PRE-TEST CHARACTERISTICS OF UNSTABLE ANGINA PATIENTS WITH OBSTRUCTIVE CORONARY ARTERY DISEASE CONFIRMED BY CORONARY ANGIOGRAPHY

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ABSTRACT

Objective As the mortality and rate of obstructive coronary artery disease (CAD) is low in patients with unstable angina (UA), better pre-test selection criteria for acute coronary angiography (CAG) is warranted. We aimed to validate the current guidelines against other clinical variables as predictors of obstructive CAD in UA patients referred for acute CAG.

Methods From 2005 to 2012, all CAGs performed at the University Hospital of North Norway, the sole provider of CAG in the region, were recorded in a registry. We included 979 admissions of UA in the primary catchment area to enable retrospective collection from patient hospital records. Obstructive CAD was defined as ≥50% stenosis and considered prognostically significant if found in the left main stem, proximal LAD or in all three main coronary arteries. Characteristics were analysed by logistic regression analysis. A score was developed using odds ratios from significant factors in a multivariable model.

Results The overall rate of obstructive CAD was 45%, and the rate of prognostically significant CAD was 11%. The ACC/AHA and ESC guidelines had an area under the curve (AUC) of 0.58. Adding clinical information increased the AUC to 0.77 (95% CI 0.74-0.80). Applying the derived score, we found that 56% (*n*=546) of patients with a score of <13 had a negative predictive value of 95% for prognostic obstructive CAD.

Conclusions CAG can be postponed or cancelled in up to 56% of UA patients, by improving pre-test selection criteria with the addition of clinical parameters to current guidelines.

KEY QUESTIONS

What is already known about this subject? Unstable angina patients have a low mortality and rate of obstructive coronary artery disease. Applying symptom characteristics to traditional risk factors improves risk prediction models in stable angina.

What does this study add? This study demonstrated that by structuring symptom characteristics and clinical variables it is possible to improve pre-test selection beyond guidelines risk criteria.

How might this impact clinical practise? Better pre-test selection criteria for acute coronary angiography in unstable angina patients will reduce cost for health care systems and avoid exposing patients to unnecessary risk of complications. Prospective studies are needed to validate our findings.

KEYWORDS

Acute coronary syndrome, myocardial ischemia, chest pain, percutaneous coronary intervention

INTRODUCTION

Acute chest pain is the second most common presentation in the emergency department.[1] It poses a challenge to health care systems, as critical conditions require prompt diagnosis and treatment, whereas benign disorders need to be eliminated early to increase patient safety and reduce costs. Acute coronary syndrome refers to chest pain presumably caused by acute myocardial ischemia, and encompasses myocardial infarction (MI) and unstable angina (UA). Patients with UA have no evidence of myocardial necrosis.[2 3] New, high-sensitive cardiac troponin (hs-cTn) assays detect myocardial necrosis in a group of patients previously diagnosed as UA, thus changing the diagnosis to MI.[4-6] Consequently, the present UA population have lower mortality and are less likely to have obstructive coronary artery disease (CAD).[5 7 8]

Despite this, the fear of missing an impending MI results in a liberal referral practice of patients with presumed UA to acute coronary angiography (CAG). ESC and ACC/AHA guidelines for the management of acute coronary syndrome in patients without ST elevation recommend performing CAG within 72 hours if there is either an intermediate GRACE risk score (109-140), relevant comorbidity, a positive electrocardiogram or stress test, or recurrence of symptoms.[3 9]

A better pre-test selection is warranted. We aimed to validate the GRACE risk score, guidelines risk criteria and other clinical factors as predictors of obstructive CAD in UA patients referred for acute CAG.

METHODS

Study population

Between January 1, 2005, and December 31, 2012, all coronary angiographies (CAG) performed at the University Hospital of North Norway were recorded in a clinical registry. The University Hospital is the sole provider of CAG in Northern Norway, serving 10 local hospitals and a population of 479,000. We included the 1,936 CAGs performed in UA patients from the local catchment area to facilitate further retrospective data collection from patient hospital records. Admissions with more than one procedure were only included once (*n*=35), and patients with a peak troponin level above the 99th percentile (*n*=813) were excluded.[2] We also excluded patients incorrectly registered with UA (*n*=46) or

the University Hospital as their local hospital (*n*=28), and foreign patients (*n*=2). Patients who had undergone percutaneous coronary intervention (PCI) within the last 30 days (*n*=33) were excluded because 91% of these patients had obstructive CAD, warranting acute CAG in these patients. Subsequently, the final cohort included 979 UA admissions. The study was a clinical audit and therefore not subject to evaluation by the Regional Committee of Ethics. It was approved by the Data Protection Official for Research at the University Hospital of North Norway (#0217).

