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Diagnosing acute coronary syndrome in primary care: comparison of the physicians' risk estimation and a clinical decision rule

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Background. Diagnosing acute coronary syndrome (ACS) in a primary care setting poses a diagnostic dilemma for physicians.

Objective. We directly compared the diagnostic accuracy of a clinical decision rule (CDR) based on history taking and physical examination in suspected ACS with the risk estimates of the attending GP.

Methods. In a prospective multicenter study, patients suspected of ACS were included by the GP. GPs were asked to estimate the probability (0%–100%) of the presence of ACS. GPs collected patient data, but they were not aware of the CDR and did not score the patient accordingly.

Results. Two hundred and ninety-eight patients were included (52% female, mean age 66 years, 22% ACS). The area under the receiver operating characteristic (ROC) curve (AUC) was 0.75 [95% confidence interval (CI) 0.68–0.82] for the GP risk estimate and 0.66 (95% CI 0.58–0.73) for the CDR. There was an agreement between the risk estimation of the GP and a CDR in 51% and the prevalence of ACS in predefined low-, intermediate- and high-risk groups was similar for the GP and CDR estimates. In the low-risk group, according to the GP, four patients (8.2%) suffered an ACS. These four patients were all identified by the decision rule as high risk.

Conclusions. The GP classified patients as ACS or no ACS more adequately than the CDR, judged by the AUC. However, the use of a CDR in patients that are considered at low risk for ACS by the GP could reduce the amount of missed myocardial infarctions.

Keywords. Cardiology, clinical diagnosis.

Introduction

Diagnosing or excluding acute coronary syndrome (ACS, comprising acute myocardial infarction and unstable angina) is a challenge for primary care physicians because signs and symptoms may be atypical and other diagnostic tools, such as cardiac biomarker testing or electrocardiography (ECG), are often not readily available in a primary care setting. There is no generally accepted clinical decision rule (CDR) for ACS although several attempts have been made to develop and validate such a rule.[1–3]

In a CDR, patient characteristics in conjunction with findings from history taking, physical examination and often other additional diagnostic tests (typically laboratory testing or imaging techniques) are combined to give an overall score, which is related to the absolute probability of the presence (or absence) of a certain disease and often guides the further diagnostic workup. A CDR, for example, the Ottawa ankle rule for the use of radiography in ankle injuries,[4] is generally developed to improve the efficacy, quality and efficiency of health care.[5–7] For instance, introduction of the Ottawa ankle rule led to a relative reduction in ankle radiography of 28%, reduction in costs and emergency room waiting times, without increasing the number of missed fractures.[8]

Many CDRs have had limited effect on physicians behaviour, and several barriers for adherence to a decision rule have been described.[7,9,10] These barriers range from unpractical use of the rule itself or lack of awareness of existence of the rule, to disagreement with the rule. In general, physicians view CDRs as oversimplified and not applicable to their specific practice population. Moreover, physicians often perceive CDRs as a reduction of their professional autonomy and they

argue that their clinical judgement is superior.[10] Physicians will be more likely to use a CDR if they are convinced that it has an additional value to their own clinical judgement in estimating risks.

In this study, we directly compared the diagnostic accuracy of a CDR in suspected ACS with the risk estimates of the attending primary care physician.

Methods

Data were collected within a large diagnostic accuracy study in which the diagnostic value of a rapid cardiac biomarker, in addition to a decision rule, was determined. The design of this study has been published previously.[11] From March 2006 until September 2008, 298 consecutive patients suspected by the GP of ACS were enrolled in three out-of-hours GP services located centrally in The Netherlands (one urban and two semi-urban), in which >150 GPs take turns being on duty during out-of-office hours. Additionally, 25 GPs from nine group practices recruited patients during daytime hours. GPs were instructed to include all consecutive patients suspected of ACS. Presenting symptoms were most often chest pain but also sudden dyspnoea or any other symptom prompting a GP to consider ACS as a possible diagnosis could lead to inclusion in this study. We excluded patients with complaints lasting >24 hours and patients requiring instant hospital emergency room referral, as judged by the GP since inclusion in our study would constitute unnecessary delay.

