ORIGINAL INVESTIGATION

Missed Opportunities in the Primary Care Management of Early Acute Ischemic Heart Disease

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Background: The role of primary care clinicians (physicians, nurse practitioners, and physician assistants) in evaluating acute cardiac ischemia is not well documented in office-based settings. Decision aids developed in the emergency department and other settings may help identify missed opportunities to intervene in symptomatic outpatients before hospitalization for acute myocardial infarction.

Methods: We conducted a case-control study of patients with no history of heart disease in a multisite group practice. Cases ("missed opportunities") were outpatients evaluated by primary care clinicians for chest pain or other anginal equivalents within 30 days of hospitalization for acute myocardial infarction and not referred for immediate hospital care (n=106). We identified 3 control patients matched to each case (n=318) using initial symptom and encounter date. We assessed the ability of several coronary risk prediction tools to identify missed opportunities.

Results: We identified 966 acute myocardial infarction hospital admissions among nearly 250 000 adults, including 261 (27.0%) with qualifying office visits in the preceding 30 days and 106 (11.0%) who were not directly referred for hospital care (cases). Chest pain (50.0%) and dyspnea (26.4%) were present in most of these cases. A Framingham risk score of 10% or greater was associated with missed opportunities (odds ratio, 19.5; 95% confidence interval, 9.3-40.6). Increased scores using the Diamond and Forrester probability and the Goldman prediction tool were also associated with missed opportunities.

Conclusions: Primary care clinicians play an important role in the management of acute cardiac ischemia. The Framingham risk score can help identify missed opportunities that warrant more intensive evaluation.

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THE DIAGNOSIS OF ACUTE ISchemic heart disease remains a challenging goal in ambulatory settings, particularly for patients with no history of coronary heart disease (CHD).[1-4] Up to 4% of symptomatic patients who present to emergency departments (EDs) are mistakenly discharged with an acute myocardial infarction (AMI),[5-7] resulting in increased mortality and significant litigation expenses[8] and spurring the development of prediction algorithms and triage strategies.[9-13] Few data exist on how frequently patients with AMI are seen in the office shortly before hospital admission and whether these visits might offer an opportunity to intervene if these high-risk patients were more reliably recognized.

Missed diagnosis of AMI has emerged as a leading cause of primary care–based malpractice litigation, suggesting a significant role for primary care clinicians (physicians, nurse practitioners, and physician assistants) in the early management of acute ischemic heart disease and the need for more accurate prediction tools in this setting.[14] Outpatient evaluation of potential AMI creates new challenges. Treatment decisions must be made without the aid of cardiac enzymes or exercise stress testing and must consider patient desires to avoid crowded EDs.[15,16]

Several validated algorithms are candidates for helping identify these high-risk symptomatic patients and prompting early aggressive evaluation and treatment.[17] The Framingham risk score (FRS) uses a combination of traditional coronary risk factors to predict the 10-year risk of developing CHD independent of symptom complex.[18] Other symptom-based algorithms predict the presence of coronary artery disease or AMI, including the Diamond and Forrester probability[19,20] and the Goldman prediction tool.[21]

We conducted a population-based case-control study to determine the proportion of AMIs preceded by primary care evaluation in patients with no history of CHD and to analyze the ability of existing prediction tools to identify missed opportunities in the early outpatient management of acute cardiac ischemia.

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METHODS

STUDY COHORT AND CASE-CONTROL DESIGN

This study was conducted in a large integrated physician group practice (Harvard Vanguard Medical Associates) consisting of 14 ambulatory health centers in eastern Massachusetts, with 110 primary care physicians caring for approximately 250 000 adult patients. During the study, most of the Harvard Vanguard Medical Associates patient population was cared for under managed care contracts, allowing the use of billing claims to identify all inpatient admissions for AMI (*International Classification of Diseases, Ninth Revision, Clinical Modification,*[22] code 410.xx) among patients at least 18 years old between January 1, 2000, and December 31, 2004. These patient records were linked to the electronic medical record system in use at all study sites to facilitate medical record review of all outpatient encounters before the index hospitalization. We identified 1523 admissions for AMI and successfully linked 1504 (98.8%) to the electronic medical record system. Because we wanted to focus this investigation on the patient population that is most challenging diagnostically, we excluded 538 patients with a known history of CHD before the index hospitalization, defined as a history of AMI, coronary angioplasty, coronary artery bypass graft surgery, or coronary artery disease demonstrated by means of noninvasive testing or cardiac catheterization.