Data collection

The registry contains data from all consecutive CAGs registered by the operator at the time of the procedure. Linkage to troponin levels from the Department of Clinical Chemistry at the University Hospital of North Norway and to patient hospital records was done by the national 11-digit identification number. From patient hospital records, we collected data on symptoms and clinical findings at presentation, preceding symptoms, stress tests, risk factors, comorbidities and medication. The extent of CAD was evaluated by the interventional cardiologist. To ensure high sensitivity, obstructive CAD was conservatively defined as ≥50% angiographic diameter stenosis in any epicardial coronary artery.[10] Prognostic significant obstructive CAD was defined as obstructive CAD in the main stem, proximal left anterior descending artery or in all three main coronary vessels (three-vessel disease).[10 11] In patients with prior coronary artery bypass grafting, only those with new obstructive CAD were labelled with obstructive CAD. From July 2009, hs-cTnT replaced standard troponin assay. A standard troponin value of 10 ng/L corresponds to 30 ng/L hs-cTnT and accordingly the troponin values measured up to July 2009 were multiplied by a factor of three.[12 13]

We registered the threshold of angina by the Canadian Cardiovascular Society grading of angina pectoris. A variation in the threshold of angina of more than two grades was defined as a variable threshold. Refractory angina was recorded if intravenous nitroglycerine was given. We defined a history of typical angina as (1) substernal chest pain or discomfort, (2) provoked by physical exertion or emotional stress and (3) relieved by rest within minutes. Atypical angina was defined as two of these characteristics, and patients with one of these characteristics were defined as having noncardiac chest pain. A positive stress electrocardiogram was defined as ≥1 mm of ST-segment depression or elevation or

stress-induced chest pain. The guideline criterion of acute heart failure was defined as Killip class II-IV. We calculated the GRACE risk score according to the Fox model for death between hospital admission and 6 months (http://www.outcomes-umassmed.org/grace/files/GRACE_ RiskModel_Coefficients.pdf). Family history of CAD was registered in patients with first-degree relatives with premature CAD or a positive family history stated in the hospital record but not further specified. Diabetes mellitus was classified as HbA1c ≥6.5% or registered in the hospital records. Hypercholesterolemia was classified as use of lipid-lowering drugs or serum cholesterol level of ≥6.5 mmol/L.

Statistical analysis

Patient characteristics were reported as counts, percentages or means ± standard deviation. Logistic regression analysis was used to investigate predictors of obstructive CAD. In the final multivariable model, we included the predictors with clinical significance and $p<0.05$. We included interaction terms significantly improving the model by *c* statistics and the Net Reclassification Improvement. The Hosmer-Lemeshow goodness-of-fit test was not significant for the final model. To investigate the main contributing variables of the GRACE risk score and guidelines risk criteria, we used a forward selection logistic regression analysis, with inclusion at $p<0.05$. Time trends in the extended cohort of UA (n=1,936) and non-ST segment elevation MI (NSTEMI) (n=1221) were significance tested by logistic regression.

An increasing number of variables with missing information was significantly associated with no obstructive CAD (OR 0.77 95% confidence interval (CI) 0.71-0.83). We tested this assumption for all variables included in the final model; it was found to be true for all variables except symptom characteristics. Therefore, missing information was combined in the reference group for the other variables, but classified as an independent predictive category for symptom characteristics.

We created a score based on the final multivariable model, weighting the variables with the odds ratio rounded off to the nearest integer. Applying the score, we estimated the proportion of patients that could have been safely discharged with a high negative predictive value, assuming no immediate yield of a CAG in patients without prognostically significant CAD. The discriminative performance of the GRACE risk score, the ESC and ACC/AHA guidelines risk criteria, and the derived model and its score were tested by *c*

statistics. Statistical analyses were performed with Stata 14.0 (Stata Corporation, College Station, TX, USA). All reported differences had two-sided p-values <0.05.

RESULTS

Patient characteristics

Of the 979 patients with UA, the overall rate of obstructive CAD was 45% (*n*=443), falling from 56% (*n*=70) in 2005 to 29% (*n*=33) in 2012 (*p* for trend=<0.001). Obstructive CAD of prognostic significance was prevalent in 11% (*n*=103) of the patients. Patient characteristics are shown in Table 1. Patients with obstructive CAD were older, more often male, smoked more, had more hypertension and hypercholesterolemia, a higher GRACE risk score and a higher rate of established CAD (Table 1).

