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Atherosclerotic Risk Factors and Their Association With Hospital Mortality Among Patients With First Myocardial Infarction (from the National Registry of Myocardial Infarction)

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Abstract

Few studies have examined associations between atherosclerotic risk factors and short-term mortality after first myocardial infarction (MI). Histories of 5 traditional atherosclerotic risk factors at presentation (diabetes, hypertension, smoking, dyslipidemia, and family history of premature heart disease) and hospital mortality were examined among 542,008 patients with first MIs in the National Registry of Myocardial Infarction (1994 to 2006). On initial MI presentation, history of hypertension (52.3%) was most common, followed by smoking (31.3%). The least common risk factor was diabetes (22.4%). Crude mortality was highest in patients with MI with

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diabetes (11.9%) and hypertension (9.8%) and lowest in those with smoking histories (5.4%) and dyslipidemia (4.6%). The inclusion of 5 atherosclerotic risk factors in a stepwise multivariate model contributed little toward predicting hospital mortality over age alone (C-statistic = 0.73 and 0.71, respectively). After extensive multivariate adjustments for clinical and sociodemographic factors, patients with MI with diabetes had higher odds of dying (odds ratio [OR] 1.23, 95% confidence interval [CI] 1.20 to 1.26) than those without diabetes and similarly for hypertension (OR 1.08, 95% CI 1.06 to 1.11). Conversely, family history (OR 0.71, 95% CI 0.69 to 0.73), dyslipidemia (OR 0.62, 95% CI 0.60 to 0.64), and smoking (OR 0.85, 95% CI 0.83 to 0.88) were associated with decreased mortality (C-statistic = 0.82 for the full model). In conclusion, in the setting of acute MI, histories of diabetes and hypertension are associated with higher hospital mortality, but the inclusion of atherosclerotic risk factors in models of hospital mortality does not improve predictive ability beyond other major clinical and sociodemographic characteristics.

The evidence is indisputable that 4 major traditional risk factors—smoking, hypertension, diabetes, and dyslipidemia—are predictive of coronary heart disease (CHD) occurrence, as initially reported from the Framingham study[1] and subsequently validated by many other investigators.[2–5] However, the relations between atherosclerotic risk factors and short-term prognosis after myocardial infarction (MI) are less well understood. We examined the relations between atherosclerotic risk factors and hospital mortality after first MI, one at a time and collectively for all the atherosclerotic risk factors combined. The main objective of this study was to use National Registry of Myocardial Infarction (NRMI) data to (1) describe the distributions of individual atherosclerotic risk factors and their associations among a cohort of patients with first MIs and (2) ascertain their relative contribution in predicting subsequent hospital mortality.

Methods

The NRMI is an industry-sponsored national registry of 2,160,671 patients admitted with confirmed MIs at 1,977 participating hospitals from 1994 to 2006. Institutional review board approval of data collection was obtained as required by the local hospitals. Given the potential complexity in studying patients with known cardiovascular disease, we first excluded patients with previous MIs, CHD, angina, heart failure, percutaneous coronary intervention, coronary artery bypass graft surgery, stroke, cerebrovascular disease, and peripheral vascular disease (n = 1,052,920). Next, any transfer patients (transfer in and transfer out) were excluded from the analysis because of the potential for incomplete reporting at initial hospital or subsequent outcome (n = 526,350). An additional 39,393 patients were excluded because of missing age, gender, weight, pulse, systolic blood pressure, and hospital characteristics. The diagnosis of MI was based on a clinical presentation consistent with MI and/or ≥1 of the following: (1) an elevated cardiac biomarker such as troponin and/or creatine kinase-MB; (2) electrocardiographic evidence of acute ST-segment elevation MI; (3) alternative enzymatic, scintigraphic, or autopsy evidence indicative of acute MI or necrosis; and (4) International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis code 410.X1. Case ascertainment and clinical data were previously validated by comparison to the Medicare-Cooperative Cardiovascular Project.[6]

Five major atherosclerotic risk factors were recorded by review of the medical record during the index hospitalization period: smoking (current or former); history of diabetes, hypertension, or dyslipidemia; and family history of CHD, defined as an immediate relative diagnosed as having CHD before 60 years of age. These risk factors were identified before and during hospitalization, as documented in the medical record, and were based on patient or family self-report or previous records. Weight was available throughout the study period, but body mass index was available only in the NRMI for 2000 to 2006.

