American Journal of Emergency Medicine (2012) xx, xxx–xxx

The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Original Contribution

Risk scores prognostic implementation in patients with chest pain and nondiagnostic electrocardiograms

Alberto Conti MD*, Claudio Poggioni MD, Gabriele Viviani MD, Yuri Mariannini MD, Margherita Luzzi MD, Gabriele Cerini MD, Erica Canuti MD, Maurizio Zanobetti MD, Francesca Innocenti MD, Riccardo Pini MD

Emergency Medicine, Department of Critical Care Medicine and Surgery, University of Florence and Careggi University Hospital, 50134 Florence, Italy

Received 17 December 2011; revised 23 January 2012; accepted 26 January 2012

Abstract

Background: Several risk scores are available for prognostic purpose in patients presenting with chest pain.

Aim: The aim of this study was to compare Grace, Pursuit, Thrombolysis in Myocardial Infarction (TIMI), Goldman, Sanchis, and Florence Prediction Rule (FPR) to exercise electrocardiogram (ECG), decision making, and outcome in the emergency setting.

Methods: Patients with nondiagnostic ECGs and normal troponins and without history of coronary disease underwent exercise ECG. Patients with positive testing underwent coronary angiography; otherwise, they were discharged.

End point was the composite of coronary stenosis at angiography or cardiovascular death, myocardial infarction, angina, and revascularization at 12-month follow-up.

Results: Of 508 patients considered, 320 had no history of coronary disease: 29 were unable to perform exercise testing, and finally, 291 were enrolled. Areas under the receiver operating characteristic curves for Grace, Pursuit, TIMI, Goldman, Sanchis, and FPR were 0.59, 0.68, 0.69, 0.543, 0.66, and 0.74, respectively ($P < .05$ FPR vs Goldman and Grace). In patients with negative exercise ECG and overall low risk score, only the FPR effectively succeeded in recognizing those who achieved the end point; in patients with high risk score, the additional presence of carotid stenosis and recurrent angina predicted the end point (odds ratio, 12 and 5, respectively). Overall, logistic regression analysis including exercise ECG, coronary risk factors, and risk scores showed that exercise ECG was an independent predictor of coronary events ($P < .001$).

Conclusions: The FPR effectively succeeds in ruling out coronary events in patients categorized with overall low risk score. Exercise ECG, nonetheless being an independent predictor of coronary events could be considered questionable in this subset of patients.

1. Introduction

Patients with chest pain (CP) represent a substantial percentage of visits to the emergency department (ED). The management of high-risk patients with abnormal

* Corresponding author. Tel.: +393397472294; fax: +390558947938.
E-mail address: aaaconti@hotmail.com (A. Conti).

0735-6757/$ – see front matter © 2012 Published by Elsevier Inc.
doi:10.1016/j.ajem.2012.01.028

electrocardiograms (ECGs) and elevated plasma level of troponin is established [1,2]. However, management is still questionable in low-risk patients with normal ECGs and normal troponin. This subset represents a large and heterogeneous population with low prevalence of coronary disease [3]: those patients with history of coronary disease need to be carefully evaluated, whereas those without could be considered for direct discharge. Moreover, in the population of patients without history of coronary disease, diagnostic strategy is costly and time consuming and represents a continuous challenge for cardiologists and emergency physicians. Determining which patients need in-hospital stress testing or outpatient evaluation is still a dilemma. Thus, effective clinical risk stratification on admission could move toward the threshold approach to clinical decision making and save resources [4]. To date, submitting patients to stress testing is usually based on nonstandardized clinical judgment [3,5]. Afterwards, several prediction rules are available for risk stratification in patients with CP; however, some of these have been tested in high-risk patients [6-10], whereas others, in low-risk patients [11-13]. In addition, some prediction rules are based on clinical data, whereas others used only major risk factors for atherosclerosis [14-16]. Therefore, which risk score to be used remains a challenge because no standardized prediction rule is yet available for stratification of patients with low-risk CP [3,17-19].

The objective of this study was to characterize a cohort of patients with CP presenting to the ED with risk scores calculated by Grace, Pursuit, TIMI, Goldman, Sanchis, and Florence Prediction Rules (FPRs) [6-9,11-13] and compare the scores to outcomes.

2. Methods

2.1. Patient selection

All consecutive adult patients with CP who presented to the ED of the tertiary care teaching Careggi Hospital were evaluated during the years 2008 and 2009. Patients with abnormal ECGs or positive troponin and patients with history of coronary disease or severe comorbidities or a life expectancy less than 6 months were excluded from the study. Patients with atypical CP were also excluded from the study. Tourists and inhabitants outside the catchment area of Careggi University Hospital serving a population of half a million were not enrolled in the study. All patients gave their consent for study participation. The study was conducted according to good clinical practice and the Declaration of Helsinki.

2.2. Management of patients and study protocol

All patients underwent a first-line, 6-hour workup including clinical evaluation, serial ECGs, and serial troponins [2,3,17-19]. Enrolled patients with CP were categorized by all the previously validated risk scores (Grace, Pursuit, TIMI, Goldman, Sanchis, and FPR) [6-13]. Patients were characterized also by the presence of coronary risk factors such as diabetes, metabolic syndrome, hypertension, high blood cholesterol, familial history of coronary disease, and current smoking. During the time of triage to the ED, a research nurse detects vital signs on admission (systolic and diastolic blood pressure, heart rate, oxygen saturation, and breaths per minute) and prospectively records variables used to calculate the scores for the risk stratification. During the visit, the resident checks the correctness of the findings and integrates them with information obtained from patients, relatives, caregivers, and previous hospital freely accessed folders available on the hospital network. To avoid overestimation of coronary risk profile, when information regarding some risk factors were unavailable, we assumed that the patient did not have that risk factor.

