Risk model for suspected acute coronary syndrome is of limited value in an emergency department

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ORIGINAL ARTICLE

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ABSTRACT

INTRODUCTION: Among patients with acute chest pain, acute coronary syndrome (ACS) is seen only in a minority of the patients, which raises the question, whether it is possible to separate a group with a high risk of ACS for admission to a cardiac care unit (CCU) from those with a low risk who would be treated at an emergency department (ED). The aim of this study was to describe a risk stratification model for a Danish context.

METHODS: This was an historic prospective cohort study of patients with suspicion of ACS. The patient was defined as a low-risk patient and admitted to the ED if: 1) electrocardiogram (ECG) was normal, 2) the patient did not have persisting chest pain and 3) there was no history of ischaemic heart disease, heart failure or cardioverter defibrillator. Otherwise, patients were admitted to the CCU. The primary outcome was whether the ACS diagnosis was confirmed or rejected.

RESULTS: We included a total of 488 patients with suspicion of ACS, 50% of whom were low-risk patients. 17% had a verified ACS; 10% of those in the low-risk group and 24% of those in the high-risk group ($p = 0.0001$). Among the verified ACS cases, 71% went primarily to the CCU. The odds ratio for an ACS if assigned to the high-risk group was 3.0. Allocation to the high-risk group, male gender and age above 60 years were associated with a higher risk of ACS. For patients fulfilling the high-risk definition, sensitivity was 71%, specificity 55%, negative predictive value 90% and positive predictive value 24% for an ACS.

CONCLUSIONS: The model for stratification separated patients into two equal groups, allocated 71% of all ACS directly to the CCU and could not be improved by any of the additional factors examined. Further development of referral strategies for chest pain patients is required.

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In Denmark, almost all acutely ill patients are admitted through an Emergency Department (ED) [1]. For patients with acute coronary syndrome (ACS), considerable improvements have been achieved in dedicated cardiac care units (CCU) [2, 3]. If a suspicion of ACS is raised in Denmark, it is recommended to call for an ambulance and upon arrival to have a pre-hospital electrocardiogram (ECG) transmission performed and to establish direct communication between the pre-hospital providers and a hospital physician who decides where the patients should be transferred to based on the reported history, clinical findings and ECG. While patients with ST-elevation myocardial infarction (STEMI) are referred for percutaneous coronary intervention (PCI) [4], the remaining patients are admitted to either a CCU or an ED. Whether a CCU or an ED is the destination may depend on local agreements between the departments based on logistic or resource reasons or on the individual physician's judgment of the likelihood of a primary coronary disease. It is known that among patients with acute chest pain, only a minority has ACS [5, 6]. This raises the question whether it is possible to separate a group of patients with an a priori high-risk-ACS group who would profit from being admitted directly to a CCU and a low-ACS-risk group of patients with chest pain who will be better cared for in the multidisciplinary ED.

In Denmark, it has been estimated that 20-33% of the patients with a suspicion of ACS could be admitted to the ED according to certain suggested criteria [7, 8], but this has only been evaluated in hospital settings quite different from those in Denmark [9-12].

We conducted a study addressing this strategy. The aim was to describe how many patients would be classified as high-risk and low-risk patients for ACS according to the suggested model [8] , what proportion would actually be confirmed as ACS, and how this stratification would perform as a diagnostic test for ACS. Finally, we sought for additional risk factors that could identify the patients at high risk for ACS in this population.

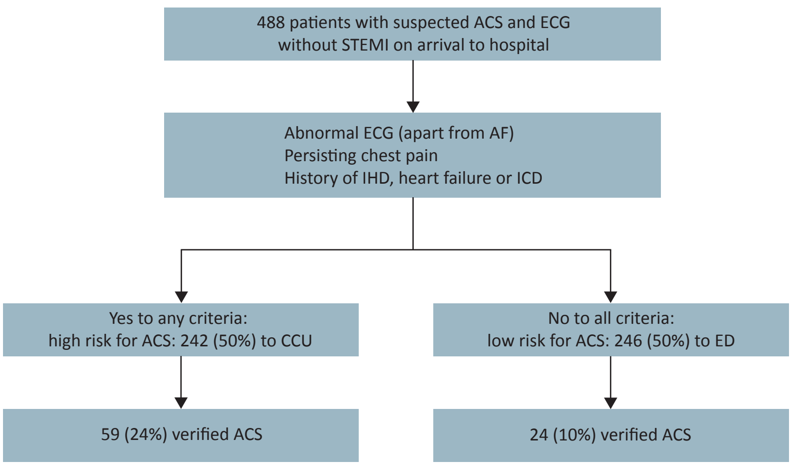
METHODS

This was a historic, prospective cohort study (a prospective study of past data) including all patients referred to Kolding Hospital with sudden onset of chest pain and the presumptive diagnosis of ACS as the primary reason for admission. Excluded from the study were patients who were transferred directly to the intensive care unit or died before an ACS diagnosis could be made based on ECG and blood test or who had a STEMI already on their first ECG.

