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Two-year survival of STEMI patients in Slovakia. An analysis of the SLOVak registry of Acute Coronary Syndromes (SLOVAKS)

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SÚHRN

V roku 2011 na Slovensku bol nepretržitý 24/7 program primárnej PKI (P-PKI) u STEMI vykonávaný v štyroch PKI centrách. Vychádzajúc z geografického rozloženie P-PKI centier a počtu obyvateľov pripadajúcich na jedno P-PKI centrum (1,37 mil. obyv./P-PKI centrum) v danom období bolo možné hodnotiť dostupnosť P-PKI ako suboptimálnu. Cieľom analýzy je vyhodnotenie 2-ročného prežívania pacientov so STEMI prijatých do nemocníc v roku 2011 a posúdenia prežívania vo vzťahu k použitej liečebnej stratégii. Pre analýzu klinických údajov bola použitá databáza SLOVenského registra Akútnych Koronárnych Syndrómov. V tejto analýze sme vyhodnotili 1 580 prípadov AKS (STEMI, NAP a non-STEMI).
Zo všetkých STEMI 80,6 % pacientov bolo hospitalizovaných v P-PKI centrách, a to buď formou primárneho, alebo sekundárneho transportu. Primárna reperfúzna liečba bola vykonaná u 76 % pacientov (64,7 % P-PKI, 11,3 % fibrinolýza). 82,3 % pacientov so STEMI bolo prijatých do 12 hodín od vzniku príznakov. Medián celkového ischemického času bol 219 min. V analyzovanej kohorte pacientov so STEMI bola nemocničná mortalita 5,99 %, 30-dňová mortalita 10,7 %, ročná mortalita 14,6 % a dvojročná mortalita 17,6 %. Dvojročné prežívanie pacientov liečených P-PKI bolo signifikantne lepšie oproti pacientom bez primárnej reperfúznej liečby (HR 0,4, $p < 0,001$) a porovnateľné s pacientami liečenými fibrinolýzou ($p = 0,66$). 90,7 % pacientov liečených fibrinolýzou však následne absolvovali koronarografické vyšetrenie a podľa potreby rescue, či odloženú PKI. Farmakoinvazívna stratégia reprezentovala podskupinu s najlepšou prognózou, avšak benefit oproti pacientom s P-PKI nedosiahol štatistickú významnosť ($p = 0,164$). V skupine zomretých pacientov liečených P-PKI medián celkového ischemického času (interval príznaky–PKI) bol 300,5 min, kým u pacientov liečených P-PKI, avšak prežívajúcich dva roky bol 230,5 min ($p = 0,043$). Signifikantne horšie dvojročné prežívanie mali diabetici (HR 1,63, 95%, $p = 0,03$).
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ABSTRACT

Four 24/7 P-PCI centres performed emergency program in 2011 in Slovakia. In view of the geographic relations and number of residents per centre (1.37 mil. residents/centre) it was possible to consider access to P-PCI as sub-optimal. The aim of the study is an evaluation of two-year survival of STEMI cohort admitted to hospitals in 2011 and confrontation of survival with used treatment strategy. Clinical outputs were analysed using data acquired from the SLOVak registry of Acute Coronary Syndromes (SLOVAKS). In this analysis we have evaluated 1 580 cases of ACS (STEMI, UAP and NSTEMI).