Diagnosis of diabetes was based on history or presence of fasting glucose greater than 125 mg/dL in at least 2 measurements or current hypoglycemic drug therapy. Diagnosis of metabolic syndrome consisted of history or presence of 3 or more of the following: high fasting glucose (>110 mg/dL), high blood pressure (systolic blood pressure >130 mm Hg and diastolic blood pressure >85 mm Hg), low high-density lipoprotein cholesterol (<40 mg/dL in men and <50 mg/dL in women), high triglycerides (>150 mg/dL), and central obesity (waist circumference >102 cm in men and >88 cm in women) [14-16]. Based on self-reported cholesterol levels, weights, and heights, mean total blood cholesterol levels of 200 mg/dL or higher were considered abnormal as is the presence of body mass index of 3.0 kg/m^2 and higher. Resting echocardiography was performed in all patients [17]. Unstable angina and acute myocardial infarction were defined according to international guidelines [1,2,20].

During observation in the ED, patients showing ischemic ECG changes and/or abnormal troponin levels and/or wall motion abnormalities at echocardiography were considered at high risk for coronary events; thus, they were referred for urgent coronary angiography [3,20].

Patients with typical CP and without history of coronary disease were considered at low risk and were submitted to early in-hospital exercise ECG by nonstandardized clinical judgment [3,5,17,21]. Patients with positive testing were considered at high risk for coronary events; they were admitted and referred for early coronary angiography. Conversely, patients with negative testing were considered at very low risk; they were discharged and followed up.

2.3. Characterization of patients by the risk scores

All patients with normal ECGs and normal troponins were considered at low risk for coronary events. They were categorized by all available risk scores: Grace, Pursuit, TIMI, Goldman, Sanchis, and FPR. Patients with at least very low scores (eg, Grace <96, Pursuit <5, TIMI <3,

Table 1 Clinical CP score

Location	Score
Substernal, precordial	+3
Left chest, neck, lower jaw, epigastrium	+1
Apex	−1
Radiation	
Either arm, shoulder, back, neck, lower jaw	+1
Character	
Crushing, pressing, heaviness	+3
Sticking, pleuritic, pinprick	−1
Associated symptoms	
Dyspnea, nausea, diaphoresis	+2

Goldman <2, Sanchis <2, and FPR <2) were considered as having a very low risk of future coronary events, whereas the remaining patients were considered as having a substantial risk of coronary events.

The novel FPR is a simple score strictly based on few clinical characteristics on presentation: CP score greater than 6, male sex, age 50 years or older, diabetes, or metabolic syndrome (Tables 1 and 2) [6-13].

2.4. Follow-up

All the enrolled patients were submitted to follow-up. Follow-up data were gathered with telephone interviews at 1 and 12 months by residents, and all events were analyzed by review of hospital records and laboratory data.

2.5. End point

End point was the composite of coronary stenosis at angiography or cardiovascular death, myocardial infarction, angina, and revascularization at follow-up.

2.6. Statistics analysis

Continuous variables were reported as mean ± standard deviation. Frequencies were shown as percentages and absolute values. Predictors of coronary event were analyzed with the logistic regression analysis by backward stepwise (likelihood ratio). Sensitivity and specificity of each prognostic score were evaluated by receiver operating characteristic (ROC) curves; the areas under the ROC curves were compared by the analysis of variance for summary data test. Continuous variables were compared through 1-way analysis of variance and t test, whereas percentages were compared with χ^2 or Fisher exact test when expected frequencies were less than 5%. Two-tailed $P < .05$ was considered statistically significant. Statistical analysis were performed using SPSS Package, version 17 (SPSS Inc, Chicago, IL).

Table 2 The FPR

CP score >6	+3
Age >50 y	+1
Male sex	+1
DM or MS	+1

DM indicates diabetes mellitus; MS, metabolic syndrome.

3. Results

3.1. Patients screened for the study

During the years 2008 to 2009, 508 patients with CP presenting nondiagnostic ECG were considered for enrollment. They underwent stress testing after the first-line evaluation inside the ED including serial ECGs and serial troponins. Of these, 320 patients (63%) had no history of coronary disease and fulfilled the inclusion criteria. Twenty-nine patients (9%) were unable to perform exercise ECG and were submitted to stress radionuclide myocardial perfusion imaging or stress echocardiography. Thus, 291 patients with nondiagnostic ECGs and normal troponins and without previous history of coronary disease were enrolled and underwent exercise ECG. No patient was lost to follow-up.

3.2. Study population

Baseline clinical characteristics of enrolled patients are reported in Table 3. Of 291 patients enrolled, 23 (8%) had positive exercise ECG, and 14 of these (61%) had coronary stenoses 50% or greater at angiography. Of these, those who presented occlusive coronary stenosis (ie, stenosis >70%, n = 7) underwent percutaneous transluminal coronary angioplasty, and 1 more patient underwent coronary artery bypass graft. The remaining 268 patients (92%) had negative testing, and 14 (5%) of these reached the end point during the 9.9 ± 4.9 months of follow-up. Of these, no patient was lost to follow-up. Thus, in our population, overall negative predictive value of exercise ECG in ruling out coronary events was 95%, and diagnostic accuracy was 92%.