A 12-lead electrocardiogram (ECG) was recorded and transmitted to the hospital or obtained immediately upon arrival. A senior medical physician evaluated the

FIGURE 1

Distribution of the patients.



ACS = acute coronary syndrome; AF = atrial flutter/fibrillation; CCU = cardiac care unit; ECG = electrocardiography; ED = emergency department; ICD = cardioverter defibrillator; IHD = ischaemic heart disease; STEMI = ST-elevation myocardial infarction.

ECG and the patient's history. The patient was considered to be at low-risk and was admitted to the ED if: 1) the ECG was normal (apart from atrial flutter/-fibrillation) [13], 2) the patient did not have persisting chest pain defined as pain not subsiding after administration of a first dose of sublingual nitro-glycerine or morphine [9] and 3) there was no history of ischaemic heart disease (IHD), heart failure or cardioverter defibrillator (ICD) [11]. In all other cases, patients were admitted to the CCU (**Figure 1**).

The ED was a 36-bed department with around 9,000 annual admissions, mainly surgical, medical, cardiologic or orthopaedic patients. The CCU had 20 beds and around 1,000 admissions per year. The ED has the same equipment for monitoring of ACS patients as the CCU does, and follows the same procedures for admittance, observation and treatment of a patient with suspected ACS. One cardiologist was employed in the ED as an emergency physician, and three specialists in cardiology were employed in the CCU. While the nursing staff in the ED was experienced in a range of acute patient problems, the CCU staff was highly trained, primarily in the handling of cardiac patients.

The primary outcome was whether the ACS diagnosis was confirmed or rejected. An ACS was defined as an ST-elevation myocardial infarction (STEMI) developing after admission, a non-ST-elevation myocardial infarction (NSTEMI) or unstable angina pectoris (UAP) [14].

Data were extracted from the patient records together with information on gender, age, smoking habits, a history of hypertension, a family history of coronary disease and a diagnosis of diabetes. All continuous comparisons were made using the Wilcoxon rank-sum test. All categorical data were compared using Fisher's exact test. Univariate logistic regression was performed to evaluate the ability of a model to identify patients with ACS, and multivariate logistic regression using backwards elimination using a p-value exceeding 0.20 was the elimination criterion. For evaluation of the different models, the likelihood ratio for positive and negative test was used together with the receiver operator curve (ROC) area equal to (sensitivity + specificity)/2.

The study was considered a quality assurance project of the implemented algorithm for the ACS referral, based only on existing data in the patient hospital records, and no ethical approval was therefore required.

Trial registration: The study was registered with the Danish Data Protection Agency (R. no. 2010-41-5444).

RESULTS

During the study period from 1 March to 8 September 2009, a total of 488 patients were admitted to the hospital with suspected ACS, 50% were considered low-risk patients and referred to the ED and 50% were considered high-risk patients for ACS and were therefore admitted to the CCU. The baseline characteristics and outcome are presented in **Table 1**.

The median age was significantly lower for the low-risk group, 55 years (p25-p75: 44-69 years) than for the high-risk group, 66 years (p25-p75: 52-77 years) (p =

TABLE 1

Baseline information and outcome for low-risk and high-risk patients suspected for acute coronary syndrome.

Variable	Low risk, n (%)	High risk, n (%)	p-value
Total	246 (50[a])	242 (50[a])	
Gender			0.01
Male	127 (52)	152 (63)	
Female	119 (48)	90 (37)	
Age, yrs			0.0001
20-40	40 (16)	14 (6)	
41-60	103 (42)	74 (31)	
61-80	73 (30)	112 (46)	
> 80	30 (12)	42 (17)	
Outcome			
STEMI	4 (2)	13 (5)	0.03
NSTEMI	18 (7)	35 (14)	0.01
Unstable angina	2 (1)	11 (5)	0.01
ACS[b]	24 (10)	59 (24)	0.0001

ACS = acute coronary syndrome; NSTEMI = non-ST-elevation myocardial infarction; STEMI = ST-elevation myocardial infarction.
a) % of total.
b) STEMI + NSTEMI + unstable angina.