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80.6% of STEMI patients have been admitted into P-PCI-centres via primary or secondary transfer. Primary reperfusion treatment was accomplished in 76.0% of patients (64.7% primary PCI, 11.3% fibrinolysis). 82.3% STEMI patients were admitted within 12 h of symptoms onset. The median of total ischemic time was 219 minutes. In the analysed cohort of STEMI patients an in-hospital mortality of 5.99% was recorded, a 30-day mortality of 10.7%, a one-year mortality of 14.6% and a two-year mortality of 17.6%. The two-year survival of patients treated with P-PCI was significantly better compared with patients without primary reperfusion treatment (HR 0.4, $p < 0.001$) and comparable with patients treated by thrombolysis ($p = 0.66$). A total of 90.7% of patients after thrombolysis, however, subsequently underwent coronary angiography and as needed a rescue or delayed PCI was performed. Pharmacoinvasive strategy represented the sub-group with the best prognosis, even though the benefit versus the sub-group treated with primary PCI did not achieve statistical significance ($p = 0.164$). In patients with P-PCI who died, the median of the total ischemic time (the symptoms–PCI interval) was 300.5 min, while in the patients who survived to two years the median was 230.5 min ($p = 0.043$). Significantly worse two-year survival was observed in diabetics (HR 1.63, 95% CI, $p = 0.03$).
Conclusions: In 2011 it was possible to record a continuation of the favourable trend in the management of patients with STEMI in Slovakia. The greatest challenge for health care workers in the coming years will be to ensure primary reperfusion treatment for patients in the desired time intervals. Our analysis confirms the excellent prognosis of patients managed through a pharmacoinvasive strategy. The mid-term survival of patients after ACS in Slovakia points to worse results in comparison with results from abroad, which could be associated with an unfavourable length of total ischemic time and less consistent secondary prevention could be speculated.

Keywords:
Mortality
Reperfusion strategy
SLOVAKS
STEMI
Survival
Time intervals

Introduction

International clinical experience has confirmed that the implementation of evidence based medicine into daily practice can on the one hand impact the incidence and prevalence of STEMI in a principal way and on the other hand affect the prognosis of these patients. Implementation of the official ESC-STEMI guidelines into clinical practice, however, is not necessarily easy and differs significantly in individual countries to the extent that it involves time delays as well as in-depth implementation. Among the possibilities for speeding up implementation there are the use of targeted activities and organisational measures. Four workplaces in Slovakia (Bratislava, Nitra, Banská Bystrica and Košice) performed 24-hour emergency medical services for primary percutaneous intervention (P-PCI) in 2011, and the theoretical net time for transport from a district hospital to PCI centres ranges from 15–120 min. In view of the geographic relations and number of residents per centre (1.37 mil. residents/centre) it was possible in 2011 to designate access to P-PCI as sub-optimal. The aim of the study is to evaluate two-year survival of STEMI cohort admitted to hospitals in 2011 and to compare survival with used treatment strategy.

Patients and methods

Changes in clinical practice and clinical outputs were analysed using data acquired from the SLOVak registry of Acute Coronary Syndromes (SLOVAKS). SLOVAKS registry was based in 2007 under the patronage of the Slovak Society of Cardiology and National Institute of Health Information and Statistics. The data from 2007 to 2008 comes from continuous all year character of data collection [1]. Since 2011 Slovak Society of Cardiology has been organizing SLOVAKS-2 registry based on periodical two--month snapshot data collection. The substantial change in methods of data acquisiton in 2011 brought better hospital compliance, improved discipline of reporting and more reliable data collecting [2]. Survival analysis relates to STEMI patients admitted to hospitals in August and September 2011. Date of death and two-year survival information in individual patient was picked up from central web portal enabling verification of current health insurance status.

Statistical analysis

Statistical analysis was performed using the SPSS programme. Descriptive statistics was used for description of the sample. χ^2-tests were used to explore associations between nominal variables and Mann-Whitney U-tests for analysis of association between mortality and continual variables. Kaplan-Meier plots were created and log-rank tests calculated to analyse the association of mortality and demographic and medical variables.

Results

We have evaluated data from 69 treatment sites in Slovakia. These sites represent 85 % of all workplaces treating ACS patients in the country, representing all cardiac centres and local hospitals as well. In this analysis we have evaluated 1 580 cases of ACS (STEMI, UAP and NSTEMI). STEMI cases represent 30.6% of all ACS (Table 1). The average age of patients with STEMI was 63.8 (± 12.8). Representation of women was 30% (Table 2). Comorbidity and risk factors are presented in Table 3.

