European Heart Journal (2002) **23,** 1190–1201
doi:10.1053/euhj.2002.3193, available online at http://www.idealibrary.com on IDEAL®

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 of Acute Coronary Syndromes (Euro Heart Survey ACS)

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Aims To better delineate the characteristics, treatments, and outcomes of patients with acute coronary syndromes (ACS) in representative countries across Europe and the Mediterranean basin, and to examine adherence to current guidelines.

Methods and Results We performed a prospective survey (103 hospitals, 25 countries) of 10 484 patients with a discharge diagnosis of acute coronary syndromes. The initial diagnosis was ST elevation ACS in 42·3%, non-ST elevation ACS in 51·2%, and undetermined electrocardiogram ACS in 6·5%. The discharge diagnosis was Q wave myocardial infarction in 32·8%, non-Q wave myocardial infarction in 25·3%, and unstable angina in 41·9%. The use of aspirin, beta-blockers, angiotensin converting enzyme inhibitors, and heparins for patients with ST elevation ACS were 93·0%, 77·8%, 62·1%, and 86·8%, respectively, with corresponding rates of 88·5%, 76·6%, 55·8%, and 83·9% for non-ST elevation ACS patients. Coronary angiography, percutaneous coronary interventions, and coronary bypass surgery were performed in 56·3%, 40·4%, and 3·4% of ST elevation ACS patients, respectively, with corresponding rates of 52·0%, 25·4%, and 5·4% for non-ST elevation ACS patients. Among patients with ST elevation ACS, 55·8% received reperfusion treatment; 35·1% fibrinolytic therapy and 20·7% primary percutaneous coronary interventions. The in-hospital mortality of patients with ST elevation ACS was 7·0%, for non-ST elevation ACS 2·4%, and for undetermined electrocardiogram ACS 11·8%. At 30 days, mortality was 8·4%, 3·5%, and 13·3%, respectively.

Conclusions This survey demonstrates the discordance between existing guidelines for ACS and current practice across a broad region in Europe and the Mediterranean basin and more extensively reflects the outcomes of ACS in real practice in this region.

(Eur Heart J, 2002; 23: 1190–1201, doi:10.1053/euhj.2002.3193)

Key Words: Acute coronary syndromes, acute myocardial infarction, unstable angina, prognosis, management, medication, percutaneous coronary intervention.

See doi:10.1053/euhj.2001.3121 and doi:10.1053/euhj.2002.3033 for the Editorial comments on this article

Revision submitted 4 February 2002, and accepted 5 February 2002.

This project was sponsored by Schering-Plough, and Centocor. We would like to thank Dr Eli I. Lev for his assistance in preparing this manuscript.

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0195-668X/02/$35.00

Introduction

The acute coronary syndromes include a variety of clinical scenarios ranging from unstable angina and myocardial infarction without persistent-ST-segment elevation to myocardial infarction with persistent-ST-segment elevation. A plethora of new pharmacological and technical approaches to acute coronary syndromes have been ushered into clinical practice in recent years. This has resulted in a significant heterogeneity in the management and treatment of patients with acute coronary syndromes.

Current knowledge regarding the characteristics, treatments and outcomes of patients diagnosed with the complete spectrum of acute coronary syndromes is by and large limited to data derived from clinical trials or from national registries[1–8]. Acute coronary syndrome patients enrolled in randomized, clinical trials are a highly selected, lower-risk subgroup[9,10]. In addition, given the wide variation between countries in the use of medications and more so invasive cardiac procedures[11], data derived from national registries of acute coronary syndromes may not be universally applicable. Moreover, many of the national registries have focused on selected acute coronary syndrome patients, usually those with ST elevation myocardial infarction[4–8], precluding conclusions regarding the remaining acute coronary syndrome patients.

The European Society of Cardiology (ESC) encompasses 47 countries across Europe and the Mediterranean basin. Task forces of the ESC[12,13] and other international organizations have formulated recommendations and guidelines for the treatment of the different types of acute coronary syndromes However, little is known about how these recommendations are implemented in the 'real-world' scenario, in particular by ESC member countries. Moreover, little is known regarding the outcomes of patients with the different presentations of acute coronary syndromes in these countries. The European Network for Acute Coronary Treatment (ENACT) Study suggested that treatments and outcomes are both inter- and intra-nationally heterogeneous and that practice guidelines are often not implemented in this region of the world[14].

In order to better delineate the characteristics, treatments and outcomes of acute coronary syndrome patients treated in representative ESC-member countries, and particularly to examine the adherence to current practice guidelines, the ESC sponsored the large-scale Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS), a prospective survey of 10 484 patients from 25 ESC member countries with a final diagnosis of acute coronary syndromes. Herein we present the in-hospital and 30-day results for these patients.

Methods

Participating clusters

The Euro Heart Survey ACS enrolled patients from 25 different countries (Fig. 1). The national co-ordinators for the EHS programme supplied a list of potential medical centres in each country that would be suitable technically to set up such a survey. For each country, the aim was to choose clusters of hospitals, composed of academic and non-academic hospitals and hospitals with and without cardiac catheterization laboratories and cardiac surgery facilities.

