

# Differences between acute myocardial infarction and unstable angina: a longitudinal cohort study reporting findings from the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA)

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## ABSTRACT

**Objectives:** The aim of this study was to compare risk factors and comorbidities in patients with a first episode of acute coronary syndrome (ACS), being either acute myocardial infarction (AMI) or unstable angina pectoris (UAP).

**Design:** Cross-sectional and prospective.

**Setting:** The Swedish population.

**Participants:** A total of 145 346 consecutive patients aged 25–105 years included in the Swedish Register of Cardiac Intensive Care Admission (Register of Information and Knowledge about Swedish Heart Intensive Care) and admitted to hospital between 1 January 1996 and 30 June 2009 with a first episode of either AMI or UAP.

**Primary and secondary outcome measures:** Type of ACS and 1-year outcome.

**Results:** Compared with patients with UAP, AMI patients were more likely to be older; men; and former or current smokers; they were also more likely to have had diabetes and peripheral artery disease, but had lower rates of prior heart failure (HF) and fewer cardioprotective medications on admission. Among patients aged <65 years, 1.4% of men and 1.6% of women with UAP died within 1 year in 2003–2006 compared with 4.2% of men and 3.1% of women AMI patients (multiple-adjusted OR 3.54 (99% CI 2.29 to 5.48) in women and 2.65 (99% CI 2.11 to 3.34) in men). Corresponding proportions in patients aged ≥65 years was 7.5% in men and 7.6% in women with UAP and 21.5% in men and 17.8% in women with AMI.

**Conclusions:** In patients with a first-time ACS episode, male sex, slightly older age, smoking, diabetes and peripheral arterial disease (PAD), but fewer cardioprotective medications, were major determinants for presenting with AMI. Despite increasingly active treatment in AMI and more inclusive diagnostic criteria in recent years, persistently worse prognosis was observed in AMI patients.

## ARTICLE SUMMARY

### Article focus

- To determine the likelihood of specific risk factors and comorbidities related to first-time diagnosis of acute coronary syndrome.

### Key messages

- Patient sex, age, smoking status; a previous diagnosis of diabetes or peripheral artery disease and the administration of cardioprotective medications had a significant influence on development of acute myocardial infarction.

### Strengths and limitations of this study

- This study examined externally validated data from the Swedish Register of Cardiac Intensive Care Admission, which as of 2009 included 72 of the 77 Swedish hospitals with coronary care units.
- Limitations include the facts that unstable angina and angina were determined by treating physicians rather than according to set guidelines, and that reclassification of AMI potentially changed the criteria of unstable angina cases studied here.

## INTRODUCTION

Acute coronary syndromes (ACS) represent a spectrum of events ranging from unstable angina pectoris (UAP) to acute myocardial infarction (AMI), with or without ST elevation.<sup>1</sup> Clinical understanding of the pathophysiology underlying ACS has greatly increased in recent years,<sup>2</sup> but there remains a lack of knowledge regarding the exact factors that determine the severity of an acute event.

The classification of UAP was introduced in 1989<sup>3</sup> and has since been validated in a number of studies.<sup>4–7</sup> Since this initial classification, clinical presentation in ACS has changed somewhat, with a decrease in mortality and reduced case-death following AMI.<sup>8–10</sup> This change in clinical presentation in AMI with less severe infarctions and better clinical outcomes may be explained by new or improved treatments and interventions.<sup>11–13</sup> In addition, changes in risk factors across various populations, such as less tobacco smoking and decreasing levels of total cholesterol, may have similarly contributed to these improved outcomes.<sup>11</sup>

UAP, in comparison with AMI, has a considerably better short-term prognosis,<sup>14</sup> although, ultimately, patients' long-term prognosis may not differ greatly between the two events.<sup>15</sup> Even though patients' development of coronary heart disease (CHD) is broadly dependent on well-known risk factors,<sup>16</sup> the condition's clinical presentation and severity might be influenced by variations in risk factor pattern.<sup>17</sup> Studies in AMI patients have shown that smoking is more common in those presenting with ST elevation MI (STEMI),<sup>14 18</sup> whereas being older or women, having no diagnosis of prior disease, and taking cardioprotective medications are associated with a decreased risk of STEMI.<sup>12</sup> However, few studies have systematically evaluated differences between AMI and UAP in the same manner as a means of understanding variation in the severity of these acute syndromes. The aim of this study was therefore to compare patients with a first episode of either AMI or UAP in relation to a wide spectrum of risk factors and comorbidities.