Participating GPs systematically collected data on the patient's presenting signs and symptoms and history taking. The GPs were asked to make a management decision based on their own judgement. For the purpose of the present study, GPs were explicitly instructed to estimate the probability of the presence of ACS on a scale from 0% to 100% after they finalized medical history taking and physical examination.

Using multivariate regression analysis, we developed a CDR using the same clinical items as in a diagnostic model previously developed by Grijseels *et al.*[12] The clinical items included in the CDR are sex, radiation of chest pain, nausea/sweating and the presence of prior coronary artery disease (Table 1). We (internally) validated this new model with bootstrapping techniques to correct for over-optimism. Although GPs did collect patient data, they were not aware of the CDR and were not asked to score the patient accordingly.

TABLE 1 *CDR for ACS in a primary care setting*

Clinical item	Score
Sex (male)	5 points
Presence of radiation of chest pain	8 points
Presence of nausea/sweating	5 points
History of coronary artery disease	2 points

ACS was defined in accordance with guidelines from the European Society of Cardiology and the American College of Cardiology.[13,14] In all patients, irrespective of whether they were referred to the hospital emergency room or not, a venous blood sample was collected between 12 and 36 hours after onset of complaints, for measurement of cardiac biomarkers [troponin, creatinin kinase (CK) and creatinin kinase–myocardial band (CK-MB)]. Also, we obtained a 12-lead ECG in every patient. In referred patients, these measurements were performed as part of routine care. Patients who were not referred to hospital were visited at home by a qualified GP laboratory service personnel for performance of these tests. An expert panel consisting of two cardiologists and one GP established a final diagnosis in each patient. The panel used all available patient information, including signs and symptoms, ECG and biomarker levels (troponin, CK and CK-MB), specialist letters in those who had been referred to hospital and follow-up results up to 1 month after the event. The study protocol was approved by the Medical Ethics Committee of the University Medical Center Utrecht, The Netherlands. All patients provided written consent.

Data analysis

First, we compared the abilities of the CDR and the GP judgement in discriminating patients with the disease from patients without the disease, using receiver operating characteristic (ROC) curve analysis. An area under the ROC curve (AUC) of 0.5 indicates no discrimination, whereas an AUC of 1.0 indicates perfect discrimination.[15] Then, we constructed a calibration plot to separately examine the agreement between the predicted probabilities of the decision rule with the observed outcome ACS and we constructed a similar calibration plot for the predicted probabilities of the GP. Perfect predictions should lie on the 45-degree line for agreement with the outcome in the calibration plot.[16] Finally, we divided patients into different risk groups and constructed a classification table to quantify the agreement between the risk estimation based on the CDR and by the GP. We made a division into low-, intermediate- and high-risk groups according to the expected probability of the outcome based on the CDR and also according to the expected probability of the outcome based on the GPs risk estimation. No previously determined threshold exists for such a division into risk categories of ACS patients and we therefore used values that seemed clinically plausible and resulted in a sufficient number of patients in each risk category: a <10% chance of ACS as low risk, a 10%–20% chance to indicate intermediate risk and

a probability exceeding 20% chance to indicate high risk. Statistical analyses were performed using SPSS version 16.0 for Windows, Chicago, USA.

Results

Patient characteristics

Three hundred and thirty-six patients were enrolled in the study. We excluded 38 patients. Of these, 12 refused informed consent, 23 had symptoms suggestive of ACS for >24 hours and 3 patients had an undetermined final diagnosis. The mean age of the 298 patients suspected of ACS by the GP was 66 (SD 14) years, 52% was female and 66 (22%) were diagnosed with ACS by the expert panel. The majority of patients (75%) had one or more cardiovascular risk factors (current smoker, diabetes, hypertension and hyperlipidaemia), while 36% of all patients had a history of coronary artery disease. The presenting symptoms involved chest pain in 278 patients (93%). The median ACS risk estimation according to the GP was 47.5% [interquartile range (IQR) 20.0%–70.0%] and 23.2% (IQR 13.8%–27.6%) according to the CDR. Of the suspected ACS patients, 73% was referred to hospital by the GP for further diagnostic testing and/or treatment (Table 2).