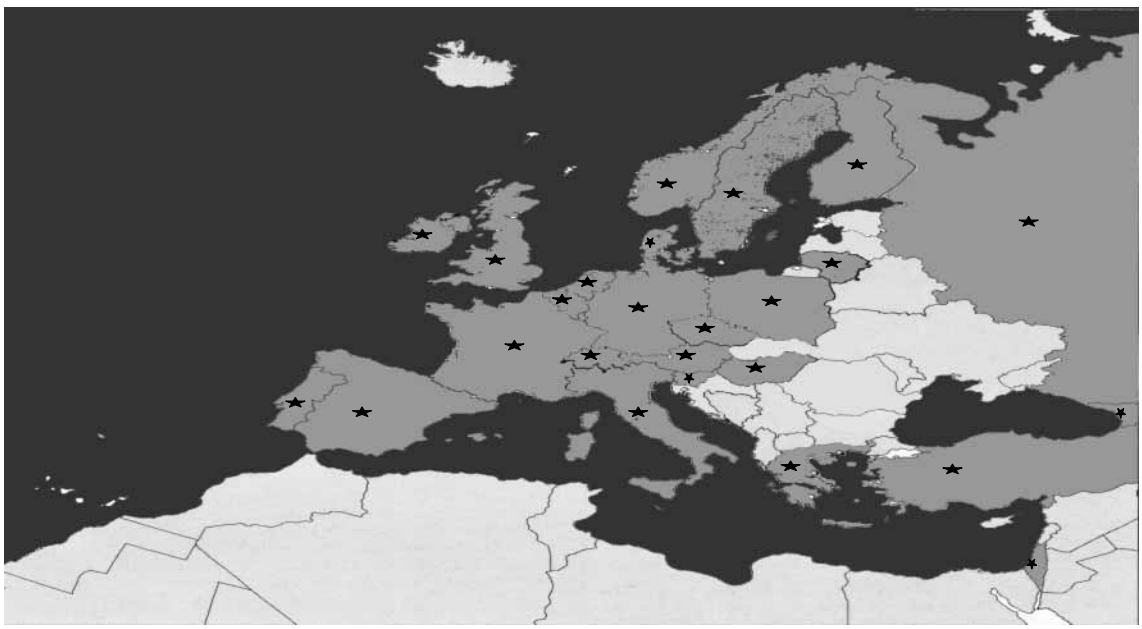

Figure 1 **Map of countries participating in the Euro Heart Survey ACS.**

Duration of survey

The survey was originally designed to include all (consenting) patients admitted during a period of up to 4 months who met the inclusion criteria. Follow-up was to be made either personally or by telephone by the local investigator at 30 days. It was anticipated that during this period each hospital within each cluster of hospitals would recruit at least 100 patients with a confirmed diagnosis of acute coronary syndromes. The enrolment period was planned from 4 September to 31 December 2000. Due to technical delays (primarily delays in approval by ethics committees in several countries), the Expert Committee decided to extend the duration of the survey to 15 May 2001, with data collection beginning in early 2001 in some countries.

Patients

All patients with suspected acute coronary syndromes, screened in an emergency room, chest pain unit, catheterization laboratory, or otherwise by the data collection officer with a tentative diagnosis of acute myocardial infarction, rule-out myocardial infarction, or suspected unstable angina were registered on a screening log (after acquisition of written informed consent if required), but they were not enrolled until the diagnosis of acute coronary syndromes was confirmed. Patients who had been in another hospital for a short (<12 h) observation period and were transferred for diagnosis and management were also registered, and information from the referring hospital was sought. However, patients who were referred only for specific treatment (i.e. cardiac catheterization or coronary bypass surgery) were not included. For all logged patients, the data collection officer recorded the tentative initial diagnosis *made by the attending physicians* based on the initial electrocardiographic pattern: acute coronary syndromes with ST elevation, acute coronary syndromes without ST elevation, and acute coronary syndromes with an undetermined electrocardiographic pattern.

The full case report form was filled out for patients with a confirmed diagnosis of unstable angina or myocardial infarction (ICD-9 subclassifications: Q wave acute myocardial infarction 410·0–410·6, non-Q acute myocardial infarction 410·7, atrial/papillary acute myocardial infarction 410·8, undetermined acute myocardial infarction 410·9, unstable angina 411·1, coronary insufficiency 411·8, nocturnal angina 413·0, variant angina 413·1). The data collection officer recorded the discharge diagnosis *made by the attending physicians* based on the following categories: unstable angina, non-Q wave myocardial infarction, and Q wave myocardial infarction. The case report form included details regarding the demographic, clinical, and electrocardiographic characteristics of the patient, the diagnostic and treatment modalities, the in-hospital complications, and the discharge status. In addition, once the diagnosis of acute coronary syndromes had been confirmed, the data collection officer was asked to interview the attending physicians regarding pre-defined queries about management and therapy. The final diagnosis of the logged patients with suspected acute coronary syndromes who were discharged with a non-acute coronary syndrome diagnosis was also recorded.

Data collection

In each hospital, data were collected using the Macro™ software (InferMed, U.K.) on portable computers and sent to a central database in the European Heart House via the internet. Initial internal edit checks for missing or contradictory entries or for values excessively out of the normal range were implemented by the software. Additional edit checks were implemented by the data management staff at the European Heart House and the Euro Heart Survey ACS data analysis centre at the Neufeld Cardiac Research Institute. Patient identification was not entered on the local computer or transferred to the central database.

Site audits for source document verification vs data collected in the central database, were randomly performed by the Euro Heart Survey staff in sample sites. Site audits were not intended to validate the accuracy of the discharge diagnosis by the attending physicians.

Results

The electronic case report form, containing 650 fields, was successfully filled out with a low rate of missing values; for the entire cohort of 10 484 patients, only 12 951 out of 6 814 600 fields (0·0019%) were incomplete.

Initial and final diagnoses

During the study period, 14 271 patients were logged, of whom 10 484 were finally diagnosed with acute coronary syndromes (Fig. 2). The initial diagnosis for these patients was acute coronary syndromes with ST elevation in 42·3%, acute coronary syndromes without ST elevation in 51·2%, and acute coronary syndromes with an undetermined electrocardiographic pattern in 6·5%. The final diagnoses (i.e. unstable angina, non-Q wave myocardial infarction and Q wave myocardial infarction) for each type of initial acute coronary syndrome pattern are presented in Figs 3–5, respectively. Among the patients with an initial diagnosis of acute coronary syndromes without ST elevation, 33·6% had no electrocardiographic change initially. Altogether, 32·8% of the patients had a final diagnosis of Q wave myocardial infarction, 25·3% non-Q myocardial infarction, and 41·9% unstable angina.

