



Epidemiology of acute myocardial infarction in the Italian CCU network

The BLITZ Study

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KEYWORDS

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Reperfusion therapy

Aims A large number of descriptive data on patients with acute myocardial infarction are based on clinical trials and registries on non consecutive patients: these data may give only a partial picture on treatment delay, patient characteristics, treatment and outcome of acute myocardial infarction in the real world.

Methods and results The BLITZ survey prospectively enrolled all of the patients with acute myocardial infarction admitted in 296 (87%) Italian Coronary Care Units from 15–29 October 2001. Data on treatment delay, therapeutic strategies, duration of hospitalization and 30-day outcome were collected. One thousand nine hundred and fifty-nine consecutive patients (mean age 67±12 years, 70% males) were enrolled, 65% with ST-segment elevation (STEMI), 30% with no ST-segment elevation (NSTEMI) and 5% with undetermined ECG. The median delay between symptom onset and hospital arrival was 2 h and 9 min with 76% of patients hospitalized within the sixth hour (26% within the first hour, 48% within the second). The median delay from hospital arrival to reperfusion therapy in STEMI was 45 min (IQR 26–85) for thrombolysis (50% of the patients) and 85 min (IQR 60–135) for primary angioplasty (15% of the patients). Coronary angiography was performed during hospital stay in 46% of the patients (STEMI 48%, NSTEMI 43%, undetermined AMI 35%), coronary angioplasty in 25% (STEMI 26%, NSTEMI 15%, undetermined AMI 13%) and coronary bypass in 1.4% (1%, 2.2% and 1% respectively). Twenty-two percent of the patients admitted to hospitals without cath-lab were transferred to a tertiary care hospital for invasive procedures. The overall median hospital stay was 10 days (IQR 7–12, STEMI 10, NSTEMI 9, undetermined AMI 11) and was not significantly different between hospitals with or without cath-lab (respectively, 9 and 10 days, $P=0.38$). After discharge and up to 30 days, coronary

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angiography was performed in 11% (STEMI 11%, NSTEMI 11%, undetermined MI 9%), angioplasty in 10% (STEMI 10%, NSTEMI 11%, undetermined MI 7%), bypass surgery in 7% (STEMI 5%, NSTEMI 11%, undetermined AMI 7%). The in-hospital and 30-day case fatality rates were 7.4% and 9.4%, respectively (7.5% and 9.5% for STEMI, 5.2% and 7.1% for NSTEMI, 18.2% and 21.2% for undetermined MI).

Conclusions Patients with acute myocardial infarction admitted to the Italian CCUs, are older than those represented in clinical trials. A high proportion of these cases has the chance to receive early reperfusion therapy. Short-term mortality is lower than expected for patients with STEMI, but higher than reported for NSTEMI.

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Introduction

Over the last few years, there have been significant changes in the diagnosis and management of patients with acute myocardial infarction (AMI), with greater emphasis on immediate diagnosis and risk stratification in order to tailor an increasing number of therapeutic options to patients' risk profile. Despite several published randomized trials and guidelines, the extent to which recommended treatments are applied to practice remains uncertain. Although the benefit of early reperfusion is universally recognized¹, the way to attain this goal, by means of fibrinolysis or primary percutaneous coronary interventions (PCI) and the role of adjunctive therapy, and in particular antithrombotic therapy, are still controversial leading to heterogeneity in the management of patients with AMI. The organizational scenarios affecting time delays in delivering reperfusion therapy, including early diagnosis and treatment on ambulance service and in the emergency room, are largely unknown and may show great differences within the same country. Current knowledge of characteristics, management and outcome of patients with AMI stems from randomized clinical trials (RCT) in highly selected and often low-risk populations. On the other hand, international and national surveys and registries have shown that the adherence to RCT derived guidelines is strongly affected by differences in multiple cultural, regional and epidemiological aspects.²⁻⁶ Thus, the need exists for robust data from unselected populations on a national basis. In Italy, since the first GISSI⁷ randomized trial, a collaborative CCU network has been developed along with a widespread diffusion of the Emergency Ambulance Service covering almost all of the national territory. This gives a unique opportunity to investigate in a reliable manner epidemiology, therapeutic interventions and outcomes in the real world. Aims of the present survey were, therefore, to determine time delays, organizational scenarios, management strategies and outcomes as well as extent of adherence to guidelines in unselected patients with AMI in Italy.

Patients and methods

Study organization

The study was designed by the Italian Hospital Cardiology Association (ANMCO) as a nationwide survey on patients admitted to the Coronary Care Units (CCU) for an AMI either with

(STE-MI) or without (NSTEMI) ST-segment elevation. The survey was aimed at collecting data from the pre-hospital phase to 1-month follow-up.

Of the 341 CCUs invited, 296 (87%) accepted to participate (Table 1) in the study, with an homogenous distribution throughout the country. The enrolling period was 15 days, between the 15 and 29 October 2001.

Patients

Each centre agreed to enrol all the patients consecutively admitted with an AMI within 48 h from symptom onset. Signed informed consent was obtained from the patients at enrolment. The diagnosis of myocardial infarction could be made either upon admission or later during the CCU stay. No other exclusion criteria, besides time from symptom onset, were used. Data on patients' demographics, medical history, clinical characteristics, electrocardiographic findings, MI definition and treatment interventions, as well as in-hospital outcomes were to be reported in a detailed standardized case record form by a trained cardiologist. The details on symptoms onset, first medical help seeking and arrival at hospital were collected as soon as patients could be interviewed. Particular care was taken to assess timing of hospital arrival, ECG execution, and reperfusion treatment. Additional items included length of stay in the CCU and overall hospital stay, timing of invasive procedures and transfer to a tertiary care hospital to undergo coronary angiography and/or revascularization.

