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The diagnoses of patients admitted with acute chest pain but without myocardial infarction

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Objective The purpose of this study was to describe the frequencies of various diagnoses in patients admitted with acute chest pain, but without acute myocardial infarction, and to evaluate a non-invasive screening programme for these patients.

Patients A total of 204 consecutive non-acute myocardial infarction patients were included. Fifty-six had a definite diagnosis within 48 h, whereas 148 patients underwent an examination programme including pulmonary scintigraphy, echocardiography, exercise electrocardiography, myocardial scintigraphy, Holter monitoring, hyperventilation test, oesophago-gastro-duodenoscopy, 3 h monitoring of oesophageal pH, oesophageal manometry, Bernstein test, physical examination of the chest wall and thoracic spine, bronchial histamine provocation test and ultrasonic examination of the abdomen.

Results According to predefined criteria, 186 patients (91%) had at least one diagnosis, 144 had one, whereas 39 had two, and three patients had three diagnoses. In 18 patients no diagnosis was obtained. The diagnoses belonged mainly to three groups: (1) ischaemic heart disease (n=64); (2) gastro-oesophageal diseases (n=85); (3) chest-wall syndromes (n=58). Less frequent diagnoses included pulmonary embolism, pleuritis/pneumonia, lung cancer, aortic stenosis, aortic aneurysm and herpes zoster.

Conclusions The high risk subset of a non-acute myocardial infarction population can be identified by means of a clinical evaluation and non-invasive cardiac examinations. Among the remainder, pulmonary embolism, gastro-oesophageal diseases and chest-wall syndromes should be paid special attention. A careful physical examination of the chest wall and an upper endoscopy seems to be the most cost-beneficial examination to employ in this subset.

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Key Words: Chest pain, diagnosis, ischaemic heart disease, oesophageal dysfunction, chest-wall syndromes.

Introduction

In more than half of the patients admitted to a coronary care unit with chest pain, acute myocardial infarction is ruled out (non-acute myocardial infarction)[1–3]. Both acute myocardial infarction and non-acute myocardial infarction patients are at high risk of subsequent cardiac events (cardiac death or non-fatal acute myocardial infarction)[1,3–5]. However, the non-acute myocardial infarction patients constitute a heterogeneous group with several diagnostic possibilities, e.g. unstable and stable angina pectoris, non-atherosclerotic cardiac pain, and non-cardiac pain. Chest pain due to causes other than ischaemic heart disease is frequent and often clinically indistinguishable from classic angina pectoris[6]. The previous studies on non-acute myocardial infarction patients have been directed towards a single organ system as the possible source of the pain[6–9]. The purpose of the present study was to perform a systematic and broad examination of the organ systems that may cause acute chest pain in a consecutive group of non-acute myocardial infarction patients in order to describe the frequency of various diagnoses and to evaluate the efficiency of various examinations in this group of patients.

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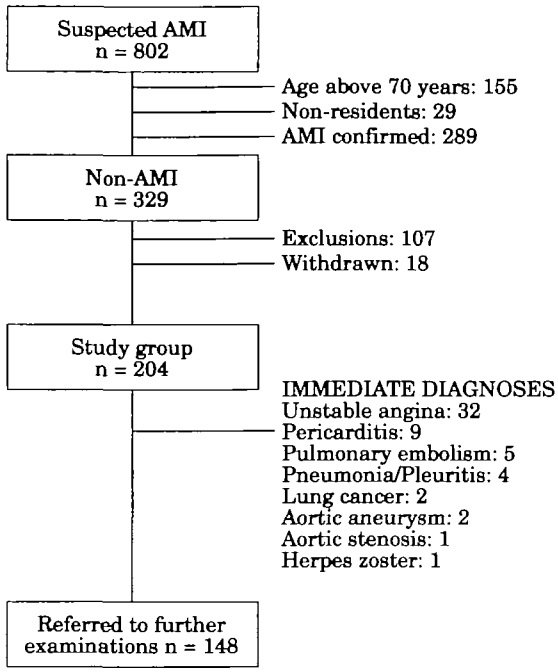

