

The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004

Lori Mandelzweig¹, Alex Battler², Valentina Boyko¹, Hector Bueno³, Nicolas Danchin⁴, Gerasimos Filippatos⁵, Anselm Gitt⁶, David Hasdai², Yonathan Hasin⁷, Jaime Marrugat⁸, Frans Van de Werf⁹, Lars Wallentin¹⁰, and Shlomo Behar^{1*} on behalf of the Euro Heart Survey Investigators

¹Neufeld Cardiac Research Institute, Sheba Medical Center, Tel Hashomer, Israel; ²Department of Cardiology, Rabin Medical Center, Petach Tikva, Israel; ³Department of Cardiology, Hospital General Universitario Gregorio Marañon, Madrid, Spain; ⁴Department of Cardiology, Hopital Europeen Georges-Pompidou, Paris, France; ⁵Department of Cardiology, Atticon University Hospital, Athens, Greece; ⁶Herzzentrum Ludwigshafen, Institut für Herzinfarktforschung, Ludwigshafen, Germany; ⁷Cardiovascular Institute, Poriah Medical Center, Tiberias, Israel; ⁸Lipids and Cardiovascular Epidemiology Unit, IMIM, Barcelona, Spain; ⁹Department of Cardiology, University Hospital Gasthuisberg, Leuven, Belgium; and ¹⁰Department of Cardiology, Uppsala Clinical Research Centre, Uppsala, Sweden

Received 16 January 2006; revised 29 June 2006; accepted 27 July 2006; online publish-ahead-of-print 14 August 2006

This paper was guest edited by Prof. Chris Granger, Duke University Medical Center, Durham, NC 27710, USA

See page 2260 for the editorial comment on this article (doi:10.1093/eurheartj/ehl240)

KEYWORDS

Acute coronary syndromes;
Acute myocardial infarction;
Unstable angina;
Prognosis;
Management

Aims Our study aimed to examine the management of acute coronary syndromes (ACS) in Europe and the Mediterranean basin, and to compare adherence to guidelines with that reported in the first Euro Heart Survey on ACS (EHS-ACS-I), 4 years earlier.

Methods and results In a prospective survey conducted in 2004 (EHS-ACS-II), data describing the characteristics, treatment, and outcome of 6385 patients diagnosed with ACS in 190 medical centres in 32 countries were collected. ACS with ST-elevation was the initial diagnosis in 47% of patients, no ST-elevation in 48%, and undetermined electrocardiographic pattern in 5% of patients. Comparison of data collected in 2000 and 2004 showed similar baseline characteristics, but greater use of recommended medications and coronary interventions in EHS-ACS-II. Among patients with ST-elevation, the use of primary reperfusion increased slightly (from 56 to 64%), with a significant shift from fibrinolytic therapy to primary percutaneous coronary intervention (PPCI). The use of PPCI rose from 37 to 59% among those undergoing primary reperfusion therapy. Analysis of data in 34 centres that participated in both surveys showed even greater improvement with respect to the use of recommended medical therapy, interventions, and outcome.

Conclusion Data from EHS-ACS-II suggest an increase in adherence to guidelines for treatment of ACS in comparison with EHS-ACS-I.

Introduction

The diagnosis, management, and treatment of the various forms of acute coronary syndromes (ACS), which include persistent ST-segment elevation myocardial infarction (MI), non-ST-segment elevation MI, and unstable angina (UA), have been rapidly evolving in recent years. European and American cardiological associations have published new guidelines to address these changes in medical practice.^{1–4}

Surveys and registries are an effective means of assessing the implementation of guidelines.⁵ Although the adherence to guidelines has been shown to be associated with improved outcomes,⁶ their implementation remains sub-optimal.^{7,8} Indeed, the first Euro Heart Survey of ACS,⁹ conducted in 25 countries in Europe and the Mediterranean basin in 2000–2001, demonstrated great variability in the implementation of the guidelines and recommendations applicable at that time period. In order to assess current management and implementation of more contemporary guidelines, we conducted the second Euro Heart Survey of ACS during 2004 in 32 countries throughout this region.

*Corresponding author. Tel: +972 3 5344703; fax: +972 3 5342392.
E-mail address: behar@sheba.health.gov.il

Methods

The second Euro Heart Survey on ACS was conducted in 190 medical centres from 32 countries in Europe and the Mediterranean basin. Within each participating country, medical centres were invited to participate in the survey on a purely voluntary basis, by a national coordinator, responsible for maintaining contact with the investigators in each of the participating centres, and for overseeing the implementation of the survey protocol (see Appendix). In addition to the recruitment efforts of the national coordinators, information about the survey was posted on the website of the European Society of Cardiology (ESC) and on the ESC web news, inviting all interested investigators to join. Announcements about the survey were also made at the European Congress of Cardiology. Among 319 centres that confirmed their participation in the survey, 129 either did not recruit any patients or did not complete any case report forms.

The enrolment period of the survey began in March 2004, and ended in October 2004. Participating centres were asked to recruit 30–50 consecutive patients fulfilling the survey inclusion criterion of a confirmed diagnosis of ACS.

In each participating centre, a data collection officer was responsible for screening consecutive patients admitted with a tentative diagnosis of ACS. Patients were followed throughout their hospitalization, and informed consent for participation in the survey was acquired when necessary. As in the first survey,⁹ case report forms were completed only after the diagnosis of ACS (UA, Q-wave, non-Q-wave, or undetermined MI) was confirmed by the attending physician. Patients with symptoms that suggested ACS, but did not fulfil the diagnostic criteria for ACS were not included in the survey.

In addition to data regarding the pre-hospital and in-hospital course, follow-up data were collected at 30 days. Patient identification was not recorded on the case report forms. The centres were instructed to keep a log of all included patients, in which their names, contact information, and study code were recorded, in order to enable follow-up. Each participating centre was also asked to complete a questionnaire, designed to provide a description of the medical centre.⁹

Electronic case report forms were used for data entry and transferred via the web to a central database located in the European Heart House, where they were edited for missing data, inconsistencies, and outliers. Additional editing of the data was performed at the data analysis centre at the Neufeld Cardiac Research Institute. In the case of two countries, participation in ACS-II involved the transfer of data collected in national ACS surveys during the recruitment period of ACS-II in 2004 (the Israeli ACSIS survey and the Spanish MASCARA survey¹⁰) to the ACS-II database at the European Heart House. ACSIS is a biennial national ACS survey conducted in all 25 operating cardiac departments in Israel since 1992. MASCARA is a nationwide prospective cohort study that included consecutive patients hospitalized for ACS in 60 randomly selected Spanish hospitals in 2004–2005. Both national surveys collected data on ACS patients using similar case report forms and the same definitions for ACS as used in EHS-ACS-II.