80.6% of STEMI patients have been admitted into PCI-centres. It was done as the primary hospitalization or secondary transfer. The proportion of STEMI admitted via EMS reached 88.7%. Primary reperfusion treatment was accomplished in 76.0% of patients (64.7% primary PCI, 11.3% fibrinolysis). 82.3% STEMI patients were admitted within 12 h of symptoms onset (Fig. 1). The median of total ischemic time in 2011 was 219 min (Fig. 2). There was a significant increase of total number STEMI patients treated with primary reperfusion therapy ($p < 0.001$) and primary PCI ($p < 0.001$) as well within years 2007 to 2011 (Fig. 3). We have documented significant hospital mor-

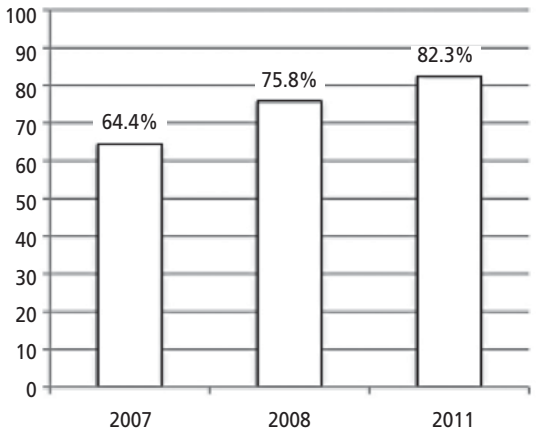

Fig. 1 – Ratio (%) of STEMI patients admitted within 12 h of symptoms onset.

Table 1 – The number of ACS cases reported in 2011 and type of ACS distribution.

	n (2-month data)	%
ACS	1 580	100
STEMI	484	30.6
NSTEMI	565	35.8
UA	518	32.8
ACS with LBBB	13	0.8

Table 2 – Age and sex distribution in STEMI patients.

	n (2-month data)	Age (average)	S.D.
All	484	63.8	12.8
Male	339 (70%)	60.9	11.5
Female	145 (30%)	70.7	13.2

tality decrease since 1998, when the first relevant STEMI analysis in Slovakia has been done (Fig. 4).

In the analysed cohort of patients with STEMI from the year 2011 an in-hospital mortality of 5.99% was recorded, a 30-day mortality of 10.7%, a one-year mortality of 14.6% and a two-year mortality of 17.6%. The two-year survival of patients is illustrated in Fig. 5. Women have a tendency towards worse survival; however, the difference versus men did not reach a level of significance ($p = 0.152$) (Fig. 6). Our analyses confirmed that patients with STEMI have a worse in-hospital prognosis than patients with ACS without elevation of ST (NSTE-ACS); however, in line with experiences from abroad it is shown that surviving to one year is gradually balanced out and in the case of NSTEMI the prognosis is in the end significantly worse (Table 4).

The two-year survival of patients treated with primary PCI was significantly better compared with patients

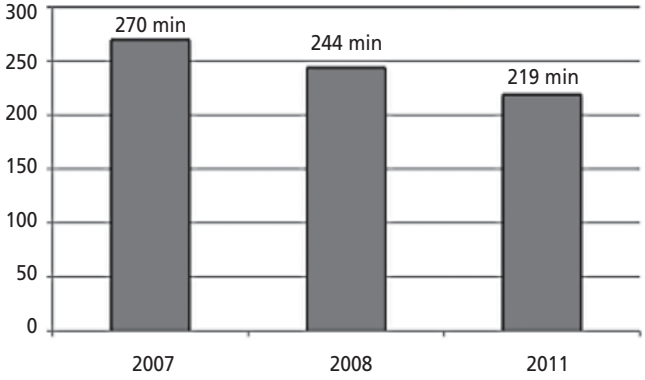

Fig. 2 – Median of interval "symptoms-PCI" (total ischemic period) in patients treated with primary PCI.

