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Patterns of Presentation and Outcomes of Patients with Acute Coronary Syndromes

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Key Words
Acute coronary syndrome · Mortality · Percutaneous coronary intervention

Abstract
Objectives: We undertook this study to assess the relationship between presentation pattern and mortality in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention. ***Methods:*** This registry included 10,455 patients with ACS, of whom 2,853 patients had ST-segment elevation myocardial infarction (STEMI), 3,060 patients had non-ST-segment elevation myocardial infarction (NSTEMI) and 4,542 patients had unstable angina. The primary outcome was 1-year mortality. ***Results:*** At 1 year there were 976 deaths, 390 (13.7%) among STEMI patients, 366 (12.0%) among NSTEMI patients and 220 (4.8%) among patients with unstable angina (OR = 1.17, 95% CI 1.01–1.35 for STEMI vs. NSTEMI; OR = 3.00, 95% CI 2.56–3.51 for STEMI vs. unstable angina, and OR = 2.58, 95% CI 2.20–3.04 for NSTEMI vs. unstable angina). In the Cox proportional hazards model ACS form was an independent correlate of 1-year mortality (HR = 0.90, 95% CI 0.73–1.13 for STEMI vs. NSTEMI; HR = 1.56, 95% CI 1.13–2.14 for STEMI vs. unstable angina; HR = 1.72, 95% CI 1.30–2.29 for NSTEMI vs. unstable angina). ***Conclusions:*** The presentation pattern affects 1-year mortality in patients with ACS, with unadjusted mortality being highest in patients with STEMI and lowest in patients with unstable angina.

Introduction

Acute coronary syndromes (ACS) refer to acute myocardial ischemic states. Despite important advances in the understanding of their pathophysiology and treatment, ACS still remain poorly characterized and are leading causes of mortality and morbidity worldwide [1–3]. Most of the information available regarding clinical presentation, therapy and prognosis of ACS comes from registries rather than from studies that have used comparable approaches for diagnosis and therapy [4–7]. These registries have reported large differences between patients with ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation ACS regarding application of noninvasive therapy, coronary angiography and invasive procedures. Of note, although it is well

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known that information obtained by angiography bears important prognostic information [8–12], in these registries coronary angiography was performed only in a proportion (usually selected) of patients. Several studies have demonstrated that invasive therapy reduces mortality in patients with non-ST-segment elevation ACS compared with conservative therapy [13, 14]; however, marked differences in applying invasive therapy among patients with STEMI and non-ST-segment elevation myocardial infarction (NSTEMI) have been reported [4, 6]. Moreover, crossovers from one form of therapy to the other (predominantly from noninvasive to invasive therapy) occurred so often that a comparison of therapeutic approaches is almost impossible [15].

The present study is based on a large prospective registry that represents the entire spectrum of patients with ACS treated with percutaneous coronary intervention (PCI). The aim of the study was to assess the relationship between presentation pattern (STEMI, NSTEMI or unstable angina) and outcome (30-day and 1-year mortality) in patients with ACS undergoing early PCI.

Methods

Patients

This prospective registry included 10,455 patients with acute coronary syndromes (STEMI, NSTEMI and unstable angina) who underwent coronary angiography and early PCI (within 12 h from the admission) in the Deutsches Herzzentrum and 1. Medizinische Klinik rechts der Isar, between September 1997 and December 2006. There were 2,853 patients with STEMI, 3,060 patients with NSTEMI and 4,542 patients with unstable angina. The diagnosis of STEMI was based on the presence of chest pain lasting ≥20 min associated with typical changes on surface ECG (ST-segment elevation of ≥0.1 mV in ≥2 limb leads or ≥0.2 mV in ≥2 contiguous precordial leads, pathological Q waves, or complete left bundle branch block of new onset). Unstable angina was diagnosed when characteristic chest pain [with an accelerating pattern or prolonged (>20 min) or recurrent episodes at rest or with minimal effort] was associated with either ST segment depression of ≥0.1 mV and/or T-wave inversion in 2 continuous leads in the electrocardiogram and with documentation of significant coronary artery disease on coronary angiography. Diagnosis of NSTEMI required clinical and electrocardiographic criteria similar to those of unstable angina plus elevated troponin T (level >0.03 μg/l) or creatine kinase or creatine kinase-myocardial band. To be included in the study all patients had to have significant coronary artery disease on coronary angiography. Patients who underwent urgent coronary artery bypass surgery (73 patients with STEMI and 93 patients with unstable angina) and those who were treated conservatively (154 patients with STEMI or NSTEMI and 210 patients with unstable angina) were not included in this analysis.

