

Management and mortality in patients with non-ST-segment elevation vs. ST-segment elevation myocardial infarction. Data from the Malopolska Registry of Acute Coronary Syndromes

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Abstract

Background: According to the presenting electrocardiogram, acute myocardial infarction (MI) can be categorised generally as non-ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI).

Aim: To assess the impact of the different acute MI categories on in-hospital management and mortality in hospitals without on-site invasive facilities.

Methods: We identified 380 NSTEMI and 334 STEMI patients treated in the Malopolska Registry of Acute Coronary Syndromes from February to March 2005 and from December 2005 to January 2006. Data concerning in-hospital management and mortality were assessed.

Results: Patients with NSTEMI were older and were more likely to have prior angina, prior MI and prior heart failure symptoms than STEMI patients. The NSTEMI patients were less likely to be transferred for invasive treatment (23.9 vs. 41.9%, $p < 0.0001$) and receive glycoprotein IIb/IIIa inhibitors during index hospital stay. The use of low-molecular-weight heparin, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin II antagonists, nitrates and statins was more frequent in NSTEMI patients. Among patients treated non-invasively, in-hospital mortality was high, but was lower in NSTEMI than STEMI patients (12.1 vs. 22.7%, $p < 0.0001$). Independent predictors of in-hospital death in this group were age, cardiogenic shock, chronic obstructive pulmonary disease, and STEMI.

Conclusions: Despite current recommendations, NSTEMI patients are still less likely to be transferred for invasive treatment than STEMI patients. Among patients treated non-invasively during index hospital stay, NSTEMI is associated with more favourable prognosis than STEMI, but the risk of in-hospital death is high. The hospital network should implement more frequently the strategy of early and urgent invasive treatment of NSTEMI patients.

Key words: myocardial infarction, pharmacotherapy, management, mortality

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Introduction

According to the presenting electrocardiogram, acute myocardial infarction (MI) can be categorised generally as non-ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI) [1]. Despite similar pathogenesis, a different clinical approach to the treatment of NSTEMI vs. STEMI has been proposed by the guidelines [2-4].

The purpose of the present study was to assess the impact of the different categories of acute MI on current in-hospital management and mortality in hospitals without on-site invasive facilities.

Methods

The Malopolska Registry

The Malopolska Registry of Acute Coronary Syndromes is a prospective, multicentre, observational registry designed to examine current epidemiology, in-hospital management and outcome of patients with acute coronary syndromes in the Malopolska region [5, 6]. A total of 29 community hospitals without on-site invasive facilities participated in the registry during two study periods: from February 2005 to March 2005 and from December 2005 to January 2006 (two separate patient enrolment periods). To minimise

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selection bias all consecutive patients with a suspected diagnosis of acute coronary syndrome (ACS) were included regardless of the treatment strategy or outcome. During the index hospitalisation, data concerning baseline demographic and clinical characteristics, relevant laboratory results, pharmacotherapy during hospital stay and adverse cardiovascular outcomes were recorded on a standardised, electronic, web-page based case report form. Standardised definitions were used for adverse events and final diagnosis. Data were collected in a central electronic database. This database was reviewed for completeness by an independent physician and site queries were generated if needed. Cardiogenic shock was defined as reduced blood pressure (systolic blood pressure <90 mmHg or a drop of mean arterial pressure >30 mmHg) and/or low urine output (<0.5 ml/kg/h), with a pulse rate >60 beats per minute with or without evidence of organ congestion [7]. The primary end point was in-hospital mortality. Occurrence of other ischaemic and bleeding events was not analysed. For the purpose of the present analysis patients were classified as NSTEMI and STEMI based on their final diagnosis. STEMI was diagnosed if ST-segment elevation more than or equal to 1 mm occurred in at least one lead or new left bundle branch block was found in the electrocardiogram with biochemical evidence of myocardial necrosis (at least one positive biochemical cardiac necrosis marker measurement). NSTEMI was diagnosed in patients with at least one positive biochemical cardiac necrosis marker measurement without new ST-segment elevation in the electrocardiogram.

