Occurrence, Characteristics, and Outcome of Patients Hospitalized with a Diagnosis of Acute Myocardial Infarction Who Do Not Fulfill Traditional Criteria

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Summary

Background: The diagnosis of acute myocardial infarction (AMI) is traditionally based on clinical history, elevation of serum enzyme activity, and typical changes in the electrocardiogram (ECG); however, not all patients who develop AMI fulfill these criteria on discharge from hospital.

Hypothesis: The aim of the study was to evaluate (1) the frequency with which the traditional criteria for AMI are not fulfilled among patients diagnosed with AMI on discharge, and (2) whether patients with and without these criteria differ in terms of characteristics, treatment, and outcome.

Methods: All patients aged < 75 years and hospitalized in the municipality of Göteborg with a discharge diagnosis of AMI were included. Fulfillment criteria for AMI were two of the following three points: (1) chest pain, (2) increase in cardiac enzymes, and (3) development of Q waves.

Results: In all, 1,188 admitted patients, 27% of whom were women, were included in the analysis. Of these, 193 (16%) did not fulfill the traditional criteria for AMI. These patients had an in-hospital mortality rate of 48%; of these, 59% died a sudden death, and of those who were autopsied (62%), 96% showed signs of a fresh AMI. The most common symptom on admission to hospital in patients who did not fulfill the traditional criteria was chest pain (34%), followed by dyspnea (27%) and fatigue (14%). Of those who died suddenly, fewer than half had been admitted to the coronary care unit.

Conclusion: Patients diagnosed with AMI who do not fulfill the traditional diagnosis criteria have high mortality. On admission to hospital, the initial suspicion of AMI is often vague. Measures for earlier detection of life-threatening coronary artery disease among these patients are warranted.

Introduction

The diagnosis of acute myocardial infarction (AMI) is traditionally based on clinical history, elevation of serum enzyme activity, and typical changes in the electrocardiogram (ECG). With the availability of new biochemical markers with high sensitivity and specificity for the detection of myocardial necrosis, patients with unequivocal biochemical evidence of acute myocardial necrosis may not fulfill the traditional criteria for AMI. For instance, patients with severe, sudden dyspnea, a typical increase in creatine kinase (CK)-MB mass concentration, and left bundle-branch block will frequently be given a discharge diagnosis of 410 (AMI) while not fulfilling the traditional AMI criteria.[1,2]

In this study, all patients aged < 75 years, living in the municipality of Göteborg, hospitalized in the two city hospitals in Göteborg and receiving a discharge diagnosis of 410 (AMI) were further evaluated. Patients who fulfilled two out of three criteria for AMI were compared with those who did not in terms of patient characteristics and outcome. The aims were to evaluate (1) the frequency with which the traditional criteria are not fulfilled, and (2) whether patients with and without these criteria differed in terms of characteristics, treatment, and outcome.

Methods

All patients living in the municipality of Göteborg, aged < 75 years, hospitalized in one of the two city hospitals, and receiving a discharge diagnosis of 410 (AMI) in 1990 and 1991 were included in the study.

In a retrospective evaluation, all cases were characterized in terms of previous history, treatment in hospital, and outcome. Furthermore, the criteria for diagnosis as well as the reason for hospitalization among those who did not fulfill the criteria for AMI were reevaluated in all patients. All information was taken from the patients' medical files.

The criteria for AMI were (1) chest pain of at least 15 min duration; (2) increase in cardiac enzymes: CK, CK-MB, or lactate dehydrogenase (LD)1; (3) development of pathologic

Q waves, defined as ≥ 0.04 s wide or, if the Q wave was ≥ 0.03 s, a Q/R wave ratio of ≥ 1:4 in at least two leads in a 12-lead standard ECG. At least two of the three criteria had to be fulfilled for a diagnosis of AMI.

Sudden death was defined as instantaneous death if there were no premonitory symptoms or if death occurred less than 1 h after the onset of final symptoms. Cardiogenic shock was defined as systolic blood pressure < 80 mmHg with simultaneous signs of poor peripheral circulation.

The prevalence of a history of AMI, angina pectoris, hypertension, diabetes, and smoking was based on information from the medical files.

In this manuscript, patients who did and those who did not fulfill the criteria for AMI are compared.

Statistical Methods

To test for differences between patients who did and did not fulfill criteria for AMI, Fisher's exact test was used for proportions and Wilcoxon's rank sum test was used otherwise. All p values are two-sided and are given in the tables if they are < 0.05.

