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Risk Stratification in Chest Pain Patients Undergoing Nuclear Stress Testing: The Erlanger Stress Score

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*Cover Letter

May 4, 2012

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Michael L. Callaham, MD, Editor in Chief
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Dear Dr. Callaham,

Enclosed is the manuscript "Risk Stratification in Chest Pain Patients Undergoing Nuclear Stress Testing: The Erlanger Stress Score" intended as a contribution to the ***Cardiology*** section of *Annals of Emergency Medicine* under the subheading ***Original Research***. Though studies have individually reported the relationship of younger age (less than 40),[1] number of cardiac risk factors,[2] and history of preexisting coronary artery disease (CAD)[3] for predicting acute coronary syndromes (ACS) in chest pain patients undergoing cardiac stress testing, no study has investigated the interplay of all of these factors on the incidence of ACS in this subgroup of patients. Furthermore, none of these studies took into account the sex of the patient though the Framingham study found that a 33 year-old male has the same risk for CAD as a 40 year-old female. In this study, we individually report the effects of age, cardiac risk factors, and presence or absence of pre-existing CAD on incidence of ACS so that our data can be directly compared to studies published by Herman et al,[1] Purim-Shem-Tov et al,[2] and Madsen et al.[3] We also developed a regression model that utilizes age, sex, risk factors, and history of CAD to predict the risk of 30-day ACS. We believe this regression tool has the potential to assist the physician in selecting the appropriate low-to-intermediate risk chest pain patients who are most suitable for stress testing.

We previously published in *Annals of Emergency Medicine (*2001;38:207-215) a manuscript entitled: "Selective dual nuclear scanning in low risk patients with chest pain to reliably identify and exclude acute coronary syndromes." This was an observational study of outcome in patients undergoing our stress testing protocol. The patient population of the current study derives from the same patient database. However, we retrospectively applied current ACC/ESC criteria for diagnosing AMI and used troponin as the gold standard whereas the previous study used modified WHO criteria for diagnosing MI and also included CK-MB measurements. As a result, there is some crossover in the patients included and excluded from the previous study as compared to present study which accounts for the small difference in study population (805 patients in former study, 800 patients in current study). ***All the reported data in the current study is original and has not been reported elsewhere.***

Though some may criticize our study for utilizing this older database, our study is derived from a consecutive patient population that underwent a standardized protocol of serial cardiac marker and ECG followed by only one type of stress testing (i.e. nuclear). Furthermore, our population of 800 patients is much larger than the investigations reported by Herman et al (220 patients),[1] Purim-Shem-Tov et al (210 patients),[2] and Madsen et al (531 patients).[3] Also, as our protocol does not exclude anyone from our chest pain evaluation protocol due to age, ability to exercise, TIMI score, presence or absence of pre-existing CAD, or any other exclusionary criteria so common in other chest pain units (see LIMITATION section), we feel our database is ideal for investigating the interplay of age, sex, coronary risk factors, and presence or absence of pre-existing CAD in predicting ACS. For comparison, Herman et al's study that investigated influence of age < 40, performed this study in a chest pain unit that excluded patients $\geq$ 50 years of age, patients unable to exercise, and patients with history of pre-existing CAD. Also, the type of stress testing in Herman's study was entirely at the discretion of the admitting physician (treadmill, echo, nuclear, or no stress testing) unlike the Erlanger protocol in which all patients underwent nuclear stress testing. Furthermore, Herman et al's study did not collect post-discharge outcome data whereas our study collected 30-day outcome.

One criticism we received during our presentation at the 2011 Research Forum of the American College of Emergency Physicians is that the risk score is too cumbersome to utilize in clinical practice. In order to facilitate use of the "Erlanger Stress Score," we have developed an internet-based decision support tool in which one can easily calculate the stress score on a computer or smart phone in order to bridge the gap between research and clinical care (http://107.22.120.83/acs/index.jsp).

We look forward to the comments of the reviewers.

Sincerely,

Francis M Fesmire

Francis M. Fesmire, MD, FACEP

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Risk Stratification in Chest Pain Patients Undergoing Nuclear Stress Testing: The Erlanger Stress Score

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Risk Stratification in Chest Pain Patients Undergoing Nuclear Stress Testing: The Erlanger Stress Score

ABSTRACT

Study Objectives: Studies have individually reported the relationship of age, cardiac risk factors, and history of preexisting coronary artery disease (CAD) for predicting acute coronary syndromes (ACS) in chest pain patients undergoing cardiac stress testing. In this study, we investigate the interplay of all of these factors on the incidence of ACS in order to develop a tool that may assist physicians in the selection of appropriate chest patients for stress testing.