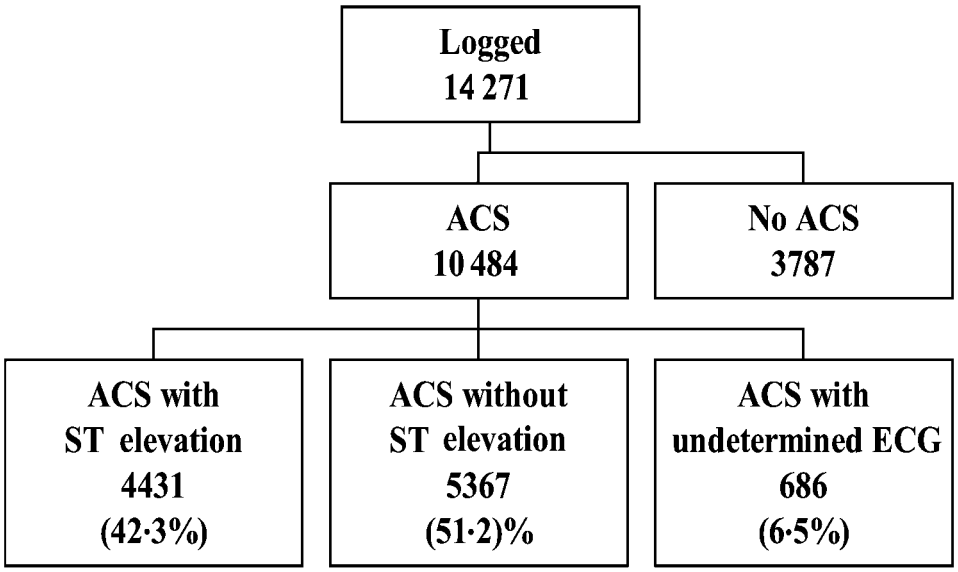

Figure 2 **Logged and enrolled patients, with the initial diagnosis provided for enrolled patients. ACS=acute coronary syndromes.**

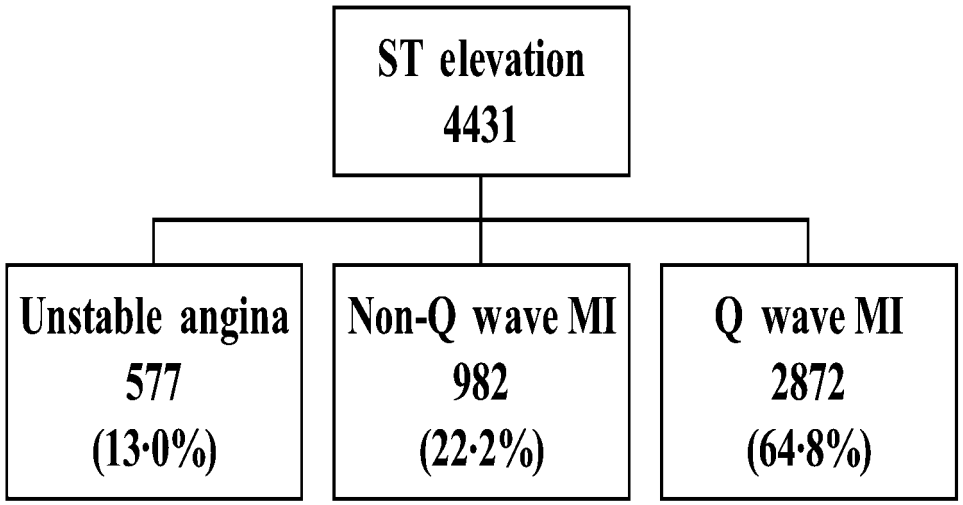

Figure 3 **Final diagnosis of enrolled patients initially diagnosed with ST elevation acute coronary syndromes.**

Demographic and clinical features

Patients with an initial diagnosis of ST elevation ACS were more likely to be males and current or former smokers (Table 1). The patients with an undetermined initial electrocardiographic pattern had the worst baseline demographic and clinical characteristics: they were older, were more likely to have antecedent heart disease (i.e. myocardial infarction, valvular heart disease, heart failure, and a permanent pacemaker) and revascularization procedures, as well as other co-morbid conditions such as diabetes mellitus, hypertension, renal failure, chronic lung disease, and peripheral vascular disease (including cerebrovascular disease).

Initial haemodynamic and clinical features

Upon presentation, the patients with an initially undetermined electrocardiographic pattern had a higher heart rate and were more likely to be in heart failure (Table 2). Although the presenting symptom was most commonly typical angina for all patients, it was least common among the patients with an initially undetermined electrocardiographic pattern.

Altogether, the patients were enrolled in 65 clusters (103 hospitals): 65% were in academic hospitals, 77% in hospitals with catheterization laboratories, and 57% in hospitals with cardiac surgery facilities. The vast majority of patients with ST elevation ACS were

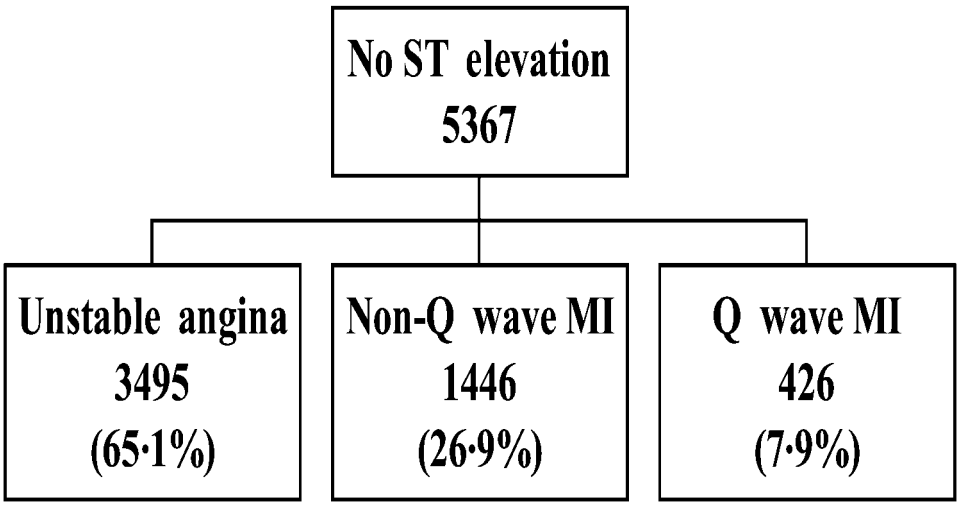

Figure 4 **Final diagnosis of enrolled patients initially diagnosed with non-ST elevation acute coronary syndromes.**

