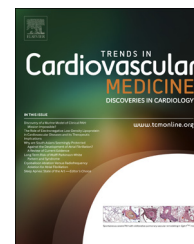


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# Why are South Asians seemingly protected against the development of atrial fibrillation? A review of current evidence

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## ABSTRACT

Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia and is strongly associated with conditions such as valvular heart disease, coronary artery disease and particularly hypertension and diabetes mellitus. The South Asian ethnic group have high rates of these conditions and so would be expected to be at significant risk of AF. However, observational studies have consistently shown that South Asians have a lower prevalence of AF compared with Caucasians. This article summarizes current evidence surrounding the development of AF and its relationship to ethnicity, offers potential reasons for this disparity and identifies future areas of research.

**Key words:** Atrial fibrillation, South Asian, Ethnicity.

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## Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia [1] with an estimated prevalence of 3% in adults aged 20 years or older [2]. This figure is expected to rise further, potentially more than doubling over the next 50 years [3]. It is associated with a five-fold risk of stroke, a three-fold incidence of heart failure [4] and a 1.5- to 1.9-fold increase in mortality [5] as well as having a significant impact on patients' quality of life. Traditional risk factors for the development of AF include advancing age, valvular heart disease, coronary artery disease [6,7] and, in particular, hypertension and diabetes mellitus which are both significant independent predictors of the condition [8]. More recently, novel risk factors have been identified including obesity [9], metabolic syndrome [10,11], obstructive sleep apnea [12–14] and physical inactivity [15] or excessive exercise [16].

The South Asian (SA) population is an ethnic group that originates from India, Pakistan, Sri Lanka, Bangladesh and Nepal and makes up more than a fifth of the world's population. This ethnic group has been shown to have higher rates of cardiovascular risk factors, especially hypertension and diabetes mellitus [17–20] (see Fig. 1 [21–24]). They have growing levels of obesity [25,26] and the metabolic syndrome [27–30] and have low levels of physical activity [31]. They also have a higher rate of ischemic stroke compared to other ethnic groups [32]. Despite a high prevalence of risk factors for the arrhythmia, the SA population has consistently been shown to have a lower prevalence of AF [17–19,33] although the reason for this disparity is currently unclear.

## Hypothesis and Objective

The mechanism of AF is thought to be related to structural and electrical remodelling within the atria [34] (see Fig. 2). We

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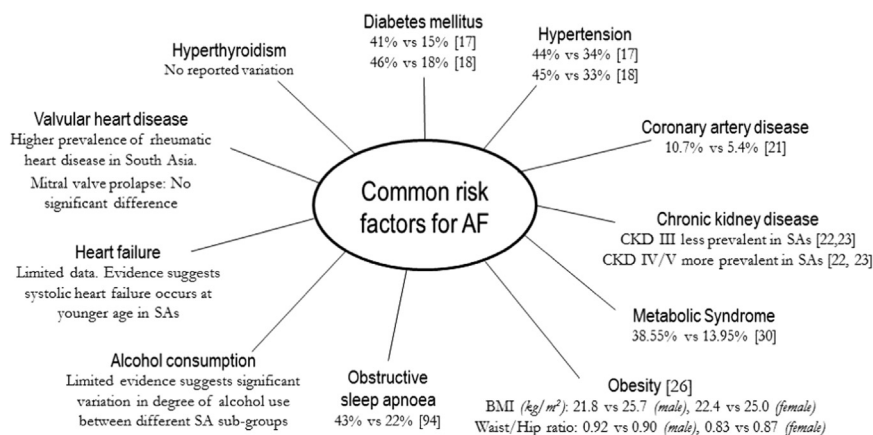
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**Fig. 1 – Common risk factors for AF and their prevalence in South Asians compared to Caucasians (South Asian % vs Caucasian %, where applicable).**

hypothesize, therefore, that individuals of SA origin have morphological or electrophysiological differences within their atria which reduce the risk of them developing AF. We aim to review and summarize current literature surrounding the mechanisms behind AF development, with an emphasis on identifying ethnic variations, to determine whether there is evidence to support or refute this hypothesis.

#### Literature search and method

Literature searches were performed in the following databases: Medline, Embase and PubMed. A combination of the key search terms included the following: atrial fibrillation, auricular fibrillation, South Asia, India, Sri Lanka, Pakistan, Bangladesh, Nepal, ethnicity, continental population groups, African, African-American, atrial size/ volume/ enlargement/ dimension/ diameter, organ size, tissue mass, body surface area, height, weight, body mass index, electrophysiology, refractory period, autonomic nervous system, acetylcholine, fibrosis, connective tissue, genes, genetics, obesity, metabolic syndrome, sleep-disordered breathing and obstructive sleep apnea. The references cited in each eligible study were considered for additional citations. The final literature search was performed on 1st August 2016.

All studies which examined AF and its relationship to atrial size, electrophysiological change, the autonomic nervous system, myocardial fibrosis and genetics were considered, together with studies that examined AF in the SA ethnic group, regardless of the publication year.

### Ethnic variations in the prevalence of AF

#### African-American/Black population

In recent years, an increasing amount of evidence has shown ethnic variations in patients diagnosed with AF. The vast majority of studies looking at ethnicity and AF have examined the African-American (AA) or black population and they have consistently shown a reduced prevalence of AF in this ethnic group compared with their Caucasian counterparts [3,7,35–37], despite AAs having a higher prevalence of

conventional risk factors for the arrhythmia. The reason for this is uncertain although some theories have been proposed.

It was previously thought that the reduced prevalence of AF in AAs was in fact caused by under-detection of the arrhythmia due to AAs having less access to healthcare [38] and being more likely to suffer from paroxysmal AF [39]. However, a recent study by Kamel et al. involved the interrogation of pacemakers in AA and white-American patients and found that during 3.7 ( $\pm 1.8$ ) years of follow-up, rates of AF were consistently lower in AAs [40]. This would seem to indicate that potential underreporting of AF does not account for the disparity between the two ethnic groups.

There is evidence demonstrating cardiac structural differences between the two groups. For instance, the black population appear to have smaller atria in comparison to Caucasians [41,42] with one study showing that in multivariate analyses, left atrial (LA) dimension in black males was 1.9mm less than in white males [41]. There is also evidence to suggest that the ethnic variation may be due to genetic differences. A study by Marcus et al. [43] showed that AAs risk of AF development increased with increasing levels of European ancestry whilst Roberts et al. [44] identified a single-nucleotide polymorphism (SNP) that partially mediated the increased risk of AF in Caucasians compared to AAs.

It is likely that the variation in AF prevalence between AAs and Caucasians is due to a combination of environmental and genetic factors although a comprehensive answer to fully explain this puzzling disparity is yet to be determined.

#### South Asian population

A similar paradox has been demonstrated within the SA ethnic group. The West Birmingham Stroke Project [17], a registry data review of 832 consecutive patients admitted with non-hemorrhagic stroke over a 2 year period demonstrated that patients of Indo-Asian origin had significantly higher rates of hypertension and diabetes mellitus but an AF rate of only 1% (compared with 13% in the Caucasian group). A study in 2005 by Newton et al. compared SA- and white- cohorts who were admitted acutely to hospital with a first presentation of heart failure [18]. Again, this study demonstrated higher rates of hypertension (45% vs. 33%) and diabetes (46% vs. 18%) in the

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