Table 3 – Comorbidity and risk factors analysis.

	All	Male	Female	*p*
Diabetes	21.90%	18.20%	30.30%	0.003
Arter. hypertension	68.00%	63.40%	78.60%	0.001
Hyperlipoproteinemia	44.80%	44.20%	46.20%	0.691
Smoking	37.60%	44.50%	21.40%	< 0.001
Previous PCI	7.00%	7.70%	5.50%	0.396
Previous CABG	0.60%	0.90%	0.00%	0.256
Previous stroke	8.30%	7.70%	9.60%	0.001
Renal insufficiency	7.60%	5.30%	13.10%	0.003
Obesity	25.40%	21.20%	35.20%	0.001

Table 4 – The comparison of mortality between various types of ACS in Slovakia (NTSE-ACS data comes from [4]).

	STEMI	UA	NSTEMI
Hospital mortality	5.99%	NA	3.90%
30-day mortality	10.70%	0.96%	7.65%
6-month mortality	13.80%	3.65%	14.59%
12-month mortality	14.60%	6.54%	19.22%

without primary reperfusion treatment (HR 0.4, 95% CI, $p < 0.001$) and comparable with patients treated by thrombolysis ($p = 0.66$). A total of 90.7% of patients after thrombolysis, however, subsequently underwent coronary angiography and as needed a rescue or delayed PCI was performed. Fig. 7 illustrates the prognosis according to the individual treatment strategies.

For the purpose of the analysis all cases of patients treated with thrombolysis and subsequently examined

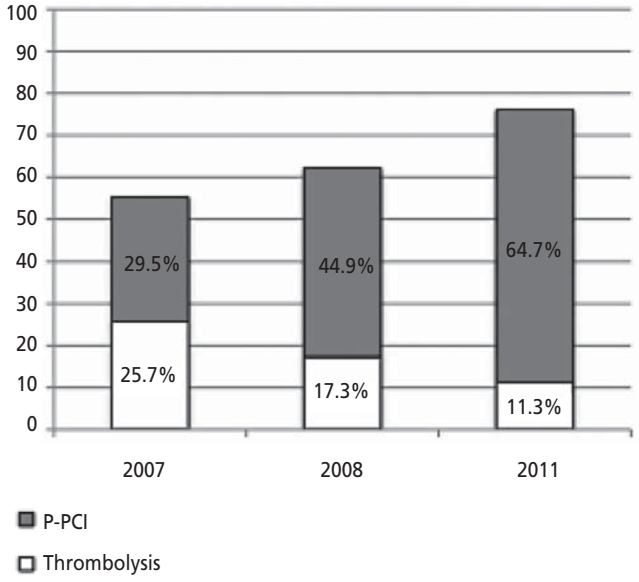

Fig. 3 – Change of reperfusion strategy within period 2007–2011.

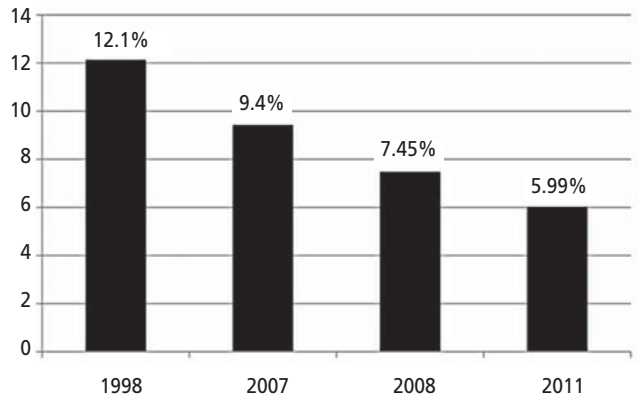

Fig. 4 – Hospital mortality in STEMI patients during 1998–2011. (Data of 1998 comes from [3].)