Methods: Retrospective analysis of a prospectively acquired database of consecutive chest pain patients undergoing nuclear stress testing. Backwards stepwise logistic regression was utilized to develop a model for predicting risk of 30-day ACS utilizing information obtained from age, sex, cardiac risk factors, and history of preexisting CAD.

Results: A total of 800 chest pain patients underwent nuclear stress testing. ACS occurred in 74 patients (9.3%). Logistic Regression analysis found only six factors predictive of 30-day ACS: age, male sex, preexisting CAD, diabetes, and hyperlipidemia. Area under the Receiver Operator Characteristic curve of this model for predicting ACS was 0.767 (95% CI 0.719 to 0.815). There were no cases of ACS in the 173 patients with predicted probability estimates less than or equal to 2.5% (95% CI 0 to 2.1%).

Conclusions: A regression model utilizing age, sex, preexisting CAD, diabetes, and hyperlipidemia is predictive of 30-day ACS in patients undergoing nuclear stress testing. Prospective studies need to be performed to determine whether this model can assist physicians in selection of appropriate low-to-intermediate risk chest pain patients for nuclear stress testing.

INTRODUCTION

Background

Studies have individually reported the relationship of age, number of cardiac risk factors, and history of preexisting coronary artery disease (CAD) for predicting acute coronary syndromes (ACS) in chest pain patients undergoing cardiac stress testing as part of chest pain unit (CPU) evaluation protocols.[1-5] Studies investigating age suggest that stress testing is not routinely indicated in patients less than 40 years of age due to low risk of ACS.[1-3] Studies investigating number of risk factors and history of preexisting CAD suggest that patients with greater than or equal to 3 risk factors or history of preexisting CAD be admitted directly to the hospital and thus be excluded from CPU protocols due to high risk of ACS.[4,5] According to Bayes' theorem, one should not perform a stress test in patient with extremely low risk of ACS due to the inherent risks of unnecessary testing resulting from false positive exams.[6] Likewise, one should not perform a stress test in high risk patients due to the risks of false negative exam. Thus it is imperative that physicians select appropriate low-to-intermediate risk chest pain patients in whom the benefits of stress testing outweigh the risks.

Importance

Chest pain represents one of the most common chief complaints for adult emergency department (ED) patients with approximately 6 million visits per year and comprising 8% of all ED visits.[7,8] Of those patients presenting with chest pain, over 850,000 have ACS.[9] Despite advances in medical technology, approximately 2% of patients with myocardial infarction and high risk ACS are missed leading to significantly increased morbidity for the patient as well as significant medicolegal risk for the physician.[10,11] In an effort to minimize risks associated with missed ACS, many centers have instituted chest pain unit (CPU) evaluation protocols with routine cardiac stress testing in those in whom MI is ruled out.[12,13]

While cardiac stress testing is useful in the evaluation of appropriate low-to-intermediate risk chest pain patients, such testing is not without risk. For example, in patients undergoing nuclear stress testing, there is long-term risk from radiation exposure as well as short term risk of adverse reaction to radio-isotope or to the pharmacologic stress testing agent utilized.[14] Furthermore, the false-positive rate for nuclear stress testing is approximately 20% for detection of coronary stenosis $\geq$ 50%.[15,16] As these patients with false-positive stress test results usually undergo coronary angiography, there is the additional risk associated with this procedure in addition to a five-fold added cost.[17]

Goal of this investigation

The goal of the present study is to determine the association of age, sex, cardiac risk factors, and presence or absence of preexisting CAD on the incidence of ACS and to develop a simple prediction tool to optimize the selection of appropriate low-to-intermediate risk chest pain patients who would benefit the most from cardiac stress testing.

MTHODOLOGY

Study Design

This is a retrospective analysis of a prospectively acquired database of 2,206 consecutive chest pain patients presenting to the ED. The study was performed with approval of the Institutional Review Committee.

Setting

This study was performed at an urban county hospital with an adult ED volume of approximately 45,000 patients per year. The hospital has full cardiac capability with both interventional cardiologists and cardiothoracic surgery available 24-hours a day.