Figure 1 **Flow-chart and examination programme. Further examinations include: ultrasonic upper abdominal examination; exercise test and myocardial scintigraphy; Holter monitoring; hyperventilation test; oesophogo-gastro duodenoscopy; oesophageal manometry; oesophageal reflux monitoring; Bernstein test; Chest-wall examination; bronchial histamine test. For 'Exclusions', see Patients and Methods section. AMI = acute myocardial infarction.**

Patients and methods

From 1 November 1988 to 30 April 1989, and from 1 September 1989 to 30 November 1990 (the inclusion being interrupted for 4 months for practical reasons without any influence on the recruitment of patients or examinations from before to after the 4 months interval) a total of 802 patients were admitted to the coronary care unit of Hillerød Hospital, Frederiksborg County, Denmark, under suspicion of acute myocardial infarction. Acute myocardial infarction was confirmed in 289 patients (Fig. 1) with characteristic elevation of myocardial enzymes (CK-MB and/or LDH-1) and/or electrocardiographic changes lasting for more than 48 h indicative of Q-wave or non-Q-wave acute myocardial infarction[10]. Patients above 70 years, who were non-residents in Frederiksborg County, who had had an admission for acute myocardial infarction during the preceding 6 months or had other significant diseases (cancer, severe pulmonary disease, severe heart failure (New York Heart Association class III and IV) or disabling disease prohibiting examination were excluded. Twelve of the patients were unwilling to participate and 18 withdrew before the examinations were started.

As a result, 204 non-acute myocardial infarction patients remained (Fig. 1). Seventy-two (36%) were women. The median age of the patients was 54, range 21–70. Further demographic data are listed in Table 1. X-ray of the chest, echocardiography, electrocardiogram and pulmonary scintigraphy were performed initially. In 56 patients one of the predefined 'immediate diagnosis' was disclosed within 48 h of admission and these patients were not examined further (Fig. 1). The remaining 148 patients were allocated to a comprehensive examination programme after discharge. The examinations were performed in varying order and the different investigators were not informed about the results of other examinations. Oesophageal manometry and Bernstein test were only included in the last 12 months of the study.

Table 1 Demographic data of the 204 non-acute myocardial infarction patients included in the study

	n	%
Male	132	65
Female	72	35
Previous AMI	26	13
Anamnestic angina pectoris	39	19
Diabetes mellitus	3	2
Hypertension	29	14
Smokers	118	59
Medication		
Beta-blockers	21	10
Ca^{2+} antagonists	25	12
Digoxin	9	4
Diuretics	25	12
Nitrates	23	11
H_2-blockers	7	3

Examination programme

Electrocardiogram (n=204)

A 12-lead electrocardiogram at rest was evaluated for signs of ischaemic heart disease according to the Minnesota code[10].

Exercise Electrocardiogram (n=148)

A maximal symptom-limited bicycle exercise test was performed. The initial work-load of 50 W was increased by 50 W every 3 min until termination of the test. The test was interrupted at the age-predicted maximal heart rate (i.e. 220 − age), or when there was severe angina or exhaustion. During exercise all 12 leads were recorded continuously.

The test was considered to be suggestive of myocardial ischaemia if ST-depression (horizontal or down-sloping) of ≥0·1 mV 80 ms after the J-point, or ST-elevation at the J-point above 0·1 mV were recorded during maximum exercise. In case of left-bundle branch block at rest or during exercise and if ST-depresion during exercise was combined with either

ST-depression at rest, left ventricular hypertrophy, left hemiblock or digoxin treatment, the test was classified as uninterpretable.