Statistical analysis

Values are expressed as mean \pm SD. Categorical variables are presented as percentages. Statistical

comparisons between subgroups were performed using chi-square test and Fisher's exact test for categorical variables and Kruskal-Wallis test for continuous variables, as appropriate. In addition, multivariate Cox regression analysis was performed to find significant predictors of in-hospital death. Forward and backward selection in Cox regression with the probability value for covariates to enter or stay in the model set at 0.05 were used. The following covariates were tested: age, body mass index, presence of diabetes, arterial hypertension, hyperlipidaemia, prior angina, prior MI, prior heart failure symptoms, prior percutaneous coronary intervention, prior coronary artery bypass graft, prior stroke/transient ischaemic attack, history of smoking, peripheral arterial disease, chronic renal insufficiency, chronic obstructive pulmonary disease, chest pain on admission, cardiogenic shock at admission and time from chest pain onset to admission. The final model was adjusted for gender. Risk of in-hospital death was expressed as odds ratios with 95% confidence intervals. All tests were 2-tailed, and a p value of <0.05 was considered statistically significant.

Results

The Malopolska Registry of Acute Coronary Syndromes database included 1414 patients with ACS admitted between February 2005 and March 2005, and between December 2005 and January 2006. A total of 700 patients with final diagnosis other than MI (e.g. unstable angina, stable angina, extracardiac cause of chest pain) were excluded from the analysis. NSTEMI and STEMI were diagnosed in 380 (26.8%) and 334 (23.6%) patients, respectively (Figure 1). Baseline demographic and clinical characteristics for both groups of patients are shown