The 30-day follow-up was conducted by hospital visits and concerned major cardiac events occurred from hospital discharge (non fatal MI, new hospitalizations for angina and heart failure, and revascularization procedures). In order to limit the percentage of missing data or misinterpretations, the first CRF filled in at each centre, and including all in-hospital data, was faxed to the Study Coordinating Center within 24 h of patient discharge, and checked by a member of the Steering Committee of the study for consistency and completeness of data. Any inconsistencies and missing data were reviewed with the investigators by telephone within 24 h. After completion of the follow-up, all of the CRFs were sent to the National Coordinating Center (Centro Studi ANMCO) for data input and statistical analysis.

Definitions

Notes were provided to assist with completion of the case record form. Each Center, was required to enrol patients who fulfilled either the classical⁸ or the new⁹ definition of MI, according to the local clinical practice. Myocardial infarction were further divided in STE-MI, NSTEMI and undetermined ECG location. STE-MI was defined by the presence of ST segment elevation ≥ 1 mm (≥ 2 mm in V1 to V3) in two or more contiguous leads. NSTEMI was defined by the presence of ST depression, T wave

Table 1 Characteristics of the participating Coronary Care Units

	<i>n</i> 296 ^a	%
Without cath-lab	164	55
With cath-lab, no intervention	40	14
With cath-lab, with intervention available <24/24 h	33	11
With cath-lab, with intervention available 24/24 h	59	20
Hospitals with cardiac surgery	52	18
Hospitals without cardiac surgery	244	82

^a*n*=number of centers; cath-lab=catheterization laboratory.

inversion, or non-significant ST-T changes. Patients with complete left bundle branch block, paced rhythm or other abnormalities that made it impossible to analyse the ST segment were defined as having an MI with undetermined ECG location. Pre-hospital delay was defined as the time interval between symptom onset and the first arrival at hospital. Delay of reperfusion treatment was defined as the time interval between arrival at hospital and start of thrombolysis (door-to-needle time) or primary coronary angioplasty (door-to-balloon time). As far as treatment strategies are concerned, patients with NSTEMI were grouped as having had an invasive or a conservative strategy. The first was considered to have occurred when the patients had undergone coronary angiography/PCI or CABG during index hospital admission, without a preliminary functional evaluation (exercise stress test, dobutamine or dipyridamole stress echocardiography or myocardial perfusion scintigraphy). All the remaining patients were considered to have followed a conservative strategy.

Statistical analysis

Categorical variables are presented as number of cases and percentages and compared by the chi-square test. Time intervals are presented as median times (and inter-quartile ranges-IQR). Other continuous variables are presented as mean±standard deviation and compared by the T-test for comparison of two groups. Observed differences are expressed as *P* value. A value of *P*<0.05 was considered statistically significant. All analyses were performed with SAS system software (SAS Institute Inc., Cary, North Carolina). Completeness of data was 100% for all the analysed variables, with the exception of 16 (most of which regarding the pre-hospital phase). The median missing values for these latter was 0.7% (range 0.1–2.2%).

Results

During the 15-day enrolment period, 1959 patients (mean 6.6 patients, range 1–20, per participating CCU) had a final diagnosis of AMI and were enrolled in the study. The mean age was 67±12 years (range 21–97) and males were 70% of the whole population.

Patients arrived primarily to CCU from outside the hospital (68%), whereas 15% were intra-hospital transfers (13% of whom from cardiological ward and 87% from a non-cardiological ward) and 17% arrived from a different hospital. Thirty-two patients (1.6%) were already hospitalized at onset of index symptoms. AMI and unstable angina accounted for the most frequent diagnosis upon admission in the CCU: respectively 86% and 8%. According to the first ECG (in 14% of the cases it was a pre-hospital ECG), patients were classified as having STE-MI in 65%,

NSTEMI in 30%, and AMI with LBBB/PM in 5% of cases. In patients with NSTEMI, the diagnosis was done in 72% of the cases upon arrival at the emergency department, and in 28% of the cases during the next 24 h in CCU. Conversely, STE-MI diagnosis was already evident at the emergency department in 93% of cases; the diagnosis of AMI in patients with LBBB or paced rhythm was made on arrival in 79% of the cases.

The demographic and historical characteristics of the study population are shown in Table 2. Compared to patients with STE-MI, NSTEMI patients were on average 2 years older and had a much higher prevalence of a previous history of ischaemic heart disease, represented by previous myocardial infarctions, chronic angina, myocardial revascularizations and heart failure. Patients with LBBB or paced rhythm were the eldest group and presented the worst overall risk profile.

Pre-hospital phase

Clinical and organizational factors during the pre-hospital phase are summarized in Table 3. In <20% of the cases, chest pain was atypical or absent; in about one-third, the index MI was preceded by chest pain episodes, half of which occurring within the previous 48 h. Seventy-five percent of the patients had symptom onset at home, in most cases (83%) with eyewitnesses. One-third of the patients reached directly the hospital emergency department (direct presentation), whereas two-thirds sought medical help by different approaches (indirect presentation): in 45% of cases the emergency territorial services, and in 43% of cases a physician (general practitioner or medical assistance at home during night or weekend). Thirty-four percent of the patients who contacted medical help arrived at hospital by own car. Overall, the median delay between symptom onset and hospital arrival was 2 h and 9 min (IQR 60–340 min), with a significant difference (*P*<0.001) between STE-MI (120 min, IQR 60–300) and NSTEMI (164 min, IQR 75–490 min). Forty-eight percent of the patients arrived within 2 h and 76% within 6 h. In patients with indirect presentation, the median decision time, defined as the interval between onset of symptoms and the decision to seek help, was 60 min (IQR 20–245 min).