Angiographic Evaluation and Stent Implantation

Coronary angiography was performed according to standard criteria. All angiographic data were analyzed in the same quantitative angiographic core laboratory. Coronary artery disease was confirmed by the presence of coronary stenoses ≥50% lumen obstruction in at least 1 of the 3 main coronary arteries. A culprit lesion was described in the presence of an acute occlusion, intraluminal filling defects (or thrombus), ulcerated plaques with contrast-filled pocket protruding into plaque with or without delayed contrast wash-out, extraluminal contrast, dissection or intraluminal flaps [16]. Offline analysis of digital angiograms was performed in the core laboratory using an automated edge detection system (CMS, Medis Medical Imaging Systems, Neuen, The Netherlands). The initial and postprocedural blood flow in the infarct-related artery was graded according to the Thrombolysis in Myocardial Infarction (TIMI) grading system [17]. A bleeding complication was defined as major if it was intracranial, or if clinically significant overt signs of hemorrhage were associated with a drop in hemoglobin of more than 5 g/dl or, when hemoglobin was not available, an absolute drop in hematocrit of at least 15%. The diagnosis of stroke required confirmation by computed tomography or magnetic resonance imaging of the head.

Stent implantation and periprocedural care were performed according to standard criteria. Bare metal stents were mostly used. Postinterventional antiplatelet therapy consisted of ticlopidine (500 mg/day) or clopidogrel (300 or 600 mg as a loading dose followed by 75 mg/day for 4 weeks to 6 months) and aspirin (200 mg/day administered orally and continued indefinitely).

Endpoints, Definitions and Follow-Up

The primary outcome of this analysis was 1-year mortality. We also evaluated occurrence of myocardial infarction, stroke and major bleeding after the procedure. The follow-up protocol after discharge consisted of a phone interview at 1 month after the procedure, a visit at 6 months and a phone interview at 12 months. Information about death was obtained from hospital records, death certificates or phone contact with relatives of the patient or attending physician. The diagnosis of myocardial infarction was made according to the TIMI criteria [17].

Patients were advised to present to the outpatient clinic or their referring physicians if they developed chest pain or other cardiac symptoms. In case of symptoms, at least 1 clinical, laboratory and electrocardiographic check-up was performed.

Statistical Analysis

Data are presented as median (with 25th and 75th percentiles) or counts and proportions (percentages). The distribution of the data was analyzed with the 1-sample Kolmogorov-Smirnov test. Categorical data were compared with the χ^2 test. Continuous data were compared with the Kruskal-Wallis test. Survival analysis was performed by applying the Kaplan-Meier method. Differences in survival were assessed with the log-rank test. Landmark analysis, with a prespecified landmark at 1 month, was performed to assess early and late relative risk of death. The Cox proportional hazards model was used to assess the correlates of mortality. All analyses were performed using the S-plus statistical package (S-PLUS, Insightful Corp., Seattle, Wash, USA). $p < 0.05$ was considered to indicate statistical significance.