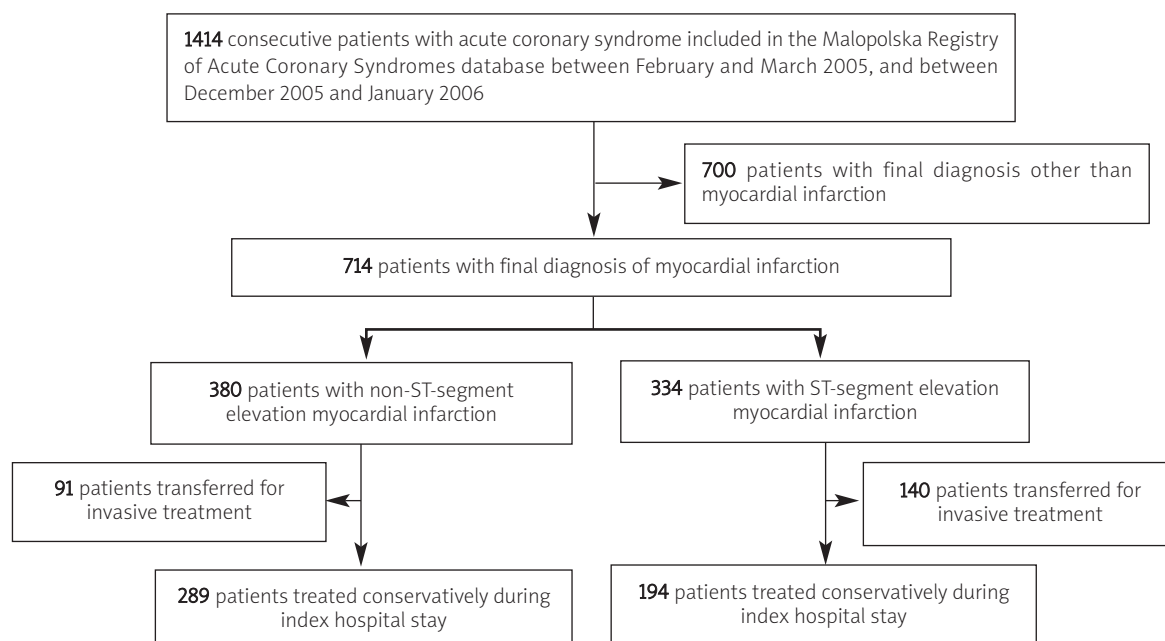


Figure 1. Scheme of group distribution in the registry

in Table I. Patients with NSTEMI were older and were more likely to have arterial hypertension, hyperlipidaemia, prior angina, prior MI and prior heart failure symptoms than STEMI patients – see Table I. Chest pain onset to admission time was similar among groups, but NSTEMI patients were less likely to have chest pain on admission than STEMI patients. Systolic blood pressure on admission as well as left ventricular ejection fraction were lower in the STEMI group. Frequency of cardiogenic shock did not differ between study groups (NSTEMI vs. STEMI, 6.8 vs. 8.4%, $p=0.48$).

Table I. Baseline demographic and clinical characteristics. Values are presented as percentages or mean \pm SD

Variable	NSTEMI N=380	STEMI N=334	p
Male gender	60.3	60.2	NS
Age [years]	70.2 \pm 11.6	66.3 \pm 13.6	<0.001
Age >75 years	37.6	28.4	0.01
Body mass index [kg/m ²]	27.3 \pm 8.3	26.9 \pm 4.5	NS
Diabetes	24.2	22.5	NS
Arterial hypertension	79.2	62.3	<0.001
Hyperlipidaemia	49.7	41.6	0.04
Prior angina	70.5	44.3	<0.001
Prior myocardial infarction	33.9	24	0.004
Prior heart failure symptoms	26.6	13.8	<0.001
Prior percutaneous coronary intervention	5.5	6	NS
Prior coronary artery bypass graft	2.9	1.5	NS
Prior stroke/transient ischaemic attack	7.1	7.8	NS
Current smoker	30	36.5	NS
Family history of coronary artery disease	13.4	13.8	NS
Peripheral arterial disease	13.4	10.5	NS
Chronic renal insufficiency	7.9	5.4	NS
Chronic obstructive pulmonary disease	13.2	9.3	NS
Chest pain on admission	63.2	71	0.03
Time from chest pain onset to admission [hours]	14.8 \pm 19.5	14.6 \pm 19.6	NS
Time from chest pain onset to admission \leq 12 hours	68.9	68.3	NS
Heart rate on admission [beats/min]	87.2 \pm 26.1	84.3 \pm 22.9	NS
Systolic blood pressure on admission [mmHg]	144.2 \pm 35.8	138.3 \pm 34.1	0.02
Diastolic blood pressure on admission [mmHg]	87.8 \pm 16.9	85.5 \pm 16.1	NS
Killip class on admission			
I	60.5	61	NS
II	24.5	23.4	
III	8.2	7.2	
IV	6.8	8.4	
Left ventricular ejection fraction [%]	50.3 \pm 13.5	47.2 \pm 13.2	0.01

The NSTEMI patients were less likely to be transferred for invasive treatment during index hospital stay than STEMI patients (23.9 vs. 41.9%, $p < 0.001$). The percentage of transferred patients was higher in patients with chest pain onset to admission time \leq 12 hours (NSTEMI vs. STEMI, 28.2 vs. 56.1%, $p < 0.001$). In the subgroup of patients in cardiogenic shock transfer rate was similar between study groups (23.1 vs. 21.4%, $p=0.99$). Out of 91 NSTEMI transferred patients only 11 (12.1%) were transferred within 6 hours (urgent invasive strategy) and 31 (34.1%) within 72 hours (early invasive strategy) from index admission. Percentages of transferred patients according to diagnosis and time from admission to transfer for invasive treatment initiation are shown in Figure 2.

Pharmacological treatment during hospital stay is shown in Table II. Thrombolytic therapy was used only in STEMI. Also, STEMI patients were more likely to receive more aggressive antiplatelet therapy including glycoprotein IIb/IIIa inhibitors, but the frequency of therapy with clopidogrel was very low in both study groups (less than 20%). Use of low-molecular-weight heparin, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin II antagonists, nitrates, as well as statins was more frequent in the NSTEMI than the STEMI patient group.