The descriptive results were stratified by the presence of 5 major atherosclerotic risk factors and further divided by gender and age. Multivariate logistic regression models were fit for successive blocks of covariates to assess the associations of atherosclerotic risk factors and hospital mortality. Variables in the mortality model were entered in a stepwise manner: (1) age, (2) atherosclerotic risk factors, (3) weight, (4) baseline and presenting characteristics (Table 1) and hospital characteristics (such as facility type, MI volumes, census region, teaching, and rural location), calendar year. Two-tailed tests were used, and p values <0.05 were considered significant. All statistical analyses were done with SAS version 9.13, service pack 4 (SAS Institute Inc., Cary, North Carolina).

Results

A total of 542,008 patients fulfilled study criteria for initial MI presentation. The most common risk factor in patients with initial MIs was hypertension (52.3%), followed by smoking (31.3%), dyslipidemia (28.0%), family history of CHD (28.0%), and the least common traditional risk factor, diabetes mellitus (22.4%) (Table 1).

The mean age was highest in patients with hypertension, followed by those with diabetes, and lowest in smokers. Whites had a greater prevalence of family history of CHD, but blacks and Hispanics had relatively higher proportions with diabetes and hypertension. Asians were the least likely to smoke. Among patients with diabetes, the next most common risk factor in combination with diabetes was hypertension, followed by dyslipidemia. In patients with family histories of CHD, almost half had hypertension, and 1/3 had dyslipidemia. Despite family histories of CHD, >40% smoked. In patients with hypertension, 1/4 had diabetes, >1/4 had dyslipidemia, 1/4 had smoking histories, and 1/4 had family histories of CHD. Smokers were most likely to have hypertension or family histories of CHD but least likely to have diabetes. More than 2/3 of the population with initial MI was either overweight or obese. The proportion of population with either obesity or morbid obesity was highest in patients with diabetes and lowest in smokers.

Patients with diabetes were more likely to delay hospital presentation (46 minutes more on average) compared to those without diabetes. Also, patients with diabetes were most likely to present in Killip class >1, although patients with diabetes or smoking histories were more likely to be in cardiogenic shock. Smokers and those with family histories of CHD were more likely to have ST-segment elevation on initial electrocardiography and inferior or posterior MI location compared to the other risk factor groups, and patients with MI with diabetes or hypertension had a slightly higher prevalence of left bundle branch block.

Overall, men with MIs tended to have a greater prevalence of smoking, to have family histories of CHD, or to be either overweight or obese (Table 2). Women with MIs had more diabetes and hypertension and were more likely to be underweight, normal weight, or morbidly obese. Smokers tended to present with initial MIs at a much younger age, a finding seen in men and women. Similarly, patients with MI with family histories of CHD were more likely to present at an earlier age. In contrast, in those with MIs, hypertension appeared to increase in prevalence with advancing age and was especially notable in those aged >55 years old in either gender. Gender differences in diabetes were more apparent in younger age groups (greater in women), and these differences appeared to attenuate with increasing age.

Crude mortality was highest in patients with MI with diabetes (11.9%) and hypertension (9.8%) and lowest in patients with smoking histories (5.4%) and dyslipidemia (4.6%) (Table 3). In the adjusted mortality model to examine the association of atherosclerotic risk factors with short-term outcomes, we first included age in the model, given its relative importance for short-term outcome (C-statistic = 0.71). After including each of the individual 5 atherosclerotic risk factors in a stepwise multivariate model, the C-statistic changed very little over and above that of age alone (C-statistic = 0.73). Similarly, the C-statistic did not change after including weight as a risk factor (C-statistic = 0.73). Last, in the final adjusted model for mortality, after including other important factors, such as race or ethnicity, gender, payer status and other presenting characteristics, and hospital characteristics, patients with MI with diabetes and hypertension had higher adjusted odds of dying in the hospital than those without diabetes or hypertension, and conversely, patients with family histories of CAD, those with dyslipidemia, and smokers had lower adjusted odds of dying.