Table 1. Baseline characteristics

Characteristic	STEMI (n = 2,853)	NSTEMI (n = 3,060)	Unstable angina (n = 4,542)	p value
Age, years	63.8 (54.2; 73.1)	68.6 (59.4; 76.8)	66.1 (57.9; 73.7)	<0.001
Female sex	738 (25.9)	789 (25.8)	1,188 (26.2)	0.927
Body mass index, kg/m^2	26.3 (24.3; 29.0)	26.3 (24.2; 29.1)	26.4 (24.4; 29.1)	0.36
Diabetes	613 (21.5)	901 (29.4)	1,104 (24.3)	<0.001
On insulin therapy	162 (5.7)	328 (10.7)	340 (7.5)	<0.001
Arterial hypertension	928 (32.5)	1,588 (51.9)	2,742 (60.4)	<0.001
Current smoking	1,096 (38.4)	716 (23.4)	999 (22.0)	<0.001
Hypercholesterolemia (≥240 mg/dl)	1,614 (56.6)	2,081 (68.0)	2,929 (64.5)	<0.001
Previous myocardial infarction	514 (18.0)	844 (27.6)	1,609 (35.4)	<0.001
Previous coronary artery bypass surgery	143 (5.0)	411 (13.4)	639 (14.1)	<0.001
Creatinine, mg/dl	1.0 (0.9; 1.2)	1.1 (0.9; 1.2)	1.0 (0.9; 1.1)	<0.001
Systolic blood pressure, mm Hg	124.0 (110.0; 140.0)	140.0 (120.0; 160.0)	145.0 (126.0; 168.0)	<0.001
Diastolic blood pressure, mm Hg	70.0 (60.0; 80.0)	70.0 (60.0; 80.0)	70.0 (60.0; 80.0)	<0.001
Heart rate, beats/min	78 (67; 89)	73 (65; 83)	70 (61; 88)	<0.001
With cardiogenic shock[a]	429 (15.0)	188 (6.1)	65 (1.4)	<0.001
Creatine kinase-myocardial band, U/l	54.6 (24.7; 124.0)	23.1 (14.0; 50.3)	13.0 (8.0; 17.0)	<0.001
Troponin I, μg/l	0.43 (0.06; 1.64)	0.23 (0.06; 0.67)	0.01 (0.00; 0.01)	<0.001

Data are medians with 25th and 75th percentiles in parentheses, or counts with percentages in parentheses, as appropriate.
[a] The diagnosis of cardiogenic shock was established at the time of PCI.

Results

Baseline Characteristics

There were 2,853 patients with STEMI, 3,060 patients with NSTEMI and 4,542 patients with unstable angina. Baseline characteristics are shown in table 1. With the exception of proportion of women and body mass index, all other parameters appeared to differ significantly among patients of various groups. Patients with NSTEMI were older and more often had diabetes and hypercholesterolemia. As expected, patients with STEMI more frequently presented with or developed cardiogenic shock and had a higher level of markers of myocardial necrosis (creatine kinase-myocardial band and troponin) than patients with NSTEMI or unstable angina. The group with unstable angina had the highest proportion of patients with arterial hypertension, previous myocardial infarction and previous coronary artery bypass surgery compared with the other 2 groups. Angiographic data are shown in table 2. The group with NSTEMI had the highest proportion of patients with multivessel disease and smaller vessel size and more distally located culprit lesions compared with patients of 2 other groups. Type of intervention and therapy at discharge is shown in table 3. For patients with STEMI and NSTEMI, median time-to-treatment interval was 7.8 h (25th and 75th percentiles 4.0 and 18.7 h, respectively).

After excluding patients with cardiogenic shock, differences between groups regarding therapy at discharge were markedly attenuated.

Thirty-Day Clinical Outcome

Within the first 30 days there were a total of 558 deaths. Of these, 280 deaths occurred in patients with STEMI, 197 deaths occurred in patients with NSTEMI and 81 deaths occurred in patients with unstable angina (Kaplan-Meier estimates of mortality 9.8, 6.4 and 1.8%, respectively; OR = 1.55, 95% CI 1.30–1.86, $p < 0.001$ for STEMI vs. NSTEMI; OR = 5.73, 95% CI 4.60–7.13, $p < 0.001$ for STEMI vs. unstable angina, and OR = 3.69, 95% CI 2.90–4.70, $p < 0.001$ for NSTEMI vs. unstable angina). Myocardial infarction occurred in 49 patients with STEMI, 101 patients with NSTEMI and 77 patients with unstable angina (Kaplan-Meier estimates 1.7, 3.3 and 1.7%, respectively; OR = 0.51, 95% CI 0.37–0.71, $p < 0.001$ for STEMI vs. NSTEMI, OR = 1.01, 95% CI 0.70–1.44, $p = 0.85$, for STEMI vs. unstable angina and OR = 1.96, 95% CI 1.47–2.63, $p < 0.001$ for NSTEMI vs. unstable angina). Death or myocardial infarction within 30 days occurred in 325 patients with STEMI, 287 patients with