Among patients treated non-invasively during index hospital stay in-hospital mortality was lower in NSTEMI than STEMI patients (NSTEMI vs. STEMI, 12.1 vs. 22.7%, $p=0.003$). Mean time to death did not differ between the groups (5.8 \pm 3.2 vs. 5.1 \pm 3.9 days, $p=0.15$). In patients with cardiogenic shock, in-hospital mortality rate did not differ significantly between groups NSTEMI vs STEMI (50 vs. 72.7%, $p=0.20$), but was significantly lower in NSTEMI vs. STEMI non-shock patients (9.3 vs. 16.3%, $p=0.04$). In multivariate Cox regression analysis, independent predictors of in-hospital death in patients treated non-invasively were age, cardiogenic shock, chronic obstructive pulmonary disease, and STEMI (vs. NSTEMI) – see Table III.

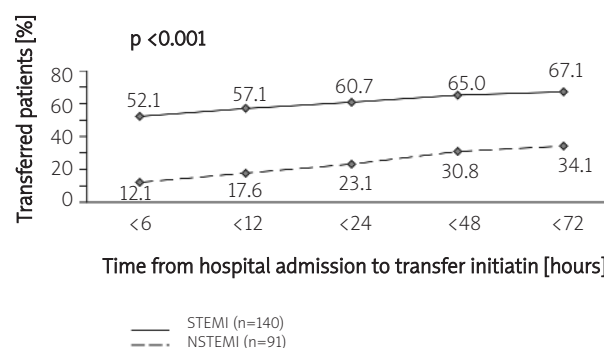


Figure 2. Percentages of transferred patients according to diagnosis and time from admission to transfer for invasive treatment initiation

STEMI – ST-segment elevation myocardial infarction (solid line), NSTEMI – non-ST-segment elevation myocardial infarction (dotted line)

Table II. Pharmacological treatment during hospital stay. Values are presented as percentages

Medication	NSTEMI N=380	STEMI N=334	p
Aspirin	95	96.1	NS
Clopidogrel	16.6	19.5	NS
Ticlopidine	19.7	13.5	0.03
Glycoprotein IIb/IIIa inhibitor	1.6	9.6	<0.001
Thrombolysis	0	16.8	<0.001
Low-molecular-weight heparin	85.8	59	<0.001
Beta-blocker	80.3	57.8	<0.001
Angiotensin-converting enzyme inhibitor/angiotensin II antagonist	76.6	53.6	<0.001
Calcium antagonist	8.4	5.1	NS
Nitrates	72.6	54.8	<0.001
Statins	83.9	70.4	<0.001

Discussion

In our study almost half of the patients admitted with suspicion of ACS had confirmed diagnosis of MI. These observations are in line with the GRACE Registry data, which demonstrated frequency of STEMI diagnosis in 30% of patients and NSTEMI in 25% of patients [8]. Similarly to previous reports, NSTEMI patients were older and were more likely to have higher prevalence of coronary artery disease risk factors, as well as comorbid conditions than STEMI patients [8-11]. In coronary angiography more severe atherosclerotic changes including multivessel disease, chronic total occlusions, and collateral flow supply is more frequently observed in NSTEMI than STEMI patients. Also in STEMI the infarct-related artery is usually occluded by a thrombus, whereas in NSTEMI the infarct-related artery is usually patent with a non-occlusive thrombus [11]. On the other hand, in some cases total occlusion of the circumflex coronary artery may be not recognised as STEMI (qualified as NSTEMI) based on the electrocardiogram, and may be associated with prolongation of the time to successful reperfusion [12, 13].

In the studied group less than one quarter of NSTEMI patients were transferred for invasive treatment during the hospital stay. Of them only one third were transferred within 72 hours as recommended by current guidelines, with urgent invasive strategy application in 12.1% of patients [2-4]. We expect that in the remaining, non-invasively treated cohort there were a significant number of patients who would have benefited from an invasive strategy. As we reported before, the transfer rate for NSTEMI patients increased between the two study periods (from February 2005 to March 2005 vs. from December 2005 to January 2006) due to changing the qualification strategy for invasive treatment and starting the 24/7 PCI programme in two additional hospitals in the Malopolska Region [6].