3.3. Comparison of risk scores and outcomes

For each risk score, event rate increased as the prediction rule increased. The areas under the ROC curves for Grace, Pursuit, TIMI, Goldman, Sanchis, and FPR were 0.589, 0.683, 0.694, 0.536, 0.663, and 0.740, respectively ($P < .05$ FPR vs Goldman and Grace, Fig. 1). Of note, the areas under the ROC curves of the FPR and exercise ECG were similar (0.740 vs 0.733, respectively; $P = .93$) (Fig. 2). Among prognostic scores, FPR was the best, but results did not reach statistical significance ($P = .56$). In patients with very

Table 3 Baseline clinical characteristics and outcomes in patients with CP, negative first-line workup, and unknown coronary disease enrolled in the study and submitted to exercise ECG (n = 291)

	Total (n = 291)	FPR 0-1 (n = 89)	FPR 2-6 (n = 202)	*P*
Age (y)	61 ± 12	57 ± 13	62 ± 11	.0004
Female sex	64 (22%)	58 (65%)	51 (25%)	<.0001
Hypertension	146 (50%)	45 (51%)	101 (50%)	.004
DM	25 (9%)	0 (0%)	25 (12%)	<.0001
Smoker	67 (23%)	19 (21%)	48 (24%)	.66
Hyperlipidemia	64 (22%)	15 (17%)	49 (24%)	.23
Obesity	14 (5%)	3 (3%)	11 (5%)	<.0001
Familiarity of coronary disease	46 (16%)	15 (17%)	31 (15%)	.23
CP episodes >1 within previous 24 h	16 (5%)	1 (1%)	15 (7%)	<.0001
CP score	6.1 ± 2.2	4.6 ± 1.3	6.7 ± 2.2	<.0001
End point	28 (10%)	2 (2%)	26 (13%)	<.0001

End point: coronary stenosis at angiography or cardiovascular death, myocardial infarction, revascularization, and angina at follow-up.

low score, considered at very low risk (n = 89, FPR 0-1, 1% expected coronary events), the exercise ECG was negative in 1 of the 2 patients with coronary event at follow-up, and ruling out accounts for 99%. Conversely, analyzing the remaining subset of patient with higher score, considered at substantial risk (n = 202, FPR 2-6, 4%-25% expected coronary events), exercise ECG missed the diagnosis in 13 patients, and ruling out accounts for 94% (P = .003). Interestingly, in very low-risk patients, ruling out coronary disease by exercise tolerance test was comparable with FPR (99% vs 98%, respectively; P, not significant). However, at the logistic regression analysis model including exercise ECG, coronary risk factors, and risk scores, only exercise ECG was an independent predictor of coronary events (P < .001).

3.4. Exploring the potential clinical impact of scores in patients with negative exercise ECG

When patients with negative exercise ECG were evaluated according to the presence of very low score (eg, FPR <2, Sanchis <2, TIMI <3, and PURSUIT <5), only 1 patient with negative exercise ECG reached the end point; in this patient, no clinical predictors were available. However, in this subset of patients, FPR effectively succeeded in recognizing patients who achieved the end point, and FPR was superior to other scores (Table 4). Conversely, in patients with higher score (FPR ≥2, Sanchis ≥2, TIMI >2, and PURSUIT ≥5), 13 reached the end point. In this subset of patients, carotid stenosis (odds ratio [OR], 12.3; 95% confidence interval [CI], 1.9-79.5) and recurrent angina (ie, >1 episode of CP

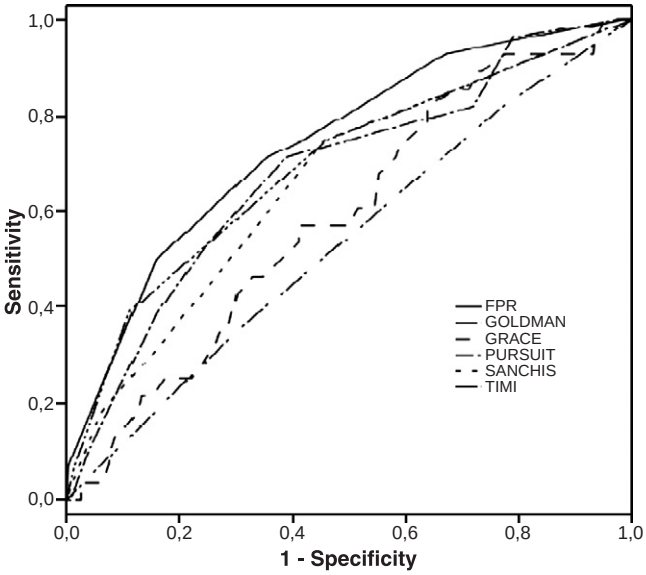

Fig. 1 Areas under the ROC curves of FPR (0.740), Goldman (0.536); Grace (0.589); Pursuit (0.683); Sanchis (0.663); TIMI (0.694); P < .05 vs Goldman and Grace.