Table 2. Angiographic data

Characteristic	STEMI (n = 2,853)	NSTEMI (n = 3,060)	Unstable angina (n = 4,542)	p value
Left ventricular ejection fraction, %	48.0 (39.0; 56.0)	51.0 (40.0; 60.0)	59.9 (49.9; 65.0)	<0.001
Extent of coronary artery disease				<0.001
1-vessel disease	951 (33.3)	600 (19.6)	1,170 (25.8)	
2-vessel disease	845 (29.6)	793 (25.9)	1,358 (29.9)	
3-vessel disease	1,057 (37.1)	1,667 (54.5)	2,014 (44.3)	
Multivessel disease	1,902 (66.7)	2,460 (80.4)	3,372 (74.2)	<0.001
Vessel treated				<0.001
Left main coronary artery	27 (0.9)	87 (2.8)	122 (2.7)	
Left anterior descending coronary artery	1,229 (43.1)	1,168 (38.2)	1,884 (41.5)	
Left circumflex coronary artery	441 (15.5)	880 (28.8)	951 (20.9)	
Right coronary artery	1,082 (37.9)	738 (24.1)	1,304 (28.7)	
Bypass graft	74 (2.6)	187 (6.1)	281 (6.2)	
Vessel size, mm	2.93 (2.60; 3.30)	2.76 (2.40; 3.14)	2.91 (2.52; 3.14)	<0.001
Culprit lesion location				<0.001
Proximal	1,211 (42.4)	1,042 (34.1)	1,872 (40.8)	
Medial	1,278 (44.8)	1,368 (44.7)	1,972 (43.4)	
Distal	364 (12.8)	650 (21.2)	718 (15.8)	
TIMI flow grade before intervention				<0.001
0	1,462 (51.2)	748 (24.4)	526 (11.6)	
1	325 (11.4)	206 (0.7)	244 (5.4)	
2	537 (18.8)	669 (21.9)	658 (14.5)	
3	529 (18.5)	1,437 (47.0)	3,114 (68.5)	
TIMI flow grade after intervention				<0.001
0	92 (3.2)	127 (4.1)	70 (1.5)	
1	56 (1.9)	45 (1.5)	24 (0.5)	
2	281 (9.9)	127 (4.2)	162 (3.6)	
3	2,424 (85.0)	2,761 (90.2)	4,286 (94.4)	

Data are median with 25th and 75th percentiles in parentheses, or counts with percentages in parentheses.

NSTEMI and 155 in patients with unstable angina (Kaplan-Meier estimates 11.4, 9.4 and 3.4%, respectively; OR = 1.24, 95% CI 1.05–1.47, p = 0.01 for STEMI vs. NSTEMI; OR = 3.64, 95% CI 2.98–4.43, p < 0.001 for STEMI vs. unstable angina, and OR = 2.93, 95% CI 2.39–3.58, p < 0.001 for NSTEMI vs. unstable angina). Major bleeding occurred in 82 patients (2.9%) with STEMI, 84 patients with NSTEMI (2.8%) and 33 patients (0.7%) with unstable angina (p < 0.001). Stroke occurred in 21 patients (0.7%) with STEMI, 23 patients (0.7%) with NSTEMI and 6 patients (0.1%) with unstable angina (p < 0.001).

One-Year Clinical Outcome

Within the first year following PCI, there were a total of 976 deaths. Of these, 390 deaths occurred in patients with STEMI, 366 deaths occurred in patients with NSTEMI and 220 deaths occurred in patients with unstable angina (Kaplan-Meier estimates of mortality 13.7, 12.0 and 4.8%, respectively; OR = 1.17, 95% CI 1.01–1.35, p = 0.031 for STEMI vs. NSTEMI; OR = 3.00, 95% CI 2.56–3.51, p < 0.001 for STEMI vs. unstable angina, and OR = 2.58, 95% CI 2.20–3.04, p < 0.001 for NSTEMI vs. unstable angina; fig. 1). Myocardial infarction occurred in 87 patients with STEMI, 139 patients with NSTEMI and 114 patients with unstable angina (Kaplan-Meier estimates 3.1, 4.5 and 2.5%, respectively; OR = 0.66, 95% CI 0.50–0.86, p = 0.002 for STEMI vs. NSTEMI; OR = 1.21, 95% CI 0.91–1.60, p = 0.17, for STEMI vs. unstable angina, and OR = 1.83, 95% CI 1.43–2.33, p < 0.001 for NSTEMI vs. unstable angina). Death or myocardial infarction occurred in 1,239 patients: 457 events in patients with STEMI, 468 events in patients with NSTEMI and 314 events in patients with unstable angina (Kaplan-Meier estimates 16.0, 15.3 and 7.0%, respectively; OR = 1.06, 95% CI 0.93–1.20, p = 0.40 for STEMI vs. NSTEMI; OR = 3.11, 95% CI 2.67–3.62, p < 0.001 for STEMI vs. unstable

