Framingham Risk Score Inadequately Identifies Patients at Risk of a First ST Elevation Myocardial Infarction

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Citation

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Abstract

The Framingham Risk Score (FRS) and ATPIII guidelines are standard tools used to assess risk of a first cardiac event and institute primary preventive therapy. The performance of these tools for predicting the occurrence of STEMI has not been evaluated. A retrospective analysis was performed on patients presenting with STEMI and without a history of coronary artery disease (CAD) or equivalent at a single institution during calendar years 2004-2007. FRS was calculated based on admission demographics and fasting lipid profiles. A total of 238 patients met study criteria. Of these, 45 (18.9%) statin pre-treated. Of the remaining 193, 46 (23.8%) had FRS and lipid profiles meeting ATPIII criteria for pharmacotherapy: 14 (7.3%) with 10 year event risk>20%, 28 (14.6%) with 10 year risk 10-20%, 2+ risk factors, and LDL>130mg/dl; and 4 (2.1%) with 10 year risk <10, 2+ risk factors, and LDL>160mg/dl. Assuming all patients in the statin group had high-risk FRS, only 45/91 (49.5%) of patients meeting criteria for lipid pharmacotherapy were appropriately treated. Of all the typical risk factors for CAD, only male sex was significantly associated with the presence of a FRS and LDL meeting criteria for statin therapy. FRS underestimated risk in the majority of patients with a first STEMI and without a history of CAD or equivalent. Furthermore, a large proportion of patients who met ATPIII criteria for statin treatment were not identified and treated pre-event. Methods for better identifying patients at risk of STEMI and facilitating institution of appropriate primary preventive therapy are needed.

INTRODUCTION

The Framingham Risk score (FRS) and ATP III guidelines are the standard tools used to assess the risk of a first cardiac event and to guide the institution of primary preventive therapy in individuals at risk of cardiovascular disease. [1,2] Recent literature supports the concept that FRS may be inadequate in identifying the majority of patients who either have sub-clinical atherosclerosis as defined by coronary calcium assessment [3] or ultimately suffer a clinical cardiovascular event. [4]

Patients who suffer ST-elevation myocardial infarction (STEMI) represent a unique subgroup of ACS patients. Patients presenting with STEMI tend to be younger and have fewer traditional risk factors versus patients presenting with other ACS. [5] How FRS performs in predicting the occurrence of STEMI has not previously been examined. In the present study we tested the hypothesis that FRS underestimates cardiac risk in first-time STEMI patients who do not have a history of coronary artery disease (CAD) or a CAD equivalent such as diabetes mellitus or peripheral or cerebrovascular disease, the patient demographics that the FRS is designed to identify cardiac risk in.

METHODS

A retrospective analysis was performed on all patients presenting to Lehigh Valley Health Network in Allentown PA with a first STEMI during calendar years 2004-2007. Data regarding past medical history, prior medicine use, admitting laboratory studies, and hospital course were extracted from an electronic medical record database. Patients were included in the analysis if they presented with a first STEMI and had no prior history of coronary, cerebral, or peripheral vascular disease by either clinical events or abnormal diagnostic testing. Additionally, because it is considered to represent a CAD-equivalent, patients with a history of diabetes mellitus were not included in the study. Patients were excluded if they had been taking non-statin lipid-lowering agents, including fibrates, fish oil, cholesterol-binding agents, or niacin within 1 month of admission.

All patients underwent emergent cardiac catheterization within 2 hours of admission or transfer to the study center. Serum lipids were assessed within 24 hours of admission, in the fasted state. The Framingham Risk Score was calculated using the admission history and fasting lipid profile for all

patients not on a statin at the time of admission. For calculation of FRS, the following definitions were used: active smoking was considered to be the use of inhaled nicotine products within 1 month of admission; treated hypertension was considered to be the use of antihypertensive therapy at the time of admission. Patients were considered to have "high risk" profiles if they met one of the following criteria: FRS 10 year event rate >20%; FRS 10 year event rate 10year risk 10-20% with 2 or more risk factors and LDL>130mg/dl; or a FRS 10 year event rate less than 10% with 2 or more risk factors and LDL>160mg/dl.