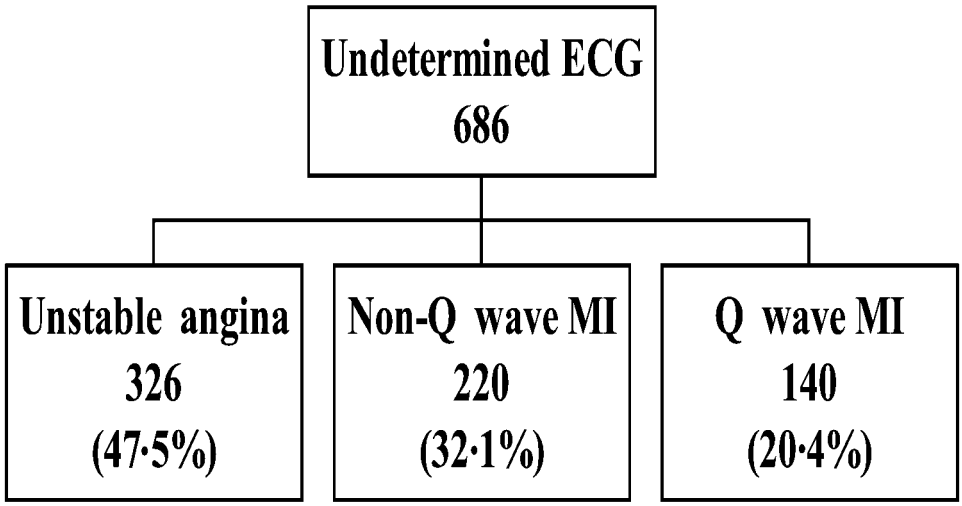

Figure 5 **Final diagnosis of enrolled patients initially diagnosed with acute coronary syndromes and an undetermined electrocardiographic pattern.**

originally admitted to coronary care units or a general cardiology ward, with only a minority of patients admitted to internal medicine wards (Table 3). Acute coronary syndrome patients with other electrocardiographic patterns were more than twice as likely to be admitted to internal medicine wards. During their hospitalization, 20·9% of patients with ST elevation were enrolled in a clinical trial, 10·4% of patients without ST elevation, and 8·5% of patients with an undetermined initial electrocardiographic pattern. The median (25th, 75th percentiles) duration of hospitalization was 8 (5, 12) days for all patients: 8 (5, 12) for ST elevation patients, 7 (4, 12) for non-ST elevation patients, and 8 (5, 13) for patients with an undetermined electrocardiographic pattern. When analysed based on the final diagnosis, the duration of hospitalization was 7 (4, 12) days for patients with unstable angina, 7 (5, 11) days for patients with non-Q wave myocardial infarction, and 8 (5, 13) days for patients with Q wave myocardial infarction.

In-hospital diagnostic and therapeutic modalities

Coronary angiography was performed in approximately one-half of the survey cohort during the initial hospitalization (Table 4). When the attending physicians were asked why coronary angiography had been performed, the response was that it was routine policy to perform coronary angiography in 25·8% of ST elevation ACS patients, 33·5% of non-ST elevation patients, and 27·4% of undetermined electrocardiographic pattern patients.

Percutaneous coronary interventions were performed more commonly in patients with ST elevation ACS

Table 1 Baseline demographic and clinical characteristics of the survey cohort categorized based on the initial electrocardiographic pattern

	ST elevation	No ST elevation	Undetermined
Age (years)	63·4 ± 13·0	65·8 ± 12·0	72·0 ± 10·3
Male gender (%)	71·6	64·4	65·5
Weight (kg)	77·9 ± 13·7	78·0 ± 14·3	77·0 ± 13·2
Height (cm)	169·9 ± 8·6	168·8 ± 9·0	168·3 ± 8·8
Prior MI (%)	22·3	35·6	45·3
Prior angina (%)	56·4	74·8	72·2
Prior HF (%)	8·2	11·9	28·0
Valve disease (%)	3·4	5·2	10·8
Pacemaker (%)	0·6	1·8	11·8
Prior CABG (%)	3·4	11·0	13·1
Prior PCI (%)	7·3	15·2	14·2
Diabetes mellitus (%)	21·1	23·5	31·7
Smoking — ever (%)	63·1	53·8	52·6
Hypertension (%)	51·6	63·6	64·0
Hyperlipidaemia (%)	46·8	54·6	46·7
Family history (%)	27·4	29·3	23·1
Cancer — ever (%)	4·9	5·8	7·8
Prior CVA/TIA (%)	5·9	8·1	13·9
Renal failure (%)	3·4	5·8	11·2
COPD (%)	8·5	8·7	13·1
PVD (%)	7·0	10·6	18·0
Prior GI bleed (%)	4·9	4·0	6·1

Continuous variables are presented as mean ± SD. MI = myocardial infarction; HF = heart failure; CABG = coronary artery bypass grafting surgery; PCI = percutaneous coronary intervention; CVA = cerebrovascular accident; TIA = transient ischaemic attack; COPD = chronic obstructive pulmonary disease; PVD = peripheral vascular disease; GI = gastrointestinal.

Table 2 Haemodynamic and clinical features of the survey cohort upon presentation categorized based on the initial electrocardiographic pattern

	ST elevation	No ST elevation	Undetermined
Heart rate (beats . min^{-1})	79 ± 20	79 ± 19	87 ± 26
SBP (mmHg)	137 ± 31	147 ± 28	142 ± 31
DBP (mmHg)	81 ± 17	84 ± 16	81 ± 17
Killip class (%)			
I	77·3	83·9	62·3
II	17·0	12·4	23·3
III	3·6	3·1	9·6
IV	2·2	0·6	4·9
Presenting symptom (%)			
Typical angina	88·7	86·9	74·1
Atypical angina	3·6	5·7	6·3
Heart failure	2·1	2·2	8·8
Syncope	1·6	1·1	2·7
Other	4·0	4·1	8·1

Continuous variables are presented as mean ± SD.

