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ORIGINAL INVESTIGATIONS

Silent Myocardial Infarction and Long-Term Risk of Heart Failure

The ARIC Study

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ABSTRACT

BACKGROUND Although silent myocardial infarction (SMI) accounts for about one-half of the total number of myocardial infarctions (MIs), the risk of heart failure (HF) among patients with SMI is not well established.

OBJECTIVES The purpose of this study was to examine the association of SMI and clinically manifested myocardial infarction (CMI) with HF, as compared with patients with no MI.

METHODS This analysis included 9,243 participants from the ARIC (Atherosclerosis Risk In Communities) study who were free of cardiovascular disease at baseline (ARIC visit 1: 1987 to 1989). SMI was defined as electrocardiographic evidence of MI without CMI after the baseline until ARIC visit 4 (1996 to 1998). HF events were ascertained starting from ARIC visit 4 until 2010 in individuals free of HF before that visit.

RESULTS Between ARIC visits 1 and 4, 305 SMIs and 331 CMIs occurred. After ARIC visit 4 and during a median follow-up of 13.0 years, 976 HF events occurred. The incidence rate of HF was higher in both CMI and SMI participants than in those without MI (incidence rates per 1,000 person-years were 30.4, 16.2, and 7.8, respectively; $p < 0.001$). In a model adjusted for demographics and HF risk factors, both SMI (hazard ratio [HR]: 1.35; 95% confidence interval [CI]: 1.02 to 1.78) and CMI (HR: 2.85; 95% CI: 2.31 to 3.51) were associated with increased risk of HF compared with no MI. These associations were consistent in subgroups of participants stratified by several HF risk predictors. However, the risk of HF associated with SMI was stronger in those younger than the median age (53 years) (HR: 1.66; 95% CI: 1.00 to 2.75 vs. HR: 1.19; 95% CI: 0.85 to 1.66, respectively; overall interaction p by MI type <0.001).

CONCLUSIONS SMI is associated with an increased risk of HF. Future research is needed to examine the cost effectiveness of screening for SMI as part of HF risk assessment, and to identify preventive therapies to improve the risk of HF among patients with SMI. (J Am Coll Cardiol 2018;71:1-8) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CMI = clinically manifested myocardial infarction

ECG = electrocardiogram

HF = heart failure

HFpEF = heart failure with preserved ejection fraction

HFrEF = heart failure with reduced ejection fraction

LVH = left ventricular hypertrophy

SMI = silent myocardial infarction

Heart failure (HF) is the final outcome of up to 15% of the patients who experience acute myocardial infarction (MI) (1–4). The proportion of this segment of the population is likely to increase, as the survival of post-MI patients has significantly improved over the last decade (5). Up to one-third of the 1 million patients who are hospitalized for HF each year in the United States have a history of MI (6). Several factors, such as recurrent MI, ventricular remodeling, mechanical MI complications, and stunned or hibernating myocardium, lead to HF post-MI (7,8). These conditions might be clinically silent and can go unnoticed for a long time.

Silent myocardial infarction (SMI), defined as evidence of MI on the electrocardiogram (ECG) in the absence of history of MI, accounts for about one-half of the total number of MIs (9). Previous reports from different populations have shown that both clinical myocardial infarction (CMI) and SMI are associated with poor prognosis (9,10). However, whether SMI is associated with HF similar to CMI is currently unclear. Furthermore, HF prevalence varies by sex and race, and hence, it is possible that sex and race modify the relationship between SMI and HF (11,12). Therefore, the aims of this study were to examine and compare the associations of SMI and CMI with HF versus those with no MI, and to examine the consistency of these associations in subgroups stratified by sex and race as well as HF risk factors.

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METHODS

STUDY DESIGN AND POPULATION. The ARIC (Atherosclerosis Risk In Communities) study is a community-based, predominantly biracial prospective cohort study that was designed to study atherosclerosis, its clinical outcomes, and variation in cardiovascular risk factors, medical care, and disease by race, sex, location, and date. Details of the ARIC study have been previously published (13). Briefly, from 1987 to 1989 (ARIC visit 1, baseline), 15,792 adults (age 45 to 64 years) from 4 U.S. communities (Washington County, Maryland; suburbs of Minneapolis, Minnesota; Jackson, Missouri; and Forsyth County, North Carolina) were prospectively enrolled in the ARIC study. They underwent a phone interview and subsequent clinic visit. Additional examinations were performed in 1990 to 1992 (visit 2), 1993 to 1995 (visit 3), 1996 to 1998 (visit 4), and 2011 to 2013 (visit 5). Participants were mostly white in the Washington County and Minneapolis sites, exclusively black in Jackson, and a mix of both in Forsyth County. The study was approved by the institutional review board at each study site. All participants provided written informed consent.

For the purpose of this analysis, all ARIC participants with good quality and complete ECG data at visits 1 through 4 as well as outcome events after visit 4 were considered. The following participants were excluded: 47 with reported race neither African-American nor white; 565 participants with ECG data that were not interpretable for the diagnosis of MI due to poor quality or suppression codes by the Minnesota ECG classification; 3,775 with missing ECG in any of the ARIC first 4 visits, including those who died during this period; 201 with missing baseline cardiovascular disease (CVD) risk factors utilized in the models; and 119 missing HF follow-up data. We also excluded 1,706 participants with a history of prevalent CVD at baseline, which was defined as the presence of ECG evidence of MI or a self-reported history of physician-diagnosed MI, coronary artery bypass surgery, coronary angioplasty, HF, or stroke. Finally, we excluded 136 cases with HF occurring between ARIC visits 1 and 4. After all exclusions (n = 6,549), a total of 9,243 participants remained and were included in the analysis.

BASELINE COVARIATES. Baseline (visit 1) age, sex, race, and smoking status were determined by self-report. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Blood samples were obtained after a 12-h fast and were examined in a central laboratory. Diabetes mellitus was defined as a fasting glucose level ≥126 mg/dl (or nonfasting glucose ≥200 mg/dl), a self-reported physician diagnosis of diabetes mellitus, or the use of antidiabetes medications. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or the use of blood pressure–lowering medications. Medication use was obtained by self-report of medication intake during the last 2 weeks and by a review of medications brought by the participants to their visit. Each medication was coded by trained and certified interviewers with the use of a computerized medication classification system. Heart rate data were obtained from the baseline ECG.

SMI AND CMI. SMI was defined as ECG evidence of new MI at ARIC visit 2, 3, or 4 that was not present at the baseline visit (visit 1) in the absence of documented CMI. CMI was adjudicated by physician review based on chest pain, cardiac biomarkers/enzymes from hospitalizations, ECG evidence