Of the 190 centres, 91 that participated in the survey were affiliated with academic institutions, 123 had catheterization laboratories, and 61 had cardiac surgery facilities. Fifty-three percent of the patients were hospitalized in medical centres that were affiliated with academic institutions, and 46% were hospitalized in tertiary care centres. Seventy-three percent of the patients were treated in hospitals that had on-site catheterization laboratories, and 37% in centres that had facilities for cardiovascular surgery. Seventy percent of the patients were hospitalized in centres in which the policy was to hospitalize ACS patients in cardiology departments, 26% were admitted to centres that treat ACS patients in both cardiology and internal medicine departments, and 4% were treated in centres that hospitalized ACS patients in internal medicine wards. Examination of the extent of enrolment in the participating centres showed that 71 centres (37%) recruited

less than 30 patients, 102 centres (54%) recruited 30–50 patients, and 17 centres (9%) included more than 50 patients.

Among the centres participating in EHS-ACS-II were 34 centres that had also participated in the first European Heart Survey on ACS. Analysis of the characteristics of 34 centres that participated in both the EHS-ACS-I and EHS-ACS-II surveys, showed that the proportion of patients hospitalized in centres with academic affiliations (70%), catheterization laboratories (92%), and cardiac surgery facilities (65%), were greater in comparison with the total group of centres participating in EHS-ACS-II.

Statistical methods

All analyses were performed using SAS software (SAS Institute Inc., Cary, NC, USA). The χ^2 test was used for comparison of proportions. All tests were two-sided and considered statistically significant if $P \leq 0.05$. No adjustment was made for multiple testing. Comparison of the outcome of patients included in the ACS-I and ACS-II surveys was performed using logistic regression analysis with adjustment for the following variables, which were considered to be potential predictors of mortality on the basis of clinical judgment, univariable analysis, and data from the literature: age, sex, prior MI, diabetes, prior stroke, chronic renal failure, hypertension, current and past smoking, Killip class ≥ 2 on admission, and ST pattern on admission ECG (ST-elevation, no ST-elevation, or undetermined pattern on ECG). In a multivariable analysis for 34 centres that participated in both the EHS-ACS-I and EHS-ACS-II surveys, a similar model was used, with the addition of the variable 'center'.

Results

The EHS-ACS-II cohort included 6385 patients with a final diagnosis of ACS. Baseline, demographic, and clinical characteristics of the EHS-ACS-I and EHS-ACS-II patients are presented in *Table 1*. The proportion of patients with an initial diagnosis of ACS with ST-elevation rose from 42% in EHS-ACS-I to 47% in EHS-ACS-II, whereas no ST-elevation ACS patients comprised 51% of the ACS-I participants and 48% of those included in ACS-II. Five percent and 6.5% of the patients in ACS-II and ACS-I, respectively, presented with an undetermined electrocardiographic (ECG) pattern, which included left bundle branch block/right bundle branch block (LBBB/RBBB), pacing, or severe left ventricular (LV) hypertrophy (LVH) without typical ST changes.

Examination of the characteristics of all patients included in the first and second EHS surveys of ACS showed a considerable degree of similarity with respect to mean age (65.2 vs. 64.7 in ACS-I vs. ACS-II), proportion of men (67.5% in ACS-I vs. 70.1% in ACS-II), and the proportion of patients with risk factors. Comparison of the characteristics of the patients in the 34 centres participating in both surveys showed much similarity in the two periods. The only noteworthy difference was the proportion of patients with ST-elevation, which rose from 40% in ACS-I to 51% in ACS-II.

The most common presenting symptom among EHS-ACS-II patients was typical angina, which was most prevalent in patients with ST-elevation. Patients with an undetermined ECG pattern were more likely to present with heart failure. Comparison of data from the two surveys showed that the proportion of patients presenting with typical angina was higher in ACS-I than ACS-II, 86.8% and 80.8%, respectively. In the second survey, more patients were hospitalized in coronary care units (70 vs. 62.4%), whereas fewer were treated in cardiology wards (19.1 vs. 22%), and

Table 1 Baseline, demographic, and clinical characteristics of ACS-I and ACS-II patients on the basis of the initial electrocardiographic pattern

	ST-elevation		No ST-elevation	
	ACS-I (n = 4431)	ACS-II (n = 3004)	ACS-I (n = 5367)	ACS-II (n = 3063)
Age (years)	63.4 ± 13.0	62.5 ± 13.1	65.8 ± 12.0	66.1 ± 12.1
Male gender (%)	71.6	74.1	64.4	67.0
BMI (mean)	27.0 ± 4.1	27.0 ± 4.3	27.4 ± 4.4	27.4 ± 4.8
Prior MI (%)	22.3	15.7	35.6	29.3
Prior PCI/CABG (%)	9.5	8.9	22.2	21.5
Diabetes mellitus (%)	21.1	21.4	23.5	26.7
Current smoker	42.8	45.6	27.0	28.0
Past smokers	20.3	22.6	26.8	29.8
Hypertension (%)	51.6	50.0	63.5	64.6
Hyperlipidaemia (%)	46.8	43.2	54.6	51.9
Family history of CAD (%)	27.4	29.8	29.3	32.6
Prior stroke/TIA (%)	5.9	5.2	8.1	7.3
Renal failure (%)	3.4	3.8	5.8	7.1
Heart rate (mean bpm)	79 ± 20	78 ± 19	79 ± 19	79 ± 20
Killip Class II, III, IV (%)	22.7	20.4	16.1	19.7

Continuous variables are presented as mean ± SD. BMI, body mass index; CAD, coronary artery disease; TIA, transient ischaemic attack.

in internal medicine wards (7 vs. 13.8%). The proportion of patients hospitalized in other wards was 3.9% in ACS-II vs. 1.8% in ACS-I.

The frequency of chronic use of cardiovascular therapies among patients prior to admission was lower among ST-elevation patients in comparison with no ST-elevation patients in both surveys. The proportions of patients receiving pre-hospital medication were similar in the two survey periods, although slight increases in the use of ACE-inhibitors/angiotensin-II receptor blockers and statins were observed in EHS-ACS-II.

Coronary angiography, percutaneous coronary interventions (PCIs), and intracoronary stents were used more frequently in ACS-II than in ACS-I (Table 2). The increase in the proportion of patients undergoing coronary angiography, PCIs, and stent implantation among those hospitalized in the 34 centres was greater than in the full ACS-I and ACS-II cohorts (from 60.5 to 82.3%, from 45.9 to 69.9%, and from 34.1 to 63.6% for patients with ST-elevation, respectively, and from 54.3 to 72.1%, from 27.3 to 46.7%, and from 19.6 to 43.6% for no ST-elevation patients, respectively).