Myocardial scintigraphy (n=144)

Planar myocardial scintigraphy was performed in three projections (anterior, left anterior oblique 45° and 70°) with a 2-day technetium-99m-Isonitril protocol: day 1 at rest and day 2 no more than a week later, with injection of tracer 1 min prior to termination of an exercise electrocardiogram, as described above. Visual comparison of smoothed, background subtracted, rest end stress scintigrams, was supplemented with evaluation of myocardial profiles. The last 33 patients were examined with both planar and tomographic myocardial scintigraphy. All the investigations were analysed blindly by one observer (B. Hesse). Defects were classified as: irreversible defects, reversible defects, combinations, or uninterpretable.

Holter monitoring (n=136)

Twenty four hour ambulatory electrocardiographic monitoring was performed using a calibrated, amplitude modulated, two-channel tape recorder. The bipolar leads recorded V5 and a modified inferior led. The tapes were analysed visually (Pathfinder II, Reynolds) and trend curves of ST-segment deviation and heart rate were obtained from the total monitoring period (ST-segment module, Reynolds). Significant ST-depression reflecting ischaemic heart disease was defined similarly as for the exercise test (with or without chest pain) and was specified as lasting for 1 min or longer.

Hyperventilation test (n=123)

Six minutes hyperventilation test was performed between 8:00 and 9:00 a.m.[11]. A 12-lead electrocardiogram was recorded continuously during the test and every second minute for 20 min after the hyperventilation. Significant ST-changes were defined as for the exercise test.

Echocardiography (n=146)

Before discharge, the patients were examined by 2-D and M-mode echocardiography. The morphology of the pericardium and the valves were evaluated and if significant abnormal valvar function was found, the patient was referred for cardiac catheterization.

Chest X-ray (n=204)

X-ray of the chest in two projections was performed prior to pulmonary scintigraphy. When pulmonary cancer was suspected, diagnostic bronchoscopy was performed before discharge.

Pulmonary scintigraphy (n=175)

Within 48 h after admission, pulmonary perfusion scintigraphy was performed in four projections (anterior, posterior and right and left posterior oblique) with technetium-99m labelled macro-aggregated albumin supplemented with krypton-81m ventilation scintigraphy if perfusion was abnormal. The results of the scintigraphy was described as: (1) normal; (2) high probability of pulmonary embolism; (3) medium probability; or (4) low probability, according to the Biello criteria[12]. Only patients with high probability were registered with the diagnosis 'pulmonary embolism'. The radiation dose for perfusion scintigraphy was 1·3–2·3 mSv, and far less from ventilation scintigraphy, (exact dose from krypton-81m is difficult to give).

Oesophago gastro duodenoscopy (n=133)

From a fibreoptic endoscopic examination of the oesophagus, stomach and duodenum, oesophagitis, ulcers and tumours were recorded. Oesophagitis grades II–IV were considered diagnostic for gastro-oesophageal reflux.

pH-monitoring in the oesophagus (n=125)

A portable system for 3 h ambulatory monitoring of oesophageal pH was used. The system consists of a pH-probe (Ingold (R)), a pH unit receiver and a 'memolog' solid phase recover[13].

Oesophageal manometry (n=108)

Lower oesophageal sphincter pressure gradient, oesophageal peristalsis and upper oesophageal sphincter gradient were evaluated[14]. For the pressure measurements a pressure probe consisting of two polyethylene catheters was used[15].

Bernstein test (n=87)

Through a catheter placed 5 cm above the lower oesophageal sphincter, isotonic glucose or 0·1 N HCL was given through a double infusion system in periods unknown to the patients. During the test, symptoms of discomfort were recorded. If symptoms during acid infusion mimicked the known thoracic pain the test was considered positive[16].

Physical examination of the chest wall (n=147)

A physical examination of the chest wall elucidating any musculo-skeletal or segmental thoracic pain source was

performed before discharge by a specialist in physical medicine. The examination included an evaluation of movement and tenderness in the cervical and thoracic spine, the shoulders and the clavicular and thoracic areas. It was noted whether palpitation or other examination procedures evoked typical chest pain as by admission, and only in this case were patients classified as having chest-wall syndrome.