Selection of Participants

The study population consists of consecutive chest pain patients greater than or equal to 18 years of age with suspected ACS presenting to Erlanger Medical Center from January 1, 1999 through January 31, 2000 who underwent nuclear stress testing as part of an accelerated chest pain evaluation protocol. Results in this patient population have been previously described.[18] Exclusion criteria for present study were as follows: injury on the initial ECG, elevated baseline troponin (see Methods of Measurement), new injury or evolving ischemia on continuous 12-lead ECG monitoring, 2-hour delta troponin greater than or equal to +0.1 ng/ml, clinical diagnosis of ACS, and patients not undergoing nuclear stress testing.

Methods of Measurement

All patients without acute ST-segment elevation MI on presentation underwent a standardized accelerated evaluation protocol consisting of baseline risk assessment based on history and ECG findings, 2-hour delta cardiac marker testing, and automated 12-lead serial ECG monitoring. This protocol has been demonstrated to reliably identify and exclude MI.[19] At the completion of this accelerated chest pain evaluation protocol, patients were reclassified into 3 groups based on the physician's estimate of likelihood of ACS: category 2 -- probable ACS (clinical diagnosis of ACS, and/or positive serum marker measurements, and/or diagnostic abnormalities on serial ECG); category 3 -- possible ACS; and category 4-- non-ACS chest pain. Category 2 patients were admitted for presumed ACS, category 3 patients underwent immediate nuclear stress testing, and category 4 patients were directly discharged from the ED unless another serious non-ACS medical condition was thought to exist. Comprehensive details of this protocol have been previously published.[18,19]

MI was defined according to current American College of Cardiology (ACC) and European

Society of Cardiology (ESC) criteria utilizing as the gold standard the lowest cutoff value of troponin above the 99th percentile in which the assay imprecision is $\leq$ 10%. [20,21] This value for the troponin I Axsym® Fluorometric Enzyme Immunoassay (Abbott Laboratories, Abbott Park, IL) utilized in this study is 0.8 ng/ml.[21] As the initial studies on this database utilized modified World Health Organization criteria for MI that was in affect at the time of prospective data collection, current ACC/ESC criteria were retrospectively applied to the entire patient population. Thirty (30)-day ACS was defined as MI within 24-hours of presentation, or percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), arteriogram revealing stenosis in major coronary vessel (or bypass graft if native vessel totally occluded) $\geq$ 70% not amenable to revascularization, life-threatening complications, or death from cardiac or unknown cause occurring within 30-days of presentation. Life-threatening complications were defined as ventricular fibrillation, sustained ventricular tachycardia, third-degree AV block, bradycardic or asystolic arrest, post ED presentation MI, cardiogenic shock, or electromechanical dissociation.

Definition of risk factors utilized in this study were was as follows: diabetes was diagnosed if patient had history of diabetes treated with diet and/or medications; in the absence of prior diagnosis, diabetes was diagnosed if ED blood glucose was $\geq$ 150 mg/dl; hypertension was diagnosed if patient had history of hypertension treated with lifestyle modification and/or medication; in the absence of prior diagnosis, hypertension was diagnosed if the patient demonstrated left ventricular hypertrophy on the initial ECG and either of the two following findings: 1) diastolic blood pressure > 100 mm Hg on two ED measurements at least $\geq$ 30 minutes apart, or 2) systolic > 140 mm Hg and diastolic > 90 mm Hg on two ED measurements at least $\geq$ 30 minutes apart; cigarette use was considered positive if the patient was a current or recent (< 1 year) cigarette smoker; dyslipidemia was diagnosed if patient had history of diagnosed dyslipidemia treated with diet and/or medications, or total cholesterol > 200 mg/dl with LDL > 130 mg/dl or HDL < 35 mg/dl; family history of CAD was defined as any first degree

relative who had any one of the following ≤ 60 years of age: MI, PCI, CABG, or sudden death of cardiac or unknown cause; obesity was defined as Body mass index > 27 kg/height $(m)^2$.