A greater proportion of patients received evidence-based medications during their hospitalization and at discharge in ACS-II compared with ACS-I, irrespective of their initial ECG diagnosis (Table 3, Figures 1 and 2). The reasons recorded for not prescribing evidence-based medications during ACS-II showed that half of the small number of patients who did not receive aspirin or beta-adrenergic blockers had contraindications to the medications. In contrast, the most frequent reason for not prescribing anticoagulants, ticlopidine/clopidogrel, ACE-inhibitors, and statins, was the lack of indication for treatment according to current guidelines.

Patients hospitalized in the 34 centres that participated in both surveys were more likely to receive evidence-based medication in comparison with the whole survey population in ACS-II, during hospitalization and upon discharge from hospitalization. Particularly noteworthy was an increase in the use of ticlopidine/clopidogrel both in-hospital and at discharge.

Analysis of the time at which medication was initiated among ST-elevation patients showed that the proportions of patients starting medication in-hospital were: 73.2% for aspirin, 51.2% for ACE-inhibitors, 64.5% for beta-blockers, and 65.6% for statins. The remaining patients to whom these medications were administered in-hospital had started taking them at least 1 month prior to hospital admission.

Comparison between the two surveys in terms of time delay showed a reduction in the median time from symptom onset to arrival at the emergency department, from 210 min (105–625) in ACS-I to 170 min (90–420) in ACS-II. This reduction was a result of decreases in both time from symptom onset to first call for help, from a median 120 min (50–450) in ACS-I to 105 min (40–306) in ACS-II, as well as time from first call for help to emergency room arrival, from a median 50 min (26–91) in ACS-I to 42 min (15–80) in ACS-II. A reduction in the length of stay in the reporting department was also observed, with a median stay of 8 days in EHS-ACS-I to 7 days in EHS-ACS-II. In the 34 centres, a reduction was also noted, from 8 to 6 days.

Among patients with ST-elevation, 63.9% received primary reperfusion treatment (51.8% of reperfused patients were treated with PPCI, 7% with facilitated PCI, and 41.2% with fibrinolytic therapy, with or without rescue interventions). The proportion of ST-elevation patients treated with primary reperfusion therapy was directly related to the time from symptom onset to emergency room arrival. The rate of primary reperfusion was 74.4% among patients with ST-elevation reaching the hospital within 6 h from symptom onset (n = 2116) and decreased to 54.8% and 25.2% for those reaching the hospital within 6–12 h (n = 301) and 12–24 h (n = 338), respectively. A total of 1084 patients presenting with ST-elevation ACS did not receive primary reperfusion therapy. The major reasons were late arrival (30.1%), uncertain diagnosis (11.2%), early resolution of ST-elevation (11.6%), and contraindications (6.5%). Additional reasons given by the treating

Table 2 The in-hospital use of invasive and non-invasive diagnostic and therapeutic techniques

	ST-elevation		No ST-elevation	
	ACS-I (n = 4431) (%)	ACS-II (n = 3004) (%)	ACS-I (n = 5367) (%)	ACS-II (n = 3063) (%)
Total angiography	56.3	70.2	52.0	62.9
Total PCI	40.4	57.8	25.4	37.1
Total stent	31.0	52.4	18.1	33.8
CABG	3.4	2.9	5.4	7.4
Echocardiography	73.1	83.1	60.5	72.2
PA catheter	3.9	1.9	2.2	2.1
IABP	2.5	2.6	0.9	1.2
AICD	0.5	0.2	0.2	0.2
Holter	13.6	11.8	7.7	8.3
Permanent or temporary pacemaker	2.8	3.1	1.8	1.5

Angiography, coronary angiography; PA, pulmonary artery; IABP, intra-aortic balloon pump; AICD, automatic internal cardiac defibrillator.

Table 3 In-hospital medical therapy

	ST-elevation		No ST-elevation	
	ACS-I (n = 4431) (%)	ACS-II (n = 3004) (%)	ACS-I (n = 5367) (%)	ACS-II (n = 3063) (%)
Aspirin	93.0	96.8	88.5	94.5
Warfarin	5.3	13.1	5.7	17.1
Heparin/LMWH	81.5	77.2	79.1	72.9
Ticlopidine/clopidogrel	36.1	69.8	27.6	67.4
GP IIb/IIIa inhibitor	19.6	30.7	10.0	20.8
ACE-inhibitors/angiotensin-II receptor blocker	63.8	75.4	58.8	69.5
IV/oral β -adrenergic blocker	78.4	83.0	76.9	82.8
Statin	49.2	80.7	50.6	73.7

GP, platelet glycoprotein; ACE-I, angiotensin-converting enzyme-inhibitor; IV, intravenous.

physician included advanced age, premature death, patient refusal, and lack of catheterization laboratory facilities.

In ACS-II, the most common complications during hospitalization were heart failure (12.4%), re-ischaemia/re-infarction (8.0%), and paroxysmal or persistent atrial fibrillation (AF) (3.3%).

As expected, the majority of patients with ST-elevation had a final diagnosis of Q-wave MI (64%), whereas patients admitted without ST-elevation were more likely to be diagnosed with UA (43%) or non-Q wave MI (38%). In the entire cohort, 34.5% had a final diagnosis of Q-wave MI, 28.2% with non-Q wave MI, 9.0% with undetermined type of MI, and 24.5% had UA. In 3.8% of the patients, the final ACS diagnosis was not specified.

Post-discharge events occurring during the 30-day follow-up period were available for 5213 hospital survivors (85%), of whom 15.9% were re-hospitalized during the first month following admission to hospital. The majority of re-hospitalizations of patients with ST or no ST-elevation were cardiac related and were due to the need for coronary angiography (4.4% and 4.8%), PCI (2.9% and 2.7%), coronary artery bypass surgery (CABG) (1.5% and 2.0%), or other cardiac surgery (0.3% and 0.2%). Among patients whose

initial ECG pattern was undetermined, the majority of re-hospitalizations were due to other cardiac-related reasons (10.8%). Non-cardiac-related reasons were the cause of re-hospitalization in 2.3% of the patients.

Comparison of patients with ST-elevation

In both surveys, the baseline characteristics of the ST-elevation patients were relatively similar (Table 1). A better adherence to the use of recommended medications was observed in the latter survey (Table 3, Figure 1).