0.0001). There were more males in the high-risk group (p = 0.01). Of the 488 patients, 72 (15%) had troponin levels above the defined cut-off value for ACS, and 83 (17%) had a verified ACS based on either development of ST elevation, increased troponin, a history of unstable angina or a combination of these findings in conjunction with the history of sudden onset of chest pain. Among the low-risk patients, 24 (10%) had a verified ACS; and in the high-risk group, the corresponding number was 59 (24%) patients (p = 0.0001). Among the patients with verified ACS, 71% were admitted primarily to the CCU (59 of 83 patients) (Figure 1).

In **Table 2**, other common risk factors for ACS were analysed together with the high-risk group definition. In the univariate analysis, the odds ratio (OR) for having an ACS if the patient belonged to the high-risk group was 3.0 (95% confidence interval: 1.8-5.0). Among the other examined risk factors for ACS, only age 60-80 years was significantly associated with ACS. In the multivariate analysis, allocation to the high-risk group, male gender and age above 60 years were all associated with a significantly increased risk of ACS.

For a patient with chest pain fulfilling the high-risk definition, the sensitivity was 71%, the specificity was 55%, the negative predictive value 90% and the positive predictive value 24% for an ACS, as shown in **Table 3**.

Since age above 60 years had an almost equal OR in the multivariate analysis, we examined this criterion alone and in combination with the high-risk definition as screening models for ACS. Our "high-risk" model and the model with "age above 60 years" for identification of ACS performed equally well, while the combination of age and "high-risk" increased the sensitivity at the expense of the predictive values. As screening models, Table 3 also shows that all three models were rather weak screening tests for ACS as expressed in the low likelihood ratios for positive tests and ROC areas, while the likelihood ratios for a negative test in the "high-risk" and age-above 60 years models indicated some usefulness in predicting that the patient did not have ACS.

DISCUSSION

We found that our stratification of the patients with suspicion of ACS into high-risk and low-risk groups divided the patients arriving to the ED with chest pain into two equally large groups. A final diagnosis of ACS was significantly more frequent in the high-risk group (24%) than in the low risk group (10%), and 71% of all ACS patients were referred primarily to the CCU. A division of the patients according to age, i.e. above or below the age of 60 years, performed equally well for detecting ACS. It was possible to increase the sensitivity by adding age > 60 years to the risk model, but this was at the expense of the model's specificity and predictive values.

TABLE 2

Risk factors for acute coronary syndrome for all admitted patients.

Variable	With ACS, n (%)	Univariate analysis OR (95% CI)	Univariate analysis p-value	Multivariate analysis OR (95% CI)	Multivariate analysis p-value
Risk groups for ACS					
Low risk	24 (10)	1.0			
High risk	59 (25)	3.0 (1.8-5.0)	0.0001	2.4 (1.3-4.2)	0.003
Gender					
Female	28 (13)	1.0			
Male	55 (20)	1.6 (0.9-2.6)	0.07	1.9 (1.0-3.3)	0.004
Age, yrs			0.0004		
20-40	4 (7)	1.0			
41-60	13 (7)	1.0 (0.3-3.2)			
61-80	41 (23)	3.7 (1.3-10.9)		3.4 (1.8-6.3)	0.0001
> 80	13 (19)	3.0 (0.9-9.7)		2.9 (1.3-6.7)	0.01
Diabetes mellitus					
No	70 (16)	1.0		–	
Yes	13 (27)	1.8 (0.9-3.5)	0.11	–	
Family history of IHD					
No or unknown	70 (19)	1.0		–	
Yes	13 (12)	2.0 (0.9-3.9)	0.06	–	
History of hypertension					
No	43 (16)	1.0		–	
Yes	40 (19)	1.2 (0.8-2.0)	0.4	–	
Smoking	0.7				
Non-smoker	25 (15)	1.0		–	
Ex-smoker	22 (18)	1.2 (0.7-2.3)		–	
Smoker	23 (14)	0.9 (0.5-1.7)		–	
Former ACS					
No	53 (15)	1.0		–	
Yes	30 (22)	1.5 (0.9-2.5)	0.09	–	
Known heart failure[a]					
No	78 (16)	1.0		–	
Yes	5 (36)	2.8 (0.9-8.6)	0.07	–	

ACS = acute coronary syndrome; CI = confidence interval; IHD = ischaemic heart disease; OR = odds ratio.
a) Ejection fraction < 45%.

