RISK FACTORS FOR ACUTE NON-ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION IN A POPULATION SAMPLE OF PREDOMINANTLY AFRICAN AMERICAN PATIENTS WITH CHEST PAIN AND NORMAL CORONARY ARTERIES

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Background: We sought to investigate the relationship between echocardiographic left ventricular hypertrophy (LVH) and acute non-ST-elevation segment myocardial infarction (NSTE-MI) in patients with chest pain and angiographically normal coronary arteries.

Methods: Retrospective analysis of patients admitted for acute chest pain in a large urban hospital serving predominantly African American patients.

Results: 131 (of 700) patients had normal coronary arteries or only minimal luminal irregularities (ie, <10% luminal narrowing) on cardiac angiography and available cardiac biomarker data to define the presence or absence of MI. Mean age was 53 ± 10 years, 76% were African Americans, 88% had a history of hypertension (49% uncontrolled) and 74% had LVH by echocardiography. Of these 131 patients, 22 (17%) had an acute NSTE-MI by creatine kinase MB criteria. The mean systolic blood pressure (BP) was significantly higher in patients with NSTE-MI compared with non-NSTE-MI group (156 ± 30 vs 143 ± 25 mm Hg, *P*=.04). Patients with NSTE-MI were more likely to have LVH (95% vs 70%, *P*=.03). NSTE-MI was present in 22% of patients with LVH compared with 3% without LVH (*P*=.02). The in-hospital course of NSTE-MI patients with LVH was not benign: 19% had persistent angina and positive stress thallium suggestive of recurrent myocardial ischemia and 48% had congestive heart failure. The results of multivariable model after adjusting for selected variables revealed that these two preexisting conditions were independently associated with NSTE-MI: LVH (OR=4.0, CI 1.06-10.05) and elevated systolic BP (OR=3.7, CI 1.01-10.64).

Conclusion: These findings provide preliminary evidence that LVH and uncontrolled hypertension predispose to NSTE-MI in this patient group. (*Ethn Dis*. 2011;21(4):421–428)

Key Words: Chest Pain, Non-ST-elevation Myocardial Infarction, Normal Coronary Angiograms, Hypertension, Left Ventricular Hypertrophy

INTRODUCTION

More than 5.5 million patients visit the emergency room in the United States every year with chest pain; of these, approximately 1.5 to 2 million are admitted to the hospital for acute myocardial infarction (MI).[1–4] About two-thirds of these MI patients are found to have non-ST-segment elevation MI (NSTE-MI, previously referred to as non-Q-wave MI).[5,6] Previous studies in selected clinical trial populations have reported that up to 15%-20% of patients with NSTE-MI undergoing angiography have little or no significant coronary atherosclerosis, suggesting insignificant (ie, non-obstructive) coronary artery disease (CAD).[5–9] Despite having less significant CAD and small-sized infarcts, patients with NSTE-MI have a greater propensity for early recurrence of myocardial ischemia, which may place them at greater risk for recurrent MI and adverse outcomes.[10,11] The reasons for the apparent dissociation between the severe clinical presentation and trivial angiographic findings remain unclear, but may largely reflect the greater burden of risk factors such as hypertension and its consequences, including left ventricular hypertrophy (LVH).

Recently, there has been growing interest in the contribution of LVH to the clinical expression of myocardial ischemia in patients with hypertension.[12,13] It has recently been suggested that LVH, whether assessed by ECG or more specifically by echocardiography, may confer a greater risk for MI (particularly NSTE-MI) and related adverse events,[6,13,14] presumably through obstructive atherosclerotic CAD. It remains unclear, however, whether LVH with or without hypertension contributes independently to acute NSTE-MI in patients with non-obstructive CAD,[8,9] and whether such information is particularly helpful in Blacks who are at higher risk for both uncontrolled hypertension and LVH and the risk of NSTE-MI.[15] We therefore sought to investigate the clinical significance and independent contribution of echocardiographic LVH as a correlate of NSTE-MI in patients presenting with acute chest pain in a large urban hospital center serving predominantly African American (AA) patients.

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We sought to investigate the clinical significance and independent contribution of echocardiographic LVH as a correlate of NSTE-MI in patients presenting with acute chest pain in a large urban hospital center serving predominantly African American (AA) patients.