Primary Data Analysis

Data was recorded on a standardized form and placed in a computer database utilizing SYSTAT® 13.0 (SPSS, Inc, Chicago, Il). Sample means were compared with the two-sample unpaired *t*-test. Categorical data were compared with $\chi 2$ test with the Yates correction for small sample size. Sensitivity, specificity, and likelihood ratios were calculated utilizing MedCalc® 11.6.1 (MedCalc Software, Belgium). Backwards stepwise logistic regression technique for development of a model for predicting the probability of 30-day ACS utilized IBM® SPSS® Statistic 19 (Armonk, New York). Initially, all the potential factors (e.g., demographic, clinical, and laboratory data) were included. Age was grouped into five classes based on the quintiles of its observed distribution. Variables with P value > 0.20 were removed by checking the probability of the likelihood-ratio statistic based on the maximum partial likelihood estimates. The remaining variables were tested one by one and were kept in the model if they were statistically significant or appeared to be confounders, which is defined as variable whose removal changed another variable's coefficient by more than 10%. Next, the variables were re-introduced one at a time. The variables were kept in the model if they were statistically significant (*P* value < 0.05) or confounders. Finally, all pairwise interactions were examined. To estimate 95% confidence intervals of the area under the receiver operator characteristic (ROC) curve for this model, 1000 bootstrap samples were generated for each sample and consisted of 1100 observations selected randomly with replacement from the original data. The 95% confidence interval was defined as the 5th and 95th percentiles of the 1000 bootstrap values. A 10-fold cross-validation was then performed to assess the level of fit of the logistic regression model and check for over-fitting of the data. First, the whole data set was randomly partitioned into 10 equal subsets. Then a randomly

selected single subset was utilized as the validation data and the remaining nine subsets were utilized as the training set. The regression coefficients were estimated for the training set and the prediction equation was applied to the validation set. This procedure was repeated such that each subset was utilized as the validation set. The ten areas under the ROC curves were calculated for the same 10 validation sets by using the original regression model developed from the whole data set. The final model found only five factors with an increased likelihood of ACS incidence: male sex, older age, prior diagnosis of coronary artery disease, prior diagnosis of diabetes, and prior diagnosis of hyperlipidemia.

RESULTS

Over a 13 month period, a total of 2,206 consecutive chest pain patients with suspected ACS underwent the Erlanger Chest Pain Protocol. Of these, 345 patients were excluded for having one or more of the following abnormalities during the initial 2-hour evaluation period: injury on the initial ECG, positive baseline troponin based on ESC/AHA/ACC redefinition of MI, new injury or evolving ischemia on continuous 12-lead ECG monitoring, or 2-hour delta troponin $\geq$ +0.1 ng/ml. Ninety-eight patients were directly admitted with a clinical diagnosis of ACS (Chest Pain Category 2). In addition, 939 patients were not felt to have ACS chest pain at the completion of the initial 2-hour evaluation period (Chest Pain Category 4) and were discharged home unless another serious non-ACS condition was felt to exist. Of these 939 patients, 1 patient underwent PCI and 1 patient underwent CABG during the 30-day follow-up period. There were no other cases of missed ACS in these category 4 patients.

Of the remaining 824 patients, 800 patients underwent nuclear stress testing in the ED (24 patients declined stress testing). The overall sensitivity and specificity of nuclear stress testing for 30-day ACS was 95.9% (95% CI 88.6-99.2) and 87.5% (95% CI 84.8-89.8) respectively (+LR 7.6, 95% CI 7.2-8.1; -LR 0.06, 95% CI 0.02-0.1). Of the 24 patients declining nuclear stress testing, there were no patients with 30-day ACS. Table 1 summarizes population demographics in patients with and without

30-day ACS for the 800 study patients. Table 2 summarizes 30-day outcome in patients with and without history of CAD. Patients with history of CAD had higher rate of 30-day ACS as compared to patients without a history of CAD (17.6% vs. 5.1%; P<0.0001; 95% CI for difference in proportion 7.6% to 17.9%). Table 3 summarizes rates of 30-day ACS according to age and according to number of risk factors. Peak rates of ACS occurred in the 51-60 age group for both patients with and without history of pre-existing coronary artery disease. Patients in the 51-60 age group had higher incidence of ACS as compared to the < 40 age group (P=0.0005; 95% CI for difference in proportions 6.5%-18.1%) and as compared to the 41-50 age group (P=0.04; 95% confidence intervals for difference in proportion 0.3%-12.5%). Patients in the >60 group also had higher incidence of ACS as compared to the < 40 age group (P=0.013; 95% CI for difference in proportions 2.3% to 12.6%). There were no other statistical significance differences among the individual age groups. Peak rate for ACS occurred in patients with 3 risk factors for patients with a history of CAD and 4-6 risk factors for patients without a history of CAD. Patients with 4-6 risk factors had a greater incidence of ACS as compared to patients with 0-1 risk factors (P=0.008; 95% CI for patients for difference in proportions 2.2%-15.1%) and patients with 3 risk factors also had greater incidence of ACS as compared to patients with 0-1 risk factors (P=0.01; 95% CI for difference in proportions 1.8%-13.3%).