Discussion

This analysis represents one of the largest studies to examine the relation of traditional atherosclerotic risk factors at presentation and their association with short-term mortality after MI. We report that hypertension was the most common risk factor, followed by smoking, and diabetes was the least common risk factor. After adjustment for extensive clinical and sociodemographic characteristics, diabetes and hypertension were independently associated with higher hospital mortality, but family history of CHD, dyslipidemia, and smoking were independently associated with lower hospital mortality. However, identification of atherosclerotic risk factors at presentation does not improve the prediction of hospital mortality significantly compared to other sociodemographic and clinical presenting characteristics available in the NRMI.

In a multivariate model examining independent predictors of mortality, after first adjusting for age, the C-statistic (the area under the receiver-operating characteristic curve, a measure of the model's ability to discriminate between survivors and nonsurvivors) changed little after introducing traditional atherosclerotic risk factors. Once extensive clinical, sociodemographic, and hospital-related factors were added, the model's ability to discriminate between survivors and nonsurvivors increased considerably. Although diabetes and hypertension were ultimately independently associated with higher odds of in-hospital death (23% and 8% higher odds, respectively), atherosclerotic risk factors were not

relatively as important in predicting hospital mortality compared to other clinical factors available in the NRMI, such as advanced age, cardiogenic shock, acute pulmonary edema, heart rate, systolic blood pressure, and ST-segment elevation myocardial infarction.

It is important to emphasize that we examined predictors of hospital death after MI, not predictors of the development of CHD or recurrent CHD events, the latter being known to be influenced by the presence of atherosclerotic risk factors, especially if poorly controlled. The observation that atherosclerotic risk factors are weak predictors of hospital death after MI may run contrary to general clinician expectations. However, although perhaps clinically surprising, this finding is consistent with many published studies. For example, the Global Registry of Acute Coronary Events (GRACE)[7] and Thrombolysis In Myocardial Infarction (TIMI) indexes[8,9] were developed to help risk-stratify and assess the prognosis (mortality) of patients who present with MI, and classic risk factors were available for multivariate model development. However, the risk factors either did not make it into the final score or contributed very little in predicting short-term mortality compared to other available clinical variables. More recently, the TIMI risk index, a newer predictive instrument for outcome after MI, may be calculated at the point of initial contact with the medical system[10] and is based solely on age, heart rate, and systolic blood pressure. The TIMI risk index, which has been externally validated, may predict hospital mortality without direct measurement of co-morbid factors, including atherosclerotic risk factors, in part because of age likely correlating well with these co-morbidities.[10]

Our analysis confirms and formally measures the minor contribution of atherosclerotic risk factors in predicting hospital mortality, and any clinical judgment regarding a patient's short-term prognosis should be based on variables such as age and acute clinical status, rather than atherosclerotic risk factors. It is apparent that most of the factors that predict hospital mortality after MI are in fact those we cannot modify at the time of hospital presentation. Hence, from a public health perspective, we should focus on modifiable factors that may potentially influence survival, such as earlier patient recognition of MI symptoms, prompt arrival to a cardiac hospital preferably by the activation of emergency medical services, wider use of aspirin, and timely restoration of anterograde coronary flow with acute reperfusion therapies.