## METHODS

### Study criteria

The Swedish Register of Cardiac Intensive Care Admission (RIKS-HIA) continuously registers all patients admitted to hospitals with coronary care units (CCU). The full protocol has been published previously,<sup>19</sup> and detailed information and the complete protocol are available online at <http://www.ucl.ac.uk/med/heart/>. On admission, patients receive written information about RIKS-HIA and other quality-of-care registries; patients are permitted to deny participation in the registry, although few of them exercise this right. According to Swedish law, written consent is not required because quality control is an inherent element of hospital and other care. Research based on the registry is approved by an institutional ethics committee and all personal identifiers are removed from the RIKS-HIA data file when used for research purposes.<sup>20</sup> RIKS-HIA started in 1995 with 19 participating hospitals; by 2008, all Swedish hospitals with CCUs were participating in the registry.

The present study is based on all consecutive patients aged  $\geq 25$  years without a history of prior AMI or UAP and admitted between 1 January 1996 and 30 June 2009. The study followed a total of 145 346 registry

participants with a first AMI or UAP; of these, 58 111 (40%) of participants were women. Participant age range was 25–105 years.

Detailed information on approximately 100 variables is reported in case records during the hospitalisation period and is filled in by nurses. For the purposes of our research, we took into consideration patients' smoking status (never smoker, ex-smoker (defined as no smoking for more than 1 month before admission to hospital) and current smoker); diagnosed hypertension; diabetes mellitus (history or medication); diagnosed heart failure (HF, history); symptomatic peripheral arterial disease (PAD) and previous pharmacological treatment on hospital admission.

### Definitions

The criteria for a diagnosis of AMI or UAP were standardised and identical for all participating hospitals using the WHO and Joint European Society of Cardiology/American College of Cardiology Committee criteria.<sup>21 22</sup> Diagnoses were coded at the treating physician's discretion according to the International Classification of diseases version 9 (ICD-9), which was used from 1987 to 1996, and version 10 (ICD-10), which was used from 1997 onward. During the study period, the biochemical criteria for these conditions were revised in accordance with the European Society of Cardiology and the American College of Cardiology Committee consensus document;<sup>22</sup> this document included more sensitive criteria for diagnosing both conditions, resulting in an increasing proportion of patients diagnosed with AMI rather than with UAP.

AMI was defined as a discharge diagnosis with a principal diagnosis of 410 (ICD-9) or I21 (ICD-10). Diagnostic codes for angina were 411B and 413 (ICD 9) and I20 (ICD 10). The number and proportions of patients who were diagnosed with 411B, 413 (ICD 9) and I20.0 at discharge from a CCU had at least one of following findings or interventions; pathological coronary angiography  $n=56$  (0.04%), percutaneous coronary intervention= $3377$  (2.3%), positive stress test  $n=10\ 933$  (7.5%), coronary artery bypass grafting  $n=33\ 502$  (23%), ECG with pathological STT changes  $n=49\ 050$  (33.7%) and  $n=47\ 565$  (32.7%) were described long-acting nitrates at discharge from hospital, leaving  $n=862$  (0.6%) without further diagnostic specification at discharge from a CCU. Planned admissions for diagnostic or therapeutic procedures were not included. Only first events were included, with a first event defined as the patient having no history of AMI and no prior hospitalisation in the register for any CHD (ICD-9 410–414 and ICD-10 I20–I25). Of 145 346 patients identified in the registry, 97 960 were diagnosed with a first AMI and 47 386 with a first UAP.

### Validation of the registry

Source data have continuously been validated by an external monitor via comparison of the information in the registry with hospital patient records. A 94%

agreement was observed between the registered information and the source data in patients' records, comprising 161 280 data points from 38 hospitals.<sup>23</sup>

### Statistical methods

We used means and percentages to describe baseline characteristics and differences in patients with AMI and UAP. The independent associations between baseline characteristics (history of tobacco smoking (never smoking, former smoking and current smoking); history of hypertension, HF, diabetes and PAD; medication usage prior to admission (eg, aspirin,  $\beta$ -blockers, ACE inhibitors, long-acting nitrate and lipid-lowering drugs and AMI) were assessed by means of logistic regression, with AMI entered as the dependent variable and age, sex and all variables above used as covariates (possible confounders) because they were either associated with type of ACS or otherwise considered to be important. To assess differences between men and women in each factor effect, we included an interaction term in the model (sex $\times$ factor). All statistical analyses were performed using SPSS software (version 20 for Windows; SPSS, Inc, Chicago, Illinois, USA). The ORs for each variable was calculated from the logistic regression model, and 95% CIs were used.

