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A 14-year follow-up study of chest pain patients including stress hormones and mental stress at index event

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ABSTRACT

Background: Knowledge of long-term outcome in chest pain patients is limited. We reinvestigated patients who 14 years earlier had visited the emergency department due to chest pain, and were discharged without hospitalization. Extensive examinations were made at that time on 484 patients including full medical history, exercise test, a battery of stress questions and stress hormone sampling.
Methods: From a previously conducted chest pain study patients still alive after 14 years were approached. Hospitalization or deaths with a diagnosis of ischemic heart disease or cerebrovascular disease were used as end point.
Results: During the follow-up period 24 patients had died with a diagnosis of ischemic heart or cerebrovascular disease, and 50 patients had been given such a diagnosis at hospital discharge. Age (OR 1.12, CI 1.06–1.19), previous history of angina pectoris (OR 9.69, CI 2.06–71.61), pathological ECG at emergency department visit (OR 3.27, CI 1.23–8.67), hypertension (OR 5.03, CI 1.90–13.76), smoking (OR 3.04, CI 1.26–7.63) and lipid lowering medication (OR 14.9, CI 1.60–152.77) were all associated with future ischemic heart or cerebrovascular events. Noradrenalin levels were higher in the event group than in the non-event group, mean (SD) 2.44 (1.02) nmol/L versus 1.90 (0.75) nmol/L. When noradrenalin was included in the regression model high maximal exercise capacity was protective of an event (OR 0.986, CI 0.975–0.997).
Conclusion: In chest pain patients previous history of angina pectoris, hypertension, smoking, pathological ECG at primary examination, and age were the main risk factors associated with future cardiovascular or cerebrovascular events.

1. Background

1.1. Chest pain

About 20% [1] of all patients seeking medical emergency departments (ED) do so for chest pain or chest discomfort. The challenge for the emergency physician is to separate patients with acute coronary syndromes (ACS) or other life threatening diseases from those with chest pain from more benign causes. Patients judged to have low risk of myocardial ischemia or other non-life threatening diseases are directly discharged from the ED or admitted for a shorter observational period until a final evaluation can be made.

1.2. Heterogeneity of chest pain patients

Acute chest pain is a multifaceted condition with cardiac as well as non-cardiac origin [2,3]. From the "Task force on management of chest pain" [4] cardiac aetiology was reported in 45%, musculoskeletal in 14%, pulmonary in 5%, gastrointestinal in 6%, psychiatric in 8% and other aetiologies in 26% of chest pain patients. Missed diagnosis of an ACS has been reported to occur in 2–8% of patients seeking the ED with chest pain [5].

1.3. Change over time

The incidence of cerebrovascular and ischemic heart disease (IHD) has decreased over several years in the western world. In Sweden, IHD declined from 782 per 100,000 in 1998 to 567 per 100,000 in 2007 in the age group 30–79 years. However, for the same age group the diagnosis of unexplained chest pain more than doubled between 1987 and 2008 [6]. In Western Sweden (health care region of Västra Götaland (VGR)) there were in 2007 a total of 3940 patients with a main hospital discharge diagnosis of acute myocardial infarction

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Table 1
Background characteristics of event group (ischemic heart disease or stroke), non-event group and non-participants.

	Event group	Non-event group	p-Values	Event + non-event groups	Non-participants	p-Values
Number of subjects	74	216		290	194	
Age, years	55 (8)	46 (11)	<0.001	48 (11)	41 (11)	<0.001
Sex, men	72	57	0.03	61	62	ns
Married or cohabiting*	75	66	ns	68	65	ns
Work status active*	54	78	<0.001	72	80	ns
Current smoker*	42	30	ns	32	43	0.04
BMI, kg/m^{2}**	26 (3)	25 (4)	0.01	25 (4)	24 (3)	0.03
Previous history of						
AMI	23	3	<0.001	8	3	0.04
Angina Pectoris	27	2	<0.001	9	3	0.01
Hypertension	37	8	<0.001	16	9	ns
Heart failure	4	0	0.03	1	0	–
Diabetes	10	2	0.03	4	3	ns
CABG	14	0.5	0.001	4	1	ns
PTCA	5	0	0.01	1	1	ns
β-blocker	41	9	0.001	17	10	ns
ASA	24	3	0.001	9	4	0.04
Lipid lowering drugs	10	1	0.01	4	2	ns

Data are mean (SD) or percent. * indicates <5% and ** 5% to <10% missing values. P-values are denoted if p≤0.05.