The probability of reaching the hospital within 2 h from symptom onset, was higher for patients who had the beginning of index symptoms at job place or on the road (66%), compared to those who had symptoms at home

Table 2 Demographic and historical characteristic of the study population

	All (n, %)	STE-MI (n, %)	NSTE-MI (n, %)	PM/LBBB (n, %)
Number of patients	1959	1275 (65)	580 (30)	99 (5)
Male	1363 (70)	902 (71)	400 (69)	59 (60)
Age (years)	67±12	66±13	68±12	74±10
Patients >75 years	529 (27)	296 (23)	182 (31)	49 (50)
Active working status	627 (32)	448 (35)	168 (29)	8 (8.1)
Familial history of ischaemic heart disease	626 (32)	401 (31)	194 (34)	31 (31)
Smoking status				
Never	823 (42)	509 (40)	257 (44)	53 (54)
Active	702 (36)	506 (40)	175 (30)	20 (20)
Prior	434 (22)	260 (20)	148 (26)	26 (26)
Diabetes	434 (22)	253 (20)	141 (24)	40 (40)
Hypertension	1087 (56)	656 (51)	363 (63)	68 (69)
History of ischaemic heart disease ^a	631 (32)	320 (25)	254 (44)	56 (57)
Prior AMI	386 (20)	190 (15)	155 (27)	41 (41)
Chronic angina pectoris (%)	401 (21)	192 (15)	176 (30)	32 (32)
Prior myocardial revascularization	155 (7.9)	66 (5.2)	74 (13)	14 (14)
PCI	85 (4.3)	41 (3.2)	40 (6.9)	4 (4.0)
CABG	85 (4.3)	28 (2.2)	43 (7.4)	13 (13)
Prior heart failure	129 (6.6)	45 (3.5)	53 (9.1)	31 (31)
Prior stroke	152 (7.8)	87 (6.8)	55 (9.5)	10 (10)
Peripheral arterial disease	210 (11)	123 (9.7)	72 (12)	15 (15)

^aHistory of ischaemic heart disease=history of chronic angina pectoris, previous myocardial infarction or previous myocardial revascularization; Prior myocardial revascularization=either PCI and CABG. In 5 patients (0.2%) the ECG was not coded. PCI=percutaneous coronary intervention; CABG=coronary artery by-pass graft.

(45%, $P<0.001$), and for patients with direct (55%) compared to indirect presentation (45%, $P<0.001$).

Hospital phase

The clinical profile upon CCU arrival is summarized in Table 4. Patients with STE-MI more frequently had ongoing chest-pain, bradycardia and hypotension at CCU admission, whereas pulmonary oedema was more frequent in patients with NSTEMI. About half of the STEMI were anterior. NSTEMI-MIs were characterized in half of the cases by ST depression, in about a quarter by negative T waves, whereas 22% had only minor ECG abnormalities. The biochemical markers used for the diagnosis of myocardial infarction were CK in 87% of the cases, CK-MB mass in 60%, CK-MB activity in 34%, cTn-I in 60%, and cTn-T in 14%. A single marker was used in 7% of cases, two markers in 36%, three in 49%, four in 7% and five markers in only two patients. In 3% of the cases, the diagnosis of AMI was done using only Troponin I or T, and in 1% using only CK-MB mass.

Reperfusion treatments

Among the 1275 patients with ST elevation, 828 (65%) received a reperfusion treatment: 642 (50%) thrombolysis and 186 (15%) primary angioplasty. The median door-to-needle time for lytic therapy was 45 min (IQR 26–85 min), and the door-to-balloon time for primary angioplasty was 85 min (IQR 60–135 min). In 63 (10%) thrombolytic-treated patients, rescue-PCI was performed with a median delay of 4 h and 30 min (IQR 150–420 min). Four hundred forty-seven patients (35%) did not receive any

reperfusion therapy: 56% of them due to late arrival, and 28% to absolute or relative contraindications. No reason was recorded in 17% of the cases. Reperfusion treatment by pre-hospital delay classes (Fig. 1) shows that the number of patients excluded from any reperfusion therapy increases with pre-hospital delay, but that the type of reperfusion therapy is not associated with the pre-hospital delay ($P=ns$). The distribution of reperfusion treatments by age classes showed that less than half of patients older than 75 years received a reperfusion treatment (34% thrombolysis, 9% primary PCI), compared to more than two-thirds of those younger than 55 (59% thrombolysis, 19% primary PCI). Among the 828 patients who received a reperfusion therapy, primary PCI was used in 23% of the cases and thrombolysis in 77%. In the three age groups considered, the use of primary PCI was 25% in patients younger than 55 years, 22% in those 55–75-year old and 21% in the elderly ($P=ns$). Among fibrinolytics, rt-PA was used in 90% of the cases and streptokinase in 6% of patients. In association with the fibrinolytic, unfractionated heparin was used in 90% of the cases and low-molecular weight heparin (LMWH) in 15% (it is likely that, in some patients, the two treatments were used consecutively). Glycoprotein IIb–IIIa inhibitors were associated with a lytic therapy in 8% of patients, and in 66% of cases with primary PCI. In patients who underwent lytic treatment, 4% experienced a major bleeding and in 0.3% of the cases a haemorrhagic stroke was reported. An ischaemic stroke occurred in 14 patients (1.1%). Patients with LBBB ($n=71$) received thrombolysis in 11% of cases (in no case followed by rescue PTCA), and primary PTCA in 6%.

Table 3 Clinical and organizational related factors during pre-hospital phase

	n (1927)	%
Symptoms at onset		
Typical chest pain	1561	81.0
Atypical chest pain	223	11.6
Without chest pain	143	7.4
Prodromal angina		
No	1259	65
Minimal effort angina <2 months	150	7.8
Rest angina >48 h	235	12.2
Rest angina <48 h	293	15.2
Setting of symptom occurrence		
Home	1446	75
Job place	102	5.3
On the road	154	8.0
Other	225	11.7
Distance from the hospital		
0–20 km	1588	82.4
>20 km	297	15.4
Unknown	42	2.2
Persons present at onset of symptoms	1603	83.2
Direct presentation	654	34
Indirect presentation	1273	66
Type of health service ^a		
Territorial emergency services	503	39.5
Ambulance services	74	5.8
Emergency territorial physician	156	12.3
General practitioner	388	30.5
Police	6	0.5
Other	157	12.3
Who sought help?		
Patient	473	37
Witness	788	62
Unknown	12	1.0

^a In some cases patients sought more than one type of health service. Patients already in hospital at symptom onset ($n=32$) were excluded from the Table.