In the NRMI, a number of atherosclerotic risk factors were observed in the younger MI cohort (age <55 years). Smoking is arguably the strongest predictor for premature heart disease in men and women. Although smoking is an important risk factor for MI at any age, the higher prevalence of smoking in the younger age group who developed MI represents an important public health opportunity. Also, a strong family history of premature CHD is an important determinant for earlier MI, and patients with this risk factor might benefit from an earlier strategy to screen and identify modifiable risk factors, possibly using even lower thresholds for instituting risk factor modification and treatments. In our study, the fact that >40% patients with family histories of CHD also smoked represents a significant opportunity for public health education. Last, although the presence of diabetes with 1 additional risk factor has been elevated to a CHD risk equivalent,[11] perhaps even earlier treatment is warranted, especially in younger women with diabetes aged <55 years.

A family history of CHD is considered by many as a predisposing risk factor but has not been established to be a significant risk factor alone after adjusting for traditional risk factors. In fact, this inheritable risk factor was not even included in the traditional Framingham risk score that is used to predict 10-year risk for heart disease.[12] It is likely that a family history of CHD may be an important contributing factor in the development of CHD through phenotypic expression of the conventional atherosclerotic risk factors such as diabetes, hypertension, and dyslipidemia.

The NRMI is an observational study, and our results may be limited by bias and unmeasured confounders. The NRMI patients and hospitals enrolled may not be representative of all patients with MI and hospitals in the United States. Also, the relative levels of risk factor exposure, such as blood pressure control, cholesterol levels, and glycosylated hemoglobin, were not readily available in our study. Last, ascertainment of risk factors was obtained through medical record review at the time of hospitalization.

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Table 1

Characteristics of patients with and without atherosclerotic risk factors and first myocardial infarctions: National Registry of Myocardial Infarction, 1994 to 2006

Variable	Atherosclerotic Risk Factors at Presentation				
	Smoking (n = 169,674 [31.3%])	Diabetes (n = 121,630 [22.4%])	Dyslipidemia (n = 151,849 [28.0%])	Hypertension (n = 283,215 [52.3%])	Family History of CHD (n = 151,595 [28.0%])
Age (years)	57.7 ± 11.0	67.4 ± 12.5	63.3 ± 12.5	68.5 ± 13.3	60.7 ± 12.5
Women	31.7%	46.9%	39.1%	47.8%	35.8%
Race/ethnicity					
White	82.7%	76.7%	84.8%	81.1%	86.8%
Black	9.1%	10.9%	5.9%	9.7%	6.0%
Hispanic	3.4%	6.0%	3.4%	3.6%	2.8%
Asian	1.4%	2.9%	2.3%	2.3%	1.1%
Other	3.4%	3.6%	3.6%	3.2%	3.3%
Smoking	100.0%	21.7%	33.1%	25.2%	40.9%
Diabetes mellitus	15.5%	100.0%	24.9%	28.7%	18.9%
Dyslipidemia	29.6%	31.1%	100.0%	32.4%	36.1%
Hypertension	42.1%	66.9%	60.5%	100.0%	48.4%
Family history of CHD	36.5%	23.6%	36.1%	25.9%	100.0%
Body mass index (kg/m^2)*	28.4 ± 6.2	30.2 ± 7.0	29.2 ± 6.1	28.8 ± 6.6	29.2 ± 6.2
Underweight	2.7%	1.9%	1.5%	2.9%	1.7%
Normal	27.0%	20.6%	21.6%	26.1%	22.5%
25–29.9	36.7%	32.5%	38.6%	34.3%	38.0%
30–39.9	29.1%	36.4%	32.9%	30.9%	32.4%
≥40	4.6%	8.6%	5.3%	5.8%	5.4%
≥30	33.7%	45.0%	38.2%	36.7%	37.8%
Initial systolic blood pressure (mm Hg)	142.7 ± 31.5	146.3 ± 33.7	146.7 ± 30.8	149.5 ± 33.8	146.4 ± 30.4
Heart rate (beats/min)	84.5 ± 22.9	90.8 ± 24.2	83.4 ± 22.0	87.5 ± 24.0	83.3 ± 21.8
Symptom onset to arrival, hours	5.3 ± 8.9	6.4 ± 10.1	5.6 ± 9.0	5.9 ± 9.5	5.6 ± 9.2
Killip class					
I	87.1%	74.9%	87.5%	80.1%	88.2%
II	8.4%	15.4%	8.2%	12.8%	7.9%
III	3.3%	8.3%	3.5%	5.9%	3.1%
IV	1.2%	1.4%	0.8%	1.1%	0.8%
Initial electrocardiographic findings					
ST-segment elevation	49.8%	36.1%	42.3%	37.1%	45.5%
ST-segment depression	31.4%	26.4%	30.4%	27.8%	30.3%
Nonspecific	26.7%	33.9%	30.1%	32.9%	29.4%
Q wave	11.8%	10.6%	11.1%	10.0%	11.7%
Left bundle branch block	2.0%	5.0%	2.8%	4.4%	2.6%
Myocardial infarction location					