Table III. Multivariate Cox regression analysis for in-hospital death

Variable	OR	95% CI	p
Gender [male]	0.91	0.56-1.45	0.68
Age [per year]	1.04	1.02-1.07	<0.001
Cardiogenic shock	5.49	3.35-9	<0.001
Chronic obstructive pulmonary disease	2.25	1.36-3.71	0.002
STEMI (vs. NSTEMI)	1.81	1.16-2.82	0.009

Abbreviations: STEMI – ST-segment elevation myocardial infarction, NSTEMI – non-ST-segment elevation myocardial infarction, OR – odds ratio, CI – confidence interval

Similarly to previous reports, the STEMI patients were more frequently qualified to invasive therapy, and received more aggressive pharmacological treatment, including glycoprotein IIb/IIIa inhibitors [9]. Thrombolytics were used in STEMI patients only. Thrombolytic therapy is not recommended for NSTEMI patients, as in non-Q wave MI it showed no benefit over standard therapy with aspirin and heparin [2-4, 14]. Glycoprotein IIb/IIIa inhibitor use was very low in both groups, but they were more frequently used in STEMI than NSTEMI patients. This is in contrast to the OPERA Registry, where they were used in more than 20% of cases and with similar frequency in both groups [9]. Use of glycoprotein IIb/IIIa inhibitors in conservative treatment of NSTEMI is generally not recommended by current guidelines [2-4]. In the OPERA and GRACE registries NSTEMI patients were less likely to receive other cardiac medications during hospital stay and at hospital discharge [8, 9]. In our registry reported use of low-molecular-weight heparin, beta-blockers, angiotensin-converting enzyme inhibitors/ angiotensin II antagonists, nitrates, as well as statins was more frequent in NSTEMI than STEMI patients treated non-invasively. Also the usage rate of clopidogrel was very low, and in almost 20% of patients ticlopidine was used rather than clopidogrel.

Similarly to the GRACE Registry data, STEMI diagnosis was associated with worse in hospital prognosis than NSTEMI [8]. Also, in patients treated with percutaneous coronary intervention in-hospital and 1-year mortality was higher in STEMI than NSTEMI patients [10]. The difference in clinical outcome may be associated with differences in baseline characteristics. There is also a risk of mortality bias between studied groups as a result of a discrepancy in the frequency of transferred patients, but the observed time to event was similar in both study groups. In contrast, in the OPERA Registry in-hospital and long-term clinical outcome was similar among NSTEMI and STEMI patients [9]. Terkelsen et al. in an unselected cohort of patients with acute MI reported higher in-hospital and 1-year mortality for NSTEMI than STEMI patients [11]. Prevalence of cardiogenic shock was similar between studied groups and cardiogenic shock occurrence was a main predictor of in-hospital death in the analysed patient population (more than fivefold

increase of the risk of in-hospital death). Similarly, the SHOCK and GUSTO II trials have found that mortality rates in cardiogenic shock complicating NSTEMI are greater than 60%, and even higher than in STEMI patients [15, 16]. Importantly, the percentage of shock patients transferred for invasive diagnostics and treatment was extremely low (less than one quarter). According to current recommendations NSTEMI patients with clinical symptoms of heart failure or haemodynamic instability, including cardiogenic shock, should be qualified for an urgent invasive strategy [2, 4]. The second independent predictor of in-hospital death was chronic obstructive pulmonary disease. Salisbury et al. have shown that patients with chronic obstructive pulmonary disease are at higher risk of death and rehospitalisation during long-term follow-up after myocardial infarction [17].

Limitations

The present study has a number of limitations. First, it has all the limitations of a registry. Second, the relatively small group size is also a limitation. The study focused only on in-hospital clinical outcomes for non-transferred patients. Data concerning mortality in the group of patients transferred for invasive treatment, as well as long-term clinical follow-up data for all patients, were not available. Also, patients were not screened for contraindications to the use of each medication, and appropriateness of the used dosage was not assessed. For that reason, to address the potential limitations of confounding biases, we used multivariable Cox analysis to control the influence of baseline characteristics and risk profiles on in-hospital mortality. However, the high-risk characteristics of NSTEMI patients, low rate of early invasive strategy, and high in-hospital mortality of NSTEMI patients are clinically important and unlikely to be influenced by the study limitations.