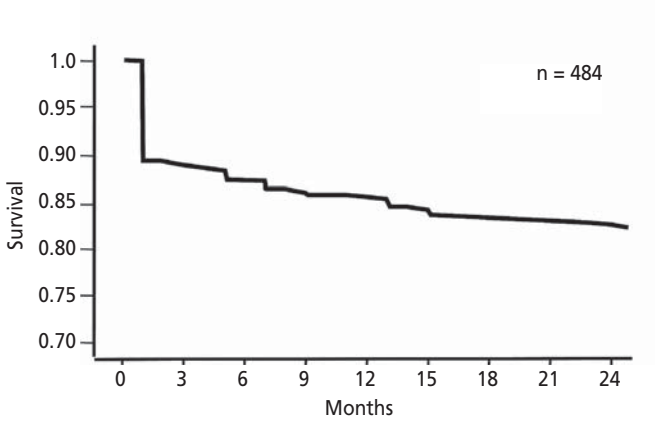

Fig. 5 – Two-year survival of STEMI patients.

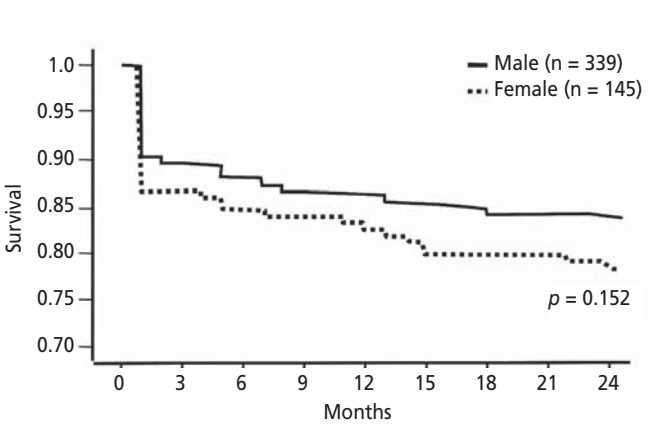

Fig. 6 – The comparison of men and women in two-year survival of STEMI patients ($p = 0.152$).

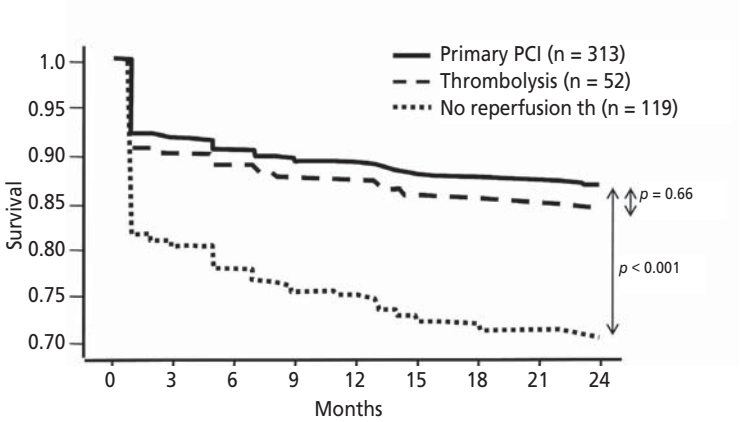

Fig. 7 – The comparison of the two-year survival in patients treated with primary PCI, thrombolysis and patients without reperfusion treatment.