Bronchial histamine provocation test (n=147)

Bronchial hyper-reactivity was evaluated by inhalation of increasing concentrations of a histamine solution (from 0 to 8 mg . ml^{-1}) and measurement of forced expiratory volume in 1 s, before and 30 and 90 s after each inhalation. A fall in the expired volume of 20% or more was considered diagnostic for bronchial hyper-reactivity.

Ultrasonic examination of the abdomen (n=148)

With the patient in the fasting state, real-time dynamic ultrasound scanning was performed on the liver, the biliary system and pancreas.

Diagnostic criteria and treatment strategy

Unstable angina

The diagnosis of unstable angina was based on repeated episodes of chest pain at rest concurrent with reversible ST–T fluctuations in the electrocardiogram at rest and no electrocardiographic or biochemical evidence of acute myocardial infarction within 24 h after admission. These patients were initially treated and stabilized with aspirin, beta-blockers, calcium antagonists and nitrates. The patients who were not stabilized by medical treatment were transferred to coronary angiography and invasive treatment. Stabilized patients had an exercise test performed before discharge and in case of low exercise capacity or other signs of severe ischaemic heart disease, coronary angiography was performed.

Ischaemic heart disease

The combination of an electrocardiogram at rest, an exercise test, myocardial scintigraphy and Holter monitoring was evaluated by a group of three cardiologists. Significant ST-deviation with or without angina and reversible myocardial perfusion defects during exercise were considered suggestive for ischaemic heart disease. In patients with irreversible defects and/or an uninterpretable exercise test the diagnostic decision was also based on the results of the electrocardiogram on admission and the ST-analysis of the Holter tape. Patients with ischaemic heart disease based on these criteria were primarily medically treated, but in case of low exercise capacity, large scintigraphic reversible defects or later instability, they were referred for invasive evaluation.

Table 2 Number and frequency of all diagnoses in 204 non-acute myocardial infarction patients; 144 with one, 39 with two, and three with three diagnoses (Percentages in parentheses)

Diagnoses	n
Gastro-oesophageal diseases	85 (42)
Ischaemic heart disease	64 (31)
Chest-wall syndromes	58 (28)
Pericarditis	9 (4)
Pleuritis/pneumonia	4 (2)
Pulmonary embolism	5 (2)
Lung cancer	3 (1·5)
Aortic aneurysm	2 (1)
Aortic stenosis	1 (0·5)
Herpes zoster	1 (0·5)

Gastro-oesophageal disease

The results of the upper endoscopy, pH-monitoring in the oesophagus, oesophageal manometry, ultrasonic examination of the abdomen and Bernstein-test were evaluated by a group of three gastroenterologists. Peptic ulcer and/or abnormal oesophageal pH-monitoring and/or oesophagitis grade II–IV by endoscopy and/or a positive Bernstein test and/or oesophageal motility disorder and/or a gall stones were considered diagnostic for gastro-oesophageal disease. These patients were treated symptomatically according to the general guidelines and routines of the department.

Other diagnoses

The results of the remaining examinations were evaluated as described above under the specific paragraphs in the section of methods.

Results

Of the 204 patients in the study population, 186 (91%) were given at least one diagnosis. The frequencies of diagnoses in the study population are shown in Table 2.

The diagnoses of the 56 patients with 'immediate diagnosis' are listed in Fig. 1. The diagnosis of unstable angina pectoris constituted the majority (32 patients). One patient with pulmonary embolism had a history of ischaemic heart disease. This diagnosis was later confirmed by exercise test and myocardial scintigraphy. The remaining 148 patients went through the examination programme. The diagnoses of these patients can be listed in three major groups: ischaemic heart disease; chest-wall syndromes; and gastro-oesophageal diseases (Table 2).

