 6-тия месец сле-
д началото на инфаркт са достоверно по-големи в
сравнение с този при мъжете (р<0.01).
Средната възраст на починалите в болницата
(70.0±12.2 г.) и на починалите след изписването до
края на 6-я месец (69.9±12.2 г.) не се различава, но
е достоверно по-голема (р<0.01), отколкото на ця-

one in 222 (74.0%) with a subsequent revascularization - thromboaspiration, dilation and stenting of the
artery, which caused the infarction. The global left
ventricular systolic function was determined echocar-
diographically before SCAG via EF using the Simson
technique. The in-hospital lethality and that by the 6th
month after the onset of MI was established by groups
depending on the timing of the revascularization after
the onset of the infarction pain. The factors determin-
ing the higher risk of a lethal outcome were sought.
The treatment of the patients before the procedure
included aspirin and clopidogrel in saturating doses,
painkillers, medications for hemodynamic stabiliza-
tion and blood pressure control (12). The post-hos-
pitalization period included antiplatelet medications
- aspirin 100 mg and clopidogrel 75 mg daily, and
in the cases of atrial fibrillation an indirect coagulant
was added. In addition, the patients received ACE-
inhibitors or ARBs, beta blockers, statins, and, when
needed, prolonged-action nitrates (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 (р<0.05) than that in Group III and Group IV.
The lethality rate in women was statistically signifi-
cantly higher than in men, both during the hospital
stay and by the end of the 6th month after the infarct-
onset (р<0.01).
The mean age of the patients who died while hospital-
ized (70.0±12.2) and that of those who died by the end
of the 6th month after discharge (69.9±12.2) was simi-
lar but statistically significantly higher (р<0.01) than

Table 1. In-hospital lethality and total lethality by the end of the 6th month

<table>
<thead>
<tr>
<th>TOTAL NUMBER OF PATIENTS</th>
<th>GROUP I</th>
<th>GROUP II</th>
<th>GROUP III</th>
<th>GROUP IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=300</td>
<td>n=81</td>
<td>n=87</td>
<td>n=66</td>
<td>n=66</td>
</tr>
<tr>
<td>In-hospital lethality</td>
<td>19 (6.3%)</td>
<td>3 (3.7%)</td>
<td>3 (3.5%)</td>
<td>8 (12.1%)</td>
</tr>
<tr>
<td>Total lethality by the 6th month</td>
<td>40 (13.3%)</td>
<td>8 (9.9%)</td>
<td>10 (11.5%)</td>
<td>12 (18.2%)</td>
</tr>
</tbody>
</table>

Table 2. Lethality by gender

<table>
<thead>
<tr>
<th>TOTAL NUMBER OF PATIENTS</th>
<th>MEN</th>
<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=300</td>
<td>n=212</td>
<td>n=88</td>
</tr>
<tr>
<td>In-hospital lethality</td>
<td>19</td>
<td>6 (2.8%)</td>
</tr>
<tr>
<td>Total lethality by the 6th month</td>
<td>40</td>
<td>18 (8.5%)</td>
</tr>
</tbody>
</table>
Prognosis in Patients with Myocardial Infarction with ST-Elevation Depending on the Timing of Interventional...

- The mean age of the deceased was 62.9 ± 11.2 years, and for survivors, it was 61.8 ± 11.4 years. From the total 40 deceased patients, 27 (67.5%) were 65 years old or older, and 13 (32.5%) were younger. (p<0.05).

- There was no difference in the echocardiographically determined ejection fraction (EF) by groups depending on the timing of the revascularization after the onset of MI. However, there was a tendency of having lower EF in groups III and IV (revascularized after the 6th hour) compared to groups I and II (revascularized by the 6th hour) (p>0.10). The global EF of the deceased at the hospital (n=19) and the total number of deceased by the end of the 6th month was significantly lower than that of the entire group of studied patients (62.9±11.2) and also that of those who have survived by the 6th month (61.8±11.4). From the total of 40 deceased patients, 27 (67.5%) were over 65 years of age and 13 (32.5%) were under 65 (p<0.05).

- There was no difference in the echocardiographically determined EF by groups depending on the timing of the revascularization after the onset of MI. However, there was a tendency of having lower EF in groups III and IV (revascularized after the 6th hour) compared to groups I and II (revascularized by the 6th hour) (p>0.10). The global EF of the deceased at the hospital (n=19) and the total number of deceased by the end of the 6th month was significantly lower than that of the entire group of studied patients (62.9±11.2) and also that of those who have survived by the 6th month (61.8±11.4). From the total of 40 deceased patients, 27 (67.5%) were over 65 years of age and 13 (32.5%) were under 65 (p<0.05).
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 (50.0%) of the patients, was thrombotic occlusion of LAD, on second place - at 96 (32%) patients was on RCA, on third - at 48 (16%) patients was on LCX, and on the fourth - at 96 (32%) patients was on LM.

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.

### Table 3. Infarction-causing artery

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

### Table 4. Lethality depending on the infarction-causing artery

<table>
<thead>
<tr>
<th></th>
<th>LM</th>
<th>LAD</th>
<th>LCX</th>
<th>RCA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deceased</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=6</td>
<td>4 (66.7%)</td>
<td>27 (18%)</td>
<td>5 (10.4%)</td>
<td>4 (4.1%)</td>
</tr>
</tbody>
</table>

### 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
Prognosis in Patients with Myocardial Infarction with ST-Elevation Depending on the Timing of Interventional ...

other authors (4-7,11,13). It should be noted that the lethality in patients with PCI, conducted by the end of the 3rd hour and by the end of the 6th hour after the onset of the infarction, 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 medications (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 жени, 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 болнично лечение е циркулаторна и остра 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

According to our data, the artery, which is most commonly responsible for STEMI, is LAD, the second most common one is RCA, followed by LCX and LM. A similar distribution of the artery responsible for infarction is observed in other studies (12). The high lethality rate in patients with LM and LAD occlusion is logical because in those cases the infarctions are more extensive, and the left ventricular systolic function – worse.

The results from our study gave grounds for the establishment and recommendation of the following factors, determining an elevated risk of death in patients with AMI with ST-elevation:

1. Revascularization after the 6th hour;
2. 65 years of age or older;
3. Female gender;
4. EF<35.0%;
5. Thrombotic occlusion of LM and LAD.

CONCLUSION

The patients with early hospitalization and revascularization by the 6th hour have lower lethality rates, both in-hospital and by the end of the 6th month after the onset of the infarction. The majority of the deceased are 65 years of age or older, more frequently women, with worse left ventricular function (EF<35.0%) and more frequently with a thrombotic obstruction of LM and LAD. The main cause of death during the hospital stay is circulatory and acute left-sided heart failure, and after discharge – SCD. The additional decrease in the lethality rate in patients with STEMI requires organizational measures, which would ensure earlier hospitalization and SCD prevention in the post-discharge period.

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

2. Bersma E, Maas DC, Deckers JW, Simoons ML.
Prognosis in Patients with Myocardial Infarction with ST-Elevation Depending on the Timing of Interventional ...