Table 4 summarizes regression coefficients and odds ratios for the individual factors included in the logistic regression model. Area under the Receiver Operator Characteristic curve of this model for predicting 30-day ACS was 0.767 (95% CI 0.719 to 0.815). Age, male sex, and presence of absence of history of CAD factored into the regression model. Of the 6 risk factors studied, only diabetes and hyperlipidemia factored into the model. The probability of 30-day ACS is equal to $1/(1+\exp^{-sum})$ where "sum" equals the sum of the constant added to the sum of regression coefficients (risk calculator is available at *http://107.22.120.83/acs/*). The Figure represents the comparison between predicted probability estimates for 30-day ACS versus actual prevalence in the 800 study patients. The predicted

probability in these patients is consistent with actual prevalence of 30-day ACS. There were no cases of 30-day ACS in the 173 patients (21.6% of total patients; 95% CI 0 to 2.1%) with predicted probability estimate $\leq$ 2.5%.

LIMITATIONS

The primary limitation of our study is its retrospective design though we feel this limitation is offset by the fact that the data collection was prospectively performed in consecutive chest pain patients undergoing a standardized chest pain evaluation protocol with all patients receiving nuclear stress testing unlike CPU protocols that allow type of provocative testing to be at the discretion of the physician.[1,22-24] Also, as the Erlanger Chest Pain Evaluation Protocol does not exclude patients from stress testing due to age > 50,[1] presence of pre-existing CAD,[1-4, 25-27] ability to exercise,[1,2,26] TIMI score >1,[24] TIMI score > 2,[27,28] or any other exclusionary factors that may be seen in other CPU protocols, we feel this lack of exclusionary criteria makes our patient population the ideal patient population for evaluating the impact of age, sex, risk factors, and presence or absence of CAD on rates of ACS in patients undergoing stress testing. Another limitation is the fact that this study utilized an older generation troponin I assay with a MI cutoff of 0.8 ng/ml to exclude patients with an abnormal baseline troponin. We have minimized this bias by also excluding patients below this cutoff value who had a 2-hour delta troponin rise of $\geq$ +0.1 ng/ml (e.g. if baseline troponin was 0.1 ng/ml and 2 hour troponin was 0.2 ng/ml, then that patient was excluded from this study). Another weakness is that our study population is only 800 patients. However, our study population is still significantly larger than the investigations by Herman et al (220 patients),[1] Purim-Shem-Tov et al (210 patients),[4] and Madsen et al (531 patients).[5] Finally, the regression score is not easily calculated. However, we have created a web-based decision support tool in which one can enter the data directly into a computer or smart

phone for determination of the regression score (The Erlanger Stress Test Score: http://107.22.120.83/acs/).

DISCUSSION

CPU protocols reported in the literature vary widely with no consensus regarding appropriate inclusion and exclusion criteria in determining which patients should undergo cardiac stress testing or type of stress test.[1-4,19,23-29] Herman et al reported on a patient population of 220 patients under the age of 40 without preexisting CAD who had AMI ruled out with serial cardiac marker tests and serial ECG.[1] In this group of patients, only 6 had positive stress tests. Two of these 6 patients underwent no further testing with no adverse events on follow-up and 4 had normal coronary arteriogram (i.e. false positive nuclear stress test). Even if both patients with a positive nuclear stress test that did not undergo coronary arteriogram had ACS, the rate of ACS in this patient population is still less than 1%. Herman concludes that patients less than 40 years of age who rule out for AMI with serial cardiac markers and ECG do not require routine stress testing. Herman's article is limited by its small sample size, retrospective design, lack of standardized stress testing protocol (73% nuclear stress testing, 22% treadmill exercise stress testing, and 5% stress echocardiography), and lack of follow-up. Also, the fact that all patients unable to perform exercise testing were excluded from the protocol indicates a significant degree of selection bias towards healthier patients. In our patient population, only 29% of patients were able to perform treadmill exercise testing during the stress phase of nuclear stress testing. The remainder of patients underwent pharmacologic stress testing (57% adenosine stress, 13% dipyridamole, and 1% dobutamine stress). Finally, Herman did not differentiate male sex from female sex though it is well established that there are definitely age related differences in risk for CAD between the sexes.[30-33] The Framingham study found that a 33 year old male had the same risk of CAD as a 40 year old female.[30] However, our data does support Herman's findings of an extremely low risk

