



The paradox of atrial fibrillation in African Americans

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Abstract

The reported lower prevalence and incidence of atrial fibrillation (AF) despite the higher prevalence of AF risk factors in African Americans compared to Caucasian whites has been referred to as the paradox of AF in African Americans. In this report we highlight this paradox and address potential explanations using data from several US populations studies. These possible explanations include limited methodology to detect AF patterns that are harder to detect (e.g. paroxysmal/intermittent AF or atrial flutter) coupled with the possibility of African Americans having more of these patterns, differential access to health care with African Americans having less access and subsequently less detected AF, survival bias with Caucasian whites living longer and subsequently having more AF, and finally differential impact of AF risk factors with Caucasian whites being more affected or African Americans less affected by AF risk factors whether this is genetically determined or via other unknown predispositions.

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Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical practice. Over 2.3 million adults in the United States have AF, and the number is expected to more than double in the next few decades [1]. The importance of AF as a public health problem stems not only from its high prevalence but also because of its associations with increased risk of morbidity and mortality [2–4]. This requires a clear understanding of the epidemiology of AF especially in the fast growing non-white races/ethnicities in the US.

Atrial fibrillation in African Americans versus Caucasian whites

Studies that addressed the risk of AF in African Americans versus Caucasian whites consistently suggest that African Americans have a lower prevalence/incidence of AF compared to Caucasian whites. We detail this consistently in 9 studies (of different design and among varying disease-free and diseased populations) and a meta-analysis below, together encompassing well over 3 million persons.

In the Cardiovascular Health Study (CHS) [5], the racial differences in incident AF were examined in 5201 adults

≥ 65 years old (≈ 95% white, 5% African-American). The authors reported that African Americans free of cardiovascular disease at baseline had a lower risk of incident AF [HR (95% CI): 0.21 (0.05, 0.86)] compared with whites after adjusting for traditional cardiovascular risk factors and potential confounders.

Data from the Atherosclerosis Risk in Communities (ARIC) study confirm the CHS results. ARIC investigators [6] studied the incidence of AF in 15,792 (≈ 27% African Americans) men and women 45 to 65 years of age at baseline. Compared to Caucasian whites, African Americans had a 41% (95% CI: 8–62%) lower age- and sex-adjusted risk of being diagnosed with AF.

A cross-sectional study of 1.89 million (≈ 85% Caucasian whites, 4% African Americans) adults 20 years or older who were enrolled in a large health maintenance organization in California also showed that AF was more common in Caucasian whites. Among persons 50 years or older, prevalence of AF was higher in Caucasian whites than in African Americans (2.2 vs. 1.5%; $P < 0.001$). In this study, AF prevalence was ascertained using hospital and outpatient diagnosis codes and an ECG database [1].

In the Evaluating Processes of Care & the Outcomes of Children in Hospital (EPOCH), African Americans had a 50% lower prevalence of AF than Caucasian whites even after adjustment for known risk factors for AF [7]. Also, in the Northern Manhattan Stroke Study, of those patients presenting with ischemic stroke, AF

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was more common in Caucasian whites (29%) than in African Americans (11%) [8].

In a large study of 664,754 US Veterans [9], the prevalence of AF (based on data from hospital discharges and out-patient clinic visits) was 5.7% in Caucasian whites, 3.4% in African Americans, 3.0% in Hispanics, 5.4% in native Americans/Alaskans, 3.6% in Asians and 5.2% in Pacific Islanders ($P < 0.001$). Ethnic/racial differences remained after adjustment for demographic and clinical characteristics.

Using data from 135,494 heart failure (HF) hospitalizations, African American patients showed markedly less AF than white patients (20.8 versus 44.8%, $P < 0.001$). Adjusting for risk factors and hospital characteristics, black race was still associated with significantly lower odds of AF (adjusted odds ratio 0.52, 95% CI 0.48 to 0.55, $P < 0.0001$) [10].

In the Losartan Intervention for Endpoint Reduction in Hypertension Study (LIFE), incident AF was examined in 518 black and 8313 nonblack hypertensive patients with electrocardiographic left ventricular hypertrophy (LVH) with no history of AF on their baseline ECG [11]. In multivariable Cox analyses, black race was associated with a 45% decreased risk of developing new AF (HR = 0.55; 95% CI = 0.35–0.87; $P = 0.01$).