Angiography, percutaneous and surgical coronary intervention

During the index admission 46% of the patients underwent coronary angiography, 25% coronary angioplasty and 1.4% coronary artery by-pass surgery (CABG).

In patients with STE-MI, coronary angiography was performed in 48% of the cases (33% not including the procedures related to primary or rescue-PCI), coronary angioplasty in 11% (excluding primary or rescue PCI), and CABG in 1.0%. Among the 580 patients with NSTEMI, coronary angiography, PCI or CABG were performed, respectively, in 43%, 15% and 2.2% of the patients. According to our definition, the invasive strategy was applied in 208 patients (36%), whereas a conservative approach was used in the remaining 372 (64%). Patients with MI and undetermined ECG underwent coronary angiography in 35% of the cases, any PCI in 13% and CABG in 1.0% of cases. Among the 898 patients admitted in hospitals without catheterization facilities, 197 (22%) were temporarily transferred to a tertiary care hospital for urgent or scheduled coronary angiography (followed

by a percutaneous revascularization in 10% of cases, and by CABG in 0.2%).

Pharmacological treatments

The use of pharmacological therapies during hospitalization (Fig. 2) and at discharge (Fig. 3) was analysed by infarct type (STE-MI vs NSTEMI).

Aspirin was given to 90% of patients, whereas the use of ticlopidine and clopidogrel in STE-MI was largely influenced by the type of reperfusion therapy. Patients treated with primary PCI received ticlopidine and clopidogrel respectively in 77% and 16% of cases.

Patients with STE-MI not treated with reperfusion therapy received a different profile of adjuvant treatments. Compared to patients treated with fibrinolysis, they received less frequently aspirin (89% vs 94%), unfractionated heparin (56% vs 85%) and beta-blockers (57% vs 71%). On the other hand, low-molecular weight heparin (43% vs 30%), GP IIb–IIIa inhibitors (11% vs 8%) and intravenous nitrates (88% vs 80%) were more often adopted; an equal use of ticlopidine (21% vs 22%) and clopidogrel (4% vs 5%) was recorded.

At discharge, an antiplatelet treatment was overall prescribed to 90% of patients, 5% less than during the hospital course. Among the other drugs, ticlopidine, clopidogrel, beta-blockers, and ACE-inhibitors were equally prescribed at discharge, whereas the use of statins increased of 5%. No marked differences were recorded within each drug, between STE-MI and NSTEMI, with the only exception of nitrates.

In-hospital outcome

One hundred and forty-four patients (7.4%) died during hospital course (Table 5). In-hospital mortality was 7.5% among STE-MI, 5.2% for NSTEMI and 18.2% in patients with LBBB or paced rhythm. Among all the patients who received a thrombolytic treatment, in-hospital mortality resulted 5.6%, and according the age classes, respectively 0.6% in patients <55 years, 4.7% in patients 55–75 years old, and 16.8% in those older than 75 years. In patients treated with primary PCI, in hospital mortality was 5.6%, and according to the age classes, respectively 1.9%, 2.8%, and 11.5%.

Among 1815 patients discharged alive, one or more major complications (heart failure, pulmonary oedema, cardiogenic shock, reinfarction, recurrent/refractory angina, mechanical complication, major bleeding, stroke) occurred in 32% of cases.

Eighty-four percent of the patients were discharged home, 15% were transferred to another hospital, and 4% were sent to a rehabilitation hospital. The overall median hospital stay was 10 days for STE-MI and 9 days for NSTEMI, half of which spent in CCU (5 days for both STE-MI and NSTEMI). Comparing hospitals with and without catheterization facilities, no differences in length of hospital stay were detected, overall and across the different types of myocardial infarctions.

Table 4 Clinical presentation in CCU

	All (n=1954) n (%)	STE-MI (n=1275) n (%) ^a	NSTE-MI (n=580) n (%) ^b	LBBB/PM (n=99) n (%) ^{c,d}
Chest pain still present	1355 (69)	992 (78)	316 (55)	44 (44)
Heart rate				
Mean±sd (bpm)	78±20	77±20	80±21	83±20
Patients with HR <60 bpm	255 (13)	182 (14)	67 (12)	6 (6.1)
Patients with HR >100 bpm	219 (11)	117 (9)	82 (14)	19 (19)
Blood pressure				
SBP/DBP (mean±SD)	137±27/80±15	135±27/80±15	141±27/82±15	136±26/77±14
Patients with SBP ≤100 mmHg	174 (8.9)	127 (10)	38 (6.6)	9 (9.1)
Patients with SBP >180 mmHg	95 (4.9)	52 (4.1)	39 (6.7)	4 (4.0)
Killip class				
Killip 1	1529 (78.1)	1015 (79.6)	458 (79.0)	52 (52.5)
Killip 2	304 (15.5)	203 (15.9)	76 (13.1)	24 (24.2)
Killip 3	89 (4.5)	33 (2.6)	38 (6.5)	18 (18.2)
Killip 4	37 (1.9)	24 (1.9)	8 (1.4)	5 (5.1)
ECG characteristics				
Anterior ST elevation	595 (30.4)	595 (46.7)		
Non-anterior ST elevation	680 (34.7)	680 (53.3)		
Anterior ST depression	203 (10.4)		203 (35.0)	
Non-anterior ST depression	90 (4.6)		90 (15.5)	
Negative T wave	159 (8.1)		159 (27.4)	
Other ST-T abnormalities	128 (6.5)		128 (22.1)	
LBBB	71 (3.6)			71 (71.7)
Pacemaker rhythm	28 (1.4)			28 (28.3)
Unknown	5 (0.3)			

^aSTE-MI=ST segment elevation myocardial infarction.

^bNSTE-MI=Non ST segment elevation myocardial infarction.

^cLBBB=left bundle branch block.

^dPM=paced rhythm; SBD/DBP=systolic/diastolic blood pressure.