The AUC for the GP risk estimate was 0.75 [95% confidence interval (CI) 0.68–0.82] and for the CDR this was 0.66 (95% CI 0.58–0.73) (Fig. 1), indicating that the GP categorized patients with and without ACS more accurately than the CDR. Calibration of the GP risk estimate showed that the GP generally overestimated the risk for ACS. For example, when the GP estimated a risk of 60%, the actual risk was ~25%. Calibration of the CDR showed good agreement between predicted and observed probabilities (Fig. 2A and B).

GPs estimated 49 (16%) patients as low risk for ACS and 209 (70%) as high risk; 8.2% and 27% of these groups, respectively, had an ACS according to the expert panel. According to the decision rule, 24 (8.1%) of patients had a low risk and 162 (54%) were high risk; the prevalence of ACS in these groups was 8.3% and 30%, respectively. The risk estimation by the GP and the decision rule showed agreement in 153 (51.3%) cases. In 27 (9.1%) cases, there was major disagreement. Of the 19 patients estimated as low risk according to the GP and high risk according to the decision rule, four patients (21%) suffered an ACS. Of the eight patients with a low risk according to the decision rule and a high risk according to the GP, two patients (25%) suffered an ACS (Tables 3 and 4). Of the patients that were estimated as low risk by both the GP and the CDR, none had an ACS.

As a sensitivity analysis, we constructed the same classification table using the lowest and highest quintiles for the GP estimation and the CDR. For the GP estimation, this yielded thresholds of <15% for low risk and >76% for high risk and for the CDR, this was <13.2% for low risk and >28.2% for high risk. Agreement between the GP estimation and the CDR was similar for these new

TABLE 2 *Demographic and clinical characteristics of included patients suspected of ACS by the GP [numbers (%)]*

Characteristics	*N* = 298
Demographics	
Age (mean, years)	66 (SD 14)
Sex (male)	143 (48)
Cardiovascular risk factors	
Presence of any of the following cardiovascular risk factors[1]	236 (79)
History of AMI, bypass, PCI and angina pectoris	108 (36)
Current smoker	69 (23)
Diabetes	68 (23)
Hypertension	145 (49)
Hyperlipidaemia	91 (31)
Symptoms	
Chest pain	278 (93)
Radiation of pain	189 (63)
Nausea/sweating	174 (58)
Referred to hospital	218 (73)
Outcome	
ACS	66 (22)
Unstable angina pectoris	14 (21)
Myocardial infarction	52 (79)

AMI, acute myocardial infarction; PCI, primary coronary intervention.

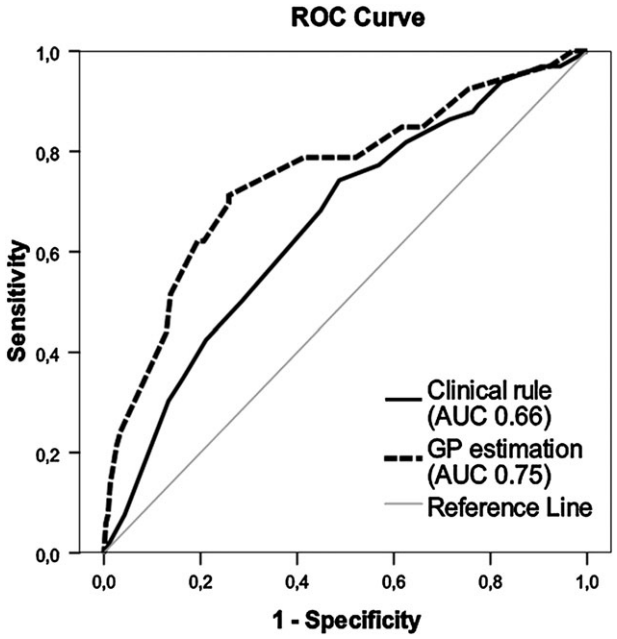

FIGURE 1 *ROC curves for the GP risk estimation and for the CDR for ACS. AUC for risk estimation GP and decision rule: 0.75 (95% CI 0.68–0.82) and 0.66 (0.58–0.73)*

thresholds (157, 52.7%); major disagreement was less prevalent (14, 4.7%).