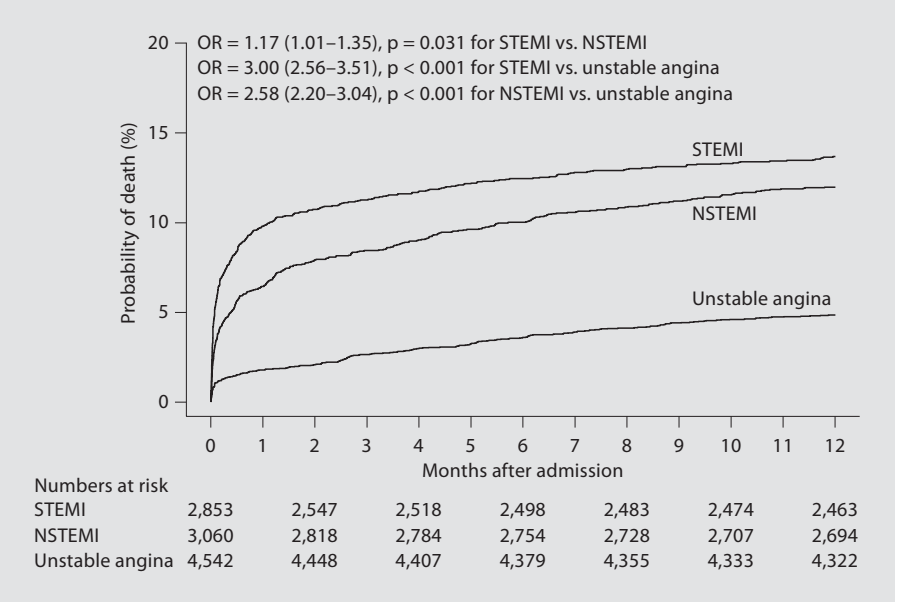

Fig. 1. Kaplan-Meier curves of 1-year mortality among patients with STEMI, NSTEMI and unstable angina.

Table 3. Type of intervention, adjunct antithrombotic therapy and therapy at discharge

Therapy	STEMI (n = 2,853)	NSTEMI (n = 3,060)	Unstable angina (n = 4,542)	p value
Type of intervention				0.06
Balloon angioplasty	223 (11.3)	398 (13.0)	517 (11.4)	
Stenting	2,530 (88.7)	2,662 (87.0)	4,025 (86.6)	
Glycoprotein IIb/IIIa receptor inhibitors	1,686 (59.1)	1,329 (43.4)	1,328 (29.2)	<0.001
Therapy at discharge				
Statins	2,382 (83.5)	2,703 (88.3)	4,031 (88.7)	<0.001
β-blocking agents	2,494 (87.4)	2,784 (91.0)	4,203 (92.5)	<0.001
Angiotensin-converting enzyme inhibitors or angiotensin II type I receptor blockers	2,499 (87.6)	2,733 (89.3)	4,045 (89.0)	0.07

Data are counts with percentages in parentheses.

angina, and OR = 2.33, 95% CI 2.03–2.68, $p < 0.001$ for NSTEMI vs. unstable angina; fig. 2).

Landmark analysis with a prespecified landmark at 1 month was performed to assess early and late relative risk of death. There were 2,573 patients with STEMI, 2,863 patients with NSTEMI and 4,461 patients with unstable angina that survived the first month after index event. Between 1 and 12 months following an acute event, there were 110 deaths among patients with STEMI, 169 among patients with NSTEMI and 139 deaths among patients with unstable angina (Kaplan-Meier estimates 4.3, 6.0 and 3.1%, respectively; OR = 0.72, 95% CI 0.56–0.91, p = 0.007 for STEMI vs. NSTEMI; OR = 1.38, 95% CI 1.08–1.77, p = 0.01 for STEMI vs. unstable angina, and OR = 1.93, 95% CI 1.54–2.40, $p < 0.001$ for NSTEMI vs. unstable angina; fig. 3).