### RESULTS

We included 145 346 patients with a first AMI (67%) or UAP (33%). Of 97 960 patients with AMI, 37.8% were women, which can be compared with 44.5% among 47 386 patients with UAP (table 1). After multiple adjustment, the OR for AMI associated with the female sex was 0.69 (95% CI 0.66 to 0.73). Patients with AMI

were slightly older than patients with UAP (mean age 69.7 vs 68.2 years). Smoking was more common in patients with AMI than in patients with UAP (25.2% vs 17.4%). After adjustment for age, sex and other concomitant conditions and medications, the OR associated with current smoking was 1.66 (95% CI 1.56 to 1.78). Hypertension was less common in AMI patients than in UAP patients, but after multiple adjustment, the OR associated with this condition was only 1.07 (95% CI 1.02 to 1.12). Diabetes was more prevalent in AMI patients (multiple-adjusted OR 1.44; 99% CI 1.34 to 1.54), as was PAD (multiple-adjusted OR 1.28 95% CI 1.13 to 1.45). HF and all medications taken prior to admission—particularly aspirin,  $\beta$ -blockers, long-acting nitrates and statins—were associated with a decreased risk of AMI; however, medication with ACE inhibitors did not retain a significant association after adjustment for other variables.

As criteria for the definition of AMI changed in 2001, we divided the data into two periods, one from 1996 to 2002 and one with the new definition from 2003 to 2009 (assuming a 1-year delay in implementing the new definition). Table 2 shows that largely all previously noted correlations remained roughly similar, with current smoking, diabetes and PAD retaining their importance over both time periods. Fewer patients were treated with nitrates in the recent period, whereas the proportion treated with statins at admission doubled: to 14.0% from 6.4% in patients with AMI and to 29% from 16.3% in patients with UAP. Still, all associations as expressed by ORs for the risk of presenting with AMI remained roughly the same, with the one exception being the weak relation with hypertension, which was no longer present during the later time period.

**Table 1** Baseline characteristics in 145 346 patients with a first event of acute myocardial infarction (AMI) or unstable angina pectoris (UAP) and OR for presenting with AMI (1996–2009)

N (%)	UAP 47386 (33)	AMI 97960 (67)	Age-adjusted and sex-adjusted OR	p Value	Multiple adjusted OR (99% CI)*	p Value
Age, mean years	68.2	69.7	1.01 (1.01 to 1.01)	<0.001	1.03 (1.03 to 1.03)	<0.001
Women	21 095 (44.5)	37 016 (37.8)	0.79 (0.68 to 0.72)	<0.001	0.69 (0.66 to 0.73)	<0.001
Never smoker	22 135 (52.9)	42 885 (48.0)	1.00 (ref)	<0.001	1.00 (ref)	<0.001
Ex-smoker	12 434 (29.7)	23 920 (26.8)	0.98 (0.95 to 1.00)	ns	0.97 (0.92 to 1.03)	<0.001
Current smoker	7281 (17.4)	22 545 (25.2)	1.87 (1.80 to 1.93)	<0.001	1.66 (1.56 to 1.78)	<0.001
Hypertension	18 116 (40.7)	35 710 (37.2)	0.95 (0.94 to 0.97)	<0.001	1.07 (1.02 to 1.12)	<0.001
Heart failure	4708 (9.9)	5806 (5.9)	0.51 (0.49 to 0.53)	<0.001	0.57 (0.52 to 0.62)	<0.001
Diabetes	7075 (14.9)	16 274 (16.6)	1.13 (1.10 to 1.17)	<0.001	1.44 (1.34 to 1.54)	<0.001
Peripheral arterial disease	1734 (3.7)	3797 (3.9)	1.00 (0.92 to 1.08)	ns	1.28 (1.13 to 1.45)	<0.001
Aspirin	20 711 (45.9)	25 293 (26.3)	0.38 (0.37 to 0.39)	<0.001	0.59 (0.56 to 0.63)	<0.001
$\beta$ -Blockers	19 571 (43.4)	25 743 (26.8)	0.47 (0.46 to 0.48)	<0.001	0.72 (0.68 to 0.76)	<0.001
ACE inhibitors	7470 (16.6)	12 680 (13.2)	0.74 (0.72 to 0.76)	<0.001	0.94 (0.88 to 1.02)	ns
Long-acting nitrates	12 253 (27.2)	8140 (8.5)	0.22 (0.21 to 0.23)	<0.001	0.34 (0.32 to 0.37)	<0.001
Statins	9818 (21.8)	10 258 (10.7)	0.44 (0.42 to 0.45)	<0.001	0.63 (0.58 to 0.68)	<0.001

