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Baseline characteristics, time-to-hospital admission and in-hospital outcomes of patients hospitalized with ST-segment elevation acute coronary syndromes, 2002 to 2005

ZLATKO PEHNEC (✉) •
ANDREJA SINKOVIČ •
BORUT KAMENIK •
MARTIN MARINŠEK, •
FRANCI SVENŠEK
Department of Internal Medicine
University Hospital Maribor
Ljubljanska 5
SI-2000 Maribor, Slovenia
Phone: 0038623212850
E-mail: zlatko.pehnec@ukc-mb.si

ZLATKO PEHNEC • ANDREJA SINKOVIČ • BORUT KAMENIK • MARTIN MARINŠEK • FRANCI SVENŠEK

ABSTRACT

Objective. The purpose of this study was to retrospectively determine baseline patient characteristics, time-to-hospital admission, utilization of reperfusion therapy and outcomes of patients hospitalized with ST-segment elevation acute coronary syndromes (ACS) between 2002 and 2005, particularly after 24-h primary percutaneous coronary intervention (PCI) was introduced in 2004.

Methods. Included were all patients admitted to the intensive care unit (ICU) from 2002 to 2005 who met the criteria for ACS. Information on patients' demographic characteristics, medical history, time-to-hospital admission, clinical characteristics on admission, laboratory examinations, ECG findings, treatments, hospital duration, and in-hospital outcomes was collected by completing a standardized case report form.

Results. There was a sustained increase in admissions between 2002 and 2005, altogether 899 patients were hospitalized. A significant decrease in time-to-hospital admission was achieved. More patients arrived within 4-6 hours (16.3% in 2002 vs. 31.5% in 2005) and less after 12 hours (35.0% in 2002 vs. 13.4% in 2005). A significant increase in primary PCI rate was achieved (16.9% in 2002 vs. 90% in 2005, $P<0.001$). Consequently, the rate of thrombolysis, postponed PCI and nonreperfusion medical therapy decreased. From 2002 to 2005, total in-hospital stay decreased significantly (15.4 ± 13.0 days vs. 7.8 ± 8.5 days, $P<0.001$), in-hospital mortality insignificantly (11.3% vs. 7.2%).

Conclusion. Despite the significant increase in primary PCI between 2002-2005, there was only an insignificant decrease in in-hospital mortality. Further shortening the time-to-hospital admission and increasing primary PCI among older hemodynamically unstable ACS patients, particularly those with cardiogenic shock, could achieve an additional decrease in mortality.

Key words: acute coronary syndrome, acute myocardial infarction, time-to-hospital admission, prognosis, management, percutaneous coronary intervention, mortality

Introduction

Advances in reperfusion therapy have contributed to a reduction in mortality and reinfarction rates. Both thrombolytic therapy and percutaneous coronary intervention may result in successful reperfusion of infarct-related arteries and lead to a decrease in morbidity and mortality. It has become increasingly evident that primary Increasingly evident that primary percutaneous coronary intervention (PCI) could be a superior reperfusion strategy if performed by an experienced team within 90 minutes of the first medical contact. (1-3)

Widespread implementation of randomized clinical trial results and guidelines has been disappointing in the USA and Europe. (4-6) Less than 25% of USA hospitals have facilities to perform primary PCI, and even fewer have

24-h availability. There are considerable geographic and urban-rural differences in quality of care for patients with acute myocardial infarction. (7,8)

In Slovenia the highest prevalence of cardiovascular diseases has been documented in the eastern region and the lowest in the western region of the country. Differences were statistically significant for stroke, angina pectoris and hypertension, but not for myocardial infarction. (9) University Hospital Maribor covers an area with approximately 820,000 inhabitants and has the facilities to perform primary PCI for the eastern part *of Slovenia. From 2004 there is 24-h access to primary PCI. Our catheterization laboratory and and Intensive care unit (ICU) have met all the criteria of a high-volume center (>200 patients/year and >75 patients/ year per interventional cardiologist). Owing to small distances and good traffic connections, door to balloon time for primary PCI is below 90 minutes for the majority of patients.