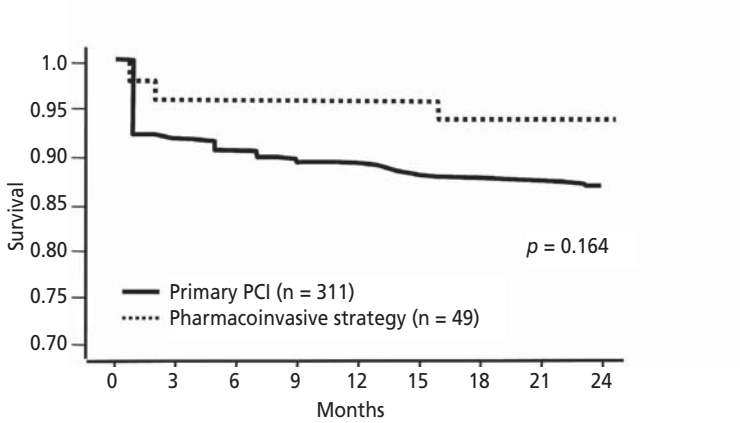

Fig. 8 – The comparison of the two-year survival between patients treated with pharmacoinvasive strategy or primary PCI.

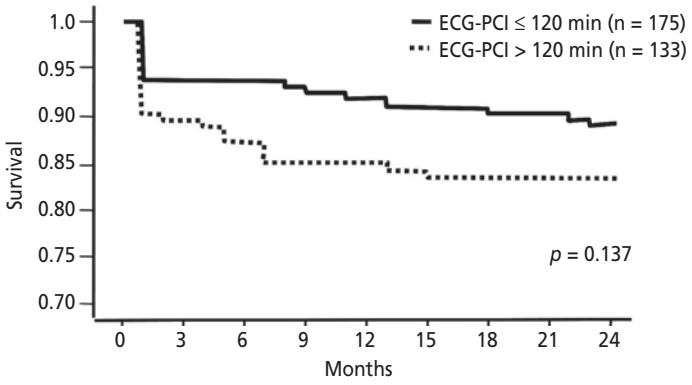

Fig. 9 – The comparison of the two-year survival between patients with primary PCI treated with ECG-PCI interval > 120 min and ECG--PCI interval ≤ 120 min.

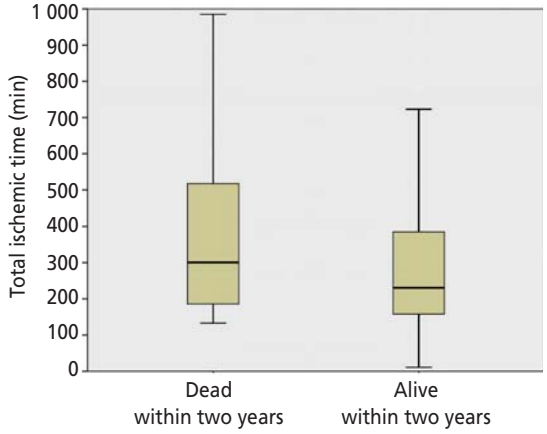

Fig. 10 – The comparison of total ischemic time (symptoms–PPCI interval) between subgroup of two-year survivors and subgroup of patients who have died.

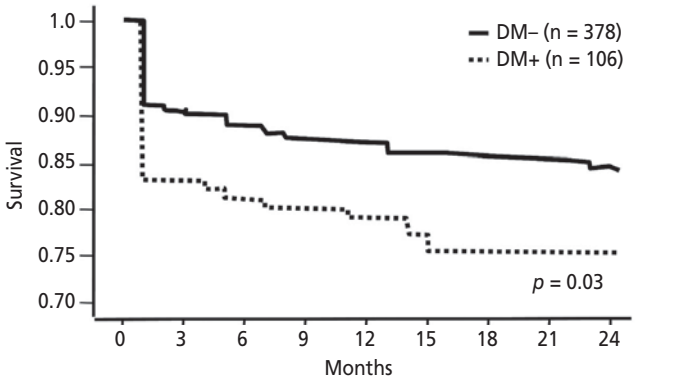

Fig. 11 – The comparison of the two-year survival between STEMI patients with diabetes and without diabetes.

by coronary angiography (± PCI) were considered as the pharmacoinvasive strategy, and this is independent of whether the subsequent coronary angiography was performed within 24 h or later. The subgroup with pharmacoinvasive strategy tended to have the best prognosis, however the benefit versus the sub-group treated with primary PCI did not achieve statistical significance (p = 0.164) (Fig. 8). The number of patients in pharmacoinvasive group was small and study was not powered to confirm superiority in this finding.