The remaining 966 patients with AMI were classified based on outpatient care received in the 30 days before the index hospitalization. Qualifying outpatient visits in this 30-day period were those involving a primary care physician, a nurse practitioner, or a physician assistant for evaluation of nontraumatic chest pain or other potential anginal equivalents, including dyspnea, shoulder pain, jaw pain, epigastric pain, upper back pain, or dizziness. Patients were divided into 3 groups: (1) "missed opportunities," or qualifying outpatient visit and not sent directly to the ED (n=106); (2) qualifying outpatient visit and sent directly to the ED (n=155); and (3) no qualifying outpatient visit (n=705).

We used a case-control study design to analyze the ability of 3 risk prediction tools to identify missed opportunities in the early management of acute ischemic heart disease. Case patients were defined as symptomatic outpatients not directly referred to the hospital and subsequently experiencing an AMI (n=106). To create an eligible control population, we used *International Classification of Diseases, Ninth Revision, Clinical Modification,*[22] diagnoses from the electronic medical record to identify all symptomatic patients first seen by general internists, nurse practitioners, and physician assistants and not experiencing an AMI within 30 days. These patients were matched to cases based on presenting symptom and encounter date (±1 month of the index outpatient visit) to account for temporal trends in the management of acute coronary syndromes and differences in patient presentation. We randomly selected control patients in a 3:1 design (n=318 controls) from this eligible patient population.

DATA COLLECTION AND PREDICTION MODELS

All the data were collected by means of outpatient electronic medical record review. Data from this system have been used extensively in evaluations of quality of care[23-25] and disease management.[26,27] Coronary risk factors, including patient age, sex, blood pressure, cholesterol level, smoking status, and diabetic status, were used to calculate the FRS (**Figure 1**).[18] Data were missing for total cholesterol in 18 patients (4%), for high-density lipoprotein cholesterol in 58 (14%), and for systolic blood pressure in 1 (0.2%). In the case of missing data, we imputed values into the Framingham risk calculator that did not raise the overall risk score (for total cholesterol, <160 mg/dL [<4.14 mmol/L]; for high-density lipoprotein cholesterol, <50 mg/dL [<1.29 mmol/L]; and for systolic blood pressure, <120 mm Hg).

The Diamond and Forrester model categorizes chest pain based on 3 characteristics: (1) location (substernal vs not substernal), (2) precipitation (exertional vs nonexertional), and (3) relief (with rest or nitroglycerin).[19] Patients with all 3 positive characteristics are classified as having "typical angina," with 2 characteristics as having "atypical angina," and with all others as having "nonanginal discomfort." The risk of coronary artery disease can then be derived by combining patient age, sex, and symptom classification (**Table 1**).[20]

The Goldman prediction tool requires knowledge of patient age, electrocardiogram (ECG) findings, and chest pain characteristics.[21] We used this model to identify patients with a predicted probability of AMI greater than 7% (**Figure 2**). If an ECG was not performed by the evaluating clinician, ECG findings were assumed to be normal. Because the Diamond and Forrester probability and the Goldman prediction tool require a description of chest pain, we limited the calculation of these risk scores to patients with chest pain.

We collected additional clinical data on missed-opportunity AMIs, including diagnosis, management, and 30-day mortality rates. Electrocardiogram readings documented in the primary care clinician's notes were compared with the final cardiologist's reading to identify misinterpretation. Unstable angina was classified based on the presence of (1) new-onset symptoms (within 48 hours), (2) symptoms at rest, or (3) worsening symptoms, such as increased frequency or duration.[28] Data on characteristics of the AMI, including cardiac enzyme levels and in-hospital treatment, were collected from hospital discharge summaries available in the electronic medical record.