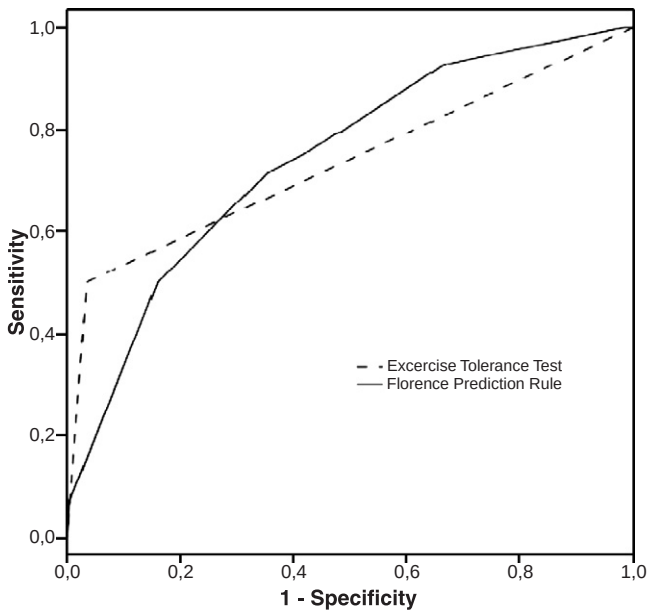

Fig. 2 Areas under the ROC curves of the FPR (0.740) and exercise tolerance test (0.733); P = .93.

Table 4 Power of prognostic scores (FPR <2, Sanchis <2, TIMI <3, and Pursuit <5) in separate patients at low risk from those at high risk in a population presenting CP and negative exercise ECG

	FPR	Sanchis	TIMI	PURSUIT
Low risk	1 (1.2%)	11 (4.9%)	11 (4.6%)	0 (0%)
Pearson χ^2	$P = .040$	$P = .633$	$P = .236$	$P = .059$
High risk	13 (7.1%)	3 (6.7%)	3 (9.7%)	14 (6.5%)

within previous 24 hours; OR, 4.5; 95% CI, 1.4-14.6) were independent predictors of coronary events (Table 5).

3.5. Patients submitted to other stress testing

Of the 29 patients unable to perform the exercise tolerance test, 5 with poor echocardiographic window underwent single photon emission computed tomography with pharmacologic stress (adenosine) (2 patients had positive test result, 1 of which was without events at follow-up; 3 patients had negative test result, and all without events at follow-up), whereas 24 patients were studied with pharmacologic stress (dobutamine) echocardiography (6 patients had positive test result, 1 of which was without events at follow-up; 18 patients had negative test result, only 1 of which was with event at follow-up). Overall, in this cohort, the negative predictive value was 95%, and positive predictive value was 75%.

4. Discussion

The present study analyzed the impact of clinical application of all the available risk scores as Grace, Pursuit, TIMI, Goldman, Sanchis, and the FPR [6-13] in a cohort of 291 patients with CP with negative first-line workup and without known coronary disease. These patients were usually labeled as low-risk patients, and they eventually showed coronary events up to 20% [3,5,17,21]. All scores effectively stratified the cardiovascular risk of patients with CP; however, which risk score could be used in the ED to improve time consuming and costly management remained to be stated. Moreover, who of the low-risk patients with CP without history of coronary disease need stress testing or can be discharged and followed up as outpatient is still a dilemma.

Results of present study showed that the novel FPR, a simple score strictly based on few clinical characteristics on presentation (CP score >6, male sex, age ≥50 years, diabetes, or metabolic syndrome), was more accurate than others in stratifying the risk of coronary events in patients with CP (Fig. 1). Areas under the ROC curves for Grace, Pursuit, TIMI, Goldman, Sanchis, and FPR were 0.59, 0.68, 0.69, 0.543, 0.66, and 0.74, respectively ($P < .05$ FPR vs Goldman and Grace). In patients with negative exercise ECG and overall low risk score, only the FPR effectively succeeded in recognizing those who achieved the end point; in patients with high risk score, the additional presence of carotid stenosis and recurrent angina predicted the end point (OR, 12 and 5, respectively). Nonetheless, the areas under the ROC curves of the FPR and exercise ECG were similar (0.740 vs 0.733, respectively; $P = .93$); only exercise ECG was recognized as an independent predictor of coronary event at logistic regression analysis ($P < .001$). Thus, exercise ECG remains to be the first-line stress testing in these patients with CP. However, ruling out coronary events by FPR accounted for 98% in patients with score 0 to 1 as compared with 99% of exercise ECG. This fact could represent an attractive option for CP screening in the ED of the crowded public health care delivery system; indeed, very low-risk patients account for one third of patients with CP in our series. In patients with negative exercise ECG, the FPR low score effectively succeeded in separating those at low from those at high risk (Table 4). Higher score eventually showed additional risk of coronary events if presenting carotid stenosis or recurrent angina (Table 5).

Thus, the hypothetical threshold approach to decision making in patients with CP matched with data of present study suggests that patients with typical CP need first-line screening by exercise ECG. When this testing is negative and the FPR is 0 to 1, patients could be safely discharged; conversely, when the FPR is 2 to 6, patients could be considered for additional stress testing, having a higher risk of coronary event. However, only patients presenting carotid stenosis or recurrent angina could be considered for the second-line costly in-hospital stress imaging. Eventually, these patients, having a risk of coronary event up to 15%, could be directly submitted to angiography.