When analysing time trends of UA and NSTEMI in our extended cohort, we found that the proportion of UA (*n*=1936) among acute CAG referrals remained stable (*p* for trend=0.304), whereas the occurrence of NSTEMI (*n*=1221) increased significantly from 2005 to 2012 (*p* for trend<0.001) with a step as hs-cTnT was implemented in 2009 (data not shown).

Table 1. Patient characteristics

	Obstructive CAD (*n* = 443)	No obstructive CAD (*n* = 536)	*P* value
Age (yr)	65±11	60±12	<0.001
Male gender (%, *n*)	67% (297)	52% (281)	<0.001
BMI (kg/m^2)	28±5	28±6	0.543
Heart rate (beats/min)	68±14	71±16	0.014
Systolic blood pressure (mmHg)	145±22	140±21	<0.001
Diastolic blood pressure (mmHg)	81±12	80±13	0.223
Use of anti-hypertensive drugs (%, *n*)	77% (339)	63% (339)	<0.001
Hypercholesterolemia (%, *n*)	74% (326)	66% (352)	0.008
Diabetes mellitus (%, *n*)	18% (79)	15% (82)	0.287

Established coronary artery disease (%, *n*)	59% (263)	39% (209)	<0.001
Previous MI (%, *n*)	36% (158)	21% (113)	<0.001
Previous PCI (%, *n*)	46% (205)	33% (177)	<0.001
Previous CABG (%, *n*)	18% (80)	14% (74)	0.069
Family history of CAD (%, *n*)	50% (220)	53% (285)	0.274
Smoking status			0.008
Current smoker (%, *n*)	29% (130)	27% (143)	
Former smoker (%, *n*)	44% (195)	38% (201)	
GRACE risk score	83±22	76±24	<0.001

Values are % (*n*) or mean±SD. BMI indicates body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction and PCI, percutaneous coronary intervention.

Performance of GRACE risk score and risk criteria from guidelines

We found that both patients with and without obstructive CAD had low GRACE risk scores, 83 versus 76, respectively. In total, less than 1% (*n*=7) of the patients with UA had a high GRACE risk score (>140), and 11% (*n*=104) had an intermediate GRACE risk score (109-140). In patients with a high GRACE score, 5 of 7 patients had obstructive CAD versus half of the patients with an intermediate GRACE score. According to the ESC guidelines, 21% (*n*=202) of the patients in our study could have been managed conservatively. However, 26% (*n*=52) of these patients had obstructive CAD and 5.5% (*n*=11) had prognostic obstructive CAD. ACC/AHA guidelines would allocate conservative treatment to 31% (*n*=299) of the patients, of which 32% (*n*=96) had obstructive CAD and 4.3% (*n*=13) had prognostic obstructive CAD. High-risk criteria from ESC and ACC/AHA guidelines were present in 25% (*n*=242) and 22% (*n*=216) of the patients, respectively. These patients did not have more obstructive or prognostic obstructive CAD than patients with intermediate-risk criteria (ESC: *p*=0.13 and *p*=0.88; ACC/AHA *p*=0.84 and *p*=0.56).

GRACE risk score, and ESC and ACC/AHA guidelines had equivalent area under the curve (AUC) for obstructive CAD, with AUC of 0.59 (95% CI 0.55-0.62), 0.58 (95% CI 0.56-0.61), and 0.58 (95% CI 0.55-0.61), respectively. Age alone had a significantly higher AUC of

0.61 (95% CI 0.58-0.65, *p*=0.037) (Figure 1). The main contributing variables in the GRACE risk score and guidelines risk criteria were age, systolic blood pressure at admission, prior PCI, Killip class and positive stress testing. We did not find more ST-T abnormalities in the electrocardiogram of patients with obstructive CAD (Table 2).