(Table 4), probably because of the higher rate of primary percutaneous coronary interventions performed in this subgroup (20·7% vs 5·1% in patients with acute coronary syndromes without ST elevation and 8·0% in patients with an undetermined electrocardiographic pattern). The attending physicians explained that performing non-primary percutaneous coronary interventions was part of routine policy which was to treat stenosed or occluded arteries (i.e. not based on strict criteria stipulated in current guidelines). This occurred in 42·6% of ST elevation patients, 60·3% of non-ST elevation patients, and in 59·0% of patients with an undetermined electrocardiographic pattern. Echocardiography was performed in the majority of patients, whereas other diagnostic and therapeutic modalities were used less commonly (Table 4).

Table 3 Initial ward in which patients were admitted categorized based on the initial electrocardiographic pattern

	ST elevation	No ST elevation	Undetermined
Coronary care unit	78·8	50·1	50·9
Cardiology	11·3	30·6	25·4
Internal medicine	8·5*	17·4**	20·5†
Other	1·4*	1·9**	3·2†

*Eventually, 6·8% were transferred to the coronary care unit or to the cardiology ward.
**Eventually, 8·8% were transferred to the coronary care unit or to the cardiology ward.
†Eventually, 10·1% were transferred to the coronary care unit or to the cardiology ward.

Table 4 The in-hospital use of invasive and non-invasive diagnostic and therapeutic techniques

	ST elevation	No ST elevation	Undetermined
Angiography (%)	56·3	52·0	41·3
PCI (%)	40·4	25·4	22·6
CABG (%)	3·4	5·4	4·4
Echo (%)	73·1	60·5	62·8
PA catheter (%)	3·9	2·2	3·5
Mech. ventilator (%)	7·0	3·4	10·4
IABP (%)	2·5	0·9	2·6
AICD (%)	0·5	0·2	0·6
EPS (%)	0·5	0·4	0·5
Holter (%)	13·6	7·7	8·9
Pacemaker (%)	2·8	1·8	5·9
Stress test (%)	22·1	24·0	13·1

Continuous variables are presented as mean ± SD. Angiography = coronary angiography; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting surgery; Echo = echocardiography; PA = pulmonary artery; Mech. ventilation = mechanical ventilation; IABP = intra-aortic balloon pump; AICD = automatic internal cardiac defibrillator; EPS = electrophysiological test.

Reperfusion therapy

Among patients with ST elevation ACS, 55·8% received some form of reperfusion therapy — 20·7% primary

percutaneous coronary interventions and 35·1% fibrinolytic therapy. When the attending physicians were asked why their patients with ST elevation ACS *did not* receive any reperfusion treatment, 35·3% responded that it was not indicated, 22·4% attributed this to a late arrival, 5·8% reported spontaneous resolution of the electrocardiographic changes in the interim, 3·7% reported that reperfusion therapy was not available, and 3·1% did not administer it due to advanced age. In the remaining cases, the attending physicians were either not certain of the diagnosis or had other reasons for not administering reperfusion therapy.

Among patients with ST elevation ACS who underwent reperfusion therapy, the median time (25th, 75th percentiles) from symptom onset to arrival in the emergency room was 176 min (90, 465) and the median time from arrival in the emergency room to reperfusion therapy was 59 min (30, 109) – 40 min (25, 70) to the initiation of fibrinolytic therapy and 93 min (60, 170) to the first balloon inflation. Among patients undergoing primary percutaneous coronary interventions in this subgroup, 45·4% received a platelet glycoprotein IIb/IIIa inhibitor and 70·7% received an intracoronary stent. When the attending physicians were asked why these patients received primary percutaneous coronary interventions rather than fibrinolytic therapy, 82·7% responded that it was their standard policy to perform primary percutaneous coronary interventions whenever possible, 5·0% responded that there was a contraindication to fibrinolytic therapy, 4·3% responded that the patient was in shock, and 1% responded that they performed primary percutaneous coronary interventions because they were unsure of the diagnosis.

Table 5 In-hospital medical therapy

	ST elevation	No ST elevation	Undetermined
Aspirin	93·0	88·5	83·1
Warfarin	5·3	5·7	11·4
Ticlopidine	13·3	11·2	6·3
Clopidogrel	23·3	16·6	16·6
Heparin	64·0	43·3	40·2
LMWH	47·8	58·1	56·7
Heparin or LMWH	86·8	83·9	80·9
IIb/IIIa	19·6	10·0	8·9
ACE-Inhib	62·1	55·8	65·0
Ang-II-Inhib	2·6	3·9	5·1
IV beta-blocker	13·5	5·9	8·3
PO beta-blocker	77·8	76·6	69·8
Dihyd. Ca-blocker	6·1	15·9	13·1
Other Ca-blocker	6·8	13·8	12·0
Digoxin	5·9	6·6	17·6
Diuretic	34·8	33·6	58·7
IV inotrope	11·3	3·6	14·4
Morphine*	25·9	10·8	20·8
Lidocaine	6·6	1·8	4·5
Amiodarone	6·4	5·1	11·2
Mg	9·3	4·5	6·6
IV nitrate	61·4	50·7	51·7
PO/topical nitrate	50·6	68·2	61·5
Statin	49·2	50·6	40·7
Fibrate	1·3	2·0	1·0

LMWH=low molecular weight heparin; IIb/IIIa=platelet glycoprotein IIb/IIIa inhibitor; ACE-Inhib=angiotensin converting enzyme inhibitor; Ang-II-inhib=angiotensin II receptor inhibitor; IV=intravenous; beta-blocker=beta-adrenergic blocker; PO=oral; Dihyd. Ca-blocker=dihydropyridine Ca-channel blocker; Mg=magnesium. *Morphine or morphine-like narcotics.

In-hospital and discharge medical therapy

While in-hospital, a substantial proportion (7%–17%) of patients with acute coronary syndromes did not receive aspirin, especially if they had an initially undetermined electrocardiographic pattern (Table 5). Unfractionated heparin was more commonly used among patients with ST elevation ACS, whereas low-molecular-weight heparin was more commonly used in the other subgroups. Altogether, platelet glycoprotein IIb/IIIa inhibitors were not commonly used in this survey cohort (8·9%–19·6%), and if they were used it was more common in the ST elevation ACS group. Although beta-adrenergic blockers were commonly used in all subgroups, their intravenous use was scarce (5·9%–13·5%).