We independently analysed the survival of the subgroup of patients treated with primary PCI in relation to whether or not they fulfilled the criterion interval of ECG-PCI ≤ 120 min. Fig. 9 illustrates the trend in favour of patients satisfying this criterion; the difference, however, did not achieve statistical significance (p = 0.137). In patients with primary PCI who died in the subsequent period, the median of the total ischemic time (the symptoms–PCI interval) was 300.5 min, while in patients who survived to two years the median was 230.5 min. This difference was statistically significant (p = 0.043) and confirms the known fact that the battle over time in patients with STEMI is relevant (Fig. 10). Significantly worse two--year survival was observed in diabetics (HR 1.63, 95% CI, p = 0.03) (Fig. 11).

Discussion

In the last 15 years in Slovakia we have systematically recorded a decrease in the mortality of STEMI. This can be explained by better organisation of the transport, improved availability of reperfusion therapy, mainly P-PCI, and introduction of modern pharmacotherapy. With the assessments of these data, however, it is necessary to be aware that the presented decrease of hospital mortality in the SLOVAKS registry, or foreign registries, do not reflect the real seriousness of the disease, since a notable portion of patients with STEMI still die before the first contact with the health care system. The most common cause of death in this phase is malignant arrhythmia, mainly ventricular fibrillation [5–7]. These patients logically do not figure into the presented statistics. This "hidden" portion of the mortality of STEMI has not changed very much. The overall mortality of STEMI is therefore the result not only of the level of immediate health care, but has a broader societal and social background. An uneducated patient who does not know the symptoms of a typical myocardial infarction can hesitate with seeking help even for several hours, and his "total ischemic time" is dramatically extended, thus increasing the risk of sudden death as a consequence of malignant dysrhythmia, or a later death resulting from cardiogenic shock due to serious dysfunction of the left ventricle. Since 2013 two additional cardiac centres have introduced continuous 24-h operation of primary PCI in Slovakia. This fact significantly contributes to increasing the accessibility of primary PCI, the shortening of overall ischemic time and thus improvement in patient prognosis nowadays.

Our analysis from 2011 documents very favourable in-hospital mortality (5.99%) in the group of STEMI patients. A comparison of the different types of ACS points

to worse in-hospital and 30-day mortality with STEMI (5.99% and 10.7%, respectively) versus NSTEMI (3.9% and 7.65%, respectively) [2,4]. In line with experiences abroad, after one year the situation is reversed in Slovakia, since 12-month mortality was 14.6% with STEMI and 19.2% with NSTEMI. In literature in-hospital mortality has been reported between 7 and 9.7% and the 30-day mortality between 11.1 and 14% [8–10]. Both in-hospital and 30-day mortality rates after STEMI have been lower in clinical trials compared to registries and reports in patients not in clinical trials. This has been explained by enrollment of a lower risk population and better adherence to proven therapies in the former.

More contemporary reports of patients not enrolled in trials have documented a continued decline in mortality in STEMI patients [11–13]. For example, outcomes were presented in a 2012 report of 6 707 STEMI patients in four French nationwide registries conducted five years apart (1995, 2000, 2005, and 2010) [14]. The following findings were noted:

There were significant decreases in crude 30-day mortality (from 13.7 to 4.4 percent) and mortality standardized to 2010 population characteristics (from 11.3 to 4.4%). These declines were seen irrespective of the type of reperfusion (fibrinolysis or PCI) and in patients who were not reperfused.

Time from symptom onset to hospital admission decreased, with a shorter time from onset to the first call, and broader use of mobile intensive care units.

During this time, the average age fell and the prevalence of most risk factors increased.

