ATRIAL FIBRILLATION AND ETHNICITY

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Atrial fibrillation (AF) and ethnicity

- The known
- The unknown
- The paradox
Why AF is important

- **AF is the most common sustained arrhythmia in clinical practice**
  - Over 2.3 million adults in the US have AF, and the number is expected to more than 10 million in 2050
  - The lifetime risk of developing AF is approximately 1 in 4
  - AF rates increase with advancing age, making AF a more relevant challenge as the population ages
  - 35% of all hospital admissions for arrhythmia are attributable to AF
Why AF is important

• AF has a considerable impact on cardiovascular morbidity and mortality
  • One of every 6 strokes occurs in patients with AF
  • The rate of ischemic stroke among patients with AF is about 5% per year; 2 to 7 times higher than that in people without AF
  • AF is independently associated with increased rates of all-cause mortality and cardiovascular mortality, and other health outcomes such as heart failure and dementia
Why AF is important

- AF imposes a substantial cost burden on the healthcare system
  - In 2001, the total annual costs for treatment of AF were estimated at US$6.65 billion
  - 2/3 of all emergency department visits with a primary diagnosis of AF result in hospital admissions
  - During the past 20 years, hospital admissions for AF have increased by 66%
  - 35% of all hospital admissions for arrhythmia are attributable to AF
Key message 1

AF is a major public health problem. Planning and budgeting for future healthcare expenditure imposed by AF require clear understanding of the pathophysiology and epidemiology of AF.
Pathophysiology of AF

Risk Factors
- Nonmodifiable
  - Age
  - Sex
  - Race
  - Genetic
- Modifiable
  - Hypertension
  - Diabetes mellitus
  - Obesity
  - Smoking

Subclinical Manifestations
- ECG
- Echo
- Artery stiffness
- Biomarkers
- Genomics

Predisposing Clinical Conditions
- Heart failure
- Myocardial infarct
- Valve disease
- Thyroid disease
- Sleep disordered breathing

Structural Substrate
- Inflammation
- Abnormal innervation
- Metabolic changes
- Fibrosis
- Atrial remodeling

Electrical Substrate
- Membrane ionic currents
- Regional heterogeneity
- Calcium dynamics

Triggers
- Ischemia
- Heart failure exacerbation
- Autonomic nervous system
- Inflammation
- Myocardial stretch

AF
- Paroxysmal
- Persistent
- Permanent

Complications
- Heart failure
- Stroke
- Dementia
- Emboli
- Diminished QOL
- Death

Pathophysiology of AF

- AF is a complex disease with a multi-factorial etiology that has been investigated mainly in Whites.

- Many traditional and novel risk factors have been linked to AF, however:
  - It is not clearly understood how these risk factors interact with each other under different genetic predispositions to AF
  - Little is known about the differential impact of these AF risk factors in non-Whites vs Whites
Key message 2

A more complete understanding of the pathophysiology of AF requires integration of our knowledge regarding the impact of individual risk factors and their interactions with age, sex and race in the context of different genetic and environmental influences.
Epidemiology of AF in non-Whites

• Few studies addressed the epidemiology of AF in Blacks vs Whites, and fewer extended this to other races
AF in Blacks vs. Whites

- **The Atherosclerosis Risk in Communities (ARIC) Study**
  - 15,792 participants (27% Blacks)
  - Age 45-65 years
  - Incident AF detected by ECG, hospital discharge codes, and death certificate from 1987 to 2004
  - Compared to Whites, Blacks had a 41% risk of AF
  - Incidence rates of AF were 6.7, 4.0, 3.9, and 3.0 per 1,000 persons per year in white men, white women, African-American men, and African-American women, respectively.

Soliman EZ, Prineas RJ, Case D, et al. Stroke 2009
AF in Blacks vs. Whites

- **The Cardiovascular Health Study (CHS)**
  - 5,201 participants (5% Blacks)
  - Age > 65 years
  - Incident AF detected by self-report, ECG and hospital discharge diagnoses from 1989-1993
  - The AF incidence was lower in Blacks than in Whites (12.0 versus 19.5 per 1000 person-years).

AF in Blacks vs. Whites

• The REasons For Geographic And Racial Differences In Stroke (REGARDS)
  • 30,239 participants (42% Blacks)
  • Age>45 years
  • Prevalent AF detected by ECG and self report from 2003-2007
  • AF was 2-3 times more common in Whites compared to Blacks

Meschia JF, Merrill P, Soliman EZ, et al. Stroke 2010
AF in Blacks vs. Whites

- The AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study
  - A cross-sectional study of 1.89 million (4% Blacks)
  - 20 years or older who were enrolled in a large health maintenance organization in California
  - AF was ascertained using hospital and outpatient diagnosis codes and an ECG database.
  - Among persons aged 50 years or older, prevalence of AF was higher in Whites than in Blacks (2.2% vs. 1.5%; $P<.001$).