METHODS

Study Population

We retrospectively selected consecutive patients who underwent cardiac catheterization for evaluation of acute chest pain and suspected myocardial ischemia in the period between January 1995 and December 1996. This analysis included only those patients with normal coronary arteries at cardiac catheterization performed during the same index hospital admission and who also had data available for cardiac markers to confirm the presence or absence of acute NSTE-MI (ie, non-Q-wave MI), as the main outcome. Acute NSTE-MI was diagnosed by positive cardiac markers (defined as serial elevations in CK-MB peaking within 24 hours or CK-MB more than twice the upper limit of normal) among patients admitted with ECG changes including ST-segment depression $\geq$0.5 mm.[5,9,13] Because ECG criterion can be equivocal in some patients with ECG evidence of LVH, a previous ECG was used for comparison when available to ensure that the observed changes are new.

Cardiovascular Risk Factors

Hypertension was defined as systolic BP $\geq$140 mm Hg and/or diastolic BP $\geq$90 mm Hg, or treatment with antihypertensive medication. Control in medicated hypertensive patients was defined by the number of controlled hypertensives (BP $<$140/90 mm Hg) divided by the number of treated hypertensives.[16] Other traditional risk factors for atherosclerotic CAD (ie, diabetes mellitus, dyslipidemia, obesity, and smoking) were recorded for each patient and defined consistent with national standards.[2–4]

Echocardiography

Two-dimensional directed M-mode echocardiograms were recorded in standard views,[17–19] and measurements were made according to the recommendations of the American Society of Echocardiography. Only echocardiographic examinations performed as close as possible temporal to the index hospital admission for NSTE-MI were used for data analysis. Among those excluded for lack of cardiac marker data, seventeen patients also did not have echocardiographic data available. All remaining patients included in the final study group had completed echocardiographic data for analysis. For purposes of this analysis, patients were grouped according to the presence or absence of LVH as previously reported in our routine clinical practice.[19]

Coronary Angiography

Cardiac catheterization was performed among patients in the final group for one or more of the following reasons: unstable angina in 36 patients; angina pectoris/exertional chest pain and/or positive stress test/abnormal stress thallium in 33 patients; atypical chest pain in 18 patients; LV dysfunction/heart failure in 22 patients; or recent MI in 22 patients with NSTE-MI. Stress thallium and coronary angiography after the acute event were completed per standard hospital protocols, mostly within the time frame of the index hospitalization before the patients were discharged from hospital. Thus, the present analysis only included procedures performed at the same index hospital admission for this acute NSTE-MI. All angiograms were read by experienced senior attending cardiologists of the hospital.[19] Angiograms were considered normal or near normal in the presence of minimal luminal irregularities (ie, a luminal diameter narrowing $<$10% of any major epicardial coronary vessel or branch). Angiograms showing any signs of plaque formation were not considered for inclusion in the analyses.

Statistical Methods

Data are expressed as mean $\pm$ SD unless otherwise specified. Groups were compared for categorical data or frequency of events using the chi-square test and for continuous variables using the Student's *t* test for unpaired data. The odds ratios (OR) with their chi-square or Fisher's exact statistic and their 95% confidence intervals (CI) were used to estimate the relative risk of MI for patients with and without each risk factor. In multivariate analysis, logistic regression was used to identify variables independently associated with acute MI. For this purpose, the results of bivariate analysis also guided the selection of factors included in the multivariate model. All tests were two-sided and a $P<.05$ was considered statistically significant.

RESULTS

Baseline Characteristics

Of 700 patients included in the chest pain database (Figure 1), we identified 180 (26%) who had angiographically normal coronary arteries or only minimal luminal irregularities. Of these 180 patients, we excluded 49 patients because cardiac marker results were not available in the database. The remaining 131 patients had complete cardiac marker data available at the index hospital admission to confirm the

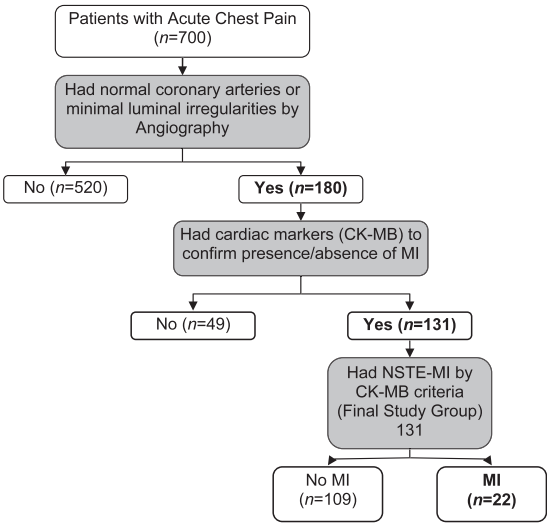

Fig 1. Flow chart detailing inclusion/exclusion selection criteria of patients from the acute chest pain database that resulted in the final study group of patients with or without non-ST elevation myocardial infarction (NSTE-MI). MI, myocardial infarction. CK-MB, MB fraction of creatine kinase