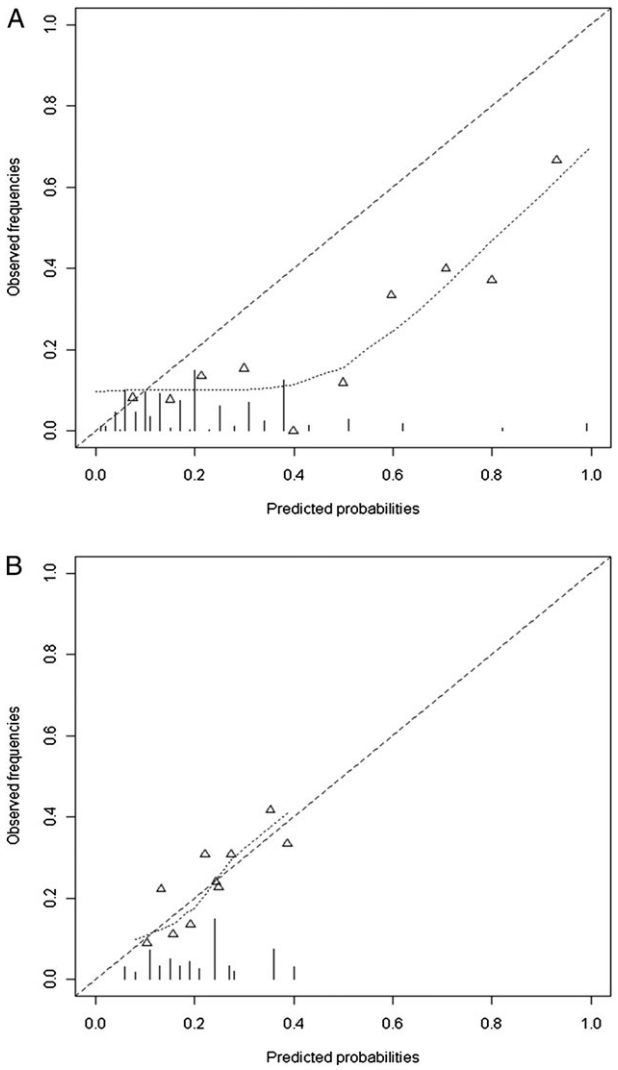

FIGURE 2 *Calibration plots of risk estimation by the GP and the CDR. (A) Risk estimation by the GP. (B) Risk estimation by the CDR*

Discussion

To our knowledge, this is the first direct comparison of a physicians' judgement with a CDR for patients suspected of ACS in primary care. Comparing the AUC of the GP estimate and the CDR revealed that the GP more adequately classified patients as ACS or no ACS than the CDR. Calibration plots showed that the GP tends to systematically overestimate a patients risk for ACS. Furthermore, in a classification table for three different risk categories (low, intermediate and high), there was a 51% agreement between the risk estimation of the GP and the decision rule. In the 49 patients judged as low risk by the GP, 4 patients (8.2%) suffered an ACS. These four patients with ACS were all identified by the decision rule as high risk. Importantly, the prevalence of ACS in the low-, intermediate- and high-risk groups according to the GP and CDR estimations was similar.

Based on our findings, we conclude that an adequate CDR for the triage of patients suspected of ACS in primary care is still lacking. The use of a CDR for ACS could increase the safety and efficiency in the diagnostic workup of patients suspected of ACS since we also show in this study that ACS patients are missed by the GP. A study in which an externally validated CDR is used could provide quantitative information on the reduction in missed ACS. The approach could be as follows: the GP performs his or her usual diagnostic workup of a patient suspected of ACS, which leads to a certain management decision. If the GP judges the patients to be at low risk for ACS, than as an extra precaution, the CDR for ACS could be performed. Patients estimated as high risk by the decision rule should then still be referred to hospital.