The purpose of this retrospective study was to determine baseline patient characteristics, time from onset of symptoms to interventional-hospital admission, application of reperfusion therapy and outcomes of patients hospitalized with ST-segment elevation acute coronary syndromes in the years 2002 to 2005, particularly for the data after 24-h primary PCI was introduced in 2004.

Patients and Methods

Included were all patients admitted to the ICU between 2002-2005 with ST-segment elevation on ECG and who met the criteria for acute coronary syndrome (ACS). The patients entered in the study had to be alive at the time of hospital presentation, had to be admitted with ACS as a presumptive diagnosis and had to have ST-segment elevation on ECG. Information on patients' demographic characteristics, medical history, time delay between onset of symptoms to PCI-hospital arrival, clinical characteristics on admission (Killip classes), laboratory findings (troponin T, electrolytes, blood glucose, urea, creatinine), ECG findings, treatment approaches, hospital duration, and in-hospital outcomes was collected by completion of a standardized case report form.

For all patients, the initial diagnosis was based on a history of sustained chest pain and the finding of ST-elevation on initial ECG. ST-elevation myocardial infarction (STEMI) was diagnosed as persistent angina pectoris for more than 20 min, ST-segment elevation of more than 1 mm in at least two standard leads or more than 2 mm in at least two contiguous precordial leads, or the presence of a left bundle branch block. It was later confirmed by an increase of at least twice the normal value of troponin T. Unstable angina was diagnosed as persistent angina pectoris for more than 20 min, ST-segment elevation, but with normal values of troponin T, or a minimal increase below twice the normal value. The discharge diagnosis was made by the attending physician and based on the following categories: anterior Q-wave myocardial infarction (anterior Q-wave MI), nonanterior Q-wave myocardial infarction (nonanterior Q-wave MI), non Q-wave myocardial infarction (non Q-wave MI), and unstable angina (UA).

Time-to-hospital admission was defined as the time between the onset of sustained chest pain and admission to the emergency department (ED) of Maribor hospital.

The Killip class was assigned to each patient on the basis of the severity of signs of heart failure at first assessment. Killip class I was defined as the absence of rales in the lung fields and the absence of an S3 heart sound; Killip class II was defined as rales in <50% of the lung fields, the presence of an S3 or jugular venous distension; Killip class III was defined as rales in >50% of the lung fields and pulmonary edema; and Killip class IV was defined as the presence of cardiogenic shock. Cardiogenic shock was defined as a clinical state of sustained hypotension characterized by systolic blood pressure of less than 90 mm Hg, lasting more than 30 min with evidence of tissue hypoperfusion such as cold and wet skin and oliguria <30 mL/h.

Primary PCI was performed in the catheterization laboratory situated close to the ED to achieve primary PCI without delay. Average door-to-balloon time was usually under 30 minutes. Thrombolytic therapy with Alteplase 100 mg over 90 minutes was performed in the ICU immediately after the patient's arrival.

The patients received morphine sulfate 2 to 4 mg IV, oxygen, sublingual nitroglycerin, aspirin (MONA) in referral hospitals or during emergency transport, and oral clopidogrel 300mg, IV glycoprotein IIb/IIIa inhibitors and unfractionated/LMW heparin in the ED or catheterization laboratory if primary PCI was planned.

Statistical methods

Statistical analysis was performed with the SPSS 12.0 statistical package. Percentage distributions, mean values and standard deviations were used to present background information. The ANOVA and chi-square tests were used to calculate statistically significant differences of background information.

Logistic regression analysis was performed to calculate the risks associated with patient death. The significance, odds ratios and confidence intervals were calculated for univariate analysis. Variables with a significant univariate association ($P<0.05$) with risk of death were included in the final multivariate binary logistic regression model calculated by Wald method. Diagnostic routines (Hosmer-Lemeshow test for lack of fit) were used for the final prediction model selection.

Results

Clinical characteristics of patients with ST-segment elevation ACS hospitalized in the ICU between 2002 and 2005 are listed in table 1. There was a sustained increase of hospitalized patients from 2002 to 2005, altogether 899 patients were hospitalized during the four years. There was a similar proportion of anterior Q-wave, nonanterior Q-wave, non Q-wave MI and UA within different years. Time-to-hospital admission was available for 784 patients. During the four-year period a significant decrea-

Table 1. Clinical characteristics of patients with ST-segment elevation acute coronary syndromes (ACS) hospitalized between 2002 and 2005 (N = 899).