presence or absence of NSTE-MI and represented the final study group. Table 1 shows the clinical characteristics for the group as a whole and separated by MI status. Overall, mean age was 53±10 years (range 28-82), 56% were women, 76% were Blacks, 19% Caucasians, and 5% Hispanics. Eighty-eight percent had hypertension with 49% uncontrolled as reflected by systolic BP>140 mm Hg or diastolic BP>90 mm Hg. Left ventricular hypertrophy was found on echocardiography in 74%. During hospitalization, 22 out of 131 patients (17%) were found to have NSTE-MI by CK-enzyme criteria (serial elevations in CK-MB peaking within 24h or CK-MB >2 times the upper limit of normal). We found NSTE-MI was common in patients aged 50 to 59 years (36%) and 40 to 49 years (27%). Further examination of selected clinical characteristics by MI status (Table 1) showed that mean systolic BP was significantly higher in patients with NSTE-MI than in the non-NSTE-MI group (156 ± 30 vs 143 ± 25 mm Hg, $P<.05$). Patients with NSTE-MI were more likely than counterparts without NSTE-MI to be Black (95% vs 72%, $P=.02$) and less likely to report obesity or use of aspirin prior to the index hospitalization. They were also more likely to have lower LV ejection fraction (EF) on angiography (51 ± 14% vs 59 ± 13%, $P<.05$) and LVH on echocardiography (95% vs 70%, $P<.05$). We found NSTE-MI was present in 21 out of 97 (22%) patients with LVH compared with 1 out of 34 (3%) patients without LVH ($P=.02$). Among the 21 NSTE-MI patients with LVH, 4 (19%) had persistent angina suggestive of recurrent myocardial ischemia as confirmed by positive exercise EKG and stress thallium performed during the course of the index hospitalization before discharge (the median length of hospital stay was 7 days). Ten patients with MI (48%) had symptoms of congestive heart failure (HF); EF was much lower among NSTE-MI patients with LVH than counterparts without LVH (49 ± 14% vs 59 ± 13%, $P<.05$).

Factors Associated with Acute NSTE-MI

To evaluate factors potentially associated with NSTE-MI, we examined all recorded clinical variables (Table 2). With univariate/bivariate analysis, a modestly significant positive correlation was found between NSTE-MI and Black race, elevated systolic BP, and the presence of LVH (Table 2). The results of the multivariable model after controlling for selected variables revealed that these two preexisting medical conditions were the strongest predictors of NSTE-MI; the presence of LVH with OR of 4.00 (95% CI 1.06-10.05) and elevated systolic BP with OR of 3.70 (95% CI 1.01-10.64) (Table 2). Other clinical variables, such as cigarette smoking, cocaine use, diabetes, and history of hypertension or CAD were not predictive of NSTE-MI. Of particular interest, race was no longer significant once LVH and high BP were accounted for in the final model.

DISCUSSION

We report a two-year experience of 700 consecutive patients who were admitted for acute chest pain symptoms at our institution, of whom 22 of 131 (17%) with normal or near-normal angiograms and available cardiac enzymes drawn at the index hospital admission had evidence of myocardial necrosis (ie, NSTE-MI). These findings are of interest in this largely African American (AA) population with a high prevalence of uncontrolled hypertension and echocardiographic evidence of LVH. Our two main findings were:

1) Although no deaths were reported during the index hospitalization, other adverse outcomes were common because more than half presented with either positive exercise ECG and/or stress thallium suggestive of residual myocardial ischemia or showed heart failure symptoms; and
2) Our data indicate that among the clinical parameters commonly available in these patients at the time of initial presentation, echocardio-

Table 1. Baseline characteristics and clinical presentation of patients with and without MI