Table 5 Risk of coronary event in patients with negative exercise ECG and different clinical characteristics

Parameter	Coronary event (OR)	95% CI
Carotid stenosis	12.3	1.9-79.5
CP episode >1 within previous 24 h	4.5	1.4-14.6
DM	0.71	0.1-3.4
Male sex	0.70	0.3-1.8

4.1. Strengths of present study

(1) To our knowledge, this is the first study in which patients with CP and initial negative workup were categorized with all the available risk scores of coronary events; (2) in patients without history of coronary disease, the novel FPR easily applicable in clinical practice seems to offer the best prognostication as compared with other risk score; (3) when FPR is low, exercise ECG prognostic yield may be

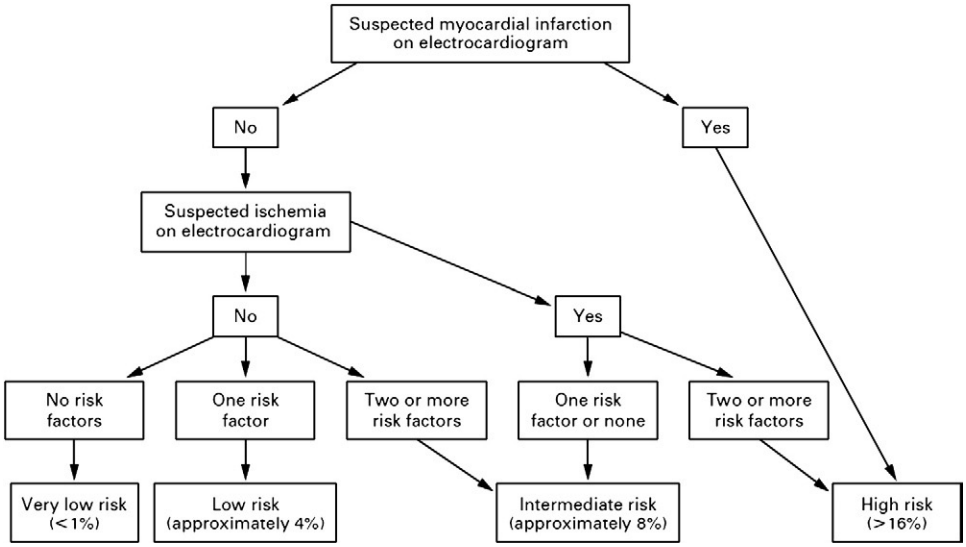

Fig. 3 Goldman algorithm. Four groups into which patients can be categorized according to risk of major cardiac events within 72 hours after admission.

questionable. Thus, these patients could be early discharged and eventually evaluated as outpatient economizing on in-hospital stress testing. (4) The remaining patients with higher score could be likely considered for early exercise ECG, and patients with negative testing eventually could be categorized as high-risk patients when presenting carotid stenosis or recent recurrent angina.

Previously multivariate algorithms have been developed in patients presenting CP to the ED. The management of high-risk patients including diagnostic ECGs and elevated plasma level of troponin is well established [6-9]; however, the management of low-risk patients with nondiagnostic serial ECGs and troponins is questionable. Indeed, low-risk patients represented a large and heterogeneous population with a low prevalence of coronary disease, and they presented different cardiovascular risk factors and clinical pattern and finally showed different outcomes. In this subset of patients, some risk scores allowed estimation for the need of intensive care [22,23]. Other models of risk scores well stratified the overall population of patients with CP [24,25]; however, they could not be easily integrated in clinical practice because of their complexity [24,25]. Other risk scores are specific in the prognostic evaluation of patients with a definite acute coronary syndrome [6-10,23]. The simplicity of the novel FPR is caused by the few variables considered and to the relevance given to clinical characteristics of CP at presentation. Indeed, the presence of high CP score has a high factor in cumulated risk score [13]. Patients with FPR low score showed a very low probability of future coronary events, less than 1%, data which are even lower than the risk reported in low-risk patients considered in previous studies [3,19].

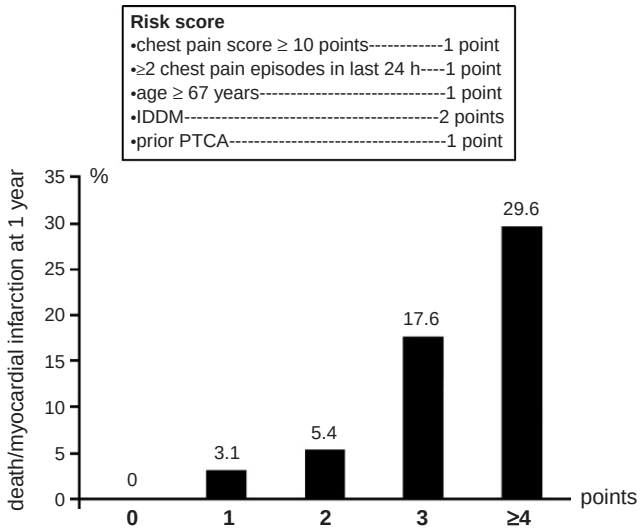

Fig. 4 Sanchis risk score. Risk categories according to risk score: very low risk, 0 points, primary end point 0%; low risk, 1 point, primary end point 3.1%; intermediate risk, 2 points, primary end point 5.4%; high risk, 3 points, primary end point 17.6%; and very high risk, 4 points, primary end point 29.6%. IDDM indicates insulin-dependent diabetes mellitus; PTCA, percutaneous transluminal coronary angioplasty.