TABLE I   Previous history

| | Fulfilled criteria for AMI | | |
	No (n = 193)	Yes (n = 995)	p Value[a]
Age (years)			
Median	69	66	<0.0001
Range	40–74	26–74	
Sex (%)			0.006
Males	65	75	
Females	35	25	
Previous history of (%)			
Myocardial infarction (2/6)[b]	40	32	0.03
Angina pectoris (2/4)	39	39	
Diabetes mellitus (2/4)	26	21	
Hypertension (2/4)	39	34	
Current smoking (2/4)	24	37	0.0005
Median delay between onset of symptoms and admission to hospital (h: min) (134/247)	2:07	2:10	
Ambulance use (%) (138/525)	71	53	0.01
Admitted to CCU (%)	43	92	<0.0001
Admitted to CCU or ICU (%)	56	94	<0.0001

[a] p Value given if < 0.05.

[b] Number of patients with missing information in the two groups, respectively.

Abbreviations: AMI = acute myocardial infarction, CCU = coronary care unit, ICU = intensive care unit.

Results

In all, 1,188 admitted patients, 315 (27%) of whom were women, were included in the analyses. Among these patients, 193 (16%) did not fulfill the traditional criteria for AMI and are compared in the following with those who did. Of the 193 patients, 34% had chest pain, 42% had enzyme elevation, and 5% had Q waves, whereas the remaining 19% fulfilled none of the criteria.

Previous History (Table I)

Patients who did not fulfill the AMI criteria differed from those who did by being older, by including more women, and by having a higher prevalence of previous AMI and a lower prevalence of current smoking. Although they were more frequently transported by ambulance, they were less frequently admitted to a coronary care unit (CCU) or intensive care unit (ICU).

Characteristics while in Hospital (Table II)

Patients who did not fulfill AMI criteria more frequently experienced cardiac arrest prior to hospital admission and less frequently had ST-segment elevation on admission to hospital. Approximately half of the patients who did not fulfill the criteria died during primary hospitalization.

Medication and Investigation in Hospital (Table III)

Patients who did not fulfill the criteria for AMI were less frequently treated with beta blockers, long-acting nitrates,

TABLE II   Characteristics while in hospital (%)

| | Fulfilled criteria for AMI | | |
	No (n = 193) %	Yes (n = 995) %	p Value[a]
Cardiac arrest prior to hospital admission (2/4)[b]	10	3	<0.0001
ST-segment elevation on admission (13/15)	22	50	<0.0001
Any Q wave on ECG	5	51	<0.0001
Enzyme elevation	42	97	<0.0001
Recurrent ischemia (3/6)	2	8	0.002
Reinfarction (3/6)	5	4	
Congestive heart failure (3/12)	37	33	
Death while in hospital	48	10	<0.0001

[a] p Value given if < 0.05.

[b] Number of patients with missing information in the two groups, respectively.

Abbreviations: AMI = acute myocardial infarction, ECG = electrocardiogram.

TABLE III Medication during hospital stay (%)

	Fulfilled criteria for AMI		
	No (n = 193) %	Yes (n = 995) %	p Value [a]
Thrombolytic agents [b]			
Beta blockers (4/5)	49	89	<0.0001
Calcium antagonists (2/6)	15	19	
Long-acting nitrates (1/7)	22	34	0.001
Intravenous nitroglycerin (1/3)	14	40	<0.0001
Lidocaine (1/4)	12	10	
Aspirin (1/4)	43	83	<0.0001
ACE inhibitors (4/134)	14	16	
Digitalis (1/5)	29	19	0.002
Diuretics (0/5)	65	52	0.0007
Anticoagulants (1/4)	11	13	
Low-dose heparin s.c. (0/5)	16	10	0.02
High-dose heparin s.c. (1/4)	1	1	
High-dose heparin i.v. (1/5)	10	17	0.01

[a] p Value given if < 0.05.
[b] Number of patients with missing information in the two groups, respectively.
Abbreviations: AMI = acute myocardial infarction, ACE = angiotensin-converting enzyme, s.c. = subcutaneous, i.v. = intravenous.

intravenous nitroglycerin, aspirin, and high-dose heparin than patients who did. They were, on the other hand, more frequently treated with digitalis, diuretics, and subcutaneous heparin. A coronary angiogram was performed in 3% of patients who did not fulfill the criteria for AMI and in 9% of patients who did (p = 0.005).

The corresponding values for echocardiography were 8 and 12%, respectively (NS).

Symptoms on Admission among Patients Who Did Not Fulfill Criteria for Acute Myocardial Infarction (Table IV)

A variety of symptoms on admission to emergency department, of which chest pain was most common but occurred in only one third of the patients, characterized these patients. A quarter of them complained of dyspnea and < 5% had pulmonary edema.

Mode of In-Hospital Death among Patients Who Did Not Fulfill Criteria for Acute Myocardial Infarction (Table V)

Of the patients who did not fulfill the AMI criteria and died in hospital, 22% died on the day of admission and 17% died the next day.