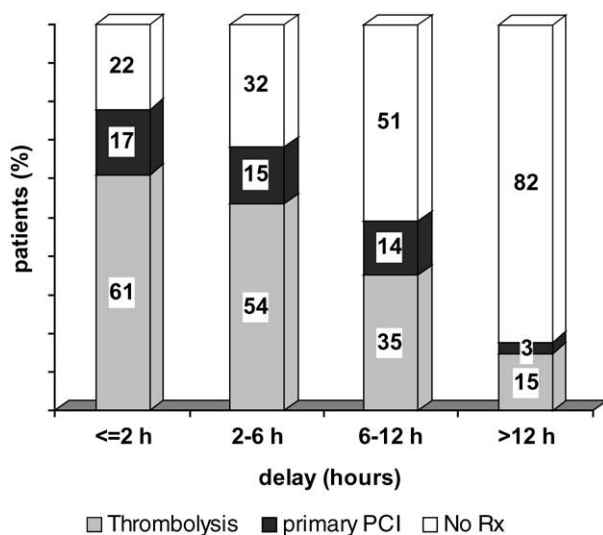


Fig. 1 Reperfusion treatment according to pre-hospital delay in patients with STE-MI. PCI=percutaneous coronary intervention; no Rx=no reperfusion treatment.

30-day follow-up

Thirty-day follow-up was completed for 99.1% of discharged patients. Between discharge and 30 days death

occurred in 2.1% of patients, a new myocardial infarction in 1.1%, and new hospital admissions for unstable angina and heart failure in 2.7% and 0.8% of patients respectively. Differences among infarct type are shown in [Table 6](#). The overall 30-day mortality was 6.4% in patients treated with thrombolysis and 6.5% in patients treated with primary PCI. After discharge and up to 30 days, coronary angiography and coronary angioplasty were done respectively in 11% and 10%, without major differences between STE-MI and NSTE-MI. However NSTE-MI patients underwent coronary artery bypass grafting twice as often as those with STE-MI (11% vs 5%).

Discussion

The aim of the BLITZ survey was to provide a reliable contemporary picture of patients with acute myocardial infarction admitted to the Italian CCU network in order to identify areas of possible improvement and to define strategies for optimal care delivery. BLITZ is the largest Italian survey on patients consecutively admitted to coronary care units with myocardial infarction, designed to study the whole clinical course, from symptoms onset to 1-month follow-up. It reflects the pattern of care applied in the management of AMI in a countrywide setting, as it has enrolled consecutive patients in 90% of the

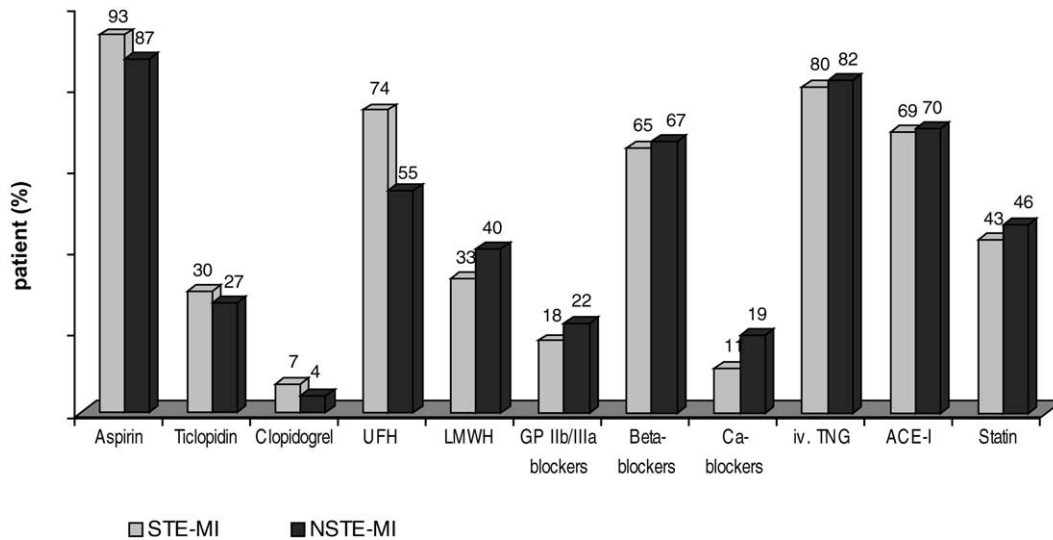


Fig. 2 Pharmacological treatment during initial hospitalization. UFH=unfractionated heparin; LMWH=low molecular weight heparin; iv. TNG=intravenous trinitroglycerine; ACE-I=ACE-inhibitors; Ca-blockers=calcium channel blockers; STE-MI=ST segment elevation myocardial infarction; NSTEMI=non-ST segment elevation myocardial infarction.

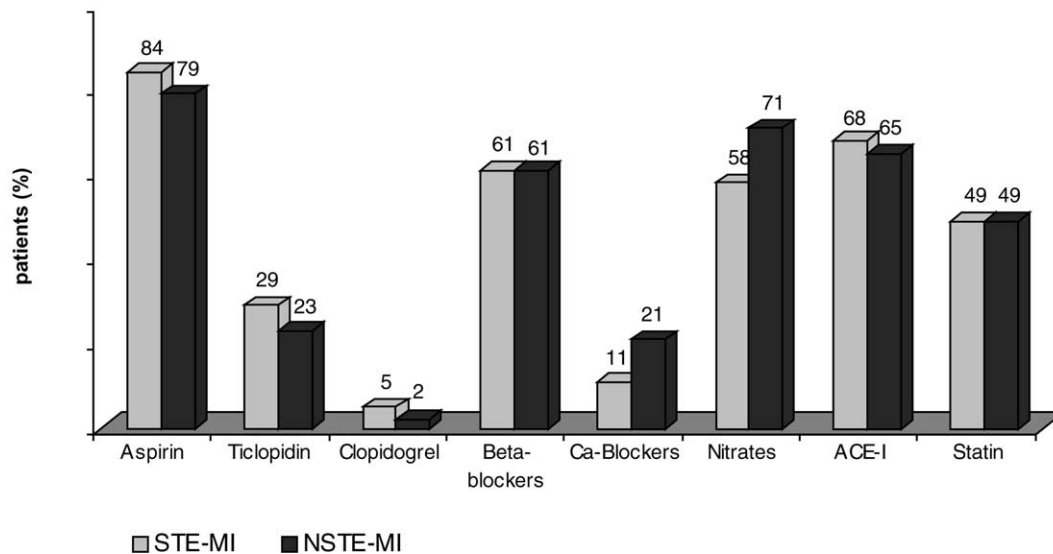


Fig. 3 Discharge medications. ACE-I=ACE-inhibitors; Ca-blockers=calcium channel blockers; STE-MI=ST segment elevation myocardial infarction; NSTEMI=non-ST segment elevation myocardial infarction.

