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Obesity and Age of First Non–ST-Segment Elevation Myocardial Infarction

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Objectives Because excess adiposity is one of the most important determinants of adipokines and inflammatory factors associated with coronary plaque rupture, we hypothesized that obesity was associated with myocardial infarction at earlier ages.

Background The developing obesity pandemic of the past 50 years has gained considerable attention as a major public health threat.

Methods The CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines) registry was a voluntary observational data collection and quality improvement initiative that began in November 2001, with retrospective data collection from January 2001 to January 2007. The CRUSADE initiative included high-risk patients with unstable angina and non–ST-segment elevation myocardial infarction (NSTEMI). We retrospectively examined, among 189,065 patients with acute coronary syndrome (between January 2001 and September 2006) in the CRUSADE initiative, the relationship of body mass index (BMI) with patient age of first NSTEMI.

Results A total of 111,847 patients with NSTEMI were included in the final analysis. There was a strong, inverse linear relationship between BMI and earlier age of first NSTEMI. The mean patient ages ($\pm$ SD) of first NSTEMI were 74.6 $\pm$ 14.3 years and 58.7 $\pm$ 12.5 years for the leanest (BMI $\leq$18.5 kg/m^2) and most obese (BMI $>$40.0 kg/m^2) cohorts, respectively ($p < 0.0001$). After adjustment for baseline demographic data, cardiac risk factors, and medications, the age of first NSTEMI occurred 3.5, 6.8, 9.4, and 12.0 years earlier with ascending levels of adiposity (BMI 25.1 to 30.0, 30.1 to 35.0, 35.1 to 40.0, and $>$40.0 kg/m^2, respectively; referent 18.6 to 25.0 kg/m^2) ($p < 0.0001$ for each estimate).

Conclusions Excess adiposity is strongly related to first NSTEMI occurring prematurely. (J Am Coll Cardiol 2008;52:979–85)

We are in the midst of an obesity pandemic. Overall, incidence rates of overweight have increased 2-fold and obesity more than 3-fold over the past 50 years (1). The National Health and Nutrition Examination Survey in 2003 to 2004 found that 33.1% and 32.2% of Americans were overweight and obese, respectively (2). Similarly, the Behavioral Risk Factor Surveillance System reported that the prevalence of obesity increased by 24% from 2000 to 2005. However, the prevalence of extreme and super obesity (body mass index [BMI] >40 and >50 kg/m^2) increased by 50% and 75%, 2 and 3 times faster, respectively (3). As obesity rates increase, so do associated cardiac risk factors including hypertension, diabetes, and dyslipidemia as well as potentially deleterious comorbidities including sleep apnea, atrial fibrillation, and chronic kidney disease (4,5). Additionally, obesity has recently been associated with emerging risk factors including systemic inflammation (6).

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Specifically, abdominal adiposity is directly related to increased inflammatory markers such as interleukin-6 produced

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Abbreviations and Acronyms

BMI = body mass index

hsCRP = high-sensitivity C-reactive protein

MI = myocardial infarction

NSTEMI = non–ST-segment elevation myocardial infarction

by adipocytes, which stimulates hepatocytes to produce high-sensitivity C-reactive protein (hsCRP) (7). We hypothesized that there might be a link between excess adiposity and occurrence of first myocardial infarction (MI) on the basis of the expected clustering of risk factors and presence of high levels of systemic inflammation in the obese (8,9).

Due to these associations, we postulated that excess adiposity might be associated with the occurrence of first MI at an earlier age. With data from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association [ACC/AHA] Guidelines) registry, we examined the relationship between BMI and patient age of onset of first non–ST-segment elevation myocardial infarction (NSTEMI), adjusting for baseline demographic data, cardiac risk factors, and medications.

Methods

The CRUSADE registry was a voluntary observational data collection and quality improvement initiative that began in November 2001, with retrospective data collection from January 2001 to January 2007 (10). The CRUSADE initiative was designed to track guideline adherence, provide feedback about performance, and develop quality improvement tools to improve adherence to ACC/AHA recommendations for the treatment of acute ischemic symptoms.