A substantial proportion of patients did not receive aspirin at discharge (11·5%–16·9%), only partially explained by the widespread use of anticoagulation agents or the other antiplatelet agents, such as ticlopidine and clopidogrel (Table 6). Although beta-adrenergic blockers were commonly prescribed (67·4%–76·9%), the use of agents blocking the angiotensin axis was less common (55·7%–64·1%). Over 50% of patients received lipid-lowering treatment with statins at discharge, the majority of whom began receiving this treatment during the hospitalization. Although current guidelines for acute coronary syndrome patients are based on the initial diagnosis, when we analysed medical therapy at discharge based on the final diagnosis (Table 7), there were no marked differences among patients with unstable angina, non-Q wave and Q wave myocardial infarction. In general, patients discharged with a diagnosis of unstable angina were less likely than patients discharged with a diagnosis of myocardial infarction to receive aspirin, beta-adrenergic blockers, and angiotensin converting enzyme inhibitors, but more commonly received nitrates and calcium-channel blockers.

In-hospital complications

In-hospital complications, especially heart failure, were common in our survey cohort (Table 8). Owing to their worse baseline status (as compared to patients with or without ST elevation ACS), the patients with an initially undetermined electrocardiographic pattern more commonly had complications, in particular severe heart failure.

Table 6 Medical therapy at discharge for surviving patients based on the initial diagnosis

	ST elevation	No ST elevation	Undetermined
Aspirin	88·5	83·1	78·0
Warfarin	5·4	5·4	11·7
Ticlopidine	12·7	9·5	5·8
Clopidogrel	22·8	14·8	15·9
LMWH	8·7	8·4	9·1
ACE-Inhib	60·7	52·5	60·3
Ang-II-Inhib	2·6	3·6	4·8
ACE or Ang-II Inhib	62·9	55·7	64·1
PO beta-blocker	76·1	71·8	67·4
Dihy. Ca-blocker	5·0	14·0	11·9
Other Ca-blocker	5·3	11·6	9·6
Digoxin	3·6	4·0	12·2
Diuretic	22·6	25·8	48·9
Oral/topical nitrate	46·8	60·0	57·9
Amiodarone	3·5	3·3	7·1
Statin	54·0	53·1	46·0
Fibrate	1·5	2·1	1·0

Of the patients who did not receive aspirin at discharge, 73·6% received no other oral antiplatelet agent (72·9% with ST elevation ACS, 72·9% with non-ST elevation ACS, and 81·2% with an undetermined electrocardiographic pattern).
Of the patients who received a dihydropyridine calcium-channel blocker at discharge, 28·2% received no beta-adrenergic blocker concomitantly (23·5% with ST elevation ACS, 28·5% with non-ST elevation ACS, and 38·9% with undetermined electrocardiographic pattern).
Of the patients who received lipid-lowering therapy, only 0·5% received a combination of statins and fibrates. Prior to hospitalization, statin therapy was given to 14·8% of patients with ST elevation ACS, 23·7% of patients with non-ST elevation ACS, and 22·0% of patients with an undetermined electrocardiographic pattern.
For explanation of abbreviations, see earlier tables.

Post-discharge event rates

Among the hospital survivors, we analysed the occurrence of subsequent hospitalization, coronary angiography, and revascularization procedures until the 30-day follow-up (Table 9). Of note, patients with ST-elevation ACS were more likely to undergo percutaneous coronary interventions in the interim between hospital discharge and the 30-day follow-up, whereas patients with non-ST elevation ACS were more likely to undergo coronary bypass surgery.

In-hospital and 30-day mortality based on initial diagnosis

In-hospital survival status was available for all patients, with a mean in-hospital death rate of 4·9% for the entire survey cohort. The in-hospital death rate for patients with ST elevation ACS was 7·0%, for patients without ST elevation ACS 2·4%, and for patients with an undetermined initial electrocardiographic pattern 11·8%. At 30 days, the death rates were 8·4%, 3·5%, and 13·3%, respectively (with 30-day survival status available for 90·7%, 88·8%, and 88·6%, respectively), resulting in a mean 30-day death rate for the entire cohort of 6·3%.

Table 7 Medical therapy at discharge for surviving patients based on the discharge diagnosis

	Q wave MI	Non-Q wave MI	Unstable angina
Aspirin	88·1	85·4	82·6
Warfarin	5·5	5·5	6·2
Ticlopidine	13·4	7·0	10·7
Clopidogrel	22·1	22·5	13·0
LMWH	9·0	9·5	7·7
ACE-Inhib	62·4	56·1	52·3
Ang-II-Inhib	2·5	3·5	3·6
ACE or Ang-II Inhib	64·5	50·9	55·3
PO beta-blocker	75·2	75·9	70·4
Dihy. Ca-blocker	3·8	8·3	15·7
Other Ca-blocker	3·9	6·7	13·6
Digoxin	3·4	4·8	4·7
Diuretic	23·0	28·4	26·6
Oral/topical nitrate	44·5	48·9	64·8
Amiodarone	3·9	3·4	3·5
Statin	53·9	52·4	52·8
Fibrate	1·2	1·4	2·4

Table 8 In-hospital complications

	ST elevation	No ST elevation	Undetermined
Heart failure			
Mild	20·2	12·7	29·8
Pulmonary oedema	7·5	4·5	13·2
Shock	7·5	1·8	8·5
Mechanical			
Free wall rupture	0·6	0·1	0·3
Septal rupture	0·3	0	0
Acute MR	0·9	0·4	0·8
Arrhythmias			
Asystole	4·9	1·5	6·7
Sustained VT	5·0	1·6	4·4
VF	5·0	1·3	3·9
At. Fib./Flutter	7·1	6·4	11·5
2°/3° AVB	4·6	1·1	3·8
Renal failure	3·3	2·7	6·8
Reversible	2·3	2·0	4·5
Reischaemia	10·4	13·5	11·2
Reinfarction	2·7	1·4	1·7
Stroke	0·8	0·7	0·8
Major Bleeding	1·6	0·9	1·8
Thrombocytopaenia	1·1	1·0	1·2

MR=mitral regurgitation; VT=ventricular tachycardia; VF=ventricular fibrillation; At. Fib./Flutter=atrial fibrillation or flutter; 2°/3° AVB=2nd/3rd degree atrio-ventricular block.