		NSTE-MI status		
	All (*n*=131)	No MI (*n*=109)	MI (*n*=22)	*P**
Demographics				
Age, yrs	53 ± 10	53 ± 11	54 ± 12	.73
Female, n (%)	73 (56)	63 (58)	10 (45)	.35
Black, n (%)	99 (76)	78 (72)	21 (95)	.02
Traditional risk factors				
Hypertension, %	88	85	91	.73
Hypercholesterolemia, %	43	49	36	.13
Diabetes mellitus, %	34	36	25	.44
Obesity, %	62	72	20	.04
Tobacco smoking, %	67	65	70	.8
Cocaine abuse, %	42	36	43	.99
Family history of CAD, %	50	52	33	.19
Medical treatment				
Hormone replacement therapy, %	9	12	0	.12
Medications, %				
Aspirin	76	84	64	.04
ACE inhibitors	43	39	59	.09
Beta-blockers	26	23	32	.42
Calcium channel blockers	54	52	59	.64
Diuretics	38	36	23	.32
Nitrates	74	81	82	.99
Lipid lowering agents	26	28	18	.43
Hypoglycemic agents	24	23	18	.78
Clinical findings on presentation				
Uncontrolled blood pressure, %	49	47	62	.24
Blood pressure, mm Hg				
Systolic	145 ± 26	143 ± 25	156 ± 30	.04
Diastolic	84 ± 18	83 ± 19	91 ± 21	.07
Mean	104 ± 20	103 ± 20	113 ± 23	.04
Pulse pressure	61 ± 17	61 ± 15	65 ± 21	.31
Echocardiographic LVH, %	74	70	95	.03
LV ejection fraction, %	58 ± 13	59 ± 13	51 ± 14	.03
Plasma cholesterol, mg/dL				
Total cholesterol	211 ± 64	212 ± 58	217 ± 118	.73
LDL cholesterol	150 ± 49	155 ± 55	147 ± 29	.74
HDL cholesterol	52 ± 25	52 ± 29	65 ± 22	.32
Triglycerides	176 ± 126	180 ± 131	117 ± 104	.26
Biochemical markers				
Peak CK, IU/l	241 ± 194	195 ± 147	471 ± 235	-
Peak fraction CK-MB, %	3.69 ± 8.50	.96 ± .97	17.08 ± 14.60	-
Peak LDH, IU/l	275 ± 103	256 ± 95	363 ± 99	-
Platelet Counts	233 ± 79	234 ± 84	231 ± 90	.88

Data are mean ± SD or *n* and/or %, of patients unless otherwise specified.

MI, myocardial infarction; CAD, coronary artery disease; ACE, angiotensin converting enzyme; LVH, left ventricular hypertrophy; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CK, creatine kinase; LDH, lactate deshydrogenase.

* Overall *P* for observed differences between the 2 groups of patients with vs without MI.

graphic LVH and elevated systolic BP (ie, uncontrolled hypertension) were significantly and independently associated with acute NSTE-MI.

Although other groups have reported an association between LVH and MI in the absence of obstructive CAD, the size of this series and the careful recording of clinical characteristics make this report particularly relevant to hypertensive AA of both sexes and of relatively young age when presenting with acute chest pain syndrome in routine clinical practice.[15]

Risk Factor Profile

This database describes a subset of adult patients with high rates of angiographically normal or minimally diseased epicardial coronary arteries (26%), who are at a higher risk for NSTE-MI than previously recognized, and may not otherwise be well-represented in large scale cohorts.[5,6,7–9] This proportion (26%) is higher than reported (up to 15%) from large scale cohorts of patients with insignificant/non-obstructive atherosclerotic CAD.[7–9,20,21] For example, our patients with NSTE-MI had similar age distribution but higher rates of risk factors such as hypertension than those from the PURSUIT cohort,[7] which did not present data for AA. In that large randomized trial involving 11000 patients with NSTE-acute coronary syndrome (ACS), a sizable proportion (12%, median age <58 years) had insignificant CAD (6% with no CAD and 6% with mild CAD) and a low incidence of adverse outcomes. More recently, the CRUSADE quality improvement initiative provided another large national sample of patients with high-risk NSTE-ACS (*n*=38,301) presenting to over 400 US hospitals and included 11% Blacks,[8] a higher percentage than most earlier published studies. Insignificant CAD (defined as coronary stenoses <50%) was present in 8.6% of patients (*n*=3,306) and was also associated with low incidence of adverse outcomes compared to patients (*n*=34,995) with obstructive CAD (>50% stenoses).[8] Altogether, these data support the observation that NSTE-MI in the absence of obstructive CAD may be a more significant problem than previously recognized, especially in this group of otherwise young adult patients who are often considered at low risk. The reason for these seemingly variable clinical presentation/outcomes is unclear, but may reflect differences in patient selection or angiographic definitions.[22–26] Alternatively, it may be further explained by the fact that in these earlier large clinical trials some