A higher use of primary reperfusion therapy was observed in ACS-II (63.9%) compared with ACS-I (55.8%), with a shift from fibrinolytic therapy to PPCI in ACS-II (Figure 3). Time from symptom onset to hospital arrival and time from hospital arrival to reperfusion were both shorter in the second survey, with a larger difference observed in time to PPCI in comparison with time to fibrinolytic therapy (Table 4). Similar improved patterns were observed for the 34 centres and, in addition, the time from emergency room arrival to fibrinolytic therapy decreased from a median of 50 min to 30 min in the 34 centres. In the ACS-II survey, a greater proportion of patients underwent coronary

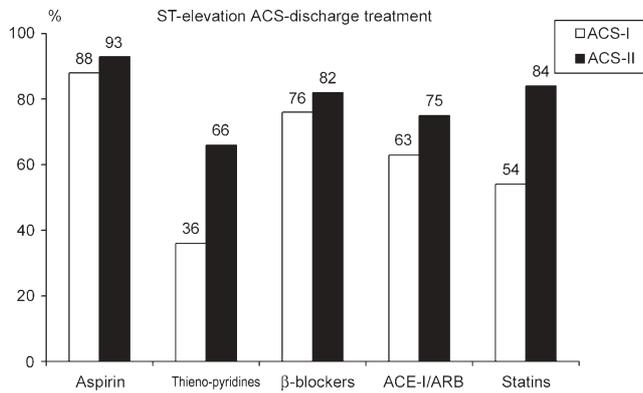


Figure 1 Comparison of treatment of ST-elevation MI patients at discharge in ACS-I and ACS-II in 34 centres that participated in both surveys.

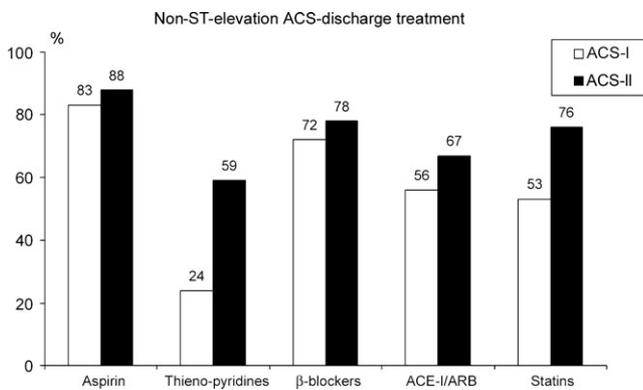


Figure 2 Comparison of treatment of no ST-elevation MI patients at discharge in ACS-I and ACS-II in 34 centres that participated in both surveys.

angiography, PCI, and stent implantation. In contrast, the proportion of patients undergoing CABG surgery was lower in ACS-II than ACS-I (Table 2). In the 34 centres, the use of PPCI was even more pronounced (79%), and only 21% were treated with fibrinolytic therapy as compared with 43% and 57%, respectively in ACS-I. In addition, the increased use of coronary procedures, except CABG, was more pronounced in the 34 centres between the two survey periods.

Comparison of patients with no ST-elevation

The baseline characteristics of the no ST-elevation patients were quite similar in both the EHS-ACS-I and EHS-ACS-II surveys (Table 1). Patients in ACS-II were more likely to be treated with evidence-based medications (Table 3, Figure 2). More coronary interventions during hospitalization were performed in the second survey, with a higher proportion of patients undergoing coronary angiography and, among them, PCIs. Among the latter, stents were placed in a greater proportion of patients in ACS-II than in ACS-I. The frequency of CABG surgery was also higher in this group of patients. Similar changes occurred in the 34 centres that participated in both surveys, but the increases were more pronounced.

In-hospital and 30-day mortality

Crude mortality in-hospital and at 30 days was lower in the total ACS-II cohort than the ACS-I cohort (Table 5). The reduction in mortality from ACS-I to ACS-II was more

Primary reperfusion for patients with ST-elevation

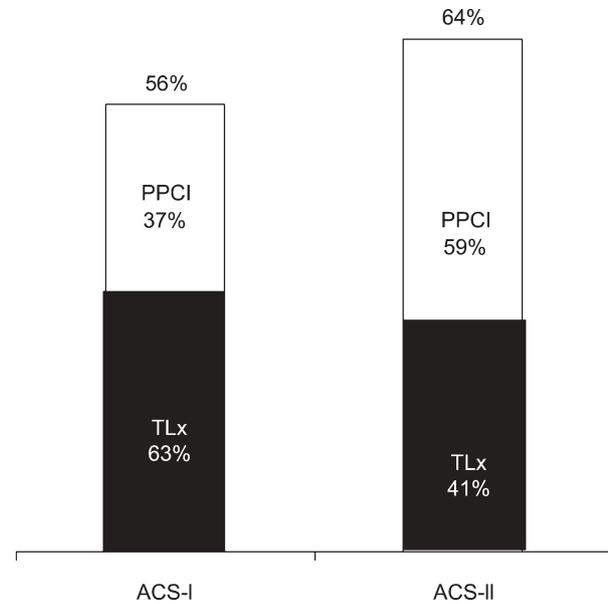


Figure 3 Comparison of the use of primary reperfusion therapy in ACS-I and ACS-II.

Table 4 Timing of reperfusion in minutes (median, interquartile range) and in-hospital coronary intervention among patients with ST-elevation—ACS-I vs. ACS-II

	ACS-I (N = 4431)	ACS-II (N = 3004)
Symptom onset to ER	176 (90–465)	145 (80–330)
ER to primary reperfusion	59 (30–109)	53 (30–96)
ER to TLx (door to lysis)	40 (25–70)	37 (20–60)
ER to PPCI (door to balloon)	93 (60–170)	70 (40–125)

ER, emergency room; TLx, thrombolytic therapy.

marked in the 34 centres, which participated in both surveys (from 5.6 to 4.4% and 6.8 to 5.6% for in-hospital and 30-day mortality, respectively). After adjustment in multivariable analysis for the 34 centres, the odds ratio (OR) for in-hospital mortality in ACS-II in comparison with ACS-I was 0.58 (95% CI: 0.40–0.83), and for 30-day mortality, 0.66 (95% CI: 0.48–0.92).

Mortality rates in ACS-II differed according to the ECG pattern on admission: the highest rates were noted for patients presenting with undetermined ECG, who can be characterized as a high-risk population with a greater prevalence of concomitant disease. The lowest rates were observed for those without ST-elevation (Figure 4). Mortality by final diagnosis was higher for patients with Q-wave MI, and highest among those with undetermined MI (Figure 4). Among 246 patients in whom the final diagnosis was not specified (MI or UA), in-hospital and 30-day mortality were 9.0 and 11.6%, respectively.

Discussion

The second Euro Heart Survey on ACS offers insight into contemporary diagnostic and therapeutic strategies applied for

ACS patients. In addition, this survey sheds light on the short- and intermediate-term prognosis of a wide spectrum of 'real world' ACS patients. Moreover, this survey, performed 4 years after the first survey, enables the assessment of temporal trends in the diagnosis, management, and outcomes of ACS.