In-hospital and 30-day mortality based on final diagnosis

When we analysed survival based on the final diagnosis, the in-hospital mortality rates were 1·0% for patients

Table 9 Hospitalizations, coronary angiography, and revascularization procedures for hospital survivors until 30-day follow-up

	ST elevation	No ST elevation	Undetermined
Hospitalization			
Cardiac-related	8·3	7·1	9·0
Non-cardiac-related	3·2	4·0	3·9
Coronary Angio*	8·5	5·6	6·6
PCI*	6·7	3·8	4·0
CABG*	3·5	5·9	2·7
Non-CABG cardiac surgery	0·8	0·8	0·2

*By 30 days, 54·7% of patients had undergone coronary angiography: 58·1% for ST elevation, 53·3% for non-ST elevation, and 42·7% for an undetermined electrocardiogram.
By 30 days 33·8% had undergone at least one percutaneous coronary intervention: 42·8% for ST elevation, 27·6% for non-ST elevation, and 23·9% for an undetermined electrocardiogram.
By 30 days, 7·7% had undergone CABG: 5·6% for ST elevation, 9·6% for non-ST elevation, and 6·0% for an undetermined electrocardiogram.

with unstable angina, 5·8% for non-Q wave myocardial infarction, and 9·3% for Q wave myocardial infarction. At 30 days, the death rates were 1·7%, 7·4%, and 11·1%, respectively.

Discussion

The Euro Heart Survey ACS is the largest survey hitherto of acute coronary syndromes in Europe and the Mediterranean basin, enrolling 10 484 patients from 25 countries. The data derived from this survey serve as a benchmark for the relative proportion of each type of acute coronary syndrome, for patient characteristics, for the diagnostic and therapeutic practices, for the in-hospital course, as well as for outcomes throughout this region.

Types of acute coronary syndromes

In this survey, 42·3% of patients presented with ST elevation, similar to the 43·0% of patients in ENACT[14]. At discharge, 41·9% of the entire Euro Heart Survey ACS cohort received a diagnosis of unstable angina, resulting in a ratio of unstable angina to myocardial infarction of 0·8, lower than the 1·2 ratio reported in ENACT[14] and in a previous report from the United States[15]. This difference occurred despite the screening of patients in all wards in our survey, as compared with patients only admitted to coronary care units in ENACT[14], perhaps because of the more widespread use of troponin assays in Euro Heart Survey ACS. The ESC consensus document regarding the redefinition of myocardial infarction primarily based on serum troponin levels was published in September 2000[16].

A substantial proportion of acute coronary syndrome patients in our survey, especially those without ST elevation or with an undetermined electrocardiographic pattern, were not treated in coronary care units, and approximately 20% were treated in general internal medicine wards. Therefore, the treatment of acute coronary syndromes in this region is not restricted to physicians in coronary care units and not even to cardiologists.

Of interest, a substantial proportion with an initial diagnosis of ST elevation ACS did not have a final diagnosis of myocardial infarction:13·0% of patients who had ST elevation at presentation at baseline had a final diagnosis of unstable angina, identical to the rate reported by others[14]. This may reflect higher rates of 'spontaneous', or more likely aspirin-induced, reperfusion in current practice, or to the more rapid administration of reperfusion therapy. Thus, the usual assumption that ST elevation ACS culminates in myocardial infarction may be erroneous in the reperfusion era.

Our results also highlight the worse baseline characteristics and the dire outcomes of the small subgroup of patients who have an initially undetermined electrocardiographic pattern. Although sicker, this group of patients was more likely to be treated by non-cardiologists, was less likely to receive medications recommended in current acute coronary syndrome guidelines, and were less likely to undergo revascularization. Based on their grim prognosis, more attention should be focused on these patients in future trials and guidelines.

Guidelines

Our results also underscore the discordance between clinical guidelines and current practice, and highlight specific areas for more intense education of cardiologists and other physicians. For example, we found that over 25% of coronary angiographies for acute coronary syndrome patients and up to 60% of non-primary percutaneous coronary interventions were performed as part of a routine policy, and not based on strict criteria stipulated in current guidelines[12,13], in line with the favourable results attained with a routine invasive strategy in recent and contemporaneous acute coronary syndrome trials[17,18]. Likewise, statins were given to over 50% of acute coronary syndrome patients during the initial hospitalization, although there are no firm guidelines advocating the acute use of statins, especially in patients with borderline or normal cholesterol levels. In contrast, we found that the use of aspirin both in-hospital and at discharge was markedly lower than expected, even when contraindications and the concurrent use of anticoagulants and other antiplatelet agents were taken into consideration, with a similar trend for heparins. Other recommendations, such as the use of intravenous beta-adrenergic blockers for the acute treatment of patients with ST elevation ACS[12], were also

scarcely implemented. Similarly, although the ESC recommendations for the treatment of patients with non-ST elevation ACS were published on the same day this survey was initiated[13], strongly advocating the use of platelet glycoprotein IIb/IIIa inhibitors, especially in the context of percutaneous coronary interventions, we found that only 10·0% of patients with an initial diagnosis of non-ST elevation ACS received any platelet glycoprotein IIb/IIIa inhibitor, and only 27·2% of these patients who underwent percutaneous coronary interventions received this treatment, perhaps due to the disappointing results with the use of abciximab for non-ST elevation ACS in the Global Use of Strategies To Open Occluded Coronary Arteries (GUSTO) IV trial presented at the time the survey took place[19]. Thus, it seems that physicians embrace certain recommendations based on their personal experience, existing conditions, and results of contemporaneous trials and reject others. Surveys such as ours not only assist in assessing the implementation of these recommendations, but also provide feedback from the field to those who formulate the recommendations to reconsider some of them.