(AMI), 3541 received a discharge diagnosis of angina pectoris and 5493 a discharge diagnosis of unexplained chest pain [7].

1.4. Outcome

There are limited data on long-term outcome in patients with chest pain. Giving the heterogeneous nature of chest pain patients, varied outcome can be expected depending on case mix, procedures used to establish diagnosis and follow-up time. Of patients not having an AMI an adverse event rate of 10% has been reported after a follow-up of 2.5 years [8]. Furthermore, elderly women with non-specific chest pain have an increased risk of a coronary event [9] and patients with unexplained chest pain have been shown to report worse quality of life (QOL) than the general population [10]. Other authors have reported excellent prognosis [11,12].

1.5. Chest pain and mental stress

In addition to conventional risk factors mental stress and/or psychosocial factors have been found to be associated with IHD [13–15]. In the INTERHEART study, stress was estimated to account for 30% attributable risk of AMI [16]. Yet, we know of no previous study also investigating perceived mental stress and objective measures of stress (stress hormones) in chest pain patients at the ED.

1.6. Aim of study

In 1992–93, a study was conducted at Sahlgrenska University Hospital on patients with chest pain where AMI or other severe disease was ruled out and the patients were discharged either from the ED directly or after a short evaluative stay at an intermediate ward. This patient group and the one-year follow-up have been previously described [17,18].

The aim of the present study was to perform a long-term follow-up of these patients. A composite endpoint of readmittance to hospital or death due to cardio- or cerebrovascular events was applied. Further aims were to test the predictive properties of stress hormone levels and results from questions on mental stress using this endpoint.

This follow-up study was approved by the Gothenburg Regional Ethics Review Board (459-05, T226-06 and T661-06) and all included alive patients gave written informed consent.

2. Patients and methods

Initially, patients were recruited from January 1992 to March 1993 at the ED of Sahlgrenska University Hospital, Gothenburg, Sweden. In short, 778 patients seeking the ED due to acute chest pain or symptoms suggestive of an AMI, but where an AMI was ruled out, were approached. These patients were offered a revisit at a cardiac outpatient clinic after approximately a week. The clinic was staffed with experienced cardiologists. Of the 778 patients, 294 were excluded for various reasons [17].

Thus, 484 patients (295 men and 189 women) with a mean age of 48 years accepted a second evaluative visit including detailed case history, exercise testing, laboratory tests for metabolic disturbances and for the stress hormones adrenalin (A), noradrenalin (NA), dopamine (D) and cortisol. They were also asked to answer questions on mental stress. Of the 484 patients 318 (66%) agreed to undergo venous and arterial blood sampling. In 87 cases, the arterial blood sampling failed due to technical difficulties.

At the evaluative visit a week after the index event 18% of the patients were judged to have IHD, 27% were given a diagnosis of musculoskeletal pain, 5% gastrointestinal pain, 12% psychogenic pain, 12% were given other diagnoses and in 26% of the patients the cause of the symptoms was unclear [17]. Patients' characteristics at study start can be viewed in Tables 1 and 2.

Table 2
Background characteristics of event group (ischemic heart disease or stroke), non-event group and non-participants.

	Event group	Non-event group	p-Value	Event + non-event groups	Non-participants	p-Value
Number of subjects	74	216		290	194	
Emergency department						
Heart rate (beats/m)**	69 (12)	72 (11)	0.04	71 (11)	74 (11)	0.01
ECG (pathological or current ischemia)**	49	12	< 0.001	21	10	0.01
Dyspnoea*	4	3	ns	4	7	ns
At exercise testing:						
Max. exercise (Watt)*	133 (36)	155 (46)	< 0.001	149 (45)	154 (46)	ns
ST depression (≥1 mm)	23	28	ns	27	23	ns
ST depression (≥2 mm)	12	6	ns	7	4	ns
Ischemia at assessment***	31	14	0.01	18	12	ns

Data are percent or mean (SD). * indicates <5%, ** 5% to <10% and *** 10% to <15% missing values. P-values are denoted if p≤0.05.