	2002 N = 160	2003 N = 183	2004 N = 277	2005 N = 279	Total N = 899	P-value
Age (years) mean ± SD	63.2 ± 13.4	63.1 ± 12.7	61.5 ± 14.4	62.0 ± 12.5	62.3 ± 13.3	0.454+
Male (%)	62.5	68.3	69.7	67.7	67.5	0.478*
Anterior Q-wave MI (%)	51.3	39.3	40.2	38.7	41.5	0.053*
Nonanterior Q-wave MI (%)	44.4	47.0	51.1	53.4	49.8	0.252*
Non-Q MI (%)	1.3	8.7	5.4	5.0	5.2	0.021*
STEMI altogether (%)	97.0	95.0	96.7	97.1	96.5	
Unstable angina (%)	3.1	4.9	3.3	2.9	3.5	0.671*
Previous MI (%)	22.5	21.3	10.1	13.3	15.6	<0.001*
Time to hospital admission (N=784)						
< 3 hours (%)	37.5	45.4	43.5	38.2	41.1	0.329*
4 – 6 hours (%)	16.3	20.9	26.9	31.5	24.9	0.003*
7 – 12 hours (%)	11.3	12.9	15.7	16.8	14.5	0.395*
> 12 hours (%)	35.0	20.9	13.9	13.4	19.5	<0.001*
Systolic blood pressure (BP) (mmHg) mean ± SD	128.3 ±28.6	127.9 ±29.4	132.5 ±25.1	128.2 ±28.8	129.2 ±28.0	0.262+
Diastolic blood pressure (mmHg) mean ± SD	74.5 ±18.5	73.0 ±17.9	78.0 ±17.8	75.5 ±16.9	75.2 ±17.8	0.038+
Peak troponin T (μg/L) mean ± SD	5,0 ± 6.2	3,9 ± 4.1	5,9 ± 5.4	5,5 ± 5.7	5,3 ± 5.4	0.001+
Killip I (%)	54.4	62.3	73.3	69.9	66.6	<0.001*
Killip II (%)	30,6	19.7	16.6	17.6	20.0	0.003*
Killip III (%)	5.0	7.7	4.3	4.3	5.1	0.368*
Killip IV (%)	10.0	10.4	5.8	8.2	8.2	0.262*
Primary PCI (%)	16.9	51.4	83.8	89.9	67.1	<0.001*
Thrombolysis (%)	37.5	18.0	1.1	0.4	10.8	<0.001*
Postponed PCI (%)	8.8	5.5	4.0	2.5	4.7	0.024*
Nonreperfusion medical therapy (%)	36.9	25.1	11.2	7.2	17.4	<0.001*
Coronary artery bypass grafting (CABG) during hospitalization (%)	3.1	6.0	1.4	3.2	3.2	0.061*
Previous CABG (%)	1.3	1.1	3.6	1.4	2.0	0.148*
Hospital stay ICU (days)	3.6 ±6.3	3.3 ±3.3	2.6 ±3.7	2.3 ±1.9	2.9 ±3.8	0.001+
Total hospital stay (days)	15.4 ±13.0	13.3 ±12.9	9.3 ±10.2	7.8 ±8.5	10.7 ±11.3	<0.001+
In hospital mortality (%)	11.3	12.0	8.3	7.2	9.2	0.243*
In hospital mortality without shock (%)	4.9	4.3	5.0	2.0	3.9	0.280*
In hospital mortality Killip I class (%)	3.4	0.0	3.0	1.0	1.8	0.138*
In hospital mortality Killip II class (%)	6.1	11.1	13.0	6.1	8.9	0.547*
In hospital mortality Killip III class (%)	12.5	21.4	8.3	0.0	10.9	0.365*
In hospital mortality Killip IV class (%)	68.8	78.9	62.5	65.2	68.9	0.718*

Anterior Q-wave myocardial infarction (Anterior Q-wave MI), Intensive care unit (ICU), myocardial infarction (MI), Nonanterior Q-wave myocardial infarction (Nonanterior Q-wave MI), Non Q-wave myocardial infarction (Non Q- wave MI), percutaneous coronary intervention (PCI), ST-elevation myocardial infarction (STEMI), Unstable angina (UA)
* Chi-square test
+ One-Way ANOVA test

se in time-to-hospital admission was achieved. Compared to 2002, in 2005 more patients arrived within 4-6 hours (16.3% vs. 31.5%) and within 7-12 hours (11.3% vs. 16.8%), and less after 12 hours (35.0% vs. 13.4%).