of ACS in patients less than age 40 as only 1 of 104 patients less than 40 years old without history of CAD had ACS. Studies by Dawson et al and Colin et al also found an extremely low risk for ACS in patients < 40.[2,3]

It cannot be over emphasized that the low risk for ACS in patients < 40 years old is only after AMI has be reliably excluded. In our entire patient population, there were 258 cases of MI and 373 cases of 30-day ACS. In the subgroup of age < 40, 20 patients (7.8%) had MI and 23 patients (6.2%) had 30-day ACS. Of interest, in patients < 40, males accounted for 70% of MI's and 74% of 30-day ACS which again supports our supposition that sex needs to be taken into account when setting age criteria for assessing risk.

Purim-Shem-Tov et al investigated the influence of number of risk factors in 243 patients without preexisting CAD who underwent a CPU evaluation protocol.[4] Of these, 210 patients underwent nuclear stress testing. They found that patients with greater than or equal to 3 cardiac risk factors had a positive stress test rate of 18.5% (the authors did not report the incidence of ACS in these 18.5% of patients with positive stress test). The authors conclude that these patients should be excluded from CPU protocols due to the high rate of positivity and admitted for further evaluation. However, as the majority of the remainder of patients would have been discharged after having a negative stress test, it seems premature to exclude this group from CPU protocols. Our investigation found a rate of ACS of 8.9% in the 247 patients without preexisting disease who had greater than or equal to three cardiac risk factors.

Madsen et al evaluated 531 patients admitted to a CPU.[23] Twenty-three percent of these patients had a history of CAD. Patients with a history of CAD had higher rates of positive stress test or coronary computed tomography angiogram as compared to patients without history of CAD (32.3% vs. 6.9%; P<.001) and higher rates of PCI or CABG (12% vs.5.9%). Madsen et al conclude that CPU's that include patients with history of CAD may wish to reconsider evaluating this high risk subgroup in

the observation setting. The results of this investigation are limited because 57% of the patients did not undergo stress testing. Our study found an ACS rate of 17.6% in patients with pre-existing CAD. We feel that this risk rate of 17.6% falls within the range of the low-to-intermediate risk patient population ideal for CPU evaluation and stress testing.

Though there is no consensus as to what constitutes a low-to-intermediate risk chest pain patient, our regression formula suggests that patients with regression score from greater than 2.5% to 20% are an ideal patient population for undergoing cardiac stress testing once AMI has been reliably ruled out. There were 172 patients with a regression score $\leq$ 2.5% without a single occurrence of ACS. If none of these patients underwent stress testing, it would have reduced the number of patients undergoing stress testing by 21.5% with a significant resource savings. There were 91 patients with a regression score of > 20% (ACS rate 25.3%). Admission of these patients to the inpatient setting for cardiology consultation would have resulted in only 7 additional admissions per month during the 13-month study period.

It is important to understand that our model was developed in a chest pain patient population that was deemed to be at low-to-intermediate risk for ACS once MI had been reliably excluded. Our model is not intended to be applied indiscriminately to all chest pain patients as our model grossly underestimates risk in category 2 chest pain patients and grossly overestimates risk in category 4 patients.

In conclusion, a regression model utilizing age, sex, preexisting CAD, diabetes, and hyperlipidemia is predictive of 30-day ACS in patients undergoing nuclear stress testing in whom AMI has been reliably excluded and in whom concern still exists that the chest pain may be ischemic in nature. Prospective studies need to be performed to determine whether this model can assist physicians in selection of appropriate low-to-intermediate risk chest pain patients for nuclear stress testing.

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Table 1. Characteristics in patients with and without 30-day ACS.