Outcomes compared with contemporaneous clinical trials

Clinical trials clearly enrol a select patient population with a better risk profile[9,10]. Among patients with ST elevation ACS in our survey, approximately 20% participated in a clinical trial, whereas only 8–10% of patients in the other two subgroups participated in clinical trials. The enrolment in a clinical trial may have affected the management of patients, such as the concurrent use of abciximab and fibrinolysis in ST elevation patients enrolled in the GUSTO V trial, which was being conducted in many of the centres participating in our survey[20]. Our results also highlight the pitfalls of relying on the results of randomized, clinical trials for determining outcomes of acute coronary syndromes: the 30-day death rates for patients with ST elevation patients enrolled in GUSTO V were reported to be 5·6–5·9% (depending on the treatment arm), as compared with 8·4% in our survey, a difference of up to 50%. In fact, because the centres that participated in this survey were mostly academic with revascularization facilities, the results of our survey may be overly optimistic, possibly underestimating the morbidity and mortality of acute coronary syndromes in a broader spectrum of clinical practice.

Limitations

Because this was not a population-based epidemiological study, an unmeasured bias may have been introduced with respect to the selection of participating countries and centres. Indeed, this survey included a high proportion of academic medical centres with revascularization facilities. The results of this survey should therefore not be generalized to all medical centres within a particular country or region. Nonetheless, Euro Heart Survey ACS is the largest survey of acute coronary syndromes hitherto in this region, providing the basis for future surveys, which may be more comprehensive and representative. In addition, on-site auditing was performed in only a minority of the centres, and the audit only focused on the accuracy of data entry and not on the validity of the diagnosis. Our analysis is based on the diagnosis made by the attending physicians, which at times may have been inaccurate. Nevertheless, because patient management was based on the working diagnosis made by the attending physician, our analysis is suitable for evaluation of patient management. Although medical centres were required to enrol consecutive patients with acute coronary syndromes, we were not able to verify this due to our limited audit. Finally, the 30-day follow-up status was missing for a small minority of patients, possibly affecting the actual death rates.

Conclusions

The Euro Heart Survey ACS is the largest survey hitherto of acute coronary syndromes in Europe and the Mediterranean basin, enrolling 10 484 patients from 25 countries, thus providing a more extensive portrait of current treatment and outcomes of acute coronary syndromes in this region. Our results clearly demonstrate the discordance between existing guidelines for the treatment of acute coronary syndromes[12,13] and current practice in this region. Moreover, our data underscore the inaccuracy of extrapolating the outcomes of randomized, clinical trials to the real world scenario. Additional regional and global[11,21] databases encompassing the complete spectrum of acute coronary syndromes are needed to broaden our understanding of how invasive and pharmacological therapies are being integrated into real practice.

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Appendix 1

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Appendix 2

Definitions of terms

Prior PCI: Percutaneous coronary intervention, successful in at least one segment

Malignancy: Other than basal and squamous cell skin cancers

Smoking: Cigarette, cigar, pipe

Hyperlipidaemia: Diagnosis previously made by physician, receiving lipid-lowering therapy, or total cholesterol $>190\ mg\ .\ dl^{-1}$ or $>5\ mmol\ .\ l^{-1}$, HDL $<40\ mg\ .\ dl^{-1}$ or $<1\ mmol\ .\ l^{-1}$, triglycerides $>190\ mg\ .\ dl^{-1}$ or $>2\ mmol\ .\ l^{-1}$

Hypertension: Diagnosis previously made by physician, receiving medications to lower blood pressure, or known blood pressure values of ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic on ≥ 2 occasions

Family history of premature coronary artery disease: History of angina pectoris, myocardial infarction, or sudden death among first-degree relatives before the age of 55 years

COPD (chronic obstructive pulmonary disease): Diagnosis previously made by physician, or patient receiving bronchodilators, or values of FEV_1 <75%, arterial pO_2 <60%, or arterial pCO_2 >50% in prior studies

PVD (peripheral vascular disease): Claudication either at rest or exertion, amputation for arterial vascular insufficiency, vascular surgery (reconstruction or bypass) or angioplasty to the extremities, documented aortic aneurysm, or non-invasive evidence of impaired arterial flow

GI Bleeding (gastrointestinal bleeding): History of occult or overt gastrointestinal bleeding

Typical chest pain: Chest pain or pressure, jaw pain, arm pain, or other equivalent discomfort suggestive of cardiac ischaemia

Atypical chest pain: Pain, pressure, or discomfort in the chest, neck, or arms not consistent with cardiac ischaemic origin

Culprit artery: Coronary artery or graft considered responsible for the acute coronary syndrome. In cases where the investigator cannot determine, the diseased vessel supplying the largest territory of myocardium should be selected

TIMI 3 flow: Complete and brisk flow

Elective: The procedure could be deferred without increased risk of compromised cardiac outcome

Urgent: Not elective and not emergent. Required during same hospitalization.

Emergent: Ongoing ischaemia including rest angina despite maximal therapy, pulmonary oedema requiring intubation, or haemodynamic instability

Shock: Clinical state of hypoperfusion characterized by systolic blood pressure <80 mmHg and central filling pressure >20 mmHg, or a cardiac index of $<1{\cdot}8\ l\ .\ min^{-1}\ .\ m^{-2}$. Also considered if intravenous inotropes and/or intra-aortic balloon pump needed to maintain systolic blood pressure >80 mmHg and cardiac index $>1{\cdot}8\ l\ .\ min^{-1}\ .\ m^{-2}$

Atrioventricular block: Second atrioventricular block refers to intermittent atrioventricular conduction failure manifested by nonconducted P waves at physiological heart rates. Third atrioventricular block refers to failure of all atrial electrical activity to be conducted to the ventricles

Major bleeding: A drop of $\geq 5\ g\ .\ 100\ ml^{-1}$ in haemoglobin levels or $\geq 15\%$ in the haematocrit

Reischaemia: Recurrent angina and/or ECG changes consistent with cardiac ischaemia

Reinfarction:

- New Q waves that are >0·03 s in width and/or a third more of the total QRS complex in continguous leads.
- Within 18 h of acute coronary syndromes with ST elevation, recurrent ST segment elevation ≥ 1 mm in amplitude in ≥ 2 continguous leads lasting ≥ 30 min.
- Post-CABG: creatine kinase-MB ≥ 5 times the upper limit of normal.
- Elevation of creatine kinase-MB to above the upper limit of normal or if not available then total creatine kinase >2 times the upper limit of normal.
- Post-percutaneous coronary interventions: Creatine kinase-MB ≥ 3 times the upper limit of normal.