Results of Multivariable Analysis

The Cox proportional hazards model was used to assess the correlates of 1-year mortality. The following variables were entered into the model: age, sex, diabetes, arterial hypertension, current smoking, hypercholesterolemia, creatinine, extent of coronary artery disease, prior myocardial infarction, prior coronary artery bypass sur-

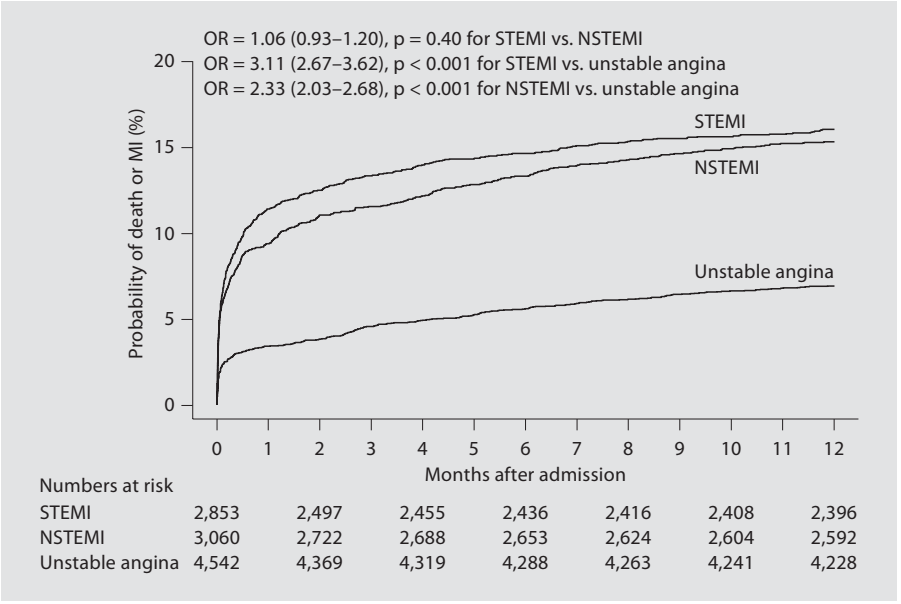

Fig. 2. Kaplan-Meier curves of 1-year composite of death or myocardial infarction (MI) among patients with STEMI, NSTEMI and unstable angina.

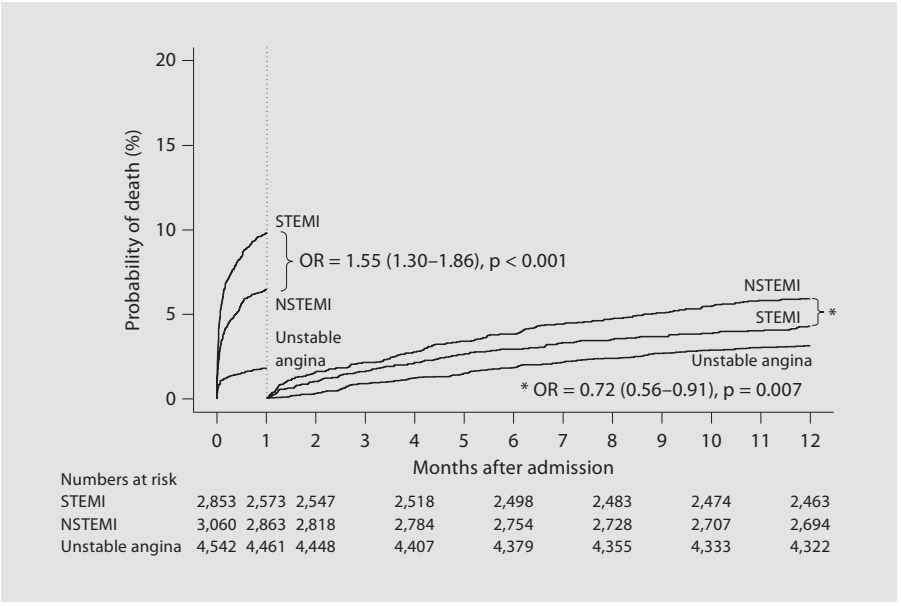

Fig. 3. Landmark analysis showing probability of early and late mortality in patients with STEMI, NSTEMI and unstable angina.

gery, left ventricular ejection fraction, TIMI flow grade before intervention, TIMI flow grade after intervention and ACS group (STEMI, NSTEMI and unstable angina). Results of multivariable analysis are shown in table 4. After adjustment for potential confounders, risk of death was significantly higher in patients with STEMI and NSTEMI compared with patients with unstable angina. However, there was no significant difference in the adjusted risk of death among patients with STEMI compared with patients with NSTEMI (table 4).