	30-Day ACS (N=74) N (%)	**No 30-day ACS (N= 726) N (%)**
Population Demographics		
Age (y)		
Age ≤ 40 (n=117)	2 (2.7)	115 (15.8)
Age 41-50 (n=228)	18 (24.3)	210 (28.9)
Age 51-60 (n=224)	32 (43.2)	192 (26.4)
Age > 60 (n=231)	22 (29.7)	209 (28.8)
Race		
White (n=627)	61 (82.4)	566 (78.0)
Black (n=161)	11(14.9)	150 (20.7)
Other (n=12)	2 (2.7)	10 (1.4)
Male sex	47 (63.5)	362 (49.9)
Diabetes	26 (35.1)	131 (18.0)
Hypertension	50 (67.6)	403 (55.5)
Cigarette Use	29 (39.2)	273 (37.6)
Hyperlipidemia	48 (50.4)	355 (48.9)
Family History CAD	24 (32.4)	242 (33.3)
Obesity	38 (51.4)	344 (47.4)
Number of Risk Factors		
0-1 (n=191)	9 (12.2)	182 (25.1)
2 (n=230)	17 (23.0)	213 (29.3)
3 (n=212)	26 (35.1)	186 (25.6)
4-6 (n=167)	22 (29.7)	145 (20.0)
History Prior MI	42 (56.8)	187 (25.8)
History Prior CABG/PCI	40 (54.1)	726 (20.8)
History of CAD	47 (63.5)	220 (30.3)

Table 2. 30-day outcome in the 800 study patients for patients with and without preexisting CAD.

	History of CAD (N=267)	**No History CAD (N= 533)**
	N (%)	**N (%)**
30-Day Outcome		
24-hr MI	3 (1.1)	4 (0.8)
30-day PCI	20 (7.5)	11 (2.1)
30-day CABG	10 (3.8)	7 (1.3)
30-day stenosis*	16 (6.0)	9 (1.7)
30-day life-threatening complication	1 (0.4)	1 (0.2)
30-day death	0	0
30-day ACS	47 (17.6)	27 (5.1)

*stenosis $\geq$ 70% on coronary arteriogram not amenable to PCI/CABG

Table 3. Rates of 30-day ACS by age category and by number of risk factors for patients with and without preexisting CAD.

	History of CAD (N=267)		No History CAD (N=533)	
	#ACS/N	**%ACS (95% CI)**	**#ACS/N**	**%ACS (95% CI)**
≤ 40	1/13	7.7 (0.2-42.9)	1/104	1.0 (0.02-5.4)
41-50	11/62	17.7 (8.9-31.8)	7/166	4.2 (1.7-8.7)
51-60	19/75	25.3 (15.3-39.6)	13/149	8.7 (4.6-14.9)
>60	16/117	13.7 (7.8-22.2)	6/114	5.3% (1.9-11.5)
Number of Risk Factors				
0-1	8/50	16.0 (6.9-31.5)	1/141	0.7 (0.02-4.0)
2	13/85	15.3 (8.1-26.2)	4/145	2.8 (0.8-7.1)
3	16/61	26.2 (15.0-42.6)	10/151	6.6 (3.2-12.2)
4-6	10/71	14.1 (6.8-25.9)	12/96	12.5 (6.5-21.8)

Table 4. Regression model for prediction of 30-day ACS in patients deemed to be low-to-intermediate risk for ACS after AMI has been ruled out with the Erlanger Chest Pain Protocol. Risk of CAD is: $1/[1 + e^{-sum}]$ where sum equals the sum of constant plus coefficient values for individual risk factors. Risk calculator is available at http://107.22.120.83/acs/.

Factor	**Regression Coefficient**	**Odds Ratio (95% CI)**
Age 43-49	1.29	3.64 (0.98-13.5)
Age 50-55	1.94	6.95 (1.97-24.5)
Age 56-64	1.74	5.69 (1.60-20.2)
Age > 64	1.53	4.62 (1.27-16.8)
Male Sex	0.68	1.97 (1.152-3.38)
Hx CAD	1.08	2.95 (1.73-5.02)
Diabetes	0.80	2.24 (1.29-3.89)
Hyperlipidemia	0.67	1.95 (1.15-3.28)
Constant	***-5.24***	