Table 2. Factors associated with acute NSTE-MI

Variable	Odds Ratio*	95% Confidence Interval		*P*†
		Lower	Upper	
Univariate/Bivariate Analysis				
Age	1.008	0.966	1.051	.72
Male (vs. female)	1.643	0.654	4.130	.29
Blacks (vs. non-blacks)	1.120	1.020	1.930	.042†
History of hypertension	1.744	0.369	8.248	.48
Blood pressure:				
Systolic	3.970	1.026	9.164	.046†
Diastolic	1.021	0.998	1.046	.079
Mean	1.024	1.001	1.047	.043†
Pulse Pressure	1.015	0.987	1.044	.307
Echo-LVH	4.865	1.001	12.249	.049†
LV ejection fraction	0.964	0.931	0.998	.039†
Obesity	0.095	0.009	0.987	.048†
Plasma cholesterol	1.001	0.995	1.007	.73
Triglycerides	0.992	0.979	1.005	.25
Diabetes mellitus	0.593	0.199	1.765	.35
Tobacco smoking	1.266	0.443	3.612	.66
Cocaine abuse	1.350	0.211	8.619	.75
Family history of CAD	0.459	0.159	1.326	.15
Ischemia on thallium	2.727	0.327	22.741	.35
Multivariate Analysis				
Echo-LVH	4.00	1.06	10.05	0.045†
Systolic blood pressure	3.70	1.01	10.64	0.047†
Ischemia on thallium	4.1	1.09	13.6	0.042†

* Odds ratio (OR) are unadjusted estimates from the bivariate analysis. An OR greater than 1 (one) indicates that patients with the characteristics (risk factor) compared to counterparts without the features have a higher odds of having an acute MI; while an OR less than one indicates a lesser odds of having MI.

† *P* for overall chi square tests that denote a significant OR because the confidence interval does not include 1 (one).

Abbreviations as in Table 1.

important, yet modifiable, co-morbid factors such as LVH were not taken into consideration in the analyses. Therefore, further quantifying the relative influence of LVH as an important correlate of NSTE-MI could help identify patients who are more likely to develop this acute coronary event and related complications, thus providing opportunity for early intervention and treatment.[8,9,26]

Relationship between LVH and NSTE-MI

Although our findings substantiate the relative importance of traditional risk factors for CAD including elevated BP/uncontrolled hypertension, we also show that these factors only explain a fraction of the risk of NSTE-MI in the absence of significant CAD; other parameters must contribute as well. In the present study, we chose to investigate the value of echocardiographic LVH as an important predisposing risk factor for NSTE-MI for three reasons. The first reason was that our urban ambulatory and hospital practice serves a very large AA population. It has been proposed that Blacks are more likely than non-Blacks to have a greater prevalence and worse outcomes from atherosclerotic CAD.[15] It remains unclear however why Blacks have disproportionately higher rates of angiographically normal or insignificantly narrowed (ie, minimally diseased) epicardial coronary arteries despite a higher prevalence of risk factors for atherosclerotic CAD. Another reason was that, we knew based on our own experience[12,17–19,27,28] and on data from the literature,[29–32] that AA continue to suffer a disproportionately more virulent course of cardiac end organ damage from hypertension. As many AA patients with hypertension are poorly controlled, not surprisingly there is an increased risk of complications such as LVH. Indeed, epidemiological studies [29,30] and findings from large autopsy series from our group [28] suggest that uncontrolled hypertension and LVH contribute most to the excess cardiovascular risk of AAs.[28–30] The final reason was that there were limited data in the literature regarding the clinical relevance and independent contribution of LVH as a potential correlate of NSTE-MI in patients with insignificant CAD,[8,9] particularly in Blacks who are at high risk for NSTE-MI and both uncontrolled hypertension and LVH.[15] Here, we found that LVH, which we previously showed to correlate closely with BP among AA patients with and without hypertension,[12,17] is also an important independent predictor of cardiac ischemic event (ie, NSTE-MI) in this ethnic group.