Italian CCUs with and without facilities for coronary revascularization.

Adjusting data for all of the CCUs in the country and throughout one year, it can be extrapolated that about 55 000 AMI/year are admitted in the Italian CCUs (2/3 STE-MI and 1/3 with NSTEMI or indeterminate ECG). Italian National Health Service¹⁰ administrative data from all hospitals report AMI as principal final diagnosis in about 80 000 patients (International Classification of Disease, 9th revision, code 410.01 through 410.91, data year 2000). This data could suggest that about 30% of AMI patients are treated out of the CCU.

The comparison with recently published international surveys is partially appropriated for differences in AMI definition, enrolling criteria and context.

Based on the ECG, we found 65% STE-MI, 30% NSTEMI and 5% undetermined MI in the BLITZ population. In Euro Heart Survey ACS¹¹ the STE-MI and NSTEMI percentages were the same as in BLITZ. Main differences exist with RIKS-HIA¹² (39% were STE-MI, 8% were LBBB/PM and 53% NSTEMI), despite similar criteria for MI definition. Possibly the older age of the population with MI (72 in RIKS-HIA vs 67 years in BLITZ) and the introduction of troponins for MI diagnosis since 1996, are factors that

Table 5 Hospital outcomes by diagnosis

	All n (%)	STE-MI ^a	NSTE-MI ^b	LBBB/PM ^{c,d}
Length of stay in hospital – days median (IQR)	10 (7, 12)	10 (7, 12)	9 (7, 12)	11 (7, 15)
Length of stay in CCU	5 (4, 7)	5 (4, 7)	5 (4, 6)	5 (4.7)
Death	144 (7.4)	96 (7.5)	30 (5.2)	18 (18.2)
<55 years	3 (0.8)	2 (0.8)	0 (0.0)	1 (25.0)
55–75 years	48 (4.5)	35 (4.9)	11 (3.5)	2 (4.4)
>75 years	93 (17.6)	59 (19.9)	19 (10.4)	15 (30.6)
Complicated hospital course	583 (32.1)	378 (32.1)	165 (30)	39 (48.2)
Type of discharge				
Home	1530 (84.3)	994 (84.3)	465 (84.6)	68 (84.0)
Transferred to an other hospital	205 (11.3)	128 (10.9)	66 (12.0)	10 (12.3)
Rehabilitation hospital	71 (3.9)	53 (4.5)	14 (2.5)	3 (3.7)
Still admitted at 30 days	9 (0.5)	4 (0.3)	5 (0.9)	0 (0.0)

^aSTE-MI=ST segment elevation myocardial infarction.

^bNSTE-MI=non ST segment elevation myocardial infarction.

^cLBBB=left bundle branch block.

^dPM=paced rhythm. HR=heart rate; IQR=interquartile range; CCU=Coronary Care Unit. Complicated hospital course=includes at least one of the following: heart failure, pulmonary oedema, cardiogenic shock, reinfarction, recurrent/refractory angina, mechanical complication, major bleeding, stroke.

Table 6 Death and cardiac events from discharge to 30-days follow-up

	All % (n=1790)	STE-MI % (n=1164) ^a	NSTE-MI % (n=540) ^b	LBBB/PM % (n=81) ^{c,d}
Death (cumulative at 30 days)	2.1(9.4)	2.1(9.5)	2.0(7.1)	3.7(21.2)
Re-infarction	1.1	1.0	1.3	2.5
Re-admission for unstable angina	2.7	2.5	2.8	4.9
Re-admission for heart failure	0.8	1.0	0.7	0.0
Coronary angiography	10.9	10.9	11.3	8.6
Coronary angioplasty	10.0	10.5	9.3	7.4
Coronary artery bypass grafting	7.2	5.3	11.1	7.4

^aSTE-MI=ST segment elevation myocardial infarction.

^bNSTE-MI=non-ST segment elevation myocardial infarction.

^cLBBB=left bundle branch block.

^dPM=paced rhythm.

play a major role, as shown by the increasing rate of STEMI diagnosis in the recent years.¹² In the GRACE Registry⁴, STE-MI was diagnosed in 54% and NSTE-MI in 46% of the cases; in the ENACT⁵ study, 73% were classified as STE-MI and 27% as NSTE-MI, but in the latter 38% of the patients classified as having an unstable angina presented troponin levels above the upper normal limit.

Pre-hospital delay

Reducing pre-hospital delay is one of the major tools for improving reperfusion therapy. In the present study, the median delay between symptom onset and hospital admission was about 2 h, with 26% of the patients arriving within the first, 48% within the second, and 76% within the sixth hour. In the GISSI-Avoidable Delay (GISSI-AD) study¹³, conducted in 1990 on 5301 patients in 118 CCUs, the median pre-hospital delay was 230 min, 120 min longer than in BLITZ. This overall reduction is to be

attributed to a shorter decision time (120 min in GISSI-AD, 60 min in BLITZ) and an increasing percentage of patients arriving within 2 h from symptom onset (GISSI-AD 34%, BLITZ 48%), whereas the proportions of patients arriving between 2 and 6 h (29% in GISSI-AD Study, 28% in BLITZ) and between 6 and 12 h (14% in GISSI-AD, 10% in BLITZ) were similar. Part of the merit for this important progress in care delivery should be ascribed to the nationwide application of the Emergency Medical Service 118 number which, however, was used as first aid only by 30% of the patients. The reductions in delay observed in the National Registry of Myocardial Infarction in about 10 years (1990 to 1999, median delay from 132 to 120 min)¹⁴ and in the Worcester Study (1986 to 1997, median delay from 132 to 120 min)¹⁵ are less impressive.