AF in Blacks vs. Whites

• The Epidemiology, Practice, Outcomes, and Costs of Heart Failure (EPOCH) study

• This racial difference in the incidence of AF has been also evidenced in heart failure patients enrolled in EPOCH where Blacks had a 50% lower prevalence of AF than Whites even after adjustment for known risk factors for AF

AF in Blacks vs. Whites

• In the US National Hospital Ambulatory Medical Care Survey, rates of visits to an emergency department with AF as the primary diagnosis were higher in Whites than in Blacks (9 vs. 5 per 10,000 person-years)

• The National Hospital Discharge Survey, which compiles data on discharges from nonfederal hospitals in the United States, also shows a higher incidence of AF hospitalizations in Whites than in Blacks

How about other races?
AF in non-Blacks non-Whites

• In a meta-analysis of data from 7 randomized clinical trials that prospectively collected information on the development of AF, Asian race was associated with significantly lower rates of AF (odds ratio 0.65, 95% CI 0.50 to 0.84) compared with White race.

AF in non-Blacks non-Whites

- These findings are consistent with a previous report that showed that AF is less common in South Asians newly hospitalized for heart failure compared with Whites (15% vs. 31%, p = 0.0002)

Newton JD, Blackledge HM, Squire IB. Heart 2005
AF in non-Blacks non-Whites

• In the Northern Manhattan Stroke Study, of those patients presenting with ischemic stroke, AF was more common in Whites (29%) than in either Black (11%) or Hispanic (11%) patient groups.

Sacco RL, Kargman DE, Zamanillo MC. Neurology 1995
AF in non-Blacks non-Whites

• In the **West Birmingham AF project**, the prevalence of AF was only 0.6% amongst Indo-Asians, who as an ethnic group comprised 65% of the 25,051 general practice population surveyed

AF in non-Blacks non-Whites

In a large study of 664,754 US Veterans (all males), the prevalence of AF (based on data from hospital discharges and out-patient clinic visits) was 5.7% in Whites, 3.4% in Blacks, 3.0% in Hispanics, 5.4% in native Americans/Alaskans, 3.6% in Asians and 5.2% in Pacific Islanders.

Key message 3

It seems there is a general agreement that Blacks (and other races) have less AF than Whites......*but does this make sense?!
The paradox of AF in Blacks

• AF risk factors are more common in Blacks compared to Whites, but many studies reported less AF in Blacks!!!

• Possible explanation?

Soliman EZ, Goff Jr DC. J Natl Med Assoc 2008
Soliman EZ, Prineas RJ, Case D, et al. Stroke 2009
Soliman EZ, Alonso A, Goff Jr DC. Future Cardiology 2009
Possible explanation of the paradox of AF in Blacks

• Limited methodology in previous studies?
• Differential under-ascertainment of AF in Blacks?
• Differential impact of AF risk factors in Blacks i.e. Blacks are less affected by AF risk factors?
• Genetic variants present in Whites but not in Blacks that made Whites more prone to the risk of AF, or genetic variants in Blacks that protect against AF?
• All of the above?
• None of the above?
Possible explanation of the paradox of AF in Blacks

• Limited methodology in previous studies?
  • 12-lead ECG [*unlikely to capture paroxysmal AF*]
  • Self-report [*subjective and prone to errors*]
  • Hospital discharge diagnosis [*affected by access to health care*]
  • Death certificate [*unlikely to capture all AF cases*]
  • Holter [may be useful but the high cost is an obstacle to use in population studies]
Possible explanation of the paradox of AF in Blacks

• Limited methodology in previous studies?
  • Limited methodology should result in an under-estimated AF prevalence across races keeping the relative distribution of AF across races intact

Soliman EZ, Alonso A, Goff Jr DC. Future Cardiology 2009
Possible explanation of the paradox of AF in Blacks

• The sensitivity of the method used to detect AF in population studies affects group-specific prevalence estimates: The REGARDS study

Possible explanation of the paradox of AF in Blacks

- **Limited methodology in previous studies?**
  - Limited methodology should result in an overall under-estimated AF prevalence across all races keeping the relative distribution of AF across races intact…unless, there is differential under-ascertainment of AF in blacks

Soliman EZ, Alonso A, Goff Jr DC. Future Cardiology 2009
Possible explanation of the paradox of AF in Blacks

• Differential under-ascertainment of AF in Blacks?
  • Why a method may disproportionately under-diagnose AF in Blacks more than Whites?
  • 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 or asymptomatic AF
Possible explanation of the paradox of AF in Blacks

• Differential under-ascertainment of AF in Blacks?
  • Is it possible that there is more paroxysmal and/or asymptomatic AF in Blacks that cannot be detected by the AF detection methods used in population studies?
  • No data on the racial differences in AF subtypes
  • No EVIDENCE that Blacks have more paroxysmal AF, but there are CLUES and SPECULATIONS!
More paroxysmal AF in Blacks??