The comparison between the two surveys is encouraging in several respects. Although the baseline characteristics of the patients were similar during the two survey periods, more extensive use of recommended medications was noted for ACS patients with and without ST-elevation, during hospitalization and at discharge, suggesting an improvement in adherence to guidelines. Moreover, in the latter survey, the use of coronary interventions such as coronary angiography and PCI was also more frequent in both patients with and without ST-elevation. However, additional analysis is needed to determine whether a more aggressive approach was administered to the patients who merit such treatment: patients at intermediate-to-high risk. Although the time from pain onset to reperfusion was shortened in

the second survey, there are still delays beyond the recommended time for reperfusion therapy, and further research is needed on how to improve public awareness of the importance of early hospital arrival.

Among patients with ST-elevation, a slight increase in the use of primary reperfusion was observed, accompanied by a significant shift from fibrinolytic therapy to PPCI. Nevertheless, a significant proportion of ST-elevation patients did not receive primary reperfusion treatment, mainly because of late arrival, uncertain diagnosis upon admission, and early ST-resolution, the latter of which is viewed by some physicians as not requiring further reperfusion therapy. Of note, the rate of primary reperfusion dropped from 74.4% among patients reaching the hospital within 6 h from pain onset, to 25.2% among those reaching the hospital 12–24 h from onset. A reduction in the time from symptom onset to arrival at the emergency room was also observed, suggesting that efforts to inform the public of the need to respond immediately to symptoms of ACS may be having an effect.

Moreover, in the 34 centres that participated in both surveys, the increases in the use of evidence-based therapies and interventions were accompanied by an even greater reduction in mortality between ACS-I and ACS-II. The relative risks of hospital and 30-day mortality were 42 and 34% lower in ACS-II in comparison with ACS-I, although patient characteristics were similar. Therefore, the improved outcome in the second survey may be partially attributed to a significant increase in guideline adherence in these centres in ACS-II vs. ACS-I. Although the latter is true as well for ST-elevation patients in the full ACS-II cohort, the increase in the use of evidence-based therapies and interventions among no ST-elevation patients seems to have even preceded the publication of new guidelines.

As 92% of the ST-elevation patients in the ACS-II survey were admitted to either coronary care units or cardiology wards, it could be said that our data reflect the state-of-the-art in cardiology departments. This may have

Table 5 Multivariable analysis of mortality: ACS-I vs. ACS-II

	ACS-I (N = 10484)	ACS-II (N = 6385)	P-value
In-hospital mortality			
n (%)	518 (4.9)	257 (4.0)	
Unadjusted OR (95% CI)	1.0	0.81 (0.69–0.94)	0.006
Adjusted OR (95% CI)	1.0	0.86 (0.73–1.01)	0.07
30-Day mortality^a			
n (%)	600 (6.2)	310 (5.1)	
Unadjusted OR (95% CI)	1.0	0.81 (0.70–0.93)	0.004
Adjusted OR (95% CI)	1.0	0.85 (0.73–0.99)	0.04

^aMissing: 7.6% in ACS-I and 4.4% in ACS-II.

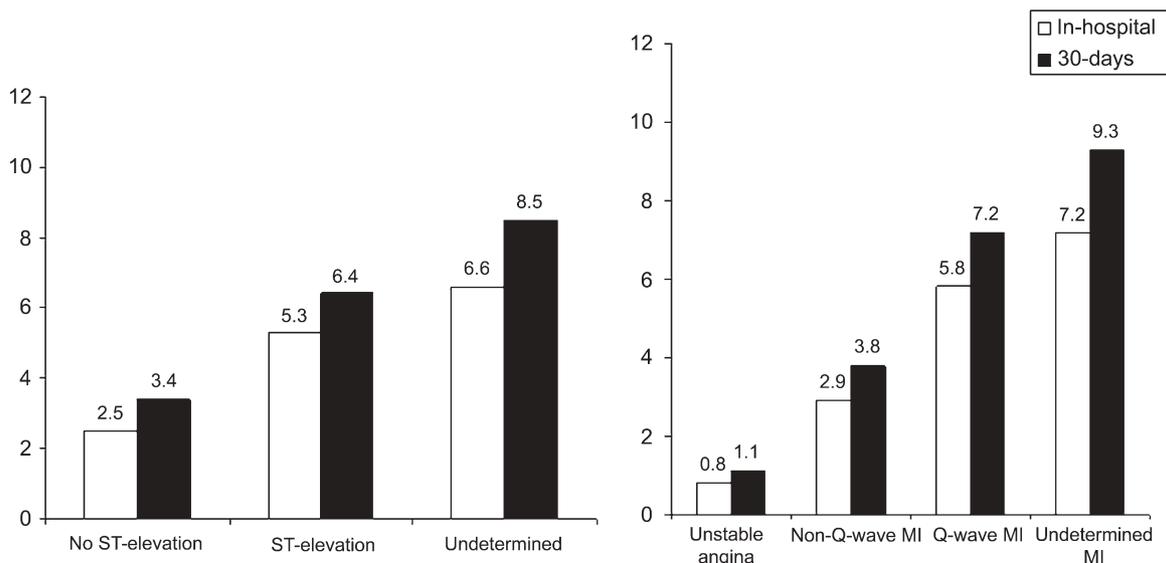


Figure 4 In-hospital and 30-day mortality by initial ECG presentation and final diagnosis (it should be noted that data on 30-day mortality were missing for 283 patients (4.4%).

been a result of the type of hospitals willing to participate in the survey on a voluntary basis.

A comparison of our current results for ST-elevation ACS patients with those of the European subpopulation of the GRACE (Global Registry Of Acute Coronary Events) registry ($n = 2729$),⁵ reveals similar rates of treatment with aspirin, beta-adrenergic blockers, calcium-channel blockers, platelet glycoprotein IIb/IIIa inhibitors, and ACE-inhibitors, whereas a greater proportion of patients in our survey were treated with thienopyridines (69.8 vs. 48%) and statins (80.7 vs. 58%). A comparison of medication at discharge yielded similar results. With regard to reperfusion therapy, the rate of use in the two surveys was similar (64 vs. 65% in EHS-ACS-II and GRACE, respectively), but PPCI was used more frequently in EHS-ACS-II. A comparison of cardiac procedures shows that a greater proportion of ST-elevation ACS patients underwent coronary angiography in EHS-ACS-II in comparison with the GRACE patients (70.2 vs. 53%). Comparison of in-hospital mortality showed a lower death rate among EHS-ACS-II patients with ST-elevation than among those in GRACE (5.3 vs. 7.8%). Although these differences may primarily reflect differences in enrolment criteria, they may also reflect a real improvement in treatment with better prognosis.

