Published in final edited form as:

Curr Cardiovasc Risk Rep. 2013 October ; 7(5): . doi:10.1007/s12170-013-0327-8.

Atrial Fibrillation and Race – A Contemporary Review

Michael K. D. Amponsah, MD¹, Emelia J. Benjamin, MD, ScM^{2,3,4,5}, and Jared W. Magnani, MD, MSc^{2,3}

¹Department of Medicine, Division of Cardiology, Newark Beth Israel Medical Center, Newark, NJ

²Department of Medicine, Boston University School of Medicine, Section of Cardiovascular Medicine, Boston, MA

³NHLBI and Boston University's Framingham Heart Study, Framingham, MA

⁴Preventive Medicine Section, Department of Medicine, Boston University School of Medicine, Boston, MA, USA

⁵Epidemiology Department, Boston University School of Public Health, Boston, MA, USA

Abstract

Atrial fibrillation (AF) is the most commonly encountered clinical arrhythmia and is associated with adverse outcomes and increased healthcare costs. Racial variations in AF are recognized yet poorly understood. In this review we summarize racial differences in AF epidemiology, risk factors, genetics, and outcomes. We identify novel risk factors, inflammatory mediators and biomarkers associated with AF, which have had limited study in racial and ethnic minorities. We describe the mismatch between risk factor burden and AF. We highlight the limited participation of minorities in trials for AF management and stroke prevention