Patient population. The CRUSADE registry included high-risk patients with unstable angina and NSTEMI, the 2 conditions that collectively comprise non–ST-segment elevation acute coronary syndromes. Data were available from 566 sites on 189,065 patients from January 1, 2001, to September 30, 2006. Patients were excluded from the analysis for the following reasons: unstable angina (n = 15,939), insufficient data regarding prior MI (n = 2,544), a history of prior MI (n = 50,733), missing age (n = 175), and inadequate data for the calculation of BMI (n = 7,827). Thus, we derived a final population of 111,847 with first NSTEMI and calculated BMI.

Inclusion criteria. All patients in the CRUSADE initiative must have presented at a participating hospital within 24 h of experiencing acute ischemic symptoms (lasting for at least 10 min) at rest. Patients with NSTEMI were required to demonstrate a characteristic rise and fall in cardiac troponin or creatine kinase-myocardial band with ≥1 confirmatory signs or symptoms including anginal chest pain equivalents, ST-segment depression ≥0.5 mm, transient ST-segment elevation 0.5 to 1.0 mm (lasting for <10 min), or an angiographically-documented occluded culprit vessel. Patients were ineligible for the CRUSADE registry if they transferred to a participating hospital >24 h after the last episode of ischemic symptoms.

Data collection. Hospitals participating in the CRUSADE registry collected detailed process of care and in-hospital outcomes data through retrospective chart review. Data were collected anonymously during the initial hospital stay with trained data collectors and standardized definitions. Information regarding height and weight were taken from the medical record, which could have been derived by patient self-report or direct measurement. Because no patient identifiers were collected, individual informed consent was not required. The institutional review board of each hospital or medical center approved participation in the CRUSADE registry. All participating institutions were required to comply with local regulatory and privacy guidelines before beginning participation in the CRUSADE registry. Blood pressure and heart rate were recorded on presentation. Serum lipids/lipoproteins were measured within the first 24 h of hospital admission.

Definitions. Body mass index was categorized into the following groups: ≤18.5, 18.6 to 25.0, 25.1 to 30.0, 30.1 to 35.0, 35.1 to 40.0, and >40.0 kg/m^2. Overweight was defined as BMI ≥25 kg/m^2, obesity class I as BMI 30.1 to 35.0 kg/m^2, obesity class II as BMI 35.1 to 40.0 kg/m^2, and extreme obesity as BMI >40 kg/m^2. Hypertension was defined as resting systolic blood pressure >140 mm Hg and/or diastolic blood pressure >90 mm Hg on repeated measurements or treatment with anti-hypertensive medications. Diabetes was defined as having an established diagnosis of diabetes mellitus or using insulin or oral hypoglycemic drugs. Hyperlipidemia was defined as total cholesterol >200 mg/dl or treatment with a lipid-lowering agent.

Statistical analysis. Patient demographic data, clinical characteristics, and prescribed medications were compared across BMI groups. Continuous variables were reported as mean ± SD, and categorical variables were reported as frequencies. To test for independence across BMI groups and patient characteristics and care patterns, stratum-adjusted Cochran-Mantel-Hanzel statistics for trend was used, where stratification is by hospital. In addition, Spearman correlation was used to evaluate the relationship between age of first NSTEMI and BMI. Furthermore, the relationship between age of first NSTEMI and BMI was evaluated, with specific reference to gender.

To investigate the factors associated with age of first NSTEMI, the generalized estimating equations method was used to adjust for patient characteristics and prescribed medications including gender, BMI categories, white race, family history of premature coronary artery disease, hypertension, diabetes, current/recent smoker, dyslipidemia, prior percutaneous coronary intervention, coronary artery bypass grafting, heart failure or stroke, renal insufficiency, electrocardiographic presentation