Other factors including obesity and associated lipid abnormalities or metabolic disorders such as diabetes (Table 2), previously shown to have a negative impact on the clinical presentation and outcome of these patients, were not predictive of NSTE-MI on multivariate analysis. It is also worth noting that medication usage was comparable between the two study groups and is therefore unlikely to have significantly influenced our results. The same is true for the potential negative influence of smoking[33] or the use of recreational drugs such as cocaine.[34]

Possible Explanations for the Adverse Impact of Hypertension and LVH

Among patients with poor BP control, systolic BP was markedly higher in those who eventually had NSTE-MI than in counterparts without

NSTE-MI. The role of elevated BP or uncontrolled hypertension in predisposing patients to NSTE-MI is unclear, but may relate to the integrated influence of cardiac morphologic changes. These early adaptive changes, characterized by elevated LV mass (ie, LVH) in response to high BP as shown in our previous studies,[17] suggest an intermediate stage whereby an incremental increase in BP may predispose individuals to the premature development of atherosclerotic cardiovascular events.[35-39] The detrimental impact of LVH independent of elevated BP (ie, uncontrolled HTN) on the risk of NSTE-MI observed in this study would suggest such a mechanistic link. While the exact mechanisms responsible for this association between LVH and NSTE-MI cannot be precisely deduced from the results of the present retrospective registry, preliminary data from our laboratory suggest that LVH may lead to impaired myocardial flow reserve and microvascular dysfunction.[12] In this preliminary study, using dipyridamole myocardial contrast echocardiography to evaluate the transmural distribution of myocardial blood flow (MBF), we found that subendocardial MBF reserve was blunted in hypertensive patients with LVH, suggesting the mechanisms of LVH-induced myocardial ischemia in hypertension.[12] In these patients, symptoms of chest pain typical for angina pectoris may be manifested prior to or at the time of the MI even in the absence of obstructive epicardial CAD.[40] The reasons are possibly related to limited flow reserve and dysfunction of the microvasculature beyond the epicardial coronary arteries which is unable to compensate for increased metabolic and oxygen demand.[26] This could predispose patients to repetitive ischemia within the subendocardial layer that eventually culminates in heart attacks without elevation of the ST segment and subsequent heart failure despite the absence of atherosclerosis or plaques build up in the coronary blood vessels as noted in the present study.

Study Limitations

First, the retrospective nature limited our ability to draw inferences about causal association between BP, LVH and NSTE-MI. Because both risk factors were obtained at the same time, we also could not determine their temporal association with adverse in-hospital outcomes. Second, the true prevalence of NSTE-MI and related putative risk factors/comorbidities may be considerably underestimated. In retrospect, our data was collected between 1995 and 1996 and might reflect the transition period before the widespread adoption of new definition of MI [4-6] with the advent of troponin as a more sensitive biomarker for diagnosing acute MI in the mid to late 1990s.[4,5,41,42] Although a more contemporary series of patients might have been relevant to the current practice using troponin, comparing and interpreting the findings in the context of previous clinical studies utilizing the CK-MB criteria would be inappropriate. It is therefore tempting to speculate that troponin T or I, as more sensitive cardiac contractile proteins/markers that allowed for detection of minor myocardial damage with greater specificity,[4,41,42] might have classified even a larger number of our patients with NSTE-MI in the absence of CAD. Finally, we have not been able to systematically analyze LV mass as a continuous variable and hence determine the magnitude of LVH in patients with MI compared with those who did not experience MI. Instead, for the purposes of this analysis, patients were grouped according to the presence or absence of LVH detected by routine echocardiography. Although this semi-quantitative approach may limit diagnostic sensitivity, specificity, and predictive accuracy, it is unanimously accepted and easy to obtain in routine clinical practice,[19] and has been shown to provide additional information with regard to cardiovascular risk of patient with hypertensive heart disease irrespective of the extent of CAD.[29,30,35]

…the presence of LVH may help identify a subset of patients with NSTE-MI and normal coronary arteries who are at particularly high risk for subsequent cardiac events.

Clinical Implications

Despite the above limitations, our findings may have important clinical implications for the management of NSTE-MI in patients with hypertensive heart disease and acute ischemic chest pain syndrome. In this context, the presence of LVH may help identify a subset of patients with NSTE-MI and normal coronary arteries who are at particularly high risk for subsequent cardiac events. Perhaps, it is this subgroup of patients who may benefit the most from early aggressive control of predisposing and potentially modifiable factors, such as BP and LVH, by appropriate pharmacological means to reduce the increased risk for both short- and long-term adverse outcomes.

SUMMARY

Echocardiographic LVH and uncontrolled hypertension were found to be independently associated with acute NSTE-MI in patients with acute chest pain and coronary arteries that appeared angiographically normal or had only minimal luminal irregularities. While further studies are needed to define the mechanisms underlying this association,

these findings may have implication for management of NSTE-MI in a high-risk subset of adult patients with hypertensive heart disease and insignificant (ie, non-obstructive) CAD.