Variable	Atherosclerotic Risk Factors at Presentation				
	Smoking (n = 169,674 [31.3%])	Diabetes (n = 121,630 [22.4%])	Dyslipidemia (n = 151,849 [28.0%])	Hypertension (n = 283,215 [52.3%])	Family History of CHD (n = 151,595 [28.0%])
Anterior/septal	25.2%	24.7%	24.0%	24.3%	25.7%
Inferior	41.8%	30.0%	37.1%	31.1%	38.5%
Posterior	6.2%	3.9%	5.6%	4.5%	5.8%
Lateral	13.8%	12.2%	13.1%	12.7%	13.8%
Right ventricle	1.1%	0.7%	0.9%	0.7%	0.9%
Unspecified	29.7%	42.7%	35.2%	41.5%	32.0%

Data are expressed as mean ± SD or as percentages. For all comparisons, $p < 0.001$.

* Body mass index is available in NRMI 4 to 5.

Table 2

Prevalence of atherosclerotic risk factors and first myocardial infarction by gender and age: National Registry of Myocardial Infarction, 1994 to 2006

Risk Factor	Age <45 Years		Age 46–55 Years		Age 56–65 Years		Age 66–75 Years		Age >75 Years	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
n (%)	11,369 (2.1%)	38,214 (7.0%)	24,102 (4.4%)	73,761 (13.6%)	36,182 (6.7%)	75,004 (13.8%)	54,011 (10.0%)	66,531 (12.3%)	98,629 (18.2%)	64,205 (11.8%)
Smoking	61.6%	63.5%	53.4%	54.4%	40.2%	39.3%	22.6%	23.1%	7.2%	10.4%
Diabetes mellitus	21.9%	11.7%	26.3%	16.5%	29.5%	21.6%	29.4%	25.5%	22.0%	23.0%
Dyslipidemia	24.1%	31.1%	32.9%	35.4%	34.7%	33.6%	31.3%	27.7%	19.5%	16.8%
Hypertension	38.8%	32.8%	49.7%	41.1%	56.4%	47.4%	62.2%	52.4%	65.9%	53.8%
Family history of CHD	41.9%	46.1%	40.5%	40.9%	33.6%	33.2%	25.0%	23.8%	14.3%	13.7%
Body mass index (kg/m^2)*										
<18.5	2.2%	0.8%	1.7%	0.8%	2.4%	1.1%	4.4%	1.8%	8.5%	4.0%
18.5–24.9	23.8%	17.6%	22.2%	17.1%	25.2%	19.3%	31.0%	25.1%	45.5%	43.2%
25–29.9	25.8%	37.6%	28.1%	40.9%	29.6%	42.1%	31.4%	44.6%	28.3%	38.1%
30–39.9	34.9%	37.7%	36.0%	35.7%	33.6%	33.4%	28.2%	26.1%	15.8%	13.8%
≥40	13.2%	6.3%	12.1%	5.4%	9.2%	4.1%	5.0%	2.4%	1.8%	0.9%

* Body mass index is available in NRMI 4 to 5. For all comparisons, $p < 0.001$.