\*Adjusted for age, smoking, hypertension, heart failure, diabetes, peripheral arterial disease, aspirin,  $\beta$ -blockers, ACE inhibitors, long-acting nitrates and statins.

**Table 2** Baseline characteristics in patients with a first event of acute myocardial infarction (AMI) or unstable angina pectoris (UAP) and ORs for presenting with AMI for two periods (1996–2002 and 2003–2009)

	UAP		AMI		Age-adjusted and sex-adjusted OR				Multiple-adjusted OR (99% CI)*			
	1996–2002	2003–2009	1996–2002	2003–2009	1996–2002	p Value	2003–2009	p Value	1996–2002	p Value	2003–2009	p Value
n	27 210	20 176	43 193	54 767								
Age, mean years	68.0	68.5	69.6	69.7	1.02 (1.02 to 1.02)	<0.001	1.02 (1.02 to 1.02)	<0.001	1.03 (1.03 to 1.03)	<0.001	1.03 (1.03 to 1.03)	<0.001
Women	12 164 (44.7)	8931 (44.3)	16351 (37.9)	20 665 (37.7)	0.67 (0.64 to 0.70)	<0.001	0.68 (0.65 to 0.72)	<0.001	0.72 (0.69 to 0.74)	<0.001	0.74 (0.70 to 0.78)	<0.001
Never smoking	13 194 (55.7)	8941 (49.2)	20 344 (51.6)	22 541 (45.1)	1.00	<0.001	1.00	<0.001	1.00	<0.001	1.00	<0.001
Former smoking	6356 (26.8)	6078 (33.5)	9218 (23.4)	14 702 (29.4)	0.93 (0.88 to 0.98)	<0.001	0.94 (0.89 to 0.99)	0.01	1.00 (0.97 to 1.04)	ns	0.97 (0.92 to 1.02)	ns
Current smoking	4144 (17.5)	3137 (17.3)	9841 (25.0)	12 704 (25.4)	1.82 (1.71 to 1.93)	<0.001	1.84 (1.72 to 1.96)	<0.001	1.72 (1.64 to 1.80)	<0.001	1.71 (1.59 to 1.82)	<0.001
Hypertension	9109 (36.6)	9007 (46.1)	13 425 (32.2)	22 285 (41.0)	0.86 (0.82 to 0.89)	<0.001	0.94 (0.92 to 0.96)	<0.001	1.05 (1.02 to 1.07)	<0.001	1.00 (0.97 to 1.03)	ns
Heart failure	3023 (11.1)	1685 (8.4)	2701 (6.3)	3105 (5.7)	0.47 (0.43 to 0.50)	<0.001	0.47 (0.43 to 0.50)	<0.001	0.62 (0.58 to 0.67)	<0.001	0.74 (0.67 to 0.82)	<0.001
Diabetes	3768 (13.8)	3307 (16.4)	6675 (15.5)	9599 (17.5)	1.14 (1.07 to 1.20)	<0.001	1.08 (1.02 to 1.14)	0.01	1.45 (1.38 to 1.52)	<0.001	1.43 (1.34 to 1.53)	<0.001
Peripheral arterial disease	1036 (3.8)	698 (3.5)	1717 (4.0)	2080 (3.8)	0.98 (0.88 to 1.09)	ns	1.04 (0.93 to 1.17)	Ns	1.32 (1.20 to 1.44)	<0.001	1.41 (1.23 to 1.61)	<0.001
Aspirin	11 879 (46.5)	8832 (45.0)	11 054 (26.2)	14 239 (26.3)	0.38 (0.36 to 0.40)	<0.001	0.39 (0.37 to 0.41)	<0.001	0.57 (0.54 to 0.59)	<0.001	0.56 (0.53 to 0.59)	<0.001
β-Blockers	10 931 (42.8)	8640 (44.1)	10 709 (25.4)	15 034 (27.8)	0.45 (0.43 to 0.47)	<0.001	0.47 (0.45 to 0.50)	<0.001	0.74 (0.71 to 0.76)	<0.001	0.74 (0.70 to 0.78)	<0.001
ACE inhibitors	4008 (15.7)	3462 (17.7)	4949 (11.7)	7731 (14.3)	0.69 (0.65 to 0.74)	<0.001	0.76 (0.71 to 0.80)	<0.001	1.00 (0.95 to 1.05)	ns	1.05 (0.98 to 1.12)	ns
Long-acting nitrates	8044 (31.6)	4209 (21.5)	4559 (10.8)	3581 (6.6)	0.23 (0.22 to 0.25)	<0.001	0.23 (0.22 to 0.24)	<0.001	0.33 (0.31 to 0.34)	<0.001	0.36 (0.33 to 0.39)	<0.001
Statins	4133 (16.3)	5685 (29.0)	2711 (6.4)	7547 (14.0)	0.37 (0.35 to 0.40)	<0.001	0.40 (0.38 to 0.42)	<0.001	0.67 (0.64 to 0.70)	<0.001	0.60 (0.56 to 0.64)	<0.001