Regarding non-ST-elevation ACS patients, the use of evidence-based medications is similar to that reported by the American CRUSADE national quality improvement initiative,¹¹ with the exception of glycoprotein IIb/IIIa inhibitors, close to that observed in the lowest adherence quartile in CRUSADE. Also, the proportion of patients discharged with aspirin and beta-adrenergic blockers is closer to the middle quartiles of CRUSADE hospitals. Thus, it seems that the treatment strategies for non ST-elevation ACS patients are similar on both sides of the Atlantic.

Limitations

Although 32 countries participated in EHS-ACS-II, the number of centres that recruited patients in each country were not representative of the countries' populations. In addition, as participation in the survey was voluntary, the majority of the centres which participated could be characterized as highly motivated, affiliated to academic institutions, likely to have catheterization laboratory facilities, and to hospitalize ACS patients in either coronary care units or cardiology departments, willing to expose their practice to criticism, and more likely to adhere to guidelines. Therefore, we are unable to extrapolate our findings to centres that did not participate in the survey. This limitation is particularly relevant to the setting in which the patients were treated in ACS-II, as the greater proportion hospitalized in coronary care units may include slightly different populations and treatment practices in comparison with alternative settings. In addition, the survey did not address the role of quality improvement interventions used in the participating centres. Therefore, we were unable to assess the extent to which the observed changes in adherence could be attributed to local efforts towards quality improvement. Furthermore, the inclusion of consecutive ACS patients could not be monitored, as on-site auditing was not required by the survey protocol. Finally, the comparison between the first and second survey is limited by the fact that not all the centres that participated

in the first survey participated in the latter survey, and additional centres were included in the second survey. However, comparison of the 34 centres that participated in both surveys yielded results that were comparable to the full populations of the two surveys.

Conclusions

Data from the second Euro Heart Survey on ACS suggest an increase in the level of adherence to guidelines for treatment of ACS. The comparison of the 34 centres that participated in both surveys suggests that the early mortality reduction observed in ACS-II was associated with improvement in management and treatment, achieved from 2000 to 2004. It is reassuring to note that in most cases of patients who did not receive evidence-based therapies, this was due to contraindications or lack of indication for treatment according to the current guidelines. This finding reinforces the idea that guidelines should be tailored individually to patients' risk profiles. It is recommended that surveys be performed periodically to continuously monitor the implementation of emerging new guidelines among ACS patients, and by doing so, improve quality of care and outcomes over time. Attention to quality improvement interventions in future surveys would also be of great benefit in understanding the mechanisms contributing to changes in guideline adherence.

Acknowledgements

The authors gratefully thank Valerie Laforest for coordinating this Euro Heart Survey. They are also grateful for the valuable contribution of all investigators and data collection officers of the participating centres.

Conflict of interest: none declared.

Appendix

Organization of the survey

Acute Coronary Syndrome Expert Committee: Alex Battler, Shlomo Behar (Chairman), David Hasdai, Israel; Nicolas Danchin, France; Anselm Gitt, Germany; Hector Bueno, Jaume Marrugat, Spain; Frans Van de Werf, Belgium; Lars Wallentin, Sweden; Yonathan Hasin, Israel and Gerasimos Filippatos, Greece (representatives of the ESC Working Group 27 Acute Cardiac Care).

Euro Heart Survey Board Committee: Anselm Gitt (Chairman), Germany; Maarten Simoons (Past-Chairman), The Netherlands; David Wood (Past-Chairman), UK; Angeles Alonso, Spain; Alex Battler, Israel; Shlomo Behar, Israel; Eric Boersma, The Netherlands; Harry Crijns, The Netherlands; Kim Fox, UK; Michel Komajda, France; Malika Manini, France; Keith McGregor, France; Barbara Mulder, The Netherlands; Sylvia Priori, Italy; Lars Rydén, Sweden; Luigi Tavazzi, Italy; Alec Vahanian, France; Panos Vardas, Greece; William Wijns, Belgium; Uwe Zeymer, Germany.

Euro Heart Survey Team (European Heart House—FRANCE): Valérie Laforest, Data Monitor; Charles Taylor, Database Administrator; Claire Bramley, Data Monitor; Malika Manini, Operations Manager.

Principal Investigator Centre (Tel Hashomer, Israel): Shlomo Behar (*Survey Chairman*), Lori Mandelzweig (*Research Coordinator*), Valentina Boyko (*Statistician*).

National Coordinators: Austria, Kurt Huber; Belgium, Guy De Backer; Bulgaria, Vera Sirakova; Czech Republic, Roman Cerbak; Denmark, Per Thyssens; Finland, Seppo Lehto; France, Jean-Jacques Blanc, François Delahaye; Georgia, Bondo Kobulia; Germany, Uwe Zeymer; Greece, Dennis Cokkinos; Hungary, Kristof Karlocai; Ireland, Ian Graham, Emer Shelley; Israel, Shlomo Behar; Italy, Aldo Maggioni; Lithuania, Virginija Grabauskiene; Netherlands, Jaap Deckers; Norway, Inger Asmussen; Poland, Janina Stepinska; Portugal, Lino Gonçalves; Russia, Vyacheslav Mareev; Serbia & Montenegro, Zorana Vasiljevic; Slovakia, Igor Riečanský; Slovenia, Miran F. Kenda; Spain, Angeles Alonso, José Luis Lopez-Sendon; Sweden, Annika Rosengren; Switzerland, Peter Buser; Turkey, Tugrul Okay; Ukraine, Oleg Sychov; UK, Peter Schofield.

There was no national coordinator in the participating countries which are not mentioned in the above list.

Participating Countries (number of patients included), Investigators, and Data Collection Officers:

Austria (116): Gunther Christ, Kurt Huber, Peter Dolliner, Kadriye Aydinkoc, Karim Kalla Vienna.

Belgium (80): Christiaan Vrints, Els Van Hertbruggen Edegem; V. Legrand, Joseph Dib Liege; E. Schroeder, Juliette Domange Yvoir.

Bulgaria (207): Assen Rachev Goudev, Desislava Bojidarova Bojadgieva Pleven; Mladen Grigorov, Georgi Todorov. Georgi Grigorov, Nina Gocheva, Elina Trendafilova, Temenuga Donova, Vera Bogdanova, Sofia; Borislav Boyanov Borisov, Stara Zagora; Vera Sirakova, Jordan Krasnaliev, Varna.

Croatia (160): Ante Samodol, Sibenik; Vjekoslava Raos, Zrinka Trstenjak, Vjeran Nikolic Heitzler, Zdravko Babic, Nikola Bulj, Zagreb.

Cyprus (29): Marios Ioannides, Larnaca; Joseph A. Moutiris, Paphos.

Czech Republic (163): J. Spinar, Jiri Spac, Ota Hlinomaz, Petr Bouchal Brno; Jindrich Florian, Sirous Yaghmae Cesky Krumlov; Alena Krizova, Pardubice; J. Bruthans, Andrej Bajo, Roudnice nad Labem.