Odds ratios of risk factors for high-risk FRS were calculated using SPSS software (Chicago, IL). The Institutional Review Board of Lehigh Valley Hospital approved the study.

RESULTS

A total of 238 patients were identified who met the study criteria. Demographics and admission lipid profiles are summarized in Table I:

Figure 1

		Range
Mean age, yrs	60	32-97
Gender, %male	70.0	N/A
% Tobacco Use	53	N/A
% with treated hypertension	27	N/A
% with FH CAD	45	N/A
Mean systolic BP, mmhg	127	79-240
Mean diastolic BP , mmhg	76	30-120
Mean total Cholesterol, mg/dL	176	87-317
Mean LDL, mg/dL	111	40-251
Mean HDL, mg/dL	36	18-71

Forty-five patients (18.9%) were prescribed statin therapy at the time of presentation. Of the remaining 193 patients not on a statin at the time of STEMI presentation, 46 (23.8%) had FRS and lipid profiles meeting ATPIII criteria for statin therapy (Table II):

Figure 2

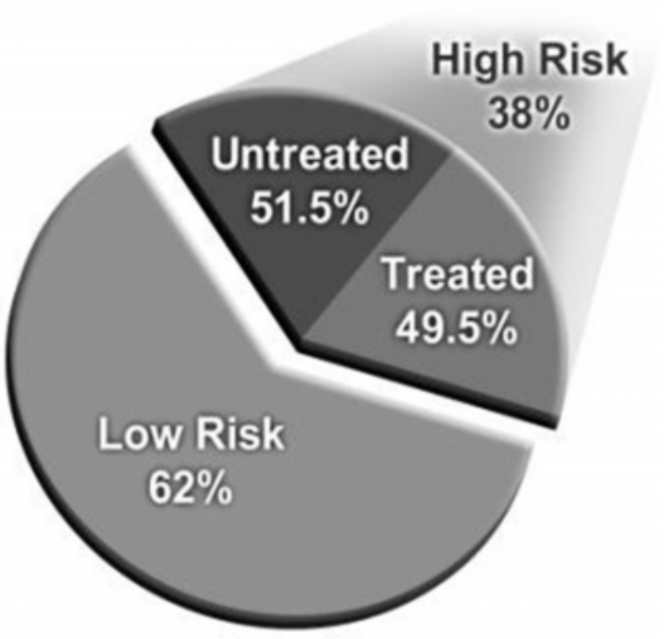
FRS	LDL	% Meeting Criteria For Statin Use
>20%	N/A	14/193 (7.3%)
10-20%	>130	28/193 (14.6%)
<10%	>160	4/193 (2.1%)
Total meeting ATP III		46/193 (23.8%)

14 (7.3%) had 10 year event risk >20%, 28 (14.6%) had 10 year risk =10-20% with 2+ risk factors, and LDL>130mg/dl, and 4(2.1%) had 10 year risk <10 with 2+ risk factors, and LDL>160mg/dl.

Making the assumption that all patients in the statin treatment group had FRS profiles meeting ATPIII criteria for statin pharmacotherapy, a total of 91 of the 238 patients in the study (38.2%) had admission FRS profiles that met criteria for pharmacologic lipid lowering. Furthermore, of these 91 patients with high risk FRS, only 45 (49.5%) were identified and appropriately treated with statin prior to the index STEMI (Figure I):

Figure I: Graphic breakdown of FRS/ATP categories of study patients. The 91 "high risk" patients were categorized as such based on prior statin use ("treated") or FRS/ATPIII assessment meeting criteria for hyperlipidemic treatment but not on therapy at presentation ("untreated").