Conclusions

Despite current recommendations NSTEMI patients are still less likely to be transferred for invasive treatment than STEMI patients. Among patients treated non-invasively during index hospital stay NSTEMI is associated with a more favourable prognosis than STEMI, but the risk of in-hospital death is high. The hospital network should implement more frequently the strategy of early and urgent invasive treatment of NSTEMI patients.

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Postępowanie wewnątrzszpitalne i śmiertelność u chorych z ostrym zawałem mięśnia sercowego bez uniesienia i z uniesieniem odcinka ST. Dane z Małopolskiego Rejestru Ostrego Zespołu Wieńcowych

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Streszczenie

Wstęp: Na podstawie zmian obserwowanych w zapisie EKG ostry zawał mięśnia sercowego może być ogólnie skategoryzowany jako przebiegający bez uniesienia (NSTEMI) i z uniesieniem odcinka ST (STEMI).

Cel: Określenie wpływu różnych kategorii zawału na przebieg postępowania wewnątrzszpitalnego i śmiertelność w szpitalach bez bezpośredniego dostępu do pracowni hemodynamiki.

Metody: W Małopolskim Rejestrze Ostrego Zespołu Wieńcowych zidentyfikowano 380 chorych z rozpoznaniem NSTEMI i 334 ze STEMI leczonych w okresie od lutego do marca 2005 r. i w okresie od grudnia 2005 do stycznia 2006 r. Oceniono dane dotyczące postępowania wewnątrzszpitalnego i śmiertelności.

Wyniki: Chorzy z NSTEMI byli starsi, częściej stwierdzano u nich wcześniejsze objawy dusznicy bolesnej i niewydolności krążenia oraz przeżyty zawał serca niż u chorych ze STEMI. Chorzy z NSTEMI rzadziej byli przekazywani w celu leczenia inwazyjnego (23,9 vs 41,9%, $p < 0,0001$) i rzadziej otrzymywali bloker receptora płytkowego IIb/IIIa w okresie hospitalizacji. Wśród 91 chorych z NSTEMI przekazanych w celu leczenia inwazyjnego jedynie 11 (12,1%) było transportowanych w okresie 6 godz. (pilna strategia inwazyjna) i 31 (34,1%) w okresie 72 godz. (wczesna strategia inwazyjna) od momentu przyjęcia. Stosowanie heparyn drobnocząsteczkowych, beta-blokerów, inhibitorów konwertazy angiotensyny lub blokerów receptora dla angiotensyny II, nitratów i statyn było częstsze u chorych z rozpoznaniem NSTEMI. Wśród osób leczonych nieinwazyjnie śmiertelność w okresie hospitalizacji była wysoka, przy czym niższa u chorych z NSTEMI niż ze STEMI (12,1 vs 22,7%, $p < 0,0001$). Niezależnymi czynnikami wystąpienia zgonu wśród osób leczonych zachowawczo były wiek, wstrząs kardiogeny, przewlekła obturacyjna choroba płuc oraz rozpoznanie STEMI.

Wnioski: Pomimo zaleceń chorzy z rozpoznaniem NSTEMI są nadal rzadziej przekazywani do leczenia inwazyjnego niż chorzy ze STEMI. Wśród osób leczonych nieinwazyjnie rozpoznanie NSTEMI jest związane z bardziej korzystnym przebiegiem klinicznym niż rozpoznanie STEMI, ale ryzyko zgonu w okresie hospitalizacji jest nadal wysokie. Strategia wczesnego czy pilnego leczenia osób z NSTEMI powinna być częściej stosowana w sieciach szpitali prowadzących leczenie ostrego zespołu wieńcowych.

Słowa kluczowe: zawał serca, farmakoterapia, postępowanie, śmiertelność

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