5. Limits of the study

Results of present study were derived from patients presenting to our tertiary care teaching hospital and need validation in other centers. Moreover, the results in this cohort of patients are not extensible to symptomatic general population because of the exclusion of patients with prior diagnosis of coronary artery disease, resting echocardiography left ventricular dysfunction, or wall motion

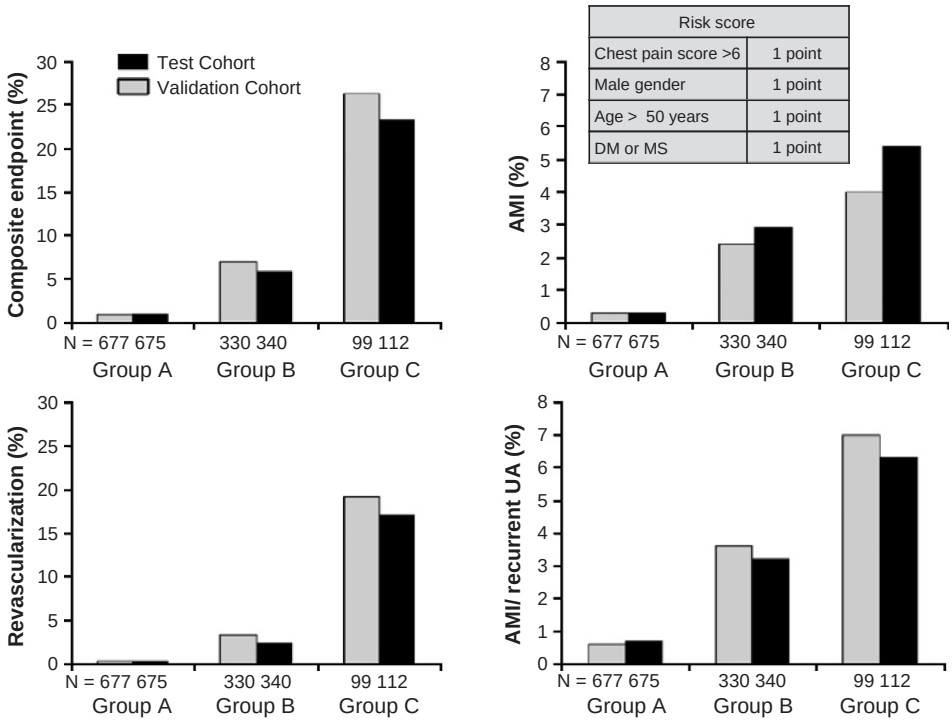

Fig. 5 Florence Prediction Rule. Rate of cardiac events including cardiovascular death, acute myocardial infarction, unstable angina, and revascularization in patients with CP, nondiagnostic ECG, and troponin. Florence Prediction Rule include the following: CP score greater than 6, 1 point; male sex, 1 point; age older than 50 years, 1 point; DM or MS, 1 point. Group A, score 0 to 1, low-risk patients, less than 1% cardiac events; group B, medium-risk, 2 to 4 points, 6% cardiac events; group C, 5 to 6 point, high-risk, 25% cardiac events. DM indicates diabetes mellitus; MS, metabolic syndrome.

abnormalities. In addition, the outcome evaluation based on dichotomy (normal/abnormal tests) may be a limitation of any screening workup in patients with CP. Finally, the optimal use of exercise ECG in patients with CP needs to be confirmed in a properly designed study beyond the preliminary results of this analysis.

PURSUIT (0–18)	Age, separate points for enrolment diagnosis	
	Decade [UA (MI)]	
	50	8 (11)
	60	9 (12)
	70	11 (13)
	80	12 (14)
	Sex	
	Male	1
	Female	0
	Worst CCS-class in previous 6 weeks	
	No angina or CCS I/II	0
	CCS III/IV	2
	Signs of heart failure	2
	ST-depression on presenting ECG	1

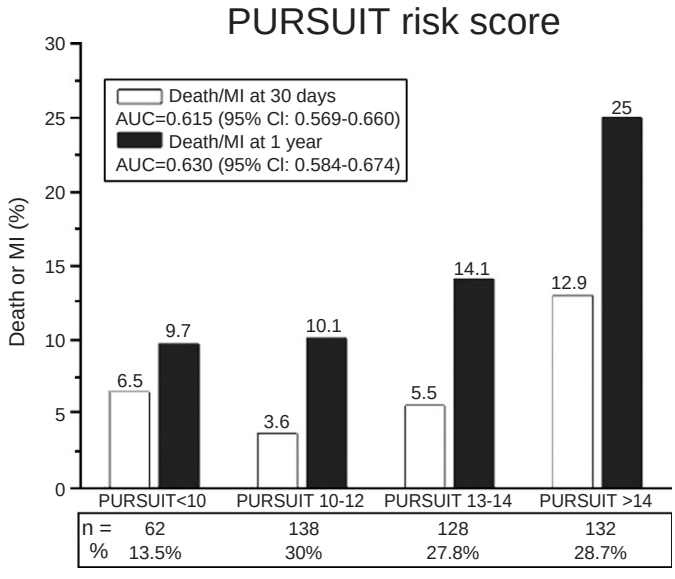

Fig. 6 Pursuit score. The 1-month and 1-year end point in the different risk groups for the Pursuit score. The Pursuit score was calculated from the initial clinical history, ECG, and laboratory values collected on admission. Pursuit score less than 10 indicates low-risk patients, MACE 10%.