Longer pre-hospital delays were observed in GRACE¹⁶ (median 139 min for STE-MI, 190 min for NSTE-MI), in the PRAIS-UK registry¹⁷ on unstable angina and NSTE-MI (180 min), and in REACT¹⁸ (including patients with chest pain), and in most thrombolysis trials.^{19,20}

Reperfusion therapy in STEMI

Timely administration of reperfusion therapy by primary angioplasty or thrombolysis is the recommended treatment for most patients with myocardial infarction and ST segment elevation.^{21,22} In the present study, pre-hospital thrombolysis has never been administered, despite a pre-hospital ECG was obtained in 14% of patients. Reperfusion treatment was administered in hospital to 65% of patients with STE-MI, with a ratio of 3.4:1 in favour of thrombolysis. Overall, this represents a very high rate of reperfusion treatment, since our population included about 15% of patients with a pre-hospital delay longer than 12 h. In addition only 5.9% of all STE-MI patients were excluded by the physician from any reperfusion therapy without a proper reason. There was no relationship between the patient's age, pre-hospital delay and rates of primary angioplasty. This finding suggests that, when Cath-lab facilities are available, Italian cardiologists are more likely to use primary PCI as preferred reperfusion strategy, rather than as an alternative strategy to thrombolysis when this is more dangerous or less effective, as respectively in the case of elderly or in patients with long time delays.

The present data also favourably compare with those of the GISSI-AD study¹³ which, in 1990, reported a very low rate of reperfusion therapy (40%) irrespective of time delays. In the GISSI-AD study, 40% of the patients admitted within 2 h did not receive reperfusion therapy, compared to 22% in BLITZ; corresponding proportions for the 2–6 h delay were 51% and 32%, for 6–12 h 79% and 51%, and for patients admitted later than 12 h from symptom onset 92% and 82% respectively.

The reperfusion rates observed in the present study are very close to those reported in the most recent surveys. In ENACT⁵ 51% of the patients received thrombolysis, and only 8% primary PCI, with wide variations among different European countries. In RIKS-HIA year 2000¹², 55% of patients received some form of reperfusion therapy (pre-hospital in only 0.6%, with a ratio thrombolysis/PCI of 5.5:1), similarly to Euro Heart Survey ACS¹¹ (56%, but with a ratio of 2.7:1). In this latter, a late admission was the cause of exclusion in only 22% and age in only 3% of the patients; most exclusions (35%) were motivated by the lack of a clear indication. The different enrolling sites could explain these differences. In the GRACE survey, 47% of STE-MI received thrombolytic treatment, and 18% primary PCI with an overall ratio similar to Euro Heart Survey ACS (2.6:1). However, huge differences were observed among different geographic areas, from a ratio of 1.6:1 in the USA to a ratio of 64:1 in the area Australia–New Zealand–Canada. Among patients in NRMI-3 presenting with ST segment elevation or LBBB within 12 h from symptom onset, 48% received thrombolysis and 24% primary PCI.

The analysis of the in-hospital delay show that only one-third of the patients received thrombolysis within 30 min, and only one-quarter underwent primary PCI within 60 min, time delays usually considered as the gold standard of reperfusion treatments.²¹ Improving these figures would require a wider use of thrombolytic therapy

in the emergency room, still seldom used in this country²³ and cath-lab available with on-site personnel 24 h per day. The comparison with the other surveys shows identical door-to-needle time in RIKS-HIA year 2000¹² (median 45 min), longer in the ESC survey (median 59 min), and shorter in NRMI-3¹⁴ registry (median, 38 min). Door-to-balloon time was 110 min in RIKS-HIA year 2000¹², 111 min in GRACE²⁴, 108 min in NMRI-3, 93 min in ESC survey, and 85 min in BLITZ, showing a positive trend in the most recent surveys.

The low rate of intracranial haemorrhage observed in BLITZ is due to the lack of event adjudication; it is likely that part of the ischaemic stroke should be diagnosed as haemorrhagic by a systematic use of CT or MRN scan. In RIKS-HIA register, the proportion of cerebral haemorrhage in patients treated with thrombolysis is identical, varying from 0.3 to 0.4% according to the type of hospital.¹²

Revascularization procedures

This survey shows that the use of cardiac catheterization and coronary revascularization in patients with acute myocardial infarction in Italy is aligned to the European average¹¹, with a significant increase over the last few years. Compared to the GISSI Prognosis Registry²⁵, performed in 1995, the present data show a 23% increase in the use of coronary angiography and a doubling of percutaneous revascularization procedures, with a concurrent reduction in the rate of CABG (from 4.4% to 1.0%). Within 1 month after the index MI, an additional 15 percent of patients underwent either percutaneous or surgical coronary revascularization.