STATISTICAL ANALYSIS

The association of each clinical characteristic, diagnosis, and treatment was assessed using conditional logistic regression to account for the matched case-control study design. The FRS, Diamond and Forrester probability, and Goldman prediction tool were all analyzed as predictors of missed opportunities using conditional logistic regression, with *P* values reported using the likelihood ratio test. The first 2 models were assessed as binary, categorical, and continuous predictors, and the Goldman prediction tool was assessed only as a binary predictor. We fit additional models for each prediction tool, including a separate adjustment term for patient sex; however, we do not present these as primary analyses because patient sex is a key component of the risk algorithms being evaluated. All analyses were performed using a statistical software program (SAS version 8.02; SAS Institute Inc, Cary, NC). This study was approved by the institutional review boards at Brigham and Women's Hospital and Harvard Vanguard Medical Associates.

RESULTS

Of 966 patients with no history of CHD admitted to the hospital with AMI, 261 (27.0%) were evaluated by primary care clinicians for chest pain or another anginal equivalent in the previous 30 days, including 155 (16%) referred directly to the ED for hospital care and 106 (11%) not referred for hospital care. Of these 106 cases of missed opportunities, the median time from initial outpatient encounter to hospital admission for AMI was 8.0 days (interquartile range, 3-15 days). Approximately one third of these case patients (n=32) presented to the ED with ST-segment elevation. Of these 106 case patients, 7 (7%)

Estimate of 10-y Risk for Men

Age, y	Points
20-34	−9
35-39	−4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Total Cholesterol, mg/dL	Age, y 20-39	40-49	50-59	60-69	70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
>279	11	8	5	3	1

	20-39	40-49	50-59	60-69	70-79
Smoker	0	0	0	0	0
Nonsmoker	8	5	3	1	1

HDL Cholesterol, mg/dL	Points
>59	−1
50-59	0
40-49	1
<40	2

Systolic BP, mm Hg	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
>159	2	3

Point Total	10-y Risk, %
<0	<1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
>16	>29

Estimate of 10-y Risk for Women

Age, y	Points
20-34	−7
35-39	−3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Total Cholesterol, mg/dL	Age, y 20-39	40-49	50-59	60-69	70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
>279	13	10	7	4	2

	20-39	40-49	50-59	60-69	70-79
Smoker	0	0	0	0	0
Nonsmoker	9	7	4	2	1

HDL Cholesterol, mg/dL	Points
>59	−1
50-59	0
40-49	1
<40	2

Systolic BP, mm Hg	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
>159	4	6

Point Total	10-y Risk, %
<9	<1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
>24	>29

Figure 1. Calculation of the Framingham risk score. To convert cholesterol to millimoles per liter, multiply by 0.0259. BP indicates blood pressure; HDL, high-density lipoprotein. Adapted from National Cholesterol Education Program.[18]

received thrombolytic agents, 64 (60%) underwent coronary angioplasty, and 12 (11%) underwent coronary artery bypass graft surgery. The median peak creatine kinase concentration was 307 U/L (interquartile range, 199-700 U/L). The 30-day mortality rate was 5.7% in cases of missed-opportunity AMI (n=6).

Case patients carried a significantly higher burden of coronary risk factors compared with matched control patients who did not experience an AMI (**Table 2**). Case patients were older and were more likely to be male, diabetic, and current smokers and to have a family history of early coronary artery disease, a higher total cholesterol level, and higher blood pressure. Approximately half of the case patients initially complained of chest pain, with the most common other complaints including shoulder pain (31%) and dyspnea (26%).