Denmark (30): P. Thyssens, Helle Cappelen Odense.

Egypt (25): Hossam Kandil, Khalid Tammam Cairo.

Estonia (37): Toomas Marandi Tallin.

Finland (115): Kari Virtanen, Mervi Pietila, Helsinki; Juha Mustonen, Irmeli Juntunen Joensuu; Seppo Lehto, Kirsti Savolainen Kuopio.

France (387): J.P. Bassand, Jerome Varini, Besancon; Yves Cottin, Dijon; Nicolas Danchin, Sylvie Marinier Paris; Hervé Le Breton, Corinne Heautot, Christine Poulain, Rennes; Jean Marco, Frederic Petit, Toulouse; Michael Angioi, Tatiana Dabrowski, Vandoeuvre les Nancy; Jean Louis Georges, G. Gibault-Genty, J. Schwob, Fadela Pousset, Versailles.

Georgia (63): David Maisuradze, Irma Aladashvili Rustavi; Bondo Kobulia, Irina Iashi, Tbilisi.

Germany (55): Ulrich Tebbe, Detmold; J. Niebauer, K. Drechsler, Leipzig; A. Gitt, Harm Wienbergen, Ludwigshafen am Rhein.

Greece (375): Gerasimos Filippatos, Virginia Markou, Ioannis Fotiadis, Dimitrios A. Korres, Athanasios Manginas, D. Cokkinos, Anastasia Tsiavou, Ilias K. Karabinos, Athens; Nikos Kafkas, Khfisia; Alexandros Gotsis, Komotini; Ioannis Skoularigis, Larisa; Fousa Stefanos, Nikolaos Patsourakos, Apostolou Thomas, Eftihia Hamodraka Pireus; Antonios Kassimatis, Kostas S. Liveris, Petros Stravopodis, Zakynthos.

Hungary (70): Istvan Preda, Eva Csoti Budapest; Janos Takacs, Mosonmagyaróvár; Aranka Kovacs, Istvan Bodonovits, Ferenc Kovacs Szentes.

Israel (592): Leonardo Reisin, Yosi Blayer Ashkelon; Doron Zahger, Irit Rabinowitz, Beer Sheva; Edo Kaluski, Jana Babkin, Beer Yakov; Avraham Shotan, Mark Kazatsker, Hadera; Haim Hammerman, Robert Dragu, Uri Rosenschein, Shmuel Rosenschein, Haifa; Jonathan Balkin, Shiri, Jerusalem; Nathan Roguin, N. Clauzner, Nahariya; Mohammed Omary, Nazareth; A. Battler, Boris Napach,

Zaza Shvili, Petach Tikva; Hanoch Hod, Shlomo Matetzky, Tel Hashomer; Arie Roth, Yehuda Levi, Tel-Aviv; Y. Hasin, Anna Bogochinsky, Hanody Saadi, Tiberias; Alon Marmour, Olga Truchin, Tsfat.

Italy (674): Giancarlo Scognamiglio, Acerra; Giuseppe Scaramuzzino, Bologna; Luigi Meloni, Enrico Onnis, Cagliari; Gaspare Ferrantelli, Castelvetrano; Francesco Gentile, Elena Mangiarotti Cinisello Balsamo; Annamaria Nicoletti, Vena Silvio, Cosenza; Grigolato Michele, Desenzano Del Garda; Silva Severi, Marco Breschi, Grosseto; Massimo Conti, Guastalla; Luigi Leonzio, Valerio Alfonso, Lanciano; Antonio Pesola, Lorenza Robiglio, Lido Di Camaiore; Felice Achilli, Andrea Farina Merate; Antonio Mafriaci, Chiara De Benedetta, Bruno Brusoni, Marco Negrini, Milan; Gianluigi Olivato, Monfalcone; Antonino Rotolo, Palermo; Federico Ferraris, Pietra Ligure; Anna Toso, Prato; Albarosa Ruggeri, Reggio Calabria; Sergio Bongioanni, Ernesto Iazzolino, Piras Rivoli; Alessandro Boccanelli, Cesare Greco, Maria Luisa Finocchiaro, Roberto Luongo Roma; Emanuele Carbonieri, San Bonifacio; Eugenio Vinci, Siracusa.

Lithuania (87): D. Vasiliauskas, Ruta Barbaskiene, Kaunas; Vitas Vysniauskas, Daiva Petraskiene, Marijampole; Birute Petrauskienė, Eduardas Subkovas, Rasa Palsauskaite, Taida Ivanauskienė, Sigita Glaveckaite, Egle Sadauskienė Vilnius.

The Netherlands (580): C. Werter, Adrie Van Den Dool Roermond; M. Bijl, Saskia Versluis, Dordrecht; R. Haan, Christel Ephraim, Harderwijk; Leo Baur, Heerlen; R. Brons, Meppel; Harry Crijns, R. Nieuwlaat, Heidi Frensen, Maastricht; D.C.A. van Hoogenhuyze, J. Deckers, Chris Jansen, M.J. Veerhoek, Maria Kamps, C.M. Leenders, Rotterdam; J.B. Winter, Herman Broers, Tilburg; J. Meeder, C. Firanescu, Venlo; R. Brons, K. Nijenbrinks, K. Thomas, Ingrid Middelveld, Zwolle.

Poland (417): Wodzimierz J. Musia, Agnieszka Kuklinska, Bialystok; Grzegorz Pulkowski, Marcin Majer, Bydgoszcz; Bogdan Zbyszynski, Ciechanow; A. Rynkiewicz, Jerzy Bellwon, Tuchacz, Gdansk; Michal Tendera, Rafal Wyderka, Katowice; Elzbieta Zinka, Wojciech Jablonski, Koszalin; A. Cielinski, Przemyslaw Mitkowski, Poznan; Janusz Kostrzewa, Roman Bytner, Rypin; Janina Stepinska, Marek Batogowski, Warsaw; Andrzej Budaj, Piotr Kokowicz, Pawel Lewandowski, Marek Roik, Grzegorz Opolski, Jerzy Rekosz, Warszawa.

Portugal (334): Maria Jose Loureiro, Almada; Rafael Ferreira, Joao Ribeiro Amadora; Pedro Monteiro, Coimbra; Jorge Mimoso, Rui Alexandre C Candeias, Faro; Decio Pereira, Funchal; Joao Carlos Araujo Morais, Leira; J. A. Correia da Cunha, Maria Jose Correia, Rui Ferreira, Antonio Fiarresga Lisbon; Cristina Gavina, teresa Pinho, Porto.

Romania (76): Maria Dorobantu, Rodica Niculescu, Bucharest; Cristian Stasescu, G. Georgescu, Radu A. Sascau Lasi.