Table 3 The distribution of the different diagnosis in 85 non-acute myocardial infarction patients with gastro-oesophageal disorders. Number in parenthesis represent percentage of 204 patients

Diagnosis	n	Single diagnosis
Gastro-oesophageal reflux	62 (30)	27 (13)
Oesophageal motility disorders	26 (13)	8 (4)
Peptic ulcer	21 (10)	8 (4)
Stones in the gall bladder	11 (5)	3 (1)

Ischaemic heart disease

In 64 patients (31%) the chest pain was thought to be related to ischaemic heart disease. In 49 patients (24%) ischaemic heart disease was the only diagnosis. During follow-up (median, 33 months) 32 of the 64 patients (50%) with the diagnosis of ischaemic heart disease were referred to coronary angiography. Sixteen patients had three-vessel disease, nine had two-vessel, five had one-vessel disease and in two patients no significant coronary stenosis were found. Only two of the 140 patients without ischaemic heart disease were referred for invasive examination and both patients were found to have one-vessel disease. During follow-up, eight cardiac deaths and four non-fatal myocardial infarctions occurred in the 64 patients with ischaemic heart disease compared to only two non-fatal infarctions and no cardiac deaths in the 140 patients without ischaemic heart disease. The prognosis is discussed further elsewhere[17].

Gastro-oesophageal disease

Gastro-oesophageal disease was found in 85 patients (42%), and as a single diagnosis in 46 (22%). 'Oesophageal disease' (oesophageal motility disorder and gastro-oesophageal reflux) was found alone in 76 of these 85 patients. The number of patients with the different gastro-oesophageal diagnoses is shown in Table 3.

Chest-wall syndromes

Chest-wall syndrome constituted the third most frequent diagnosis and was found in 58 patients (28%). It was the only diagnosis in 25 patients (12%). In 33 patients it was one of two or three possible explanations of the chest pain leading to admission.

Other diagnoses

The diagnoses pericarditis, pulmonary embolism, lung cancer, herpes zoster, aortic aneurysm, stenosis of the aortic valve and pleurisy were obtained within 48 h, except for one case of lung cancer, which was not diagnosed initially. Bronchial histamine provocation test showed hyper-reactivity in five patients, all with well-known obstructive lung disease. Hyperventilation test was negative in all patients, although satisfactory hyperventilation was documented by arterial pH, pCO_2 and pO_2.

Discussion

The main interest in coronary care units usually focus upon patients with acute myocardial infarction or with severe ischaemic heart disease. The prognosis regarding cardiac events and death is related to the presence of ischaemic heart disease[1,3–5], and the exclusion of ischaemic heart disease is consequently important. However, non-acute myocardial infarction patients (with and without ischaemic heart disease) often have repeated admissions with chest pain indistinguishable from an acute myocardial infarction. In order to try to reduce morbidity and mortality, it is important to get information about the frequency of the different diagnoses and to establish a cost efficient examination programme.

Ischaemic heart disease

Of 64 patients with ischaemic heart disease, 32 had unstable angina but the diagnosis of ischaemic heart disease could have been missed in the remainder if further estimations had not been performed. Although coronary angiography was only performed in 32 of these patients, the angiographic data available indicate that significant coronary artery disease was present in most of these patients.

Gastro-oesophageal diseases

In previous studies 30–58% of non-acute myocardial infarction patients have signs of gastro-oesophageal reflux or oesophageal motility disorders[6–8]. We found oesophageal dysfunction in nine out of 32 non-acute myocardial infarction patients (28%)[2]. This is in accordance with the present study in which oesophageal dysfunction was found in 36%. Peptic ulcer was found as the only diagnosis in eight patients (4%), but as one of two or three diagnoses in 20 (10%) of the patients and may be secondary to mental and physical stress. Stones in the gall bladder were found in 11 patients (5%), and as the only diagnosis in three patients. Two of these patients later underwent cholecystectomy, followed by complete relief of symptoms. The frequency of gall stones in non-acute myocardial infarction patients is in the same order of magnitude as in asymptomatic individuals[18], and thus a rare differential diagnosis. Patients with gastro-oesophageal conditions often have recurrent chest pain, leading to repeated admissions, creating anxiety and deterioration of the quality of life[19,20], but

a correct diagnosis and treatment may improve their physical and mental condition[21]. But gastro-oesophageal disease is not rare in asymptomatic individuals[22,23], and abnormal findings may be accidental. Some studies have suggested a relationship between ischaemic heart disease and oesophageal dysfunction[7,24], which further complicates the interpretation of the diagnostic tests.