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REFERENCES

1. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med*. 2000;342:1163–1170.
2. Braunwald E, Antman EM, Beasley JW, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). *J Am Coll Cardiol*. 2002; 40:1366–74.
3. The American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). ACC/AHA guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction—2002: Summary Article. *Circulation*. 2002; 106:1893–1900.
4. The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined—a consensus document of the Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction. *Eur Heart J*. 2000;21:1502–13.
5. Maier B, Thimme W, Schoeller R, et al. Berlin Myocardial Infarction Registry. Improved therapy and outcome for patients with acute myocardial infarction–data of the Berlin Myocardial Infarction Registry from 1999 to 2004. *Int J Cardio.l*. 2008;130:211–9.
6. Rogers WJ, Frederick PD, Stoehr E, et al. Trends in presenting characteristics and hospital mortality among patients with ST elevation and non-ST elevation myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. *Am Heart J*. 2008;156:1026–34.
7. Roe MT, Harrington RA, Prosper DM, et al. Clinical and therapeutic profile of patients presenting with acute coronary syndromes who do not have significant coronary artery disease. The Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) Trial Investigators. *Circulation*. 2000;102:1101–1106.
8. Patel M, Chen A, Peterson E, et al. Prevalence, predictors, and outcomes of patients with non–ST-segment elevation myocardial infarction and insignificant coronary artery disease: Results from the Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines (CRUSADE) initiative. *Am Heart J*. 2006; 152:641–647.
9. Roe MT, Halabi AR, Mehta RH, et al. Documented traditional cardiovascular risk factors and mortality in non-ST-segment elevation myocardial infarction. *Am Heart J*. 2007;153:507–514.
10. Goldberg RJ, Steg PG, Sadiq I, et al. Extent of, and factors associated with, delay to hospital presentation in patients with acute coronary disease (the GRACE registry). *Am J Cardiol*. 2002;89:791–796.
11. Terkelsen CJ, Lassen JF, Nørgaard BL, et al. Mortality rates in patients with ST-elevation vs. non-ST-elevation acute myocardial infarction: observations from an unselected cohort. *Eur Heart J*. 2005;26:18–26.
12. Lapu-Bula R, Ofili E. From hypertension to heart failure: the role of nitric oxide-mediated endothelial dysfunction and emerging insights from myocardial contrast echocardiography. *Am J Cardiol*. 2007;99[suppl]:7D–14D.
13. Barrabés JA, Figueras J, Cortadellas J, et al. Usefulness of electrocardiographic and echocardiographic left ventricular hypertrophy to predict adverse events in patients with a first non–ST-elevation acute myocardial infarction *Am J Cardiol*. 2009;103:455–460.
14. Boden WE, Kleiger RE, Schechtman KB, et al. Clinical significance and prognostic importance of left ventricular hypertrophy in non-Q-wave acute myocardial infarction. *Am J Cardiol*. 1988;15:62(16):1000–1004.
15. Clark L, Lingegowda U. Acute coronary syndromes in Black Americans: is treatment different? should it be? *Curr Cardiol Reports*. 2005;7:249–254.
16. Wolf-Maier K, Cooper RS, Kramer H, et al. Hypertension treatment and control in five European countries, Canada, and the united states. *Hypertension*. 2004;43:10–17.
17. Lapu-Bula R, Quarshie A, Lyn D, et al. The 894T allele of endothelial nitric oxide synthase gene is related to left ventricular mass in African Americans with high-normal blood pressure. *J Natl Med Assoc*. 2005;97:197–205.
18. Ofili EO, Cohen JD, St Vrain JA, et al. Effect of treatment of isolated systolic hypertension on left ventricular mass. *JAMA*. 1998;279: 778–780.
19. Ofili EO, Mayberry R, Alema-Mensah E, et al. Gender differences and practice implications of risk factors for frequent hospitalization for heart failure in an urban center serving predominantly African-American patients. *Am J Cardiol*. 1999;83:1350–1355.
20. Pecora MJ, Roubin GS, Cobbs BW, et al. Presentation and late outcome of myocardial infarction in the absence of angiographically significant coronary artery disease. *Am J Cardiol*. 1988;62:363–367.
21. Zimmerman FH, Cameron A, Fisher LD, et al. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (Coronary Artery Surgery Study Registry). *J Am Coll Cardiol*. 1995;26: 654–661.
22. Alpert JS. Myocardial infarction with angiographically normal coronary arteries. *Arch Intern Med*. 1994;154:265–269.
23. Raymond R, Lynch J, Underwood D, et al. Myocardial infarction and normal coronary arteriography. A 10-year clinical and risk analysis of 74 patients. *J Am Coll Cardiol*. 1988;11:471–477.
24. Dacosta A, Tardy-Poncet B, Isaaz K, et al. Prevalence of factor V Leiden (APCR) and other inherited thrombophilias in young patients with myocardial infarction and normal coronary arteries. *Heart*. 1998;80:338–340.
25. Gehani AA, al-Mulla AW, Chaikhouni A, et al. Myocardial infarction with normal coronary angiography compared with severe coronary artery disease without myocardial infarction: the crucial role of smoking. *J Cardiovasc Risk*. 2001;8:1–8.
26. Reis SE, Holubkov R, Conrad Smith AJ. WISE Investigators. Coronary microvascular dysfunction is highly prevalent in women with chest pain in the absence of coronary artery disease: results from the NHLBI WISE study. *Am Heart J*. 2001;141:735–741.
27. Bransford TL, Ofili EO. The paradox of coronary heart disease in African-American females. *J Natl Med Assoc*. 2000;92:327–333.