TABLE 3

Screening tests for identification of acute coronary syndrome.

Screening variable	Screening model: high risk	age > 60 yrs	high risk or age > 60 yrs
Test positive, n (%)	242 (50)	257 (53)	400 (82)
Patients with ACS, n (%)	83 (17)	83 (17)	83 (17)
Sensitivity, %, median (95% CI)	71 (60-81)	76 (65-85)	86 (76-92)
Specificity, %, median (95% CI)	55 (50-60)	52 (47-57)	19 (15-23)
PPV, %, median (95% CI)	24 (19-30)	25 (19-30)	18 14-22)
NPV, %, median (95% CI)	90 (86-94)	91 (87-95)	86 (77-93)
LHR, median (95% CI)			
Positive test	1.6 (1.3-1.8)	1.6 (1.4-1.8)	1.1 (1.0-1.2)
Negative test	0.5 (0.4-0.7)	0.5 (0.3-0.7)	0.8 (0.4-1.4)
ROC area, median (95% CI)	0.6 (0.6-0.7)	0.6 (0.6-0.7)	0.5 (0.5-0.6)

ACS = acute coronary syndrome; CI = confidence interval; LHR = likelihood ratio; NPV = negative predictive value; PPV = positive predictive value; ROC = receiver operator curve.

Deciding where to handle acute chest pain – in the emergency department or in the cardiac care unit – requires an electrocardiography and clinical information.

The use of a low-risk group for ACS resulted in a higher frequency of ACS in patients referred to the ED than expected. We could not improve our model for stratification into a high- and low-risk group based on the examined variables. While the model was able to direct almost three quarters of the patients with ACS to the CCU, it remains a matter of concern that 10% of the patients who remained in the ED had an ACS and needed subsequent transfer to the CCU. This study did not examine whether the prognosis in this group differed from the prognosis of the patients with ACS who were referred directly to a CCU. Further studies are warranted to elucidate this aspect.

A recent review concluded that the identification of the high-risk ACS patient could be improved by a combination of several methods, including medical history, ECG, point-of-care testing, cardiac imaging, exercise tests and a chest pain unit evaluation [15]. In Austria, the UK and the US, little association was found between the typical characteristics of ACS and their diagnostic value for ACS [10, 16, 17]. In one Spanish study, patients arriving to the ED with typical chest pain and co-morbidity like diabetes, a history of aspirin use or aged more than 65 years were considered high-risk patients, comprising 15% of all chest pain patients, and 6.5% of these high-risk patients had an ACS [18]. Another study showed that absence of diabetes, no previous coronary disease and absence of retrosternal pain suggested no ACS [19]; while in the US, previous coronary intervention and arm pain was associated with ACS [20]. It is, however, difficult to apply these prevalence rates to the Danish population where access to the hospital system is quite different.

The present study has some limitations and weaknesses. It is a historic, prospective study based on patient records. This means that in some cases information on risk factors etc. was missing. Furthermore, while the classification “high-risk” patient was clearly defined, it was not possible to determine whether the patient was “high-risk” because of pain, ECG or patient history. The definition of the “high-risk” patient is also somewhat vague since the term “chest pain” is often modified by age, gender, culture, other diseases, pain-relieving treatment and the medical staff’s experience. Since this study was performed, the troponin test has been replaced with new and more sensitive tests, and the detection threshold for ACS has been lowered. This might increase the number of patients who are admitted to the ED, but turn out to have ACS. Finally, the decision of admission to the ED or the CCU was made upon arrival. This decision could be made already in the pre-hospital setting, since all the information can be obtained at this time point.

Despite these limitations, we believe that our results add to the limited knowledge of how to refer patients with suspected ACS to the right care level, i.e. the CCU or the ED in Danish acute hospitals. If the present model is used, almost three quarters of the ACS will be admitted directly to the CCU and half of the patients to the ED; and we will need to accept that, among these patients, 10% will need to be transferred to the CCU due to ACS after the troponin analysis. We suggest that these strategies be evaluated in a larger prospective cohort study using the revised definition of ACS based on highly sensitive troponin analysis.

CONCLUSIONS

Our model for stratification into high-risk and low-risk patients separated patients in whom there was a suspicion of ACS into two groups of equal size, and allocated 71% of all patients with ACS directly to the CCU. The model could not be improved by any of the additional factors examined. We believe that development of referral strategies for chest pain patients allowing these to be treated at either ED or CCU in acute hospitals in Denmark is required.

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