\*Adjusted for age, smoking, hypertension, heart failure, diabetes, peripheral arterial disease, aspirin, β-blockers, ACE inhibitors, long-acting nitrates and statins.

**Table 3** Age-adjusted ORs (95% CI) for presenting with acute myocardial infarction (AMI) in patients admitted to Swedish coronary care units (CCUs) with either AMI or unstable angina pectoris (UAP) by sex, age and period

	Women 1996–2002		Men 1996–2002		Women 2003–2009		Men 2003–2009		p for interaction	
	<65 years				7149		19333			
	7087		17088							
Current smoker	2.50 (2.23 to 2.80)	1.53 (1.42 to 1.66)	<0.001		2.22 (1.97 to 2.50)	1.59 (1.46 to 1.73)	<0.001			
Hypertension	0.89 (0.81 to 0.98)	0.72 (0.67 to 0.78)	0.001		0.94 (0.90 to 0.99)	0.92 (0.89 to 0.95)	ns			
Heart failure	0.62 (0.45 to 0.85)	0.39 (0.31 to 0.48)	0.013		0.81 (0.57 to 1.16)	0.43 (0.34 to 0.56)	0.005			
Diabetes	1.22 (1.06 to 1.39)	1.06 (0.96 to 1.16)	0.090		1.18 (1.03 to 1.35)	0.95 (0.86 to 1.04)	0.008			
Peripheral arterial disease	1.61 (1.15 to 2.24)	0.88 (0.69 to 1.12)	0.003		1.20 (0.86 to 1.68)	0.80 (0.62 to 1.05)	ns			
	65 to 105 years				22477		26014			
	21428		24800							
Current smoker	2.34 (2.11 to 2.60)	1.59 (1.46 to 1.74)	<0.001		2.46 (2.20 to 2.76)	1.59 (1.44 to 1.76)	<0.001			
Hypertension	0.97 (0.92 to 1.02)	0.84 (0.80 to 0.88)	<0.001		0.96 (0.93 to 0.98)	0.94 (0.92 to 0.96)	ns			
Heart failure	0.47 (0.43 to 0.51)	0.42 (0.38 to 0.46)	0.003		0.60 (0.55 to 0.66)	0.52 (0.47 to 0.57)	0.006			
Diabetes	1.33 (1.24 to 1.44)	1.03 (0.96 to 1.11)	<0.001		1.28 (1.18 to 1.38)	1.02 (0.95 to 1.10)	<0.001			
Peripheral arterial disease	1.33 (1.17 to 1.53)	0.75 (0.67 to 0.84)	<0.001		1.25 (1.08 to 1.45)	0.94 (0.83 to 1.08)	0.003			

The p for interaction sex×type of ACS.

The increased risk for AMI associated with smoking, diabetes and PAD was stronger for women than for men, whereas the lower risk associated with HF was more pronounced for men (table 3). Aside from the variable of diabetes in women aged <65 years in the first time period (1996–2002), formal tests for interactions between sex and type of ACS were significant for all variables studied here. For the second time period (2003–2009), the effects of smoking and diabetes were stronger in women than in men (p for interaction <0.001 and 0.008, respectively), as was the effect of PAD in women aged 65 and older (p for interaction 0.003), whereas the lower risk of AMI associated with HF was stronger in men than in women (p for interaction 0.006).