EVALUATION AND MANAGEMENT

Among cases and controls, approximately half of the patients underwent an ECG (**Table 3**). This proportion increased to 67% in patients with chest pain. Once per-

Table 1. Calculation of the Diamond and Forrester Probability of Coronary Artery Disease*

	Nonanginal Chest Pain		Atypical Angina		Typical Angina	
Age, y	Men, %	Women, %	Men, %	Women, %	Men, %	Women, %
30-39	5	1	22	4	70	26
40-49	14	3	46	13	87	55
50-59	22	8	59	32	92	79
60-69	28	19	67	54	94	91

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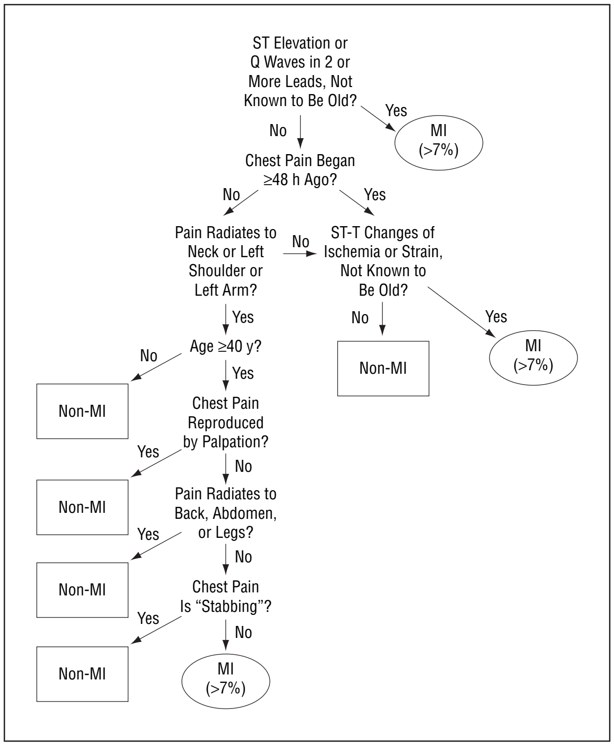

Figure 2. Prediction of myocardial infarction (MI) using the Goldman prediction rule. Adapted (2006) with permission from Goldman et al.[21] (Copyright © 1988, Massachusetts Medical Society. All rights reserved.)

formed, ECGs were more likely to be interpreted by the clinician during office visits for case patients vs controls (94% vs 83%; $P=.05$). Of the ECGs interpreted by the clinician, misinterpretation was more common in case patients vs control patients (20% vs 7%; $P=.02$), with T-wave changes reflecting the most common source of misinterpreted ECG findings (Table 3).

The evaluation plan involved exercise stress testing for a few patients and was planned more frequently among case patients vs control patients (25% vs 17%; $P=.03$). There were 2 case patients for whom cardiac enzyme analyses were ordered as outpatients and subsequently returned positive results after the patient had left the office.

Angina, musculoskeletal pain, and gastroesophageal reflux disease accounted for most clinician diagnostic considerations (**Table 4**). The diagnosis of angina was considered in less than one third of the patients overall, with case patients more likely than controls to be assigned this diagnosis (31% vs 20%; $P=.008$). Of the patients diagnosed as having angina (n=96), at least 1 criterion for unstable angina was present in 45% of cases compared with 25% of controls ($P=.29$). Treatment plans reflected the diagnostic considerations, with pain medications and antacids representing most of the prescribed medications. Treatments for suspected coronary artery disease, including aspirin, β-blockers, and nitrates, were prescribed to only a few patients (Table 4).