28. Onwuanyi A, Hodges D, Avancha A, et al. Hypertensive vascular disease as a cause of death in blacks versus whites: autopsy findings in 587 adults. *Hypertension*. 1998;31:1070–1076.
29. Cooper ES, Kuller LH, Saunders E, et al. Cardiovascular diseases and stroke in African-Americans and other racial minorities in the United States: a statement for health professionals. *Circulation*. 1991;83:1462–1480.
30. Liao Y, Cooper RS, McGee DL, et al. The relative effects of left ventricular hypertrophy, coronary artery disease, and ventricular dysfunction on survival among black adults. *J Am Med Assoc*. 1995;273:1592–1597.
31. Douglas JG, Bakris GL, Epstein M, et al. Hypertension in African Americans Working Group of the International Society on Hypertension in Blacks. Management of high blood pressure in African Americans: Consensus statement of the hypertension in African Americans working group of the International Society of Hypertension in Blacks. *Arch Intern Med*. 2003;163:525–541.
32. Flack JM, Ferdinand KC, Nasser SA. Epidemiology of hypertension and cardiovascular disease in African Americans. *J Clin Hypertens*. 2003;5(suppl 1):5–11.
33. Garoufalis S, Kouvaras G, Vitsias G, et al. Comparison of angiographic findings, risk factors, and long term follow-up between young and old patients with a history of myocardial infarction. *Int J Cardiol*. 1998;67: 75–80.
34. Zimmerman FH, Gustafson GM, Kemp HGJr. Recurrent myocardial infarction associated with cocaine abuse in a young man with normal coronary arteries: evidence for coronary artery spasm culminating in thrombosis. *J Am Coll Cardiol*. 1987;9:964–968.
35. Levy D, Garrison RJ, Savage DD, et al. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Eng J Med*. 1990;322:1561–1566.
36. Koren MJ, Devereux RB, Casale PN, et al. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann Intern Med*. 1991;114:345–352.
37. Ghali JK, Liao Y, Cooper RS. Influence of left ventricular geometric patterns on prognosis in patients with or without coronary artery disease. *J Am Coll Cardiol*. 1998;31:1635–1640.
38. Schillaci G, Verdecchia P, Porcellati C, et al. Continuous relation between left ventricular mass and cardiovascular risk in essential hypertension. *Hypertension*. 2000;35:580–586.
39. Kannel WB, Vasan RS, Levy D. Is the relation of systolic blood pressure to risk of cardiovascular disease continuous and graded, or are there critical values? *Hypertension*. 2003;epub: 453–456.
40. Hasdai D, Holmes DR, Higano S, et al. Prevalence of coronary blood flow reserve abnormalities among patients with non-obstructive coronary artery disease and chest pain. *Mayo Clin Proc*. 1998;73:1133–1140.
41. Hamm CW, Ravkilde J, Gerhardt W, et al. The prognostic value of serum troponin T in unstable angina. *N Engl J Med*. 1992;327: 146–50.
42. Holmvang L, Lüscher MS, Clemmensen P, et al. Very early risk stratification using combined ECG and biochemical assessment in patients with unstable coronary artery disease (A thrombin inhibition in myocardial ischemia [TRIM] substudy). The TRIM Study Group. *Circulation*. 1998;98:2004–2009.

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