Temporal changes in 30-day and 1-year mortality between the two time periods were observed across all age, sex and diagnosis categories (table 4). In patients aged <65 years, 30-day mortality in UAP was very low, but it was 2–3% in those aged ≥65 even in the last period. In AMI patients aged <65 years, 30-day mortality was some 2% in the second period. Still, given the very low mortality in young female UAP patients, the adjusted OR comparing AMI with UAP in the second period was 9.03 (95% CI 3.51 to 23.2) in women. The 30-day mortality in men and women with AMI did not differ greatly, and in men the corresponding OR was 3.34 (95% CI 2.06 to 5.42) in the second time period. One-year mortality in UAP patients aged <65 years changed comparatively little over time, ranging between 1% and 2%. In women <65 years with AMI, 1-year mortality in the second time period was 4.2%, decreasing from 6.1% in the first period, with a corresponding decrease among men from 4.9% to 3.1%. The OR in AMI patients compared with UAP patients was 3.54 (95% CI 2.29 to 5.48) in women and 2.65 (2.11 to 3.34) in men for the second time period.

Both 30-day and 1-year mortality were noticeably higher in older patients, particularly in patients with AMI; roughly one in five, or 21.5% of the women and 17.8% of the men, with this condition died in the first year after hospitalisation in the second period. Although this represented an improvement from the early part of the study in which approximately one in four such patients died, the multiple-adjusted OR for 1-year mortality in AMI patients when compared with patients with UAP was 3.01 (95% CI 2.65 to 3.42) in women and 2.68 (95% CI 2.36 to 3.04) in men for the second time period.

## DISCUSSION

### Key findings

In the present study, we found that in patients presenting with either AMI or UAP as a first ACS episode, smoking, diabetes and PAD were associated with an increased risk of presenting with AMI, whereas prior HF, as well as prior use of aspirin, β-blockers, long-acting nitrates and statins, were associated with lower risk. AMI

**Table 4** Case-death (n%) after 30 days and 1 year in patients admitted to Swedish coronary care units (CCUs) with either acute myocardial infarction (AMI) or unstable angina pectoris (UAP) by sex, age and period and ORs (ORs, 95% CI) for fatal outcomes in patients diagnosed with AMI relative to UAP

	UAP Period	AMI	Crude odds ratio (99% CI)	Adjusted odds ratio (99%CI) *	p Value	UAP Period	AMI	Crude odds ratio (99% CI)	Adjusted odds ratio (99% CI)*	p Value
	1996–2002					2003–2009				
<b>&lt;65 years</b>										
Women (n)	3711	3376				2617	4532			
30-day mortality	17 (0.5)	118 (3.5)	7.87 (4.72 to 13.1)	8.50 (4.62 to 15.63)	<0.001	7 (0.3)	95 (2.1)	7.98 (3.70 to 17.2)	9.03 (3.51 to 23.24)	<0.001
1-year mortality	53 (1.4)	206 (6.1)	4.48 (3.30 to 6.09)	5.53 (3.77 to 8.12)	<0.001	31 (1.3)	172 (4.2)	3.39 (2.31 to 4.99)	3.54 (2.29 to 5.48)	<0.001
Men (n)	6422	10666				4869	14464			
30-day mortality	41 (0.6)	327 (3.1)	4.92 (3.55 to 6.82)	4.48 (3.09 to 6.47)	<0.001	21 (0.4)	244 (1.7)	3.96 (2.53 to 6.19)	3.34 (2.06 to 5.42)	<0.001
1-year mortality	126 (2.0)	521 (4.9)	2.57 (2.11 to 3.12)	2.65 (2.11 to 3.34)	<0.001	73 (1.6)	401 (3.1)	1.93 (1.50 to 2.49)	1.83 (1.39 to 2.43)	<0.001
<b>65–105 years</b>										
Women (n)	8453	12975				6314	16133			
30-day mortality	253 (3.9)	2268 (17.5)	6.86 (6.01 to 7.84)	6.03 (5.16 to 7.05)	<0.001	117 (1.9)	1803 (11.2)	6.66 (5.52 to 8.05)	5.87 (4.66 to 7.39)	<0.001
1-year mortality	807 (9.5)	3581 (27.6)	3.61 (3.33 to 3.92)	3.43 (3.10 to 3.79)	<0.001	436 (7.5)	3117 (21.5)	3.36 (3.02 to 3.73)	3.01 (2.65 to 3.42)	<0.001
Men (n)	8624	16176				6376	19638			
30-day mortality	289 (3.4)	2338 (14.5)	4.87 (4.30 to 5.52)	5.09 (4.36 to 5.93)	<0.001	129 (2.9)	1826 (9.3)	4.96 (4.14 to 5.95)	5.08 (4.07 to 6.35)	<0.001
1-year mortality	925 (10.7)	3808 (23.5)	2.56 (2.37 to 2.77)	2.87 (2.61 to 3.16)	<0.001	449 (7.6)	3141 (17.8)	2.62 (2.36 to 2.01)	2.68 (2.36 to 3.04)	<0.001