Table 2. Initial Characteristics of Cases and Controls

Characteristic	Cases (n = 106)	Controls (n = 318)	P Value
Cardiac risk factors			
Age, mean ± SD, y	63.6 ± 14	49.7 ± 16	<.001
Men, No. (%)	67 (63)	99 (31)	<.001
Diabetes mellitus, No. (%)	35 (33)	30 (9)	<.001
Current smoker, No. (%)	29 (27)	50 (16)	.01
Family history of heart disease, No. (%)	32 (30)	50 (16)	<.001
Total cholesterol, mean ± SD, mg/dL	216 ± 44	206 ± 41	.02
HDL cholesterol, mean ± SD, mg/dL	45 ± 12	55 ± 18	<.001
LDL cholesterol, mean ± SD, mg/dL	135 ± 34	131 ± 35	.45
Systolic blood pressure, mean ± SD, mm Hg	137 ± 18	127 ± 18	<.001
Diastolic blood pressure, mean ± SD, mm Hg	82 ± 12	79 ± 9	.004
Initial symptoms, No. (%)			
Chest pain	53 (50)	166 (52)	.35
Shoulder pain	33 (31)	64 (20)	.01
Dyspnea	28 (26)	86 (27)	.86
Neck/jaw/throat pain	21 (20)	32 (10)	.002
Upper back pain	17 (16)	62 (20)	.27
Epigastric pain	16 (15)	46 (14)	.78
Weakness	15 (14)	35 (11)	.37
Dizziness	11 (10)	37 (12)	.60
Nausea	8 (8)	31 (10)	.45
Framingham risk score, No. (%)			<.001
<10%	16 (15)	237 (75)	
10%-19%	33 (31)	36 (11)	
≥20%	57 (54)	45 (14)	
Diamond and Forrester probability, No. (%)*			<.001
<10%	5 (10)	76 (52)	
10%-19%	9 (18)	28 (19)	
≥20%	35 (71)	43 (29)	
Goldman prediction tool, >7%, No. (%)*	21 (43)	13 (9)	<.001

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein.
SI conversion factor: To convert cholesterol to millimoles per liter, multiply by 0.0259.
*Calculated only in patients with chest pain.

MULTIVARIABLE DECISION AIDS

When used as binary predictors, elevated risk scores on all 3 algorithms were strongly associated with a missed opportunity for treatment of early acute cardiac ischemia (**Table 5**). When used as continuous predictors, the FRS (odds ratio [OR], 1.19; 95% confidence interval [CI], 1.14-1.24) and the Diamond and Forrester model (OR, 1.03; 95% CI, 1.02-1.04) demonstrated an increase in the odds of a missed opportunity for each 1% increase in risk score. After adjusting for patient sex, the FRS was independently associated with missed-opportunity AMIs, although there was slight attenuation of the effect sizes. Using a binary cutoff FRS of 10% or greater, the sex-adjusted odds ratio was 16.5 (95% CI, 7.8-34.8), and using the FRS as a continuous predictor, the sex-adjusted OR was 1.17 (95% CI, 1.13-1.22). When used as a categorical predictor with FRS less than 10% as the reference group, the sex-adjusted OR for FRS 10% to 19% was 12.4 (95% CI, 5.3-28.6) and for 20% or greater was 20.8 (95% CI, 9.1-47.7). Similar patterns of modest attenuation of effect sizes for the Diamond and Forrester model and the Goldman prediction tool were noted after adjusting for sex (data not shown). We determined the sensitivity and specificity of these instruments using different risk score thresholds to better define their utility in the clinical setting (**Table 6**). Using a moderate risk score as the cutoff point, the sensitivities of the FRS, Diamond and Forrester probability, and Goldman risk tool were 85%, 90%, and 43%, respectively, and the specificities were 75%, 52%, and 91%.

EVALUATION AND TREATMENT OF HIGH-RISK PATIENTS

We examined the evaluation and treatment of case patients with a moderately elevated FRS (≥10%) to better characterize missed opportunities for early management of acute cardiac ischemia. Of these 90 patients, only 33% were given a diagnosis of possible angina, and ECGs were performed only 51% of the time. Only 12% of these patients began aspirin treatment, and only 8% started taking a β-blocker.

COMMENT

We found that more than one quarter of the patients admitted to the hospital with AMI without known previous CHD had primary care visits in the preceding month for symptoms suggestive of coronary disease, and 41% (106/261) of these patients were not referred for hospital care. This rate of missed opportunities for early intervention is obviously much higher than rates of missed diagnoses of AMI in EDs.[7] The higher prevalence of coronary risk factors among these missed opportunities suggests that the FRS could help identify higher-risk patients during office visits.

This is the first US study, to our knowledge, that provides a population-based estimate of the role of primary care in the period immediately preceding hospitalization for AMI. A study from Germany reported a rate of "missed outpatient" AMI of 29%,[29] potentially reflecting differences in practice patterns between the 2 health systems.