Patients with NSTEMI enrolled in BLITZ were older, more frequently female, and with a longer history of coronary heart disease compared to those with STE-MI. As in other recent surveys^{6,17,26} the present study shows that there was no relationship between the patient's risk profile and rates of invasive procedures. Indeed, the strategy adopted was largely influenced by the availability of catheterization facilities and not by established clinical indicators of worse outcome. Similar findings were already present in the EARISA Registry.²⁷

In-hospital and discharge medical therapy

The present study confirms the very high rate in aspirin use during hospital stay and at discharge, consistent with the rates reported by other observational studies. In Italy, ticlopidine is still the most frequently prescribed thienopyridine (ratio of 5:1 with clopidogrel, both in STE-MI and in NSTEMI), differently from the European average, which shows an opposite fraction. This difference may be ascribed to the fact that clopidogrel was still not reimbursed at the time of the present survey. In comparison with the other most recent studies^{4,11}, the rate of use of unfractionated heparin is still very high, compared to LMWH, in both types of MI. In the present study, the use of glycoprotein IIb/IIIa inhibitors in NSTEMI was low (22%), but comparable to that observed in GRACE (20%)⁴ and higher than in the Euro Heart Survey

ACS (10%)¹¹ and ENACT (6%).⁵ At the contrary the use of glycoprotein IIb–IIIa inhibitors was associated to primary PCI in two-thirds of cases, a higher proportion than the observed in Euro Heart Survey ACS (45%).¹¹ Beta-blockers are significantly less prescribed, compared to other surveys, both during admission and at discharge, with absolute differences up to 10–23%.^{3,4,11,12} On the contrary, ACE-inhibitors were used, both during admission and at discharge, 15 to 20% more frequently than reported in recent surveys^{4,11,12}, and almost twice than in Euroaspire-II.³ Statins were prescribed in about half of the patients at discharge, similar to the overall rate observed in the ESC (54%), in RIKS-HIA (48%) and in GRACE (47%), and somewhat higher than observed in Euroaspire II (43%).

In-hospital and 30-day outcome

The duration of hospital course was one of the longest (10 days for STE-MI and 9 days for NSTEMI) compared to other contemporary national and international surveys, both for patients with and without ST elevation. Half of the hospital stay was spent in the CCU. The direct comparison shows that the median total length in STEMI was 8 days in the Euro Heart Survey ACS¹¹ and in the GRACE Registry⁴; in the latter also about half of the time was spent in the CCU. In GRACE, patients with NSTEMI stayed in hospital for 7 days. In Prais-UK¹⁷ and Strateg-SIA registry²⁶, the median hospital stay were even shorter, but both included also patients with unstable angina. During the 10 years of NRM registry, the duration of hospital stay of patients with myocardial infarction in the USA declined from a median of 8.3 days in 1990 to 4.3 days in 1999, independently of whether patients were treated with primary PCI or thrombolysis. A similar very short length of stay (median 5 days) for patients with MI was achieved in Sweden in year 2000.¹² Overall, it seems unlikely that the longer hospital stay observed in Italy in comparison with Europe and the USA may be attributed to different rates of early revascularization. More likely, a significant proportion of the hospital stay of Italian patients is due to the high rate of execution of non invasive pre-discharge risk stratification.²⁵ In addition, in some hospitals there are no step-down wards, and MI patients complete their whole hospital stay in CCU.

Despite better risk profile, patients with STE-MI showed a higher fatality rate in comparison with those with NSTEMI, for any age class. Similar data are reported in recent surveys.¹¹ The higher in hospital mortality reported in the Swedish registry (10.1%) is abolished by age stratification (in hospital mortality is 2.8%, 6.4% and 16.2% respectively for <65 years, 65–74 years, and >74 years old age classes).¹² The factors that in BLITZ could have contributed to the low 30-day mortality in STE-MI patients are, in our opinion, the high rate of reperfusion therapy, and particularly of PCI procedures, (either primary, rescue or delayed). In addition, the separate analysis of patients with LBBB ($n=71$, 13 deaths, mortality 18.3%) could have contributed to a further reduction. However, STE-MI mortality depurated from LBBB represents a more comparable rate, because generally it's not

known how many LBBBs are of new onset, both in the registries (over inclusion, with higher mortality) and in the thrombolytic trials (under inclusion, leading to lower mortality). Hence, the direct comparison with the most recent randomized clinical trials is of particular interest. In the present registry, the overall 30-day mortality of patients with STE-MI resulted about 3.0 to 3.5% higher than what observed in ASSENT trial²⁸ (6.2%) and in GUSTO-V²⁹ (5.9%) which, however, included only thrombolytic eligible patients within 6 h from symptom onset.

However, mortality of BLITZ patients who received a thrombolytic treatment resulted almost identical to that observed in GUSTO V (5.6% in-hospital, and 6.4% at 30-days), in HERO-2³⁰ (6.7% at 30-days, in western countries), and also in the elderly (19.3% in patients >75 years in ASSENT-2 trial).

Study limitations

Although the participating centres were asked to enrol all consecutive patients with a final diagnosis of acute myocardial infarction, we were not able to verify this task, due to the lack of administrative auditing. Outcome results reflect those of patients admitted to Coronary Care Units, and may not apply to all of the patients admitted to cardiology departments, and even less to patients with an MI admitted to non cardiological units. In addition, restriction of the registry to patients who are admitted may have resulted in the exclusion of patients who died early on arrival in the Emergency Department, or were not able to sign the patients consent.

Conclusions

The results of the BLITZ survey give a reliable picture of patients admitted to Italian CCUs with a myocardial infarction. In this setting, STE-MI still represents the majority of patients with MI. A remarkable reduction of the pre-hospital delay was observed over the last decade but, despite the wide diffusion of the emergency ambulance service, less than one-third of the patients dial 118, and the pre-hospital thrombolysis is not yet implemented. Thrombolytic treatment is delivered to nearly all suitable patients (though with a still long in-hospital delay), but a high number of patients with contraindications are not treated with primary PCI. Adherence to adjuvant pharmacological therapy in-hospital and at discharge is overall satisfactory, with some relevant exceptions (e.g. glycoprotein inhibitors in NSTEMI). As a result, in-hospital and 30-day mortality of CCU-admitted patients resembles that of recent randomized trials, despite the fact that in BLITZ about a fourth of STE-MI patients was over 75 years old. Major concern arises from two important issues. First, the proportion of patients who need to be transferred to a tertiary care hospital to undergo invasive procedures is high and represents a potential limitation to the adherence to guidelines, especially for patients with NSTEMI. Second, the long hospital stay, especially in CCU, is not justified. A significant shortening is mandatory to increase the availability

of Italian CCUs to admit more patients for intensive cardiological care.

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Appendix A

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