TIMI (0–7)	Age ≥65 years	1
	≥3 risk factors for CAD	1
	Use of ASA (last 7 days)	1
	Known CAD (stenosis ≥50%)	1
	>1 episode rest angina in <24 h	1
	ST-segment deviation	1
	Elevated cardiac markers	1

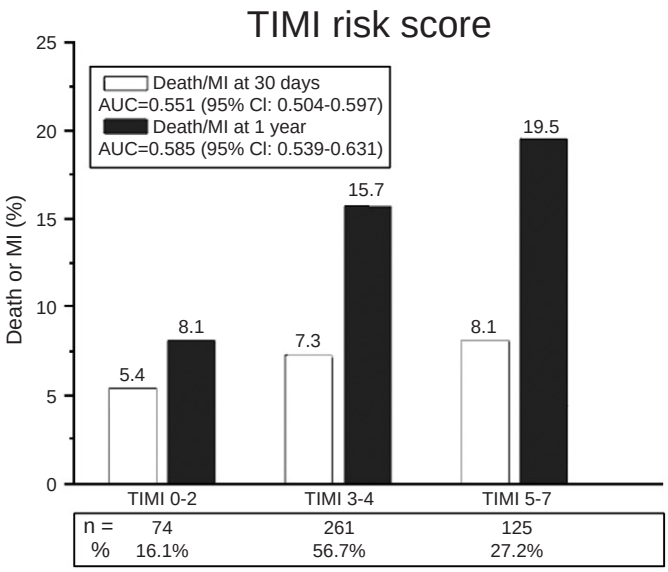

Fig. 7 TIMI risk score. The 1-month and 1-year end point in the different risk groups for the TIMI score. The TIMI score was calculated from the initial clinical history, ECG, and laboratory values collected on admission. TIMI score less than 3 indicates low-risk patients, MACE 8%.

GRACE (0–258)	Age (years)	
	<40	0
	40–49	18
	50–59	36
	60–69	55
	70–79	73
	≥80	91
	Heart rate (bpm)	
	<70	0
	70–89	7
	90–109	13
	110–149	23
	150–199	36
	>200	46
	Systolic BP (mmHg)	
	<80	63
	80–99	58
	100–119	47
	120–139	37
	140–159	26
	160–199	11
	>200	0
	Creatinine (mg/dL)	
	0–0.39	2
	0.4–0.79	5
	0.8–1.19	8
	1.2–1.59	11
	1.6–1.99	14
	2–3.99	23
	>4	31
	Killip class	
	Class I	0
	Class II	21
	Class III	43
	Class IV	64
	Cardiac arrest at admission	43
	Elevated cardiac markers	15
	ST-segment deviation	30

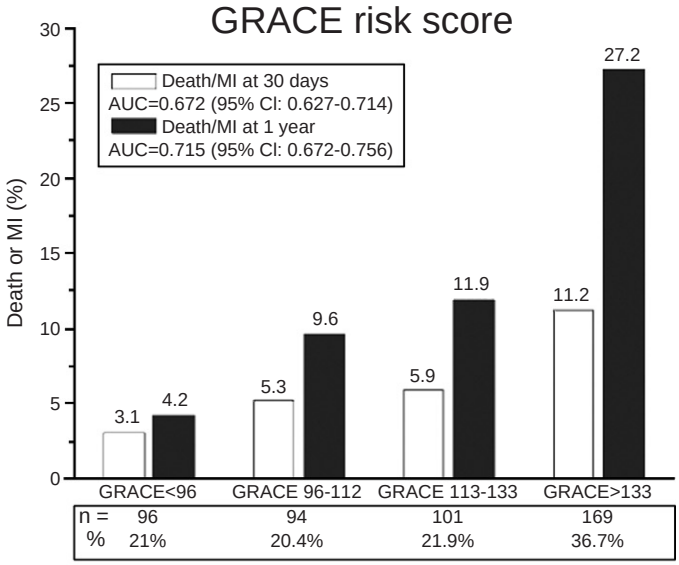

Fig. 8 Grace score. The 1-month and 1-year end point in the different risk groups for the GRACE score. The Grace score was calculated from the initial clinical history, ECG, and laboratory values collected on admission. Grace score less than 96 indicates low-risk patients, MACE 4%.

6. Conclusions

Florence Prediction Rule accurately predicts the risk of coronary events in patients with CP and nondiagnostic ECG, without existing known coronary disease, and may be a valuable tool for guiding management by threshold approach to clinical decision making. In these patients, FPR showed the best prognostication as compared with the other available risk scores such as Grace, Pursuit, TIMI, Goldman, and Sanchis. Overall, exercise ECG added prognostic value to the FPR, but its role was questionable in the subset of patients with very low score. In these patients, both exercise ECG and the FPR showed the same power in ruling out coronary events. Finally, in our series, patients with higher score and negative exercise ECG need additional stress imaging when presented carotid stenosis or recurrent angina, which were recognized as predictors of coronary events.