Discussion

The main findings of this study are as follows. (1) The presentation pattern of patients with ACS was associated with significant differences in the 30-day and 1-year mortality, with unadjusted mortality being highest in patients with STEMI and lowest in patients with unstable angina. (2) There were significant differences in the timing of death across the spectrum of patients with ACS, with early death (within 30 days) predominantly occur-

ring in patients with STEMI and late death (from 1 month to 1 year) occurring significantly more often in patients with NSTEMI than in patients with STEMI or unstable angina. (3) After adjustment for the extent of cardiovascular risk associated with each ACS form, the 1-year risk of death did not differ significantly between patients with STEMI and NSTEMI, while both continued to have a higher risk of death than patients with unstable angina.

Previous studies have reported large differences in the noninvasive or invasive therapies and marked selection bias in the application of these therapies in various subsets of patients with ACS [4–7]. In the current study the possibility of differentiated impact of treatment on prognosis has been eliminated because all patients underwent an early invasive treatment that has been proved to improve survival in patients with STEMI [18], NSTEMI [13, 14] and unstable angina [4]. Moreover, the recently reported reductions in the 6-month rates of new heart failure and mortality in patients with ACS may be attributed, at least in part, to the progressive increase in the use of primary PCI in these patients [19].

Since STEMI is associated with the most extensive ischemic damage compared with NSTEMI or unstable angina, STEMI patients had the highest proportion of cardiogenic shock. Thus, it comes as no surprise that patients with STEMI have the highest rate of early mortality as compared with 2 other ACS presentations. However, as it has recently been reported, patients with cardiogenic shock who survive for 30 days after STEMI have a favorable prognosis with annual mortality rates of 2–4%, which are approximately similar to those of patients without shock [20]. With regard to mortality in patients with NSTEMI, the present study reports some important observations. As in previous studies, we found that the NSTEMI group had a significantly more adverse cardiovascular risk profile that included older age, more prevalent diabetes and a higher proportion of patients with hypercholesterolemia. Such increased risk is important and may underlay the fact that these patients continue to experience higher mortality than patients with STEMI up to 10 years [21]. Especially in older patients with ACS, mortality during follow-up has been attributed to re-infarction and congestive heart failure [22, 23]. The finding that myocardial infarction occurred significantly more often in patients with NSTEMI between 1 month and 1 year suggests that myocardial infarction may be one of the contributing factors of higher rates of late mortality in patients with this category of ACS.

Previous studies have demonstrated that angiographic information bears important prognostic information [8–12]. Of note, angiographic information available in all patients in this study showed that patients with NSTEMI had more extensive coronary artery disease, a smaller size of vessels with culprit lesions and a more distal location of culprit lesions. Since a recent study has suggested that more distally located culprit lesions are more prone to spontaneous reperfusion following thrombotic occlusion [24], this latter fact might also have implications for the pathophysiology of NSTEMI. In contrast to patients with STEMI who showed higher rates of early mortality, patients with NSTEMI showed higher rates of mortality between 1 month and 1 year following PCI. Thus, persistence of increased demographic and angiographic cardiovascular risk could be an important factor that underlies the elevated risk of death in patients with NSTEMI compared with other types of ACS.

Another observation from this study pertains to distribution of the risk of 1-year mortality among patients with STEMI, NSTEMI and unstable angina. A recent study by Montalescot et al. [6] concluded that despite differences in the management, STEMI and NSTEMI have similar prognosis and independent correlates of outcome. Other researchers [25] suggest that STEMI and NSTEMI are distinct pathologies and that there may be a predilection of some patients to develop repeat occlusive thrombi and STEMI or repeat nonocclusive thrombi and NSTEMI [26]. Based on the course of the mortality curves and unadjusted estimated risk over 1 year, our data clearly demonstrated that mortality over 1 year was slightly higher in patients with STEMI than in patients with NSTEMI. How-