Between 2002 and 2006 there was no significant difference in Killip classes (Killip I/II 85.0% in 2002, vs. 87.5% in 2005, Killip III/IV 15.0% in 2002 vs. 12.5% in 2005). From 2002 to 2005 a significant increase in primary PCI rate was achieved (16.9% vs. 90%); consequently thrombolysis, postponed PCI and non-reperfusion medical therapy rate decreased (37.5% vs. 0.4%; 8.8% vs. 2.5% and 36.9% vs. 7.2% respectively).

From 2002 to 2005 there was a significant decrease in total in-hospital stay (15.4±13.0 days vs. 7.8±8.5 days) and a tendency to decrease in-hospital mortality (11.3% vs. 7.2%).

In patients with heart failure the mortality rate remained high, particularly in those with cardiogenic shock. Total in-hospital mortality for patients in Killip classes II and III was 5 to 6 times higher and in Killip class IV even more than 30 times higher in comparison with Killip class I (table 1). As shown in table 2, non-survivors were older (72.1 vs. 61.2 yrs, P<0.001), with more frequent anterior infarction (61.4% vs. 39.5%, P<0.001), longer time-to-hospital admission (4-6 hours 11.1% vs. 26.1%, and >12 hours 31.7% vs. 18.4%), lower blood pressure (108.6/63.8 mmHg vs. 131.4/76.6 mmHg, P<0.001), with a great deal of Killip class IV at presentation (61.4% vs. 2.8%, P<0.001), with less primary PCI (41.5% vs. 69.7%, P<0.001), more nonreperfusion medical therapy (43.9% vs. 14.7%, P<0.001) and longer ICU hospital stay (5.9 days vs. 2.5 days, P<0.003).

To determine the most significant risk factors for death, a multivariate prediction model was calculated with logistic

Table 2. Comparison of survivors and nonsurvivors with ST-segment elevation acute coronary syndromes ACS hospitalized between 2002 and 2005 (N = 899).

	Survivors N = 816	Non-survivors N = 83	chi-square	OR	95% CI	p-value
Age (years)	61.2	72.1	45.4	1.08	1.06-1.10	<0.001
Male (%)	68.1	61.4	1.5	0.75	0.47-1.19	0.216
Anterior Q-wave MI (%)	39.5	61.4	14.2	2.44	1.54-3.88	<0.001
Non-anterior Q-wave MI (%)	51.0	37.3	5.5	0.57	0.36-0.91	0.019
Non-Q MI (%)*	5.8	0.0	/	/	/	0.017
Unstable angina %	3.7	1.2	1.2	0.32	0.04-2.37	0.264
Previous MI (%)	15.0	22.0	2.7	1.60	0.92-2.79	0.098
Time-to-hospital admission (N = 784)						
< 3 hours (%)	41.2	39.7	0.1	0.94	0.56-1.59	0.815
4 – 6 hours (%)	26.1	11.1	6.4	0.35	0.16-0.79	0.011
7 – 12 hours (%)	14.3	17.5	0.5	1.27	0.64-2.51	0.494
> 12 hours (%)	18.4	31.7	6.3	2.06	1.17-3.61	0.012
Systolic BP (mmHg)	131.4	108.6	39.0	0.97	0.96-0.98	<0.001
Diastolic BP (mmHg)	76.6	63.8	28.1	0.96	0.95-0.98	<0.001
Peak troponin T (μg/L)	5.1	6.6	4.6	1.04	1.00-1.08	0.032
Killip I (%)	72.1	13.3	72.0	0.06	0.03-0.11	<0.001
Killip II (%)	20.1	19.3	0.0	0.95	0.54-1.68	0.859
Killip III (%)	5.0	6.0	0.2	1.21	0.47-3.16	0.694
Killip IV (%)	2.8	61.4	167.9	54.95	29.98-100.73	<0.001
Primary-PCI (%)	69.7	41.5	24.8	0.31	0.19-0.49	<0.001
Thrombolysis (%)	10.7	12.2	0.2	1.16	0.58-2.34	0.670
Postponed-PCI (%)	4.9	2.4	1.0	0.49	0.12-2.04	0.324
Non-reperfusion medical therapy (%)	14.7	43.9	38.6	4.54	2.82-7.32	<0.001
CABG during hospitalization (%)	3.3	2.4	0.2	0.72	0.17-3.09	0.660
Previous CABG (%)	2.1	1.2	0.3	0.57	0.08-4.36	0.591
Hospital stay ICU (days)	2.5	5.9	27.8	1.17	1.10-1.23	<0.001
Total hospital stay (days)	10.9	9.1	2.1	0.98	0.95-1.01	0.151