Table 3

Association of each atherosclerotic risk factor and adjusted mortality in patients with and without cardiovascular risk factors and first myocardial infarction: National Registry of Myocardial Infarction, 1994 to 2006

Risk Factor	Odds Ratio (95% Confidence Interval)	Wald Chi-Square
Model 1: age by 10-year intervals	1.77 (1.75–1.78)	21,027
Model 2: age, atherosclerotic risk factors (n = 5)		
Diabetes mellitus	1.35 (1.32–1.38)	727
Hypertension	0.89 (0.88–0.91)	127
Smoking	0.93 (0.90–0.95)	31
Family history of CHD	0.62 (0.60–0.64)	1,231
Dyslipidemia	0.49 (0.48–0.51)	2,684
Model 3: age, atherosclerotic risk factors, weight		
Diabetes mellitus	1.41 (1.38–1.44)	947
Hypertension	0.91 (0.89–0.92)	98
Smoking	0.89 (0.87–0.92)	72
Family history of CHD	0.63 (0.61–0.64)	1,152
Dyslipidemia	0.51 (0.49–0.52)	2,484
Model 4: full model		
Diabetes mellitus	1.23 (1.20–1.26)	299
Hypertension	1.08 (1.06–1.11)	56
Smoking	0.85 (0.83–0.88)	122
Family history of CHD	0.71 (0.69–0.73)	545
Dyslipidemia	0.62 (0.60–0.64)	1,071
Age by 10-year intervals	1.43 (1.41–1.44)	3,397
Weight (kg)		
<50	1.16 (1.11–1.21)	50
50–<60	1.00 (referent)	
60–<70	0.93 (0.90–0.96)	18
70–<80	0.87 (0.84–0.90)	57
80–<90	0.79 (0.76–0.83)	133
90–<100	0.76 (0.73–0.80)	132
100–<110	0.76 (0.71–0.80)	87
110–<120	0.85 (0.79–0.92)	17
≥120	0.93 (0.87–0.99)	5
Female gender	0.99 (0.96–1.01)	2
Race/ethnicity		
White	1.00 (referent)	
African American/black	1.05 (1.00–1.09)	5
Asian/Pacific-Islander	1.06 (0.99–1.14)	3

Risk Factor	Odds Ratio (95% Confidence Interval)	Wald Chi-Square
Hispanic	1.00 (0.95–1.06)	0
Insurance		
Medicare	1.36 (1.32–1.41)	351
Medicaid and/or uninsured	1.36 (1.30–1.43)	183
Systolic blood pressure	0.98 (0.98–0.98)	10,002
Pulse	1.01 (1.01–1.01)	2,178
Prehospital delay (hours)		
0–2	1.00 (referent)	
2–<4	0.80 (0.76–0.83)	129
≥4	0.97 (0.94–1.00)	4
Killip class		
I	1.00 (referent)	
II	1.52 (1.48–1.56)	949
III	1.91 (1.85–1.98)	1,250
IV	8.30 (7.84–8.78)	5,352
Calendar year	0.97 (0.96–0.97)	317
ST-segment or left bundle branch block	1.74 (1.70–1.78)	2,000
MI location (anterior)	1.27 (1.24–1.30)	417
Admission diagnosis		
Unstable angina/other	1.00 (referent)	
MI	0.76 (0.75–0.78)	428
Rule out MI	0.51 (0.49–0.53)	1,647
MI volume quartile		
1	1.00 (referent)	
2	1.02 (0.97–1.07)	0
3	1.01 (0.96–1.06)	0
4	0.99 (0.94–1.04)	0
Percutaneous coronary intervention noncapable	1.00 (referent)	
Interventional	0.65 (0.63–0.67)	882
Interventional without open-heart surgery	0.79 (0.76–0.83)	103
Census region		
East	1.00 (referent)	
West	1.15 (1.11–1.19)	62
South	1.24 (1.19–1.28)	152
Midwest	1.14 (1.10–1.17)	54
Hospital type		
Nonurban	1.00 (referent)	
Urban teaching	0.99 (0.94–1.04)	0
Urban nonteaching	0.99 (0.96–1.03)	0