Russian Federation (90): Nikolai. A. Gratsiansky, A.D. Erlikh, Simon Matskeplishvili, Yuri Buziashvili Moscow; Dmitry Duplyakov, Togliatti.

Serbia and Montenegro (177): Mirko Colic, Milosav Tomovic, Zorana Vasiljevic, Gordana Krljanac, Milutin Miric, Natasa Markovic, Belgrad; N. Radovanovic, Tijana Momcilov Popin, Sremska Kamenica.

Slovenia (48): Miran Sebestjen, Andrej Pernat, I. Kranjec, Ljubljana.

Spain (1030): Antonio Radován, Girona; Gurruchaga, Guipúzcoa; Dra. Martín, Zamora; Laperal/Casado, Zaragoza; Dra Bisbe y Loubad, Girona; Vicente Bartomeu y Dra. Carrillo; Eduardo Benítez Cano, Plasencia; Miguel De Miguel; Franciso Penas, Pontevedra; Casares; Juan Ortega Bernal, Cartagena; Francisco Calvo Iglesias, Vigo; Joaquín Barba/Jesús Herreros; Agustín Ardiaca, Lleida; Salvador/Pablo Aguar, Valencia; Munilla, Logroño; Fernando Arós/Emilio Sanz, Vitoria; Félix Noriega, Povisa; Velasco y Joaquina Belchi, Valencia; Valdepeñas; Pastor Torres y Dra. Melguizo, Sevilla; Jesús Aguirre, Bilbao; Ángel Llamas, Donostia; Martos, Almería; Eduardo De Teresa, Málaga; Carlos Pagola, Jaén; Luis Rodríguez Padial, Toledo; Sogorb Garri/Dra. Oliver,

Alicante; Magda. Heras/Amadeo Betriu, Barcelona; Antonio Merchán, Badajoz; Enric Esplugas/M. Ribas, Barcelona; Martin Luengo/Pedro Pabón; Barrenechea Benguria, Baracaldo; Placer/J. Sánchez, Zaragoza; José M. Cruz Fernández, Sevilla; Atilano Sánchez/Poveda, Santander; Federico Vallés, Córdoba; Carlos Macaya/J. Ferrero, Madrid; Cayetano Permanyer, Barcelona; Burgos Cornejo, Sevilla; Héctor Bueno, Madrid; Jose Luis Martí, Granada; Francisco Fernández Avilés/Pedro Luis Sánchez; Jordi Bruguera/L. Recasens, Barcelona; Abizanda; Iñaki Lecuona; Lorenzo Lopez Bescos/Ana Huelmos; J. Farré/Romero, Madrid; Luis Alonso Pulpón Javier Ortigosa, Madrid; Alfredo Bardají, Tarragona; Antonio Montón, Burgos; Joan Sala, Girona; Carmen Corona/Dra. Adamuz, Úbeda.

Sweden (157): Annika Rosengren, Gorel Hulthberg-Olsson, Lena Bjorck, Göteborg; Juhlin Tord, Birgitta Ohlsson, Malmö.

Switzerland (48): Dominique Evequoz, Ian Charvat, Brig.

Tunisia (28): Habib Gamra, Khaldoun Ben Hamda, Faten Triki, Zohra Dridi, Faouzi Addad, Fethi Betbout, Monastir.

Turkey (30): Zeki Ongen, Hakan Erkan, Istanbul.

Ukraine (63): Olena Koval, Andrey P. Ivanov, Pavel A. Kaplan, Dnipropetrovsk; Vasyl Netiazhenko, Lykov Oleg, Kiev.

UK (42): P.M. Schofield, G. Charman, Cambridge; K. Fox, D. Peter, I. Hassan.

Industry Sponsor: Eli Lilly.

References

1. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith SC Jr, Alpert JS, Anderson JF, Faxon DP, Furster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzkin LF, Hunt SA, Jacobs AK, Ornato JP. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *J Am Coll Cardiol* 2004;44:E1-E211.
2. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, Jones RH, Kereiakes D, Kupersmith J, Levin TN, Pepine CJ, Schaeffer JW, Smith EE III, Stewart DE, Theroux P, Gibbons RJ, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Hiratzka LF, Jacobs AK, Smith SC Jr. American College of Cardiology; American Heart Association, Committee on the management of patients with unstable angina and non-ST segment elevation myocardial infarction. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST segment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the management of patients with unstable angina). *J Am Coll Cardiol* 2002;40:1366-1374.
3. Van de Werf F, Ardissino D, Betriu A, Cokkinos DV, Falk E, Fox KAA, Julian D, Lengyel M, Neumann FJ, Ruzyllo W, Thygesen C, Underwood SR, Vahanian A, Verheugt FWA, Wijns W. The Task Force on the management of acute myocardial infarction of the European Society of Cardiology. Management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2003;24:28-66.
4. Bertrand ME, Simoons ML, Fox KAA, Wallentin LC, Hamm CW, McFadden E, De Feyter PJ, Specchia G, Ruzyllo W. The Task Force on the management of acute coronary syndromes of the European Society of Cardiology. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2002;23:1809-1840.
5. Carruthers KF, Dabbous OH, Flather MD, Starkey I, Jacob A, MacLeod D, Fox KAA, on behalf of the GRACE Investigators. Contemporary management of acute coronary syndromes: does the practice match the evidence? The global registry of acute coronary events (GRACE). *Heart* 2005;91:290-298.
6. Bassand JP, Piori S, Tendera M. Evidence-based versus 'impressionist' medicine: how best to implement guidelines. *Eur Heart J* 2005;26:1155-1158.
7. Lenfant C. Clinical research to clinical practice—Lost in translation? *N Engl J Med* 2003;349:868-874.
8. Bassand JP, Danchin N, Filippatos G, Gitt A, Hamm C, Silber S, Tubaro M, Weidinger F. Implementation of reperfusion therapy in acute myocardial infarction. Proceedings from the policy conference on implementation of reperfusion therapy in acute myocardial infarction. *Eur Heart J* 2005;26:2733-2741.
9. Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, Fioretti PM, Simoons ML, Battler A. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin: The Euro Heart Survey on Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J* 2002;23:1190-1201.
10. Permanyer-Miralda G, Ferreira-Gonzalez I, Marrugat de la Iglesia J, Bueno H. Bases conceptuales y metodológicas del estudio MASCARA: el reto de la efectividad. *Med Clin (Barc)* 2005;125:580-584.
11. Ohman EM, Roe MT, Smith SC, Brindis RG, Christenson RH, Harrington RA, Gibler WB, Peterson ED, for the CRUSADE Investigators. Care of non-ST-segment elevation patients: Insights from the CRUSADE national quality improvement initiative. *Am Heart J* 2004;148:S34-S39.