Anterior Q-wave myocardial infarction (Anterior Q-wave MI), blood pressure (BP), coronary artery bypass grafting (CABG), Intensive care unit (ICU), myocardial infarction (MI), Nonanterior Q-wave myocardial infarction (Nonanterior Q-wave MI), Non Q-wave myocardial infarction (Non Q- wave MI), percutaneous coronary intervention (PCI), ST-elevation myocardial infarction (STEMI), Unstable angina (UA)

* Unable to calculate

regression using the Wald method. All significant variables from the univariate analysis presented in table 2 were included in the multivariate prediction model calculation.

The calculated prediction model had a specificity of 93.6 % and sensitivity of 80.7 %. The Hosmer-Lemeshow test was not significant, indicating little deviation from perfect fit (chi-square 4.147, degrees of freedom 6, P = 0.653).

The most significant risk factors for death were age above 65 years and Killip class IV (table 3). When those two variables were met, the risk of death reached 60% of probability.

The equation based on the prediction model allowing an estimation of the odds ratios for death was calculated as: exp (-3.306 + [1.763 x age > 65 yrs] + [-1.102 x Killip class I] + [3.505 x Killip class IV] + [-0.944 x Primary PCI]).

Table 3. Variables independently related to risk of death.

Variable	Chi-square	OR	95% CI	P-value
Age > 65 yrs	20.9	5.83	2.74-12.41	<0.001
Killip I	6.4	0.36	0.17-0.80	0.011
Killip IV	79.0	33.29	15.36-72.11	<0.001
Primary PCI	8.8	0.39	0.21-0.73	0.003

Percutaneous coronary intervention (PCI)

Discussion

From 2002 to 2005 we observed an increase in ST-segment elevation ACS patients, especially since 24-h primary PCI was introduced in 2004, ranging from 343 patients in 2002-2003 compared to 556 patients in 2004-2005 (table1). The increased number of admissions to our interventional center was the consequence of more frequent transfers from referral nonintervention hospitals. In a few years our center thus covered an area of approximately 820,000 inhabitants. Comparing ST-segment elevation ACS admissions from 2002 to 2005 we observed insignificant differences in mean age, gender, the incidence of anterior Q-wave MI, nonanterior Q-wave MI, non Q-wave MI and unstable angina, and the only significant differences in previous MI, more frequently in patients before 2004.

Comparing time-to-admission form 2002 to 2005 we observed that patients arrived at the hospital earlier - an encouraging result, which is the consequence of many factors. Therefore the major components of time delay have to be analyzed separately: time for patients to recognize symptoms and seek medical attention, transportation to hospital, in-hospital decision-making and door-to-balloon time for primary PCI procedure. (2) Physicians and health care systems should work to minimize door-to-balloon times and take door-to-balloon time into consideration when choosing a reperfusion strategy. (10)