Table 3. Outpatient Evaluation of Cases and Controls

Variable	Patients, No. (%) Cases (n = 106)	Controls (n = 318)	*P* Value
Physician training level			
Physician	84 (79)	258 (81)	.66
Nurse practitioner or physician assistant	22 (21)	60 (19)	
Electrocardiographic findings			
Performed during visit	52 (49)	133 (42)	.14
Interpreted during visit*	49 (94)	111 (83)	.05
Misinterpreted†	10 (20)	8 (7)	.02
ST-segment depression	1 (10)	0	
T-wave changes	7 (70)	4 (50)	
Q waves	1 (10)	3 (38)	
Poor R-wave progression	1 (10)	1 (13)	
Planned evaluation			
Cardiac stress test	27 (25)	53 (17)	.03
Radiographs	15 (14)	78 (25)	.02
Echocardiogram	4 (4)	9 (3)	.62

Abbreviations: NA, not available.
*Calculated only in patients who underwent electrocardiography.
†Calculated only in patients whose electrocardiograms were interpreted.

Table 4. Physician Diagnoses and Treatment Plans for Cases and Controls

Variable	Patients, No. (%) Cases (n = 106)	Controls (n = 318)	*P* Value
Outpatient diagnostic considerations*			
Angina	33 (31)	63 (20)	.008
Musculoskeletal pain	26 (25)	116 (36)	.003
Gastroesophageal reflux/heartburn	19 (18)	68 (21)	.34
Upper respiratory tract infection	15 (14)	16 (5)	.003
Congestive heart failure	7 (7)	12 (4)	.23
Asthma/chronic obstructive lung disease	7 (7)	29 (9)	.32
Anxiety	4 (4)	31 (10)	.04
Treatment*†			
Pain medication	28 (26)	86 (27)	.89
Antacid	18 (17)	59 (19)	.67
Inhaled bronchodilators	13 (12)	22 (7)	.07
Nitrates	13 (12)	7 (2)	<.001
Aspirin	12 (11)	15 (5)	.01
Antibiotics	12 (11)	11 (3)	.003
β-Blockers	7 (7)	5 (2)	.01
Diuretics	6 (6)	3 (1)	.005

*The values total more than the number of cases and controls because physicians often assigned multiple diagnoses and treatments.
†These treatments reflect new initiation of therapy during the office visit and do not include the continuation of previously prescribed medications.

The high rates of missed opportunities in the primary care setting are not surprising given the lack of structured evaluation and triage protocols. Half of the patients did not have an ECG performed during the office visit, and among those who did, this ECG was not always interpreted before the patient left the office. In addition, increasingly crowded EDs may tempt primary care clinicians to attempt outpatient management of unstable coronary syndromes.

Table 5. Comparison of 3 Models for the Prediction of Missed-Opportunity Acute Myocardial Infarction

Risk Score, %	FRS Model Odds Ratio (95% CI)	*P* Value	DF Model Odds Ratio (95% CI)*	*P* Value	Goldman Risk Tool Odds Ratio (95% CI)*	*P* Value
≥10	19.5 (9.3-40.6)	<.001	8.3 (3.2-21.7)	<.001	NA	NA
>7	NA	NA	NA	NA	12.1 (4.1-35.6)	<.001
<10	1.0	NA	1.0	NA	NA	NA
10-19	14.8 (6.5-33.6)	<.001	4.3 (1.3-13.8)	<.001	NA	NA
≥20	24.7 (10.9-56.0)	<.001	10.3 (3.8-27.5)	<.001	NA	NA
Per 1% increase	1.19 (1.14-1.24)	<.001	1.03 (1.02-1.04)	<.001	NA	NA

Abbreviations: CI, confidence interval; DF, Diamond and Forrester; FRS, Framingham risk score; NA, not applicable.
*The DF model and the Goldman risk tool were used only in patients with chest pain.