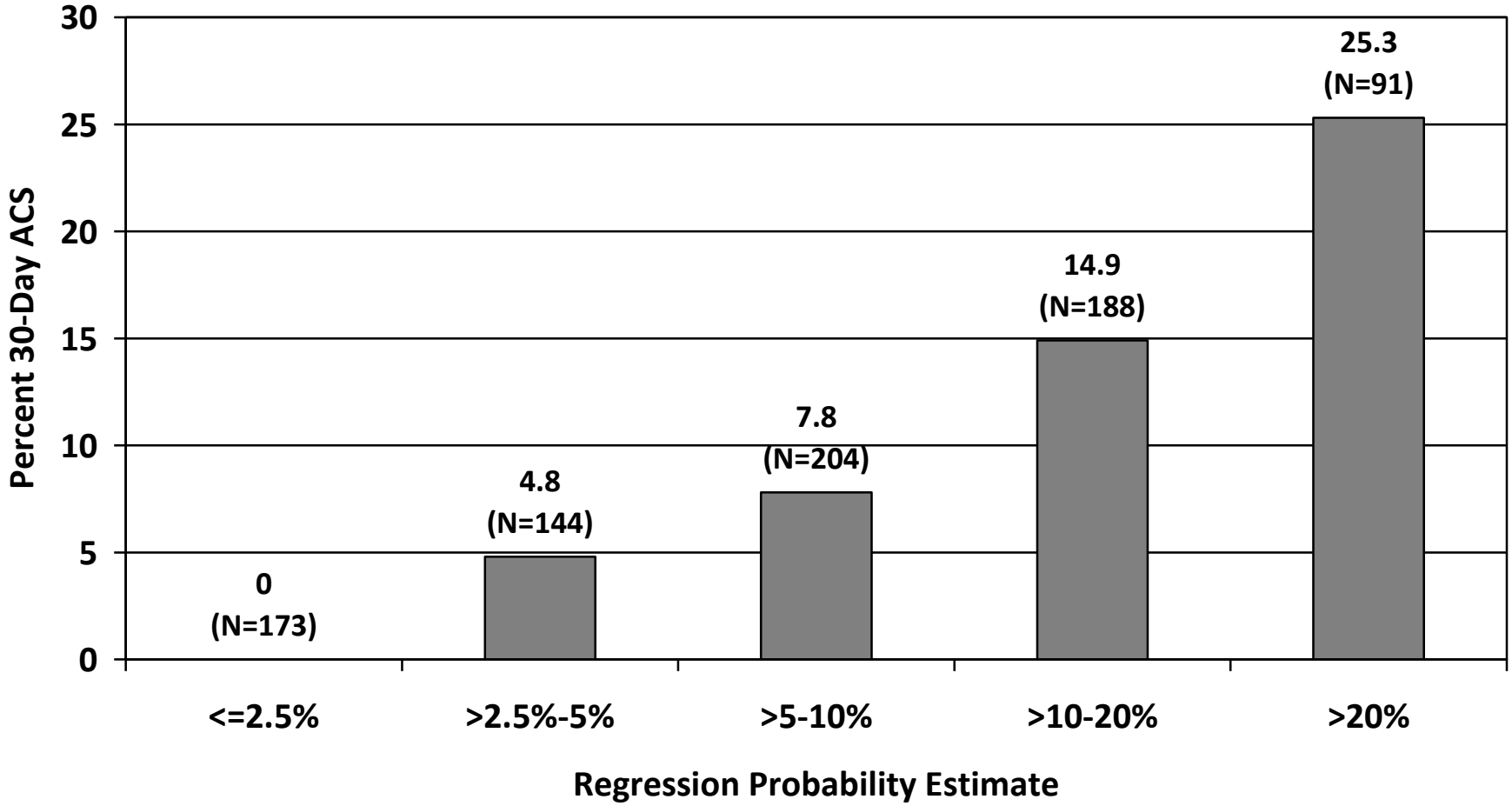
30
25
20
15
10
5
0
Percent 30-Day ACS
0
(N=173)
4.8
(N=144)
7.8
(N=204)
14.9
(N=188)
25.3
(N=91)
<=2.5%
>2.5%-5%
>5-10%
>10-20%
>20%
Regression Probability Estimate

Figure. Comparison between probability estimates of the regression model versus actual incidence of 30-day ACS in the 800 study patients.