More than half the patients who died in hospital died a sudden death. An autopsy was performed in 62% of these patients and almost all showed a fresh AMI on autopsy.

Of the patients who died a sudden death while in hospital, 26 (51%) were not admitted to the CCU/ICU. One of these

TABLE IV Symptoms on admission among patients who did not fulfill criteria for AMI (%)

	n = 187 [a]
Chest pain	34
Epigastrial pain	6
Other pain	6
Pulmonary edema	4
Congestive heart failure	6
Ventricular arrhythmia	6
Supraventricular arrhythmia	3
Syncope	6
Vertigo	4
Dyspnea	27
Fatigue	14
Asthma	5
Fever	7
Deterioration in diabetes	2
Other symptoms	50
Only other symptoms	16

[a] Information was missing for six patients.
Abbreviation: AMI = acute myocardial infarction.

had ST elevation on admission, and the initial symptoms were dyspnea (5), chest pain (4), other pain (4), fatigue (4), congestive heart failure (3), ventricular arrhythmia (3), syncope (3), epigastric pain (2), deterioration in diabetes (2), vertigo (1), asthma (1), and fever (1).

Mortality during 1 Year (Fig. 1)

The total mortality rate during 1 year after hospital admission was 57% among patients who did not fulfill the AMI criteria compared with 16% among those who did (p < 0.0001). This difference was mainly but not totally explained by far higher mortality during the initial hospital phase among those who did not fulfill the AMI criteria. Among these, the 1-year mortality rate was 47% among patients initially admitted and 69% among patients not admitted to the CCU/ICU (p = 0.004).

TABLE V Mode of death among patients who did not fulfill criteria for AMI (%)

	n = 92
Sudden death (9) [a]	59
Death from cardiogenic shock (12)	9
Death from pulmonary edema (12)	2
Other mode of death (11)	36
Autopsy performed (10)	62
If yes, signs of fresh AMI (1)	96
If yes, signs of pulmonary edema (2)	29

[a] Number of patients with missing information.
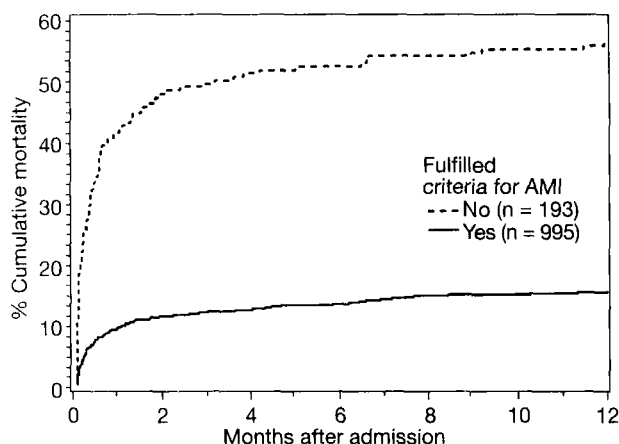Abbreviation as in Table IV.

Fig. 1 Mortality during 1 year after hospital admission among patients who did and did not fulfill the criteria for acute myocardial infarction (AMI).

Multivariate Analysis (Table VI)

In a multivariate analysis taking account of all the factors listed in Table I, plus whether or not patients had a cardiac arrest prior to hospital admission, we found that the criteria for AMI not being fulfilled appeared as a strong independent predictor of death during 1 year after initial hospital admission. Other factors identified as independent predictors included age, a history of angina pectoris and diabetes, admission to a ward other than the CCU or ICU, and cardiac arrest prior to hospital admission.

Discussion

We found that 16% of patients aged < 75 years, who were hospitalized and given a discharge diagnosis of 410 (AMI), did not fulfill criteria for AMI according to our definition. This study has the advantage of being representative of the municipality of Göteborg, as it compares the total population of patients aged < 75 years who were hospitalized with a diagnosis of AMI. The 193 patients who did not fulfill the AMI criteria represented, as expected, a heterogeneous population with a wide variety of symptoms on admission to hospital.

The very high mortality in this subset could be explained to some extent by the fact that the 410 diagnosis was based at least in part on autopsy findings. Many of these patients died a sudden death, and there was therefore no time for the development of enzyme elevation to appear in serum or ECG changes. This may have been particularly common among patients who died on the day of admission.

The percentage of these patients who were admitted to the CCU was low. It is possible to argue whether the diagnostic accuracy of AMI is lower in general wards than in CCUs due to the lower frequency of ECG recordings and enzyme samples being taken. However, enzyme samples and ECG recordings were taken at least once every morning during the first 3

TABLE VI Independent predictors of death within 1 year after hospital admission

	O.R.	95% CI	p Value
Criteria fulfilled for AMI	0.28	0.21–0.38	< 0.0001
Cardiac arrest prior to hospitalization	2.93	1.86–4.60	< 0.0001
Diabetes mellitus	1.79	1.37–2.34	< 0.0001
Age (years)	1.04	1.02–1.06	< 0.0001
Angina pectoris	1.56	1.22–2.01	0.0005
Admitted to CCU or ICU	0.60	0.44–0.82	0.002
Smoking	0.72	0.54–0.98	0.04

Abbreviation: O.R. = odds ratio.
Other abbreviations as in Table I.

days in general wards, which should create an opportunity to detect AMI in the majority of cases.

