JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.

VOL. 64, NO. 6, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.03.056

ORIGINAL INVESTIGATIONS

Incidence of and Risk Factors for Sick Sinus Syndrome in the General Population

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ABSTRACT

BACKGROUND Little is known about the incidence of and risk factors for sick sinus syndrome (SSS), a common indication for pacemaker implantation.

OBJECTIVES This study sought to describe the epidemiology of SSS.

METHODS This analysis included 20,572 participants (mean baseline age 59 years, 43% male) in the ARIC (Atherosclerosis Risk In Communities) study and the CHS (Cardiovascular Health Study), who at baseline were free of prevalent atrial fibrillation and pacemaker therapy, had a heart rate of ≥50 beats/min unless using beta blockers, and were identified as of white or black race. Incident SSS cases were identified by hospital discharge International Classification of Disease-revision 9-Clinical Modification code 427.81 and validated by medical record review.

RESULTS During an average 17 years of follow-up, 291 incident SSS cases were identified (unadjusted rate 0.8 per 1,000 person-years). Incidence increased with age (hazard ratio [HR]: 1.73; 95% confidence interval [CI]: 1.47 to 2.05 per 5-year increment), and blacks had a 41% lower risk of SSS than whites (HR: 0.59; 95% CI: 0.37 to 0.98). Incident SSS was associated with greater baseline body mass index, height, N-terminal pro-B-type natriuretic peptide, and cystatin C, with longer QRS interval, with lower heart rate, and with prevalent hypertension, right bundle branch block, and cardiovascular disease. We project that the annual number of new SSS cases in the United States will increase from 78,000 in 2012 to 172,000 in 2060.

CONCLUSIONS Blacks have a lower risk of SSS than whites, and several cardiovascular risk factors were associated with incident SSS. With the aging of the population, the number of Americans with SSS will increase dramatically over the next 50 years. (J Am Coll Cardiol 2014;64:531–8) © 2014 by the American College of Cardiology Foundation.

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Manuscript received January 14, 2014; revised manuscript received February 22, 2014, accepted March 11, 2014.

ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CI = confidence interval

CKD = chronic kidney disease

CRP = C-reactive protein

CV = cardiovascular

ECG = electrocardiogram

HR = hazard ratio

ICD-9-CM = International Classification of Disease-revision 9-Clinical Modification

NT-proBNP = N-terminal pro-B-type natriuretic peptide

SSS = sick sinus syndrome

Sick sinus syndrome (SSS) is a cardiac conduction disorder characterized by symptomatic dysfunction of the sinoatrial node. On the electrocardiogram (ECG), SSS usually manifests as sinus bradycardia, sinus arrest, or sinoatrial block, and is sometimes accompanied by supraventricular tachyarrhythmias ("tachy-brady" syndrome). Typical symptoms of SSS include syncope, dizziness, palpitations, exertional dyspnea, easy fatigability from chronotropic incompetence, heart failure, and angina (1-3). Clinically significant SSS typically requires pacemaker implantation. Approximately 30% to 50% of pacemaker implantations in the United States list SSS as the primary indication (4).

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Epidemiological information about SSS is limited. Although past studies have described the characteristics of individuals hospitalized for SSS, the incidence of SSS in the general population remains unclear. Additionally, no prior epidemiological studies have evaluated potential risk factors for incident SSS. The goals of this analysis were to determine the age and sex-specific incidence of SSS in white and black participants in the ARIC (Atherosclerosis Risk In Communities) study and the CHS (Cardiovascular Health Study), as well as to investigate associations of cardiovascular (CV) risk factors with incident SSS.

METHODS

STUDY POPULATION. The prospective cohort ARIC study comprised 15,792 individuals aged 45 to 64 years of age when recruited between 1987 and 1989 from 4 U.S. communities: Forsyth County, North Carolina; Jackson, Mississippi (blacks only); Washington County, Maryland; and the northwestern suburbs of Minneapolis, Minnesota. The prospective cohort CHS study consisted of 5,888 community-dwelling adults age 65 years of age or older from 4 U.S. communities: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania. From 1989 to 1990, CHS recruited 5,201 participants; 687 blacks were included from 1992 to 1993. The ARIC and CHS design and recruitment are described in detail elsewhere (5-7).

IDENTIFICATION OF INCIDENT SSS. Incident SSS was ascertained during cohort follow-up from hospitalization records (8,9). Medical records were reviewed for hospitalizations that included International Classification of Disease-revision 9-Clinical Modification (ICD-9-CM) code 427.81 (SSS, sinoatrial node dysfunction, tachycardia-bradycardia syndrome, persistent sinus bradycardia) in any position. We considered SSS to be present if the medical record included a diagnosis of SSS and symptoms or signs consistent with SSS (e.g., syncope, dizziness, bradycardia, sinus pauses), with no evidence of other conditions responsible for the episode, such as atrioventricular block or medication use.

In the ARIC study, 294 individuals had ICD-9-CM code 427.81 in at least 1 hospitalization. Of these participants, we obtained medical records in 195, from which we confirmed 130 (67%) of the 195 cases after medical record review. In the CHS study, ICD-9-CM code 427.81 was present in 179 individuals, and medical records were available for 169, from which we confirmed 99 cases (59%) after record review.

To determine the negative predictive value of ICD-9-CM code 427.81 for SSS, we reviewed medical records for a random sample of participants with selected non-SSS ICD-9-CM codes (426.0 and 426.1, atrioventricular block; 426.6, other heart block; 427.89, other atrial arrhythmia; 37.8, insertion, placement, and revision of pacemaker; V45.01, status post-pacemaker implantation; and V53.31, fitting and adjustment of cardiac pacemaker). Among 178 ARIC and CHS participants with these selected ICD-9-CM codes, the medical records documented a diagnosis of SSS in 5 of them (2.8%), suggesting excellent negative predictive value for the absence of the 427.81 code.

In the incidence rate calculations, we included validated SSS cases and a random sample of 63% of the 109 individuals with ICD-9-CM code 427.81 for whom medical records were not available. This sampling proportion was based on the positive predictive value of the ICD-9-CM code 427.81 in those with available medical records. We included only validated cases in the risk factor analysis; unvalidated cases were classified as noncases.

RISK FACTOR ASCERTAINMENT. Similar methods were used in the ARIC and CHS studies to assess most risk factors, as described previously (10,11). Participants underwent a baseline study examination that included height and weight measurement, blood pressure measurement by a random-zero sphygmomanometer, and 12-lead resting ECG. Race, smoking, and alcohol consumption information were determined by self-report. Information was collected on medication use, and blood was collected with the participant in a fasting state, from which glucose, high-density lipoprotein and low-density lipoprotein cholesterol, C-reactive protein (CRP), N-terminal