Figure 3



Given the fact that prior studies have supported the concept

that STEMI patients tend to have fewer traditional risk factors than other ACS patients [6], we explored the relationship between the individual components of the FRS and the presence of a "high risk" FRS 10-year event rate in patients presenting with STEMI (Figure II):

Of all of the individual risk factors that are included in the FRS calculation, only male gender was significantly associated with a FRS mandating pharmacologic therapy (odds ratio 3.1, 95% CI 1.2-7.9). In contrast, age >60, tobacco use, and the presence of hypertension did not associate significantly with a high risk FRS.

DISCUSSION

Despite significant improvements in management options for acute coronary syndromes [78] and the resultant reduction in CAD mortality in the past decade, the burden of CAD mortality has remained high. (aha statement) [9] Our inability to robustly impact the development of CAD in many of these patients is likely due in part to the fact that our ability to adequately identify and thus target preventive therapy to patients at risk of coronary events has lagged behind advancing technology in treatment. The FRS and ATP III guidelines are the standard tool that is used to identify patients at risk of cardiac events. [12] However, recent studies have concluded that these methods of risk stratification may fail to identify up to three quarters of patients who ultimately suffer an ACS. [4]

Given the fact that patients who present with acute myocardial infarction and ST elevation represent a population with fewer traditional risk factors versus other ACS [6], one would hypothesize that FRS and ATP III are also relatively inadequate at identifying patients destined to suffer STEMI. In the present study we assessed the sensitivity of FRS for the identification of patients at risk of a first STEMI by retrospectively calculating the FRS 10 year event risk in patient presenting with a first STEMI. Less than 40% of these patients were either pre-treated with statins or had FRS 10 year event rates that mandated anti-hyperlipidemic pharmacotherapy by ATP III guidelines. [2] Thus, the majority of our cohort of patients presenting with a first STEMI would not have been identified prior to the event as being at high risk using FRS and ATP III. Furthermore, the majority of patients that did have high risk clinical characteristics by FRS were not treated with statin therapy. Taken together these data point out 2 gaps in our primary preventative efforts in this patient population: identification of at-risk patients and application of evidence-based therapy to these individuals.

A major criticism of the FRS is that it overemphasizes age as a risk factor for the occurrence of cardiac events. [10] Surprisingly, in our cohort there was no significant association between patients greater than 60 years of age and the occurrence of a high risk FRS (data not shown). The only component of FRS that was significantly associated with a high risk 10 year event rate was male gender. This finding confirms prior studies that have suggested that Framingham does an inadequate job of identifying women who are at high risk of suffering acute cardiac events and illustrates the particular need to define methods of identifying at-risk females beyond the FRS. [11]

The present study has several obvious weaknesses. It is a relatively small, retrospective study and needs to be confirmed in a larger database. The FRS was calculated using lipid data obtained in the first 24 hours after admission, and it is possible that in this setting the LDL may be falsely lowered due to the effects of acute medical illness on lipid metabolism, resulting in an increase in the number of first-STEMI patients with low FRS. However, recent data has suggested that the effect of STEMI on fasting lipids is not clinically significant. [12]

By what means can we improve on FRS for the identification of patients at risk of a first STEMI? An accumulating body of data supports the use of techniques to identify systemic inflammation using measurement of C-reactive protein (CRP) or imaging techniques to define subclinical atherosclerosis, such as coronary calcium scoring and ultrasound measurement of carotid intima-media thickness. [1314] In addition, a recent study suggested that measurement of concentrations of plasma homocysteine is superior to FRS in predicting cardiac events in older individuals. [15] While the evidence supporting these techniques is rapidly growing, there is a lack of data demonstrating the specific ability of CRP assessment or subclinical atherosclerosis imaging to identify patients at risk of STEMI.

In conclusion, the present study demonstrates that FRS underestimated cardiac risk in the majority of patients presenting with a first STEMI who did not have a history of cardiovascular disease or diabetes. Furthermore, of patients who had a high-risk FRS, greater than 50% were not identified and treated with appropriate preventative therapy.

Thus, methods for better identifying patients at risk of STEMI and institution of appropriate primary preventive treatments are needed.

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