The use of reperfusion therapy increased from 50 to 75%, driven mostly by an increase of the use of PCI, as did the use of recommended preventative medical therapies.

In contrast to the short-term outcomes, which are worse with ST-elevation myocardial infarction (STEMI), long-term outcomes have been similar or worse with non-ST elevation myocardial infarction (NSTEMI). The largest direct comparison comes from the GUSTO-IIb trial performed in the early 1990s of 12,142 patients with STEMI, NSTEMI (using only CK-MB, not troponins, for diagnosis), or unstable angina [15]. The mortality rate at 30 days was lower with NSTEMI than STEMI (3.8 versus 6.1%). In contrast, the mortality at one year was similar (8.8 for NSTEMI versus 9.6% for STEMI). However, outcomes from patients with NSTEMI managed more recently were lower in the ISAR-REACT 4 trial, in which mortality at one year was about 4.4% [16].

Even though direct comparison of Slovak data with data from abroad is problematic, it is obvious that upon comparing the mortality, the data mainly from the in-hospital phase holds up worthily. The mid-time survival of patients in Slovakia tends to be markedly worse compared with data from abroad. The explanations for this could be varied; however, the possibility of worse secondary prevention is suggestive and in patients with STEMI also the on-average longer total ischemic time, resulting in worse functioning of the left ventricle upon discharging. There is still remarkable portion of patients treated with primary PCI with ECG-PPCI interval above recommended 120 (resp. 90) minutes [17]. Results of STREAM [18] study and SLOVAKS registry as well confirm the idea of pharmacoinvasive strategy suitable for all patients where recommended ECG-PPCI interval is unreachable. The National guidelines related to prehospital management of STEMI patients were published recently and this could help to improve total ischemic time and optimize antithrombotic medical treatment in Slovakia for the future [19].

Limitations of the SLOVAKS registry follow from the voluntary basis of reporting cases of ACS. It was not possible to verify whether the linked workplaces reported all consecutive cases of ACS in the subsequent period, and several workplaces in Slovakia were not connected to the registry at all. According to a qualified estimate, however, the SLOVAKS registry in 2011 covered 80% of cases in-hospital STEMI, which allows for the assumption of sufficient representativeness of the analysed sample. According to some works, the occurrence of STEMI is higher in the winter months; therefore, the annual calculation of our analysed two-month sample (August-September) could be an underestimate.

Conclusion

In 2011 it was possible to record a continuation of the favourable trend in the management of patients with STEMI in Slovakia. Our experience showed that targeted initiatives aimed at implementing official ESC guidelines into clinical practice are meaningful and can significantly change the management of patients and improve clinical outcomes in a relatively short period of time. The share of patients admitted within 12 h grew significantly; the share of patients treated with primary PCI improved; the overall ischemic time was shortened; and the in-hospital mortality of STEMI declined significantly. A detailed analysis, however, points out several aspects in which there is potential for further improvement of both the short-term and long-term prognosis of patients with STEMI. It will be possible to markedly influence the total ischemic time primarily through further educational activities focused on typical symptoms of STEMI and the need for timely calling of emergency medical help. The greatest challenge for health care workers in the coming years will be to ensure primary reperfusion treatment for patients in the desired time intervals. In 2011 the importance of pre-hospital fibrinolysis provided to patients by EMS personnel when it is not possible to reach primary PCI in the required time window was still undervalued. Our analysis confirms the excellent prognosis of patients managed through a pharmacoinvasive strategy. The mid-term survival of patients after ACS in Slovakia points to worse results in comparison with results from abroad, which could be associated with less consistent secondary prevention and in patients with STEMI with an unfavourable length of total ischemic time.

Conflict of interest
There exists no actual or potential conflict of interest related to this paper.

Funding body
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Ethical statement
The research related to this paper was done according to ethical standards.

Informed consent
The patients agreed to participate in the research related to this paper. Informed consent has been signed as a part of the protocol.

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