AF risk factors

P-wave and PR abnormalities on the ECG (P-wave indices)

Paroxysmal AF → Chronic (Permanent) AF

Soliman EZ, Prineas RJ, Case D, et al. Stroke 2009
More paroxysmal AF in Blacks??

• To overcome the limitations of the current approaches of estimating the racial distribution of AF, we suggested using the racial distributions of P-wave abnormalities (P-wave indices) on the ECG as surrogates for racial distribution of future AF in the ARIC study.

• Our results showed that:
  • Chronic (permanent) AF was significantly less common in Blacks compared with Whites (similar to what has been reported in previous studies) but,
  • Blacks had significantly more abnormal P-wave indices

Soliman EZ, Prineas RJ, Case D, et al. Stroke 2009
More paroxysmal AF in Blacks??

- With the assumption that the racial distributions of P wave indices could be used as surrogates for the racial distribution of AF (which was confirmed in this study), these results support the contention that Blacks might actually have a higher prevalence of AF that might have been missed by previous studies owing to limited methodology.

**Speculations?!**
More paroxysmal AF in Blacks??

• In the REGARDS study, the association between AF and race (Black vs White) was inversely related to the sensitivity of the method used to detect AF; as test sensitivity increased, the association became attenuated.

More paroxysmal AF in Blacks??

• These findings suggest that if a more sensitive approach for AF detection is employed (which will detect more paroxysmal AF), it might result in an estimate showing a reversed distribution of AF, with Blacks having a higher, or at least equal, prevalence of AF, compared to Whites.

More speculations?!

How about self-reported AF in individual who require regular medical attention (e.g. CKD)?

More paroxysmal AF in Blacks??

The Chronic Renal Insufficiency Cohort (CRIC)
• 3,267 participants (50% Blacks)
• Age 21-74 years
• AF detected by ECG and self report
• Results:
  • AF by ECG: Blacks had less AF compared to whites
  • AF by ECG or self-report:
    • Unadjusted and demographic adjusted models: Black had more AF risk [odd ratio and 95% CI: 1.24 (1.04-1.49); and 1.25 (1.03-1.52) respectively]
    • Demographic and clinically adjusted model: **No significant difference** between Blacks and Whites [1.07 (0.86-1.34)]
Possible explanation of the paradox of AF in Blacks

• Differential impact of AF risk factors in Blacks i.e. Blacks are less affected by AF risk factors?
  • Yes
  • No
  • May be
Possible explanation of the paradox of AF in Blacks

• Genetic variants present in Whites but not in Blacks that made Whites more prone to the risk of AF, or genetic variants in Blacks that protect against AF?
  • Yes
  • No
  • May be

• European ancestry is a risk factor for AF in Blacks…..
•…..but what type of AF; paroxysmal, chronic or both?

Possible explanation of the paradox of AF in Blacks

• Limited methodology in previous studies?
• Differential under-ascertainment of AF in Blacks?
• Differential impact of AF risk factors in Blacks i.e. Blacks are less affected by AF risk factors?
• Genetic variants present in Whites but not in Blacks that made Whites more prone to the risk of AF, or genetic variants in Blacks that protect against AF?
  • All of the above?
  • None of the above?
  • Do not know!!
Key message 4

- The less AF in Blacks compared to Whites contradicts with the high rates of AF risk factors in Blacks; the AF paradox in Blacks
- The inability to explain the paradox of AF in Blacks is complicated by lack of data on the racial distribution of AF subtypes, especially paroxysmal AF
- Lack of data on the racial distribution of AF subtypes relates mainly to the inherent limitations of the current AF detection methods used in epidemiologic studies
Racial disparities in awareness and treatment of AF

• In the REGARDS study, Blacks were less likely than Whites to be aware of having AF or to be treated with warfarin:

  • The odds of Blacks being aware of their AF were one third that of whites (odds ratio 0.32; 95% CI: 0.20 to 0.52).

  • Among those aware, the odds of blacks being treated with warfarin were only one fourth as great as whites (odds ratio 0.28; 0.13 to 0.60).

Meschia JF, Merrill P, Soliman EZ, et al. Stroke 2010
Concluding remarks

• We know little about the pathophysiology and epidemiology of AF in non-Whites

• The little we know sometimes contradicts with logic; the paradox of AF in Blacks

• Our limited knowledge of the epidemiology and pathophysiology of AF in non-whites is an obstacle to effectively address the racial disparities in cardiovascular morbidity and mortality