Chest-wall syndromes

The third large diagnostic group was chest-wall syndromes. We found chest-wall syndromes in 58 patients (28%) and as the only diagnosis in 25 (12%). This is in keeping with a previous study of patients with chest pain, in which 29% of the patients without acute myocardial infarction had chest-wall syndromes[9].

Non-atherosclerotic, cardiac causes

In a previous study of non-acute myocardial infarction patients, pericarditis was found in eight of 320 patients (2·5%), but systematic evaluation for pericarditis was not performed[25]. We found that nine patients (4%) had pericarditis. Finally, two patients had dissecting aortic aneurysms and one patient had severe valvular aortic stenosis.

Pulmonary causes

Twelve patients were thought to have pulmonary causes of their chest pain. Pulmonary embolism was diagnosed in five patients. The prognosis improves significantly, when patients with pulmonary embolism are treated with anticoagulants[26], and the diagnosis is consequently important not to overlook. Three patients had lung cancer and four patients presented themselves with infectious, parenchymal lesions and/or pleural effusion on their chest X-ray. Bronchial asthma is not generally regarded as a cause of chest pain and the results of our study do not indicate anything else. We found that only five patients had positive bronchial provocation tests but none of these had asthmatic symptoms at admission and bronchial asthma was not considered to be the cause of chest pain in any patient.

No diagnosis

In spite of the comprehensive programme, 18 patients were left without any diagnosis. Since abnormal psychiatric conditions were not systematically evaluated, a few of our patients may have had chest pain of such causes[27,28].

Clinical implications

Since the serious prognosis in non-acute myocardial infarction patients is closely related to the presence of ischaemic heart disease it is important to perform an exercise test in all non-acute myocardial infarction patients to make this diagnosis likely or unlikely. Myocardial scintigraphy is indicated in patients not able to exercise (scintigraphy with pharmacological stress) and furthermore in equivocal cases. Holter monitoring and a hyperventilation test did not provide further information.

Pulmonary scintigraphy may be considered in non-acute myocardial infarction patients without unstable angina in view of the difficulty in diagnosing pulmonary embolism and also the serious prognosis of untreated patients, even if the patient is not anamnestically predisposed. Echocardiography can be employed if pericarditis or valvular heart disease is suspected.

Although cardiac diagnoses and pulmonary embolism are the most important diagnoses to exclude, it is not satisfactory to leave two-thirds of the non-acute myocardial infarction patients with reassurance of a low risk but without an explanation of the symptoms. Based on the result of this study we find that the majority of this subset seems to suffer from chest-wall syndromes or gastro-oesophageal disorders. The most useful supplementary examinations were a careful physical examination of the chest wall and an upper endoscopy. Subsequently oesophageal pH-monitoring and ultrasonography may be used. However, abnormal test results do not necessarily mean disease. They are common findings in an asymptomatic population.

Limitations

Because of the comprehensive examination programme patients above 70 years and patients with severe heart failure were excluded, reducing the frequency of patients with ischaemic heart disease. Coronary angiography was not used routinely, but the results of the follow-up indicate that the non-invasive examination programme was useful in identifying the subset of non-acute myocardial infarction patients with ischaemic heart disease.

The 56 patients with an immediate diagnosis did not undergo further diagnostic evaluation and other diagnoses in these patients may have been missed.

In this study no attempt was made to indicate which diagnosis was the most important regarding chest pain in patients with more than one diagnosis.

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