

The Association Between Atrial Fibrillation and Sudden Cardiac Death

The Relevance of Heart Failure

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- Objectives** The purpose of this study was to evaluate the role of congestive heart failure (CHF) in the association between atrial fibrillation (AF) and sudden cardiac death (SCD).
- Background** Recent studies have reported the possibility of an independent association between AF and SCD. We hypothesized that a history of CHF is a significant confounder of this association.
- Methods** In a prospective case-control analysis from the community (The Oregon-SUDS [Sudden Unexpected Death Study], 2002 to 2012), SCD cases (n = 652) with clinical records available (including electrocardiography and/or echocardiography) were compared with age- and sex-matched control patients with coronary artery disease. The association between AF and SCD was analyzed using multivariable logistic regression and propensity score matching.
- Results** Cases (age 67.3 ± 11.7 years, 65% male) were more likely than control patients (age 67.2 ± 11.4 years, 65% male) to have a history of AF (p = 0.0001), myocardial infarction (p = 0.007), CHF (p < 0.0001), stroke (p < 0.0001), and diabetes (p < 0.0001). In multivariate analysis without considering CHF, AF was a significant predictor of SCD (odds ratio [OR]: 1.6; 95% confidence interval [CI]: 1.2 to 2.0; p = 0.002). However, in a model that included CHF, the AF-SCD association was no longer significant (OR: 1.1; 95% CI: 0.8 to 1.5; p = 0.45), whereas CHF was a significant predictor of SCD (OR: 3.1; 95% CI: 2.4 to 4.1; p < 0.0001). Results on the basis of propensity score matching were consistent.
- Conclusions** Our findings suggest that a history of CHF, including both systolic and diastolic symptomatic dysfunction, may partially explain the AF-SCD association. (J Am Coll Cardiol HF 2014;2:221-7) © 2014 by the American College of Cardiology Foundation

Atrial fibrillation (AF) remains the most common cardiac rhythm abnormality, accounting for significant morbidity and major financial costs to the healthcare system (1-5). It has also been demonstrated that AF is associated with a significant increased risk of overall mortality, even after adjustment for cardiovascular risk factors and structural heart disease (3,6-9). Recent data have suggested that history of AF is independently associated with a higher risk of sudden cardiac death (SCD) (10,11). A better

understanding of this association is of major importance due to the burden of both AF and SCD worldwide, and the potential implications for the mechanistic understanding and risk stratification of SCD.

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On the one hand, there are a number of exciting electrophysiological observations, as well as recent data on ventricular structural remodeling, suggesting that AF itself might have ventricular proarrhythmic effects (12-14). On the other hand, in most cases AF is associated with multiple cardiac comorbidities, making the potential association between AF and SCD particularly complex. In this context, congestive heart failure (CHF) remains of special interest, because it is an important cause of AF and also contributes to a significant proportion of SCD cases (15,16). Although systolic ventricular dysfunction may be relatively easily assessed by left ventricular ejection fraction (LVEF)

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Manuscript received December 20, 2013; accepted December 26, 2013.

**Abbreviations
and Acronyms****AF** = atrial fibrillation**BNP** = B-type natriuretic peptide**CHF** = congestive heart failure**CI** = confidence interval**ECG** = electrocardiogram**EF** = ejection fraction**LV** = left ventricular**LVEF** = left ventricular ejection fraction**OR** = odds ratio**SCD** = sudden cardiac death

evaluation, diastolic dysfunction or CHF with preserved ejection fraction has been shown to be nearly as prevalent as systolic ventricular dysfunction (17). The latter condition is more difficult to evaluate and has not been incorporated in any consistent fashion within published analyses. In the present large, ongoing, community-based, case-control study, we test the hypothesis that a history of CHF explains at least part of the observed association between AF and SCD.