For thrombolytic and primary PCI therapy the time to reperfusion is critical. There is a positive linear relationship between duration of ischemic time and poor outcome. In animal models, infarct size is significantly affected by the duration of coronary occlusion. (11) Therefore, late reperfusion is expected to result in less myocardial salvage and in a higher mortality rate even when optimal mechanical reperfusion is achieved. Data from Dutch and some other studies show a significant correlation between time from symptom onset to balloon inflation and mortality. The one-year mortality is increased by 7.5% for each 30-minute delay. (12) In patients with STEMI treated by primary angioplasty, symptom-onset-to-balloon time - but not door-to-balloon time - is related to mortality, particularly in higher-risk patients and in the absence of preprocedural anterograde flow. (13) Prolonged ischemic time is associated with higher mortality, mainly due to impaired myocardial perfusion and larger infarct size. (14)

After 2004, primary PCI became the main reperfusion strategy in our institution. In 2005, thrombolysis was performed only once when the interventional equipment broke down for a brief period. The increase of primary PCI in comparison to thrombolytic and nonreperfusion medical therapy after 2004 is an important achievement, namely primary PCI is more effective for treating STEMI, (15) if the transport to an interventional-hospital takes two hours or less. (16) In addition, facilitated percutaneous intervention offers no benefit over primary PCI. (17) One of the important advantages of 24-hour access to primary PCI is a significantly shorter mean in-hospital stay. The decrease of in-hospital stay together with the improved quality of life of numerous ST-segment elevation ACS patients after primary PCI can exert an important impact on the health care budget. We also noted an in-hospital mortality reduction that did not reach statistical significance.

Comparing survivors and nonsurvivors we observed that primary PCI was significantly more likely performed in survivors than in nonsurvivors. The causes for underused primary PCI in nonsurvivors are different and various. Most often symptomatic treatment of life-threatening events, such as cardiopulmonary resuscitation in case of cardiac arrest, orotracheal intubation with subsequent mechanical ventilation in case of respiratory arrest due to shock, delays the arrival to the catheterization laboratory, thus causing a substantial delay in salvation of the jeopardized myocardium. In cases with unsuccessful resuscitation with death in most severely affected patients, primary PCI is not even started, and such cases are classified as having been treated noninvasively. In addition, late admissions due to ST-segment elevation ACS are generally neither treated with reperfusion therapy nor with primary PCI.

We observed that reperfusion therapy with primary PCI was significantly underused in nonsurvivors, particularly those with cardiogenic shock – Killip class IV, thus confirming indirectly the conclusions of other studies evaluating the mode of therapy among STEMI patients with cardiogenic shock, which demonstrated poor implementation of recent guidelines advocating an aggressive invasive approach. (18,19) Based on the results of the SHOCK trial, (20) and guidelines for the management of ST-elevation ACS, (2,3) primary PCI was advocated as the reperfusion therapy of choice for patients with cardiogenic shock. Moreover, the guidelines recommended the use of intra-aortic balloon pump counterpulsation (IABP) among hemodynamically unstable ACS patients, especially those with cardiogenic shock.

Within the last few years a lot of effort was necessary to implement contemporary treatment guidelines for STEMI patients at our institution, to which patients from the entire Maribor area and including those from five regional hospitals are referred, with transfer distances not exceeding 100 km. However, late treatment - especially in patients with extensive infarctions – contributes significantly to mortality.

The time delay at the start of therapy is in part the consequence of negligence on the part of the patient, underevaluation of symptoms of acute myocardial infarction, but also the result of unnecessary waiting in emergency departments prior to hospital admission, repetition of laboratory tests, prolonged waiting for adequate transportation to an interventional center, etc.

The average prehospital delay in the USA is several hours, and the majority of this delay comes from the patient's delaying seeking medical attention. (21) Our observations suggest that the introduction of primary PCI claims changes in the organization of the medical services, including family practitioners, emergency medical services, hospitals, referral and interventional centers performing primary PCI. (22) Apart from resources, a sufficient number of trained medical staff is necessary to satisfy the needs of patients with acute evolving myocardial infarction. (23,24)

Conclusions

After 2004 the patients arrived to hospital earlier and primary PCI became the main reperfusion therapy. In patients with heart failure the mortality rate remained high, particularly in those with cardiogenic shock. An additional decrease in mortality could be achieved by further shortening the time-to-hospital admission and increasing primary PCI among older hemodynamically unstable ACS patients, particularly those with Killip class IV at first assessment.

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