Table 4. Independent predictors of 1-year mortality

Characteristic	HR (95% CI)	p value
Cardiogenic shock	6.65 (5.27–8.40)	<0.001
Age (for 10 year increase)	1.62 (1.47–1.79)	<0.001
Female sex	1.31 (1.07–1.61)	0.009
Diabetes	1.22 (1.01–1.49)	0.040
Serum creatinine (for 1 mg/dl increase)	1.12 (1.09–1.14)	<0.001
Multivessel disease	1.65 (1.23–2.22)	<0.001
LV ejection fraction (for 10% decrease)	1.78 (1.54–2.04)	<0.001
TIMI flow grade after intervention (0 vs. 3)	3.03 (2.22–4.00)	<0.001
ACS group		
STEMI vs. unstable angina	1.56 (1.13–2.14)	<0.001
NSTEMI vs. unstable angina	1.72 (1.30–2.29)	<0.001
STEMI vs. NSTEMI	0.90 (0.73–1.13)	0.366

LV = Left ventricle.

ever, after adjustment in the multivariable model for various cardiovascular risk factors, differences in mortality were no longer significant and in fact there was a trend for higher mortality in patients with NSTEMI than in those with STEMI demonstrating that, at least in terms of prognosis, STEMI and NSTEMI are close to each other.

With regard to patients with unstable angina, our study shows that these patients have a low risk of death over 1 year after PCI, significantly lower than the risk of death for patients with STEMI or NSTEMI. Thus, our data clearly show that reporting efficacy of any novel treatment or assessing prognosis of patients with non-ST-segment elevation ACS with patients with NSTEMI and unstable angina grouped together, as has been the case in previous studies [5, 7, 27], could be misleading because these 2 subsets may have inherent differences that may shape the response to treatment or affect prognosis. As recently demonstrated, patients with NSTEMI but not those with unstable angina benefited from antithrombotic therapy with abciximab in the setting of urgent PCI [27]. In terms of the response to treatment and outcome, patients with unstable angina were more close to patients with stable coronary artery disease undergoing elective PCI [28] than to patients with NSTEMI. It may be said hypothetically that these differences in response to treatment and prognosis among patients with NSTEMI and unstable angina may explain existing controversies regarding timing of early PCI [29–31] in patients with non-ST-segment elevation ACS. Considering the impact of peri-PCI bleeding on mortality [32], lower rates of bleeding in patients with unstable angina could also be a factor that explains low mortality in these patients.

Some observations regarding the extent of cardiovascular risk and outcomes in each of the ACS presentations may have clinical implications. Although patients with STEMI and NSTEMI seem to have differences in their cardiovascular risk profiles, with patients with NSTEMI having a more adverse risk profile, clinical outcomes such as 1-year mortality seem be relatively similar in both ACS presentations. On the other hand, patients with NSTEMI and unstable angina seem to have a similar cardiovascular risk profile; however, these ACS forms showed significant differences regarding outcome. This comparative analysis of cardiovascular risk and outcome among patients with ACS demonstrates that syndrome itself (i.e. type of ACS) plays an important prognostic role. Thus, non-ST-segment elevation ACS includes a heterogeneous group of patients with striking differences in their response to treatment and prognosis, which stresses the need to separate these patients into NSTEMI and unstable angina groups. This strategy may have far reaching therapeutic implications. Specifically, patients with NSTEMI may need a therapeutic strategy similar to that of STEMI patients in terms of early PCI.

Although all patients included in this registry were treated with a PCI-based invasive strategy, the evolution of treatment modalities including the use of drug-eluting stents, new antithrombotic agents and prolongation of dual antiplatelet therapy up to 1 year after PCI procedure might have impacted the efficacy of invasive treatment during the course of the study. However, since the primary objective of the study was a comparison of clinical outcomes across the ACS spectrum and patients were consecutively included on the registry, we believe that such an evolution of therapy has not disproportionately affected the clinical outcome in different groups of patients.

In conclusion, data from this large prospective registry showed that presentation pattern affects 1-year mortality in patients with ACS with unadjusted mortality being highest in patients with STEMI and lowest in patients with unstable angina. Adjusting for the extent of cardiovascular risk associated with each of the ACS types attenuated differences between STEMI and NSTEMI regarding 1-year mortality. Both conditions, however, continued to have a higher adjusted risk of death than patients with unstable angina. These data strongly suggest that current consideration of NSTEMI and unstable angina within a unitary group of ACS is not justified and future studies on treatment strategies should distinguish between these 2 pathologies.

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