Appendix A. The scoring for the decision rules

Updated available risk scores in patients with CP are listed below, and Figs. 3 to 8 show the various scoring system. The risk scores that should be used as a tool for risk stratification and decision making on admission of patients with CP with nondiagnostic ECG and troponin in the ED are Goldman algorithm, Sanchis Score, FPR, TIMI risk score, Pursuit score, and Grace score [6-13]. They use clinical information as well as findings on an ECG to determine a percentage likelihood that a given patient is likely having a Major Adverse Coronary Event (MACE). These tools are more sensitive and more specific than clinicians for predicting MACE. However, these tools do not replace clinical judgment but serve as an aid in decision making. In the present study, patients with low-risk profile of future cardiac events were enrolled and stratified with all the aforementioned risk scores.

References

[1] Pollack Jr CV, Antman EM, Hollander JE. 2007 focused update to the ACC/AHA guidelines for the management of patients with ST-segment elevation myocardial infarction: implications for emergency department practice. Ann Emerg Med 2008;52(4):344-55.

[2] Van de WF, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2008;29(23): 2909-45.

[3] Lee TH, Goldman L. Evaluation of the patient with acute chest pain. N Engl J Med 2000;342(16):1187-95.

[4] Pauker SG, Kassirer JP. The threshold approach to clinical decision making. N Engl J Med 1980;302(20):1109-17.

[5] Stein RA, Chaitman BR, Balady GJ, Fleg JL, Limacher MC, Pina IL, et al. Safety and utility of exercise testing in emergency room chest pain centers: an advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association. Circulation 2000;102(12):1463-7.

[6] Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non–ST elevation MI: a method for prognostication and therapeutic decision making. JAMA 2000;284(7):835-42.

[7] Peterson JG, Topol EJ, Roe MT, Sapp SK, Lincoff AM, Deckers JW, et al. Prognostic importance of concomitant heparin with eptifibatide in acute coronary syndromes. PURSUIT Investigators. Platelet glycoprotein IIb/IIIa in unstable angina: receptor suppression using integrilin therapy. Am J Cardiol 2001;87(5):532-6.

[8] Fox KA, Dabbous OH, Goldberg RJ, Pieper KS, Eagle KA, Van de WF, et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). BMJ 2006;333(7578):1091.

[9] Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. Circulation 2000;102(17):2031-7.

[10] de Araujo GP, Ferreira J, Aguiar C, Seabra-Gomes R. TIMI, PURSUIT, and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTE-ACS. Eur Heart J 2005;26(9):865-72.

[11] Goldman L, Cook EF, Brand DA, Lee TH, Rouan GW, Weisberg MC, et al. A computer protocol to predict myocardial infarction in emergency department patients with chest pain. N Engl J Med 1988;318(13):797-803.

[12] Sanchis J, Bodi V, Nunez J, Bertomeu-Gonzalez V, Gomez C, Bosch MJ, et al. New risk score for patients with acute chest pain, non–ST-segment deviation, and normal troponin concentrations: a comparison with the TIMI risk score. J Am Coll Cardiol 2005;46(3):443-9.

[13] Conti A, Vanni S, Taglia BD, Paladini B, Magazzini S, Grifoni S, et al. A new simple risk score in patients with acute chest pain without existing known coronary disease. Am J Emerg Med 2010;28(2): 135-42.

[14] Isomaa B, Almgren P, Tuomi T, Forsen B, Lahti K, Nissen M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001;24(4):683-9.

[15] Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287(3):356-9.

[16] Executive summary of the third report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001;285(19):2486-97.

[17] Erhardt L, Herlitz J, Bossaert L, Halinen M, Keltai M, Koster R, et al. Task force on the management of chest pain. Eur Heart J 2002;23(15): 1153-76.

[18] Fox K, Garcia MA, Ardissino D, Buszman P, Camici PG, Crea F, et al. Guidelines on the management of stable angina pectoris: executive summary: the Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology. Eur Heart J 2006;27(11):1341-81.

[19] Hamm CW, Braunwald E. A classification of unstable angina revisited. Circulation 2000;102(1):118-22.

[20] Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol 2002;40(7): 1366-74.

[21] Polanczyk CA, Johnson PA, Hartley LH, Walls RM, Shaykevich S, Lee TH. Clinical correlates and prognostic significance of early

negative exercise tolerance test in patients with acute chest pain seen in the hospital emergency department. Am J Cardiol 1998;81(3):288-92.
[22] Goldman L, Cook EF, Johnson PA, Brand DA, Rouan GW, Lee TH. Prediction of the need for intensive care in patients who come to the emergency departments with acute chest pain. N Engl J Med 1996;334(23):1498-504.
[23] Ramsay G, Podogrodzka M, McClure C, Fox KA. Risk prediction in patients presenting with suspected cardiac pain: the GRACE and TIMI risk scores versus clinical evaluation. QJM 2007;100(1):11-8.
[24] Morise AP, Detrano R, Bobbio M, Diamond GA. Development and validation of a logistic regression-derived algorithm for estimating the incremental probability of coronary artery disease before and after exercise testing. J Am Coll Cardiol 1992;20(5): 1187-96.
[25] Morise AP, Jalisi F. Evaluation of pretest and exercise test scores to assess all-cause mortality in unselected patients presenting for exercise testing with symptoms of suspected coronary artery disease. J Am Coll Cardiol 2003;42(5):842-85.