Table 6. Utility of 3 Models in Identifying Missed-Opportunity Acute Myocardial Infarction by Risk Score

	FRS Model, %		DF Model, %*		Goldman Risk Tool, %*	
Risk Score	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Low (≥5%)	96 (102/106)	61 (193/318)	96 (47/49)	32 (47/147)	NA	NA
Moderate (≥10%)†	85 (90/106)	75 (237/318)	90 (44/49)	52 (76/147)	43 (21/49)	91 (134/147)
High (≥20%)	54 (57/106)	86 (273/318)	71 (35/49)	71 (104/147)	NA	NA

Abbreviations: DF, Diamond and Forrester; FRS, Framingham risk score; NA, not applicable.
*The DF model and the Goldman Risk tool were used only in patients with chest pain.
†Moderate risk score is defined as greater than 7% for the Goldman risk tool.

The results of this study support previous findings[17] of the utility of coronary risk prediction tools in identifying high-risk patients in the primary care setting. Although a previous study[30] in the ED setting demonstrates that individual risk factors do not add substantially to the prediction of AMI, the present data suggest that the combination of risk factors using the FRS produces a measure that is strongly associated with the occurrence of AMI. This association was stronger than that obtained using either the Diamond and Forrester probability or the Goldman prediction tool, which were designed for use in different populations and require additional clinical information.

The ability of the FRS to identify high-risk symptomatic outpatients presents an opportunity to prompt early intervention by primary care clinicians. The real-time calculation of the FRS can be readily automated through electronic medical records or might simply be calculated intermittently and placed on the patient problem list. The presentation of an elevated FRS (≥10%) to a clinician might raise rates of ECG performance in outpatients or influence the interpretation of borderline abnormalities.

In addition to triggering a more aggressive evaluation, the presence of an elevated FRS might prompt initiation of cardioprotective medications or hospital evaluation in high-risk patients. We identified low prescription rates for β-blocker and aspirin therapy among these symptomatic outpatients with elevated risk scores, and recent guidelines[31] suggest aspirin therapy for patients with an elevated FRS even in the absence of symptoms. More aggressive intervention in these symptomatic patients, particularly those with characteristics of unstable angina, may have prevented their AMI.

The present study findings should be interpreted in the context of the study design. The case-control study design precludes estimation of the positive predictive value of the FRS; thus, before routine use of the FRS in clinical settings is considered, further research should determine whether the prevalence of AMI among outpatients with these symptoms is so low that such a tool might generate more false alarms than averted missed opportunities. We relied on claims data for the diagnosis of AMI. However, the positive predictive value associated with using claims data to identify hospital admission for AMI in patients with no history of CHD is nearly 95%.[32] Because we relied on outpatient medical records, it is possible that control patients experienced hospital admissions for AMI not detected in the electronic system, although this is highly unlikely given the severity of such admissions and the complete follow-up data available in this patient population. Finally, the individual who performed the medical record review could not avoid knowing whether patients experienced an AMI; thus, risk factor data were recorded by clinicians prospectively, but their collection by the investigators was not blinded.

Half of the patients in this study did not have ECGs performed, making it impractical to analyze the utility of other risk prediction tools that rely heavily on ECG findings, such as the Acute Cardiac Ischemia Time-Insensitive Predictive Instrument.[33] However, the present data reflect "real-world" evaluation of symptomatic outpatients, where ECGs are not routinely performed on all patients, highlighting the importance of developing risk prediction tools that do not rely on performance or interpretation of this test but may instead prompt clinicians to obtain it. The FRS is subject to similar limitations in availability of data, as many studies highlight low rates of assessment for important components of this risk score, including cholesterol testing and tobacco counseling.[34]

In conclusion, this study demonstrates a substantial role of primary care clinicians in the identification and management of early acute cardiac ischemia. A significant number of missed opportunities in this early management were identified, and the FRS represents an attractive instrument to identify these patients and prompt more aggressive intervention. These findings should stimulate the performance of prospective trials designed to improve the treatment of symptomatic outpatients with potential acute cardiac ischemia through the use of risk assessment tools.

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