\*Adjusted for age, smoking, hypertension, heart failure, diabetes, peripheral arterial disease, aspirin,  $\beta$ -blockers, ACE inhibitors, long-acting nitrates and statins.

patients were also slightly older, and the registry data indicated a higher proportion of men than women with this condition. The differences for smoking, diabetes and PAD were more pronounced in women than in men. Although there were changes in the definition of AMI during the inclusion period, all associations were roughly similar before and after the implementation of the new criteria. Both short-term and long-term outcomes were markedly better in UAP compared with AMI; these differences persisted even after the adoption of new criteria for AMI in 2001.

Sex differences in the clinical presentation of CHD have long been recognised,<sup>24 25</sup> with men more likely than women to have an initial presentation of AMI, whereas presenting with UAP is more common in women. In recent studies in patients with ACS, women were found to present more often with UAP.<sup>26</sup> However, in the Euro Heart Survey,<sup>14</sup> this difference was found to be restricted to younger patients (<65 years). Our data are in line with these earlier observations.

Of the studied variables, smoking was observed to be the factor most strongly associated with a first-time presentation with AMI; this was only moderately the case in men, whereas the difference in smoking prevalence between patients presenting with AMI or UAP was more pronounced in women. Half of all women <65 years with AMI were current smokers, a slightly higher proportion than in men with AMI (43%).

Virtually all studies of AMI patients have shown diabetes to be more common in women, but the influence of diabetes on clinical presentation has only rarely been assessed. In the Euro Heart Survey on diabetes, the influence of diabetes on presenting symptoms and clinical course was similar in men and women;<sup>27</sup> however, this population represented a mixture of patients with both chronic and acute forms of CHD. In contrast, in the Euro Heart ACS survey,<sup>28</sup> diabetes was associated with more severe forms of ACS. Women, but not men, with diabetes had a higher risk of presenting with ST elevation ACS and developing Q wave MI, suggesting a differential effect of diabetes on the pathophysiology of ACS based on the sex of the patient. Although we did not specifically study outcomes associated with diabetes, diabetes in both men and women with AMI is known to affect short-term and long-term outcomes adversely.

### Limitations

The present study has several limitations that require appropriate acknowledgement, such as using data largely collected for other purposes than research. The definitions of unstable angina and angina used in the present study are based on each treating physician's judgements and ECG changes, as ST elevation, ST depression and pathological T wave and were not strictly validated. Whereas there are strict and objective criteria for a diagnosis of AMI, there is in routine clinical practice no optimal way of validating UAP. With the reclassification of AMI criteria in 2001, a proportion of UAP

episodes before that year would now be reclassified as small infarcts. However, reclassifying these episodes as AMI by using available laboratory markers did not seem to appreciably influence our findings. Even so, the heterogeneity of markers and cut-off values that were used between hospitals precluded a systematic analysis.

A proportion of the patients with ACS may have had chest pain of non-cardiac origin. However, using data on coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting, positive stress test, ECG with pathological STT changes during hospitalisation, and long-acting nitrates at discharge from hospital, only 0.6% did not have any further evidence in support of their diagnosis specification. Given the overall high prevalence of CHD in the general population,<sup>29 30</sup> it is more likely that CHD is underdiagnosed; thus, excluding all patients with no objective signs of ischaemia would undoubtedly provide a distorted view of patients with UAP.

### CONCLUSIONS

In patients presenting for the first time with an ACS episode, male sex, slightly older age, smoking, diabetes and PAD were major determinants for presenting with AMI (and not UAP), suggesting a different phenotype for these two manifestations of CHD. Patients with UAP more often used cardioprotective medications. Despite increasingly active treatment for patients with AMI and more inclusive criteria, a worse prognosis in AMI persists.

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