One further possible explanation might be that treatment outside the CCU is less aggressive and less successful, which explains the high mortality in patients who do not fulfill the AMI criteria. However, when simultaneously considering whether patients were admitted to the CCU/ICU, not fulfilling the criteria for AMI still appeared to be a strong independent predictor of death. The observation that admission to the CCU/ICU also appeared to be a predictor of a lower risk of death is of interest as it again emphasizes the fact that patients with AMI should be treated in such a unit.

Cardiac arrest prior to hospital admission was another independent predictor of death and was also more common among patients who did not fulfill the criteria for AMI. Most probably, the majority of these patients had ventricular fibrillation. Previous studies have indicated that, among CCU-treated patients with AMI, the development of ventricular fibrillation while in hospital is associated with an adverse prognosis during the hospital phase but not during long-term follow-up.[3–5]

It is obvious that a large percentage of the patients who did not fulfill the criteria for AMI did, in fact, develop a true infarction. This could only be stated with certainty in patients who died and were autopsied. However, the aim of this study was not to answer this question but rather to describe the occurrence, characteristics, and outcome of patients receiving a diagnosis of AMI without fulfilling the AMI criteria.

Only one third of these patients had chest pain on admission to hospital; some of the other patients obviously had an AMI without chest pain. Such patients have previously been reported by us and by others[6–10] as being older and having high mortality, which agrees well with the findings in this study.

Syncope, shock, and pulmonary edema instead of chest pain have often been accepted as criteria for AMI if they are combined with elevated serum enzyme activity or the development of Q waves. In this study of patients who did not fulfill the AMI criteria, 10% suffered a prehospital cardiac arrest, 6% had syncope, and 4% had pulmonary edema on admission to hospital. Some of these patients also had raised enzymes or Q waves and were thus regarded by many as fulfilling the criteria for AMI. The reason why Q waves were used as the ECG

criterion for AMI was that this is the only ECG abnormality reflecting myocardial necrosis.

Pain caused by myocardial ischemia or infarction is not always localized in the chest.[11, 12] In this study, some of the patients who did not fulfill the AMI criteria had pain that was localized in parts of the body other than the chest.

We found that patients who did not fulfill the criteria for AMI were treated less aggressively than those who did. There are several possible explanations. First, these patients were less frequently admitted to the CCU/ICU and consequently were less often treated by a cardiologist. Second, their ECG changes indicating acute ischemia were probably less frequent. Third, many of the patients died on the day of admission before anti-ischemic medication could be initiated.

Many previous studies have tried to define high-risk patients in populations with AMI.[13, 14] We have recently reported that patients without ST elevation on admission constitute a high-risk group of this kind.[15] In this study, we have defined another group with high mortality, that is, patients who did not fulfill the traditional criteria for AMI. The fact that their presentation was less typical, which might explain why less than half were admitted to the CCU (only one third had chest pain and only one fifth had ST elevation), highlights the importance of finding new tools for the early detection of AMI.

This was further highlighted by the fact that admission to the CCU/ICU was a significant predictor of increased survival and, furthermore, that more than half of the patients who did not fulfill the criteria for AMI and died a sudden in-hospital death had been admitted to wards other than the CCU/ICU.

The clinical relevance of these observations is that, in the very early phase of a suspected acute coronary syndrome, patients without ST-segment elevation on the ECG are at high risk of early complications as well, and that early monitoring and aggressive medication during the early phase might save many lives in this patient population. In other words, the patients with the most typical symptoms and ECG signs of AMI are not necessarily those who need the most careful attention in the early phase of an acute coronary syndrome.

Current smoking at the time of hospital admission was associated with a favorable prognosis. Similar results have previously been reported among patients with AMI[16] and this has been explained by a tendency for smokers to develop AMI very early in the course of their atherosclerotic disease.

Conclusion

A substantial percentage of patients diagnosed with AMI do not fulfill the AMI criteria if they are defined as fulfilling at least two of the following three: chest pain, increased cardiac enzymes, and Q waves. These patients have a high mortality, and the majority who die while in hospital die suddenly. A substantial percentage of these patients have actually suffered an AMI. On admission to hospital, the initial suspicion of AMI is often vague. Measures for earlier detection of an acute coronary syndrome and particularly AMI are warranted.

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