In the Southern Community Cohort Study (SCCS) which included participants aged >65 years receiving Medicare coverage from 1999 to 2008 ($N = 8836$), AF prevalence was significantly lower among African Americans (11%) than Caucasian whites (15%) ($P < 0.0001$). Odds ratios for African Americans compared to Caucasian whites persisted after adjustment for AF cardiovascular risk factors (odds ratio 0.64, 95% confidence interval 0.55 to 0.73) [12].

A meta-analysis that included 10 studies totaling 1,031,351 participants, including some of the studies mentioned earlier, showed that African American race/ethnicity was associated with less AF prevalence as compared to Caucasian race (odds ratio 0.51, 95% CI 0.44 to 0.59). In subgroup analyses, African American race/ethnicity was significantly associated with a lower prevalence of AF in the general population, those hospitalized or greater than 60 years old, post-coronary artery bypass surgery patients, and patients with heart failure [13].

The Paradox of Atrial Fibrillation in African Americans

African Americans have a well-documented greater prevalence of AF risk factors than Caucasian whites, including hypertension, obesity, heart failure, diabetes and others [6,11,14–16]. This increased prevalence of AF risk factors in African Americans compared to Caucasian whites is at odds with the reported lower prevalence/incidence of AF in African Americans: the AF paradox [17–20]. Such a paradox mandates rethinking the epidemiology of AF and revising the current knowledge of the ethnic distribution of AF.

Possible explanations for the AF paradox in African Americans

At this stage, efforts to explain the AF paradox in African Americans can only be speculative (Table 1).

Limited methodology to detect AF in population studies

Most of the methods of AF detection in population studies (12-lead resting ECG and self-reported history of previous physician diagnosis) do not take into account the paroxysmal/intermittent/asymptomatic nature of AF in most cases. It could be argued, however, that a limited AF detection method with a low sensitivity would equally under-diagnose AF in African Americans and Caucasian whites; thus, the proportionate distribution of AF between these two groups would not be affected. If this is true, the proportionate difference in AF (i.e. relative risk) between African Americans and Caucasian whites should be similar regardless of the method of AF detection. However, this is not the case according to results from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study in which the relative risk of AF in African Americans vs. Caucasian whites differed according to the sensitivity of the AF detection method used [21].

The REGARDS study investigators conducted an analysis on 18,833 black and white participants from a number of US states. Levels of sensitivity to detect AF, from presumed least to most sensitive, were created for combinations of self-report (SR) and ECG methods, as follows: (a) both SR and ECG required, (b) ECG alone, (c) SR alone, and (d) either SR or ECG. For the four methods used to detect AF, the strength of association between black race/ethnicity and AF progressively decreased with increasing test sensitivity (ORs: 0.20, 0.40, 0.70, and 0.71 respectively). Therefore, it is possible that differential under-ascertainment of AF in African Americans is playing a role in the paradox of AF. The question then would be, why is there such a differential under-ascertainment of AF in African Americans?

Differential distribution of AF sub-types

It would be appropriate to think that the ability to accurately estimate the incidence/prevalence of AF in any population would be dependent on the proportion of individuals with the difficult-to-detect AF patterns such as paroxysmal and asymptomatic AF or atrial flutter [20]. That is to say, if groups differ in the prevalence of paroxysmal/asymptomatic AF, detection of AF by ECG or self-report will differ among groups. At present, there are too few data on the racial differences in the prevalence/incidence of AF

Table 1
Possible explanations of the paradox of atrial fibrillation (AF) in African Americans.

- Limited methodology to detect all AF sub-types in population studies.
- Differential under-ascertainment of AF in African Americans due to differential distribution of AF “sub-types”.
- Differential access to healthcare and subsequently less detection of AF in the group with less access to healthcare i.e. African Americans.
- Survival bias: increased mortality in African Americans at younger age.
- Differential impact of AF risk factors in African Americans i.e. African Americans are less affected by AF risk factors.
- Biological factors.
- Genetic differences: genetic variants present in whites but not in African Americans that made whites more prone to the risk of AF, or vice versa.

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