However, widely accepted decision rules for the diagnosis of ACS do not exist and available prediction rules for ACS have major methodological limitations, as was shown in a systematic review on the diagnostic accuracy of clinical prediction rules for excluding ACS in an emergency room setting.[17] These limitations included verification bias [failure to use the same reference standard ('gold standard') in all patients], lack of blinding and lack of external validation of the

TABLE 3 *Comparison of the risk estimation by the GP and the CDR with the outcome ACS*

	GP risk estimate				CDR			
	Number (%)	Outcome ACS			Number (%)	Outcome ACS		
		N	% Within risk group	% From total		*N*	% Within risk group	% From total
Low risk	49 (16)	4	8.2	1.3	24 (8)	2	8.3	0.7
Intermediate risk	40 (13)	6	15	2.0	112 (38)	15	13.4	5.0
High risk	209 (70)	56	27	19	162 (54)	49	30	16
Total	298 (100)	66	–	22	298 (100)	66	–	22

TABLE 4 *Concordance of the estimations of the GP and the CDR with absolute number of patients with ACS (in grey italics)*

		CDR			Total
		Low risk	Medium risk	High risk	
Risk estimation GP	Low risk	10	20	19	49 (16)
		0	*0*	*4*	*4*
	Medium risk	6	17	17	40 (13)
		0	*4*	*2*	*6*
	High risk	8	75	126	209 (70)
		2	*11*	*43*	*56*
	Total	24 (8.1)	112 (38)	162 (54)	298 (100)
		2	*15*	*49*	*66*

CDR, which all could have led to overestimation of diagnostic performance of the CDR.

It is important to realize that the CDRs that were developed in a secondary care setting cannot be applied uncritically to the primary care setting, even when performed in patients in whom the same diagnostic problem exists. In primary care, the prevalence of ACS is lower as compared to secondary care (because only the medium- and high-risk patients are referred to hospital) and in primary care patients present at in an earlier stage after symptom onset. Patient characteristics and symptoms will therefore differ and it is possible that an item that provides considerable diagnostic information in secondary care will be of little additional value for a CDR in a primary care setting. In general, in diagnostic research, the positive predictive value of a diagnostic test is higher in secondary care, while on the other hand, the negative predictive value will be higher in primary care.

Some limitations of our study deserve further discussion. A drawback of our study is that the decision rule that we developed in this study was not externally validated in a different patient set. ROC curve analysis shows that the discriminative power of the CDR that we used in our study was moderate. This is explained because we only included signs and symptoms in our CDR and no additional diagnostic information such as ECG or biomarker testing. It is notoriously difficult to diagnose ACS based on clinical parameters only.[14,18] A previous study that derived and validated a clinical prediction score to rule out coronary heart disease in primary care found an AUC of 0.75 upon external validation using a CDR with eight signs and symptoms.[1] Although we did not externally validate our CDR, so-called 'overfitting' of the CDR for ACS that we derived is less likely because we used prespecified items that were previously used in another CDR for ACS in primary care not items that we derived from our own data.[12,19] The original decision rule that formed the basis of the presented CDR also included abnormal ECG examination at the time of patient presentation. In our study, no ECGs at the time of presentation to the GP were available, however. An ECG was performed later (but within 24 hours), on arrival in hospital or at the patient's home in case of non-referral. We therefore only included the clinical items of the original decision rule, which may also explain the CDR's restricted performance. This is, however, according to Dutch clinical practice: although many Dutch GPs have an ECG facility in their practice, they often do not have portable facilities to record an ECG at the patients home in case of a house call.

Another limitation of our study is that one can argue whether we chose the correct threshold for low-, intermediate- and high-risk groups. No established thresholds for such risk stratification exists and we chose thresholds of 10% and 20% since they seemed reasonable thresholds given the average ACS risk of 22% in our population. To test for the validity and robustness of our findings, we performed a sensitivity analysis using the lowest and highest quintiles as thresholds. This analysis yielded similar results with respect to overall agreement and unjustified low risk estimations by the GP.

Conclusion

Judged by the AUC, the GP more accurately classified patients as with or without ACS than the CDR and there was an agreement between the risk estimation of the GP and a CDR in 51% of patients suspected of ACS. Also, GPs systematically overestimate a patient's risk for ACS, while on the other hand, a small number of ACS patients were missed by the GP in this study. Our study shows that in the diagnostic accuracy of ACS without ECG, the CDR adds to ruling in cases that based on the judgement by the GP would have been missed.

Declaration

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Ethical approval: The study protocol was approved by the Medical Ethics Committee of the University Medical Center Utrecht, The Netherlands. All patients provided written consent.

Conflict of interest statement: All authors are fully independent from the funder. Funder is not involved in gathering, analysing and publishing of data. No other conflicts of interest.

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