Table 2. The main contributing variables of the GRACE risk score and ESC and ACC/AHA guidelines risk criteria predicting obstructive coronary artery disease

Variables in GRACE risk score, and ESC and ACC/AHA guidelines risk criteria	Odds ratios (95% confidence interval)	
	Univariable model	Forward selection model (p <0.05)
Age (yr)*	1.04 (1.03-1.05)	1.03 (1.02-1.04)
Heart rate (beats/min)*	0.99 (0.98-1.00)	
Systolic blood pressure (mmHg)*	1.01 (1.00-1.02)	1.01 (1.00-1.01)
Creatinine (µmol/L)*	1.01 (1.00-1.01)	
Estimated GFR < 60 mL/min/1,73m^{2}†	1.43 (0.88-2.32)	
Killip class*†	1.49 (1.02-2.16)	1.50 (1.01-2.22)
Diabetes mellitus†	1.20 (0.86-1.69)	
Left ventricular ejection fraction < 40%†	2.10 (0.95-4.63)	
Positive stress test†	1.60 (1.21-2.11)	1.73 (1.28-2.33)
Refractory angina†	0.97 (0.58-1.61)	
Prior CABG†	1.38 (0.97-1.94)	
Prior PCI‡	1.75 (1.35-2.26)	1.67 (1.27-2.20)
Prior PCI < 6 months§	1.31 (0.78-2.20)	
Electrocardiogram		
ST-segment deviation*	1.03 (0.62-1.73)	
New ST-depression§	1.29 (0.68-2.44)	
Dynamic ST-T changes‡	0.80 (0.49-1.31)	

CABG indicates coronary artery bypass graft; GFR, glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; and PCI, percutaneous coronary intervention. *GRACE risk score; †both guidelines; ‡ESC guidelines; §ACC/AHA guidelines

Prediction of obstructive coronary artery disease

A prior history of typical angina symptoms, Canadian Cardiovascular Society angina grade 3 or 4, no variable threshold of exertional angina, no history of palpitations, prior PCI, positive stress testing, smoking, hypertension, age over 65 years and male gender all added independently significant information in a multivariable model, increasing the AUC for obstructive CAD to 0.77 (95% CI 0.74-0.80) (Table 3, Figure 1), significantly higher than the GRACE risk score and guidelines risk criteria. The significant interaction between age and prior PCI was also included. From the model, we derived a score predicting obstructive CAD with an odds ratio of 1.40 (95% CI 1.33-1.47) per score level increase. With a cut-off level of <13, the negative predictive value was 95% for prognostic obstructive CAD in 56% (*n*=546) of UA patients referred for acute CAG. For the 44% (*n*=295) of patients with a score <12 the negative predictive value was 97%. Stratified by sex, a cut-off level of <14 gave a negative predictive value of 95% for 82% (*n*=330) of females, and a cut-off level of <12 and <13 gave negative predictive values of respectively 96% for 20% (*n*=177) and 93% for 43% (*n*=251) of males (Table 4).

In univariable analysis, shorter pain duration predicted obstructive CAD (<2-6 h, OR 1.82, 95% CI 1.34-2.48), whereas chest pain related to change in body posture (*n*=23) gave lower odds for obstructive CAD (OR 0.18, 95% CI 0.05-0.68). We found that pain relief by nitrates, dyspnoea, pain radiation, and number of chest pain episodes during the last 24 hours were not associated with obstructive CAD. Neither were chest wall pain, pain related to breathing or self-reported similarity to prior CAD symptoms, but most patient records lacked this information. The few patients with typical angina symptoms at admission (*n*=11) did not have a significantly increased risk of obstructive CAD (OR 1.49, 95% CI 0.41-5.41), but those with atypical symptoms had (*n*=121) (OR 2.07, 95% CI 1.11-3.86). A GRACE risk score ≥109 was not significantly associated with obstructive CAD (OR 1.37, 95% CI 0.92-2.04).

Table 3. Univariable and multivariable predictors of obstructive coronary artery disease in unstable angina patients.

Characteristics	*n* = 979	Univariable model, OR (95% CI)	Multivariable model, OR (95% CI)	Score

Age > 65 years	410	1.92 (1.49-2.49)	2.94 (1.97-4.41)	3
Male gender	578	1.85 (1.42-2.40)	2.03 (1.48-2.79)	2
Prior PCI	382	1.75 (1.35-2.26)	1.85 (1.21-2.81)	2
Hypertension*				
1	303	2.79 (1.82-4.28)	2.26 (1.36-3.75)	2
2	151	2.27 (1.40-3.69)	2.08 (1.20-3.61)	2
3	372	3.05 (2.01-4.63)	2.36 (1.43-3.89)	2
Current smoker	273	1.48 (1.06-2.06)	2.53 (1.70-3.77)	3
Previous smoker	396	1.58 (1.17-2.14)	1.37 (0.97-1.95)	1
Positive stress test	278	1.60 (1.21-2.11)	1.85 (1.34-2.56)	2
Best CCS grade				
1	84	1.59 (1.01-2.51)	0.91 (0.54-1.56)	0
2	91	2.12 (1.36-3.30)	1.05 (0.62-1.78)	0
3-4	107	4.71 (2.97-7.48)	1.83 (1.03-3.26)	2
No variable threshold	253	4.03 (2.96-5.48)	1.96 (1.28-2.99)	2
Symptoms before admission				
Noncardiac pain	243	2.50 (1.58-3.96)	1.89 (1.14-3.14)	2
Atypical angina	284	5.75 (3.67-9.01)	3.40 (2.01-5.75)	3
Typical angina	141	6.49 (3.90-10.8)	3.65 (1.99-6.69)	4
Missing	145	3.10 (1.87-5.12)	2.36 (1.36-4.08)	2
No palpitations	844	1.93 (1.26-2.94)	1.71 (1.07-2.74)	2
Interaction: Prior PCI and age over 65 years			0.50 (0.28-0.91)	-2
AUC			0.77 (0.74-0.80)	

AUC indicates area under the curve; CI, confidence interval; CCS, Canadian Cardiovascular Society grading of angina pectoris; GRACE, Global Registry of Acute Coronary Events; PCI, percutaneous intervention and OR, odds ratio. *1: Use of antihypertensive drugs and normal blood pressure on admission, 2: high blood pressure on admission, 3: 1+2.

Table 4. Prevalence of obstructive coronary artery disease in unstable angina patients by score level.

Score	*n*	Obstructive CAD, *n* (row %)	Prognostic obstructive CAD, *n* (row %)	Revascularized, *n* (row %)
≤ 5	25	-	-	-
6-7	54	4 (7.4%)	-	3 (5.6%)
8	74	15 (20%)	2 (2.7%)	15 (20%)
9	53	12 (23%)	2 (3.8%)	12 (23%)
10	114	26 (23%)	3 (2.6%)	23 (20%)
11	106	42 (40%)	7 (6.6%)	35 (33%)
12	120	49 (41%)	12 (10%)	36 (30%)
13	101	56 (55%)	17 (17%)	46 (46%)
14	90	63 (70%)	11 (12%)	51 (57%)
15	84	49 (58%)	10 (12%)	46 (55%)
16-17	97	78 (80%)	23 (24%)	69 (71%)
≥ 18	61	49 (80 %)	16 (26%)	46 (75%)
AUC		0.77 (0.74-0.79)	0.72 (0.68-0.77)	0.75 (0.71-0.78)

AUC indicates area under the curve and CAD, coronary obstructive artery disease.

DISCUSSION

In our population-based cohort, we have demonstrated that among patients with UA referred for acute CAG the rates of obstructive CAD were low, despite clinical decision making before referral to CAG. By structuring symptoms characteristics and clinical information, it is possible by applying a new risk score with obstructive CAD as endpoint instead of mortality to exclude a higher number of patients with a higher accuracy than the guidelines risk criteria.

There is to our knowledge no other studies using symptoms to predict obstructive CAD in UA patients. The HEART score includes the clinicians suspicion of critical disease to predict MACE in an all-cause chest pain population.[14] In stable angina, typical angina

symptoms added to risk scores is known to improve the prediction of obstructive CAD,[15 16] while in UA patients, typical angina symptoms predicts positive stress tests.[17] In our study, we found that a history of typical angina with a stable or consistently decreasing threshold in the time prior to the acute admission was strongly associated with obstructive CAD.

Prognostic implication of revascularisation in unstable angina

There is limited knowledge of the prognostic implications of CAG and an invasive strategy for UA patients. Available trials do not report separate findings for UA or have not implemented newer troponins to discriminate between MI and UA. The most recent meta-analyses of existing trials up to 2015, did not show an appreciable benefit of routine revascularisation for UA and NSTEMI on mortality or MI rates as a previous meta-analyses did.[18-21] As 90% of NSTEMI patients have obstructive CAD,[22 23] it seems fair to assume that the potentially prognostic benefit in the UA population with no necrosis, low GRACE risk score, and a low rate of obstructive CAD applies to few of the patients. In stable angina patients, evidence supports prognostic benefit from revascularisation if obstructive CAD in left main stem, proximal left anterior descending artery or three vessel disease.[10 11]

The interaction term between age and prior PCI attenuate the high risk of new obstructive CAD in elderly for those with prior revascularization indicating a possible benefit of secondary prevention.

High-sensitive troponins: A game changer?

While UA was regarded as high-risk patients in the past, we now observe that the present-day UA population have both low mortality and morbidity. This is likely due to the implementation of increasingly sensitive troponins detecting myocardial necrosis and reclassifying high-risk UA patients as MI, thereby leaving a healthier UA population. This is supported by increasing rates of NSTEMI following implementation of hs-cTn,[4 13 24 25] and no difference in mortality between hs-cTn-negative patients and the background population.[5] Further, trials demonstrate a 90-day mortality and MI rate for hs-cTnT-negative UA patients of 0.6% and 1.7%, respectively, and a 30-day combined death and MI rate in high-risk UA patients of approximately 2%.[7 8 26]

High-sensitivity troponins seem to be the major discriminating risk factor for non-ST segment elevation acute coronary syndrome, and should perhaps receive a larger part in discriminating risk than in current guidelines.[3 9] Further, it has been suggested that

increasingly sensitive troponins, will lead to UA becoming a redundant diagnosis.[27] However, we did not find the expected reciprocal decrease in UA.[4 13 24 25] A plausible reason for the stable frequency of UA is that a larger proportion of the UA patients previously treated conservatively, are now referred for acute CAG. As the UA diagnosis is based on clinical suspicion of myocardial ischemia and negative troponins ruling out MI, we have no objective rule-out test. In a time of health anxiety and overdiagnosis, the fear of uncertainty among clinicians and patients may lead to the overuse of presumed UA as indication for acute CAG, even in patients with low clinical suspicion of CAD. This is consistent with the low and falling rate of obstructive CAD and emphasize the need of a better pre-test selection, also in the hs-cTn era. In a stable chest pain population referred to a cardiologist, two fifths were found to have a panic disorder.[28] In our UA population, we found that palpitations, a known symptom of panic disorder, predicted no obstructive CAD.[29] Panic attacks is likely the cause of chest pain in some of our presumed UA patients.

Relevance of guidelines risk criteria and GRACE risk score in the low mortality unstable angina population

The GRACE risk score predicts 3-year mortality in acute coronary syndrome with a superior AUC of 0.82.[30] The overall low GRACE score observed in both patients with and without obstructive CAD is reassuring and supports a low mortality in the present-day UA population. It may also explain why the GRACE risk score and guidelines encompassing NSTEMI had poor discriminative ability for obstructive CAD in UA patients.[3 30] Accordingly, a low rate of obstructive CAD, MI and death, as well as an unsure prognostic benefit of revascularisation in the hs-cTn-negative UA patients, questions the resource utilization of acute CAG in most UA patients. A better pre-selection of UA patients before acute CAG will alleviate this. Guidelines would allocate one fourth of the UA patients in our study to conservative treatment. However, by adding symptoms to traditional risk factors, our study indicates that it is possible to rule out or delay CAG in well over half of the UA patients with less obstructive CAD using clinical variables added to traditional risk factors.

Strengths and limitations

The major strengths of our study are the inclusion of all acute CAGs performed in UA patients within a confined geographical area for eight subsequent years, the application of the Third Universal Definition of MI to the whole cohort, and that all variables included in

our risk score are obtained in daily clinical practice. A potential limitation is the relatively small numbers of patients with prognostic obstructive CAD. We have exclusively investigated UA patients referred to CAG, and thereby do not know how the score performs in an extended chest pain/UA population. The accuracy and consistency of the information collected from hospital records as well as many missing variables are further limitations. To minimize observer bias, the CAG results were not available during the data collection. However, if the CAG was soon after followed by coronary artery bypass grafting or gastroscopy, this was visible as separate notes labelled accordingly, indicating the CAG result. Since we excluded patients with PCI within 30 days, we could not test post-MI angina and the ACC/AHA criterion of PCI within 6 months was only applicable for 1-6 months. Further, we did not have enough information on ESC guidelines' recurrence of symptoms to validate its potential role. We applied the peak troponin value, thereby excluding UA patients with chronically elevated troponin, presumably leaving a healthier cohort. As the adjustment for standard troponin to hs-cTnT was only applicable for patients with troponin values above the limit of detection, we may have included NSTEMI patients before the implementation of hs-cTnT in 2009. The same yearly numbers of UA patients throughout the study period highlights that UA is still a relevant issue in the high-sensitive troponin era.

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DISCLOSURES

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FIGURE LEGENDS

Figure 1. Prediction of obstructive coronary artery disease in unstable angina patients referred for coronary angiography. Receiver operating characteristics curves for age, GRACE risk score, ESC and ACC/AHA guidelines risk criteria, and the new risk score model. AUC indicates area under the curve.