Methods

Study case-control population. Detailed methods of the Oregon-SUDS (Sudden Unexpected Death Study) have been published earlier (18–20). Briefly, the Oregon-SUDS has prospectively identified out-of-hospital SCD occurring among residents of the Portland, Oregon metropolitan region (population approximately 1,000,000) since February 1, 2002. Residents of all ages who experience SCD are identified from several sources: the emergency medical response system, the state medical examiner's office, and 16 area hospitals (20). The county has a 2-tiered emergency medical response system. Advanced cardiac life support-staffed fire engine companies provide the first response with backup by advanced cardiac life support-transporting ambulances. Investigators are alerted to cases by the emergency medical services agency or by the office of the county medical examiner. Since 2005, cases from the emergency medical services system are included only if resuscitation was attempted. This study was approved by the institutional review boards of Cedars-Sinai Medical Center, Oregon Health and Science University, and participating hospitals.

A comprehensive evaluation was performed for each case of unexpected death, including analysis of the circumstances of arrest, medical records, and available autopsy data. Identified cases were screened to identify subjects with presumed cardiac arrest and eventually those that met the criteria for SCD according to prospective assessment with in-house adjudication. Independent assessments were made by 3 physicians, followed by a consensus review. In the event of a disagreement regarding a specific case, the determination was based on the majority opinion.

Control subjects were from the same geographic area and time period and were enrolled concomitantly with SCD cases. Since at least 80% to 85% of SCD occurs in the setting of existing coronary artery disease (21), control subjects for this analysis were restricted to individuals alive with documented chronic as well as acute coronary artery disease, but no history

of cardiac arrest or ventricular arrhythmias. This approach allows for examination of risk factors for SCD in the setting of coronary artery disease. Control patients were enrolled from clinics of participating health systems, individuals receiving a coronary angiogram, patients transported by emergency medical services for complaints suggestive of ongoing coronary ischemia, and among members of a local health maintenance organization. Documented coronary artery disease was defined as having $\geq 50\%$ stenosis of a major coronary artery or a history of myocardial infarction, coronary artery bypass grafting, or percutaneous coronary intervention. Medical records for each potential control patient were reviewed by the adjudicating committee to confirm the presence of coronary artery disease as well as the absence of a history of fatal ventricular arrhythmias before inclusion in the Oregon-SUDS database.

Previous medical history of case and control patients was obtained from a comprehensive assessment of inpatient as well as outpatient medical records/visits (general medicine as well as specialty medicine consultation) in any Portland, Oregon medical system. If available, cardiac evaluations (prior to the arrest for cases) were obtained, including electrocardiograms (ECGs), echocardiograms, and angiograms. These data were recorded and entered into the database after further review according to pre-specified criteria and definitions.

In accordance with the hypothesis being tested, in the present analysis, we considered case and control subjects age ≥ 18 years with a history of specific cardiac evaluation, including an electrocardiogram and/or an echocardiogram. Of the 2,436 subjects (1,743 cases and 693 control subjects) enrolled from February 2002 to January 2012 with pre-arrest physician records available, 1,614 (935 cases and 679 control subjects) met these criteria, and finally, 652 cases were sex- and age-matched to 652 control patients.

Definitions of SCD, history of AF, and CHF. SCD was defined as a sudden unexpected pulseless condition occurring within 1 h of symptom onset; if unwitnessed, subjects were to have been seen alive and symptom free within 24 h of their sudden arrest. Patients with known noncardiac causes of arrest (e.g., trauma, overdose, pulmonary embolism, cerebrovascular accident, and terminal illness such as cancer not in remission) were excluded (20,22).

A history of AF was defined as any documentation of paroxysmal, persistent, or permanent AF or atrial flutter in the past records of the patients, as noted by a physician, by ECG, or by other recording (e.g., ambulatory monitor). Of note, all ECG recordings were over-read by a study cardiologist.

Patients categorized as having CHF were those with a physician-documented history of CHF in clinical records prior to arrest (including outpatient visits as well as hospital records), with substantiating evidence for CHF (clinical as well as laboratory/tests). Overall, CHF criteria, including both diastolic as well as systolic patterns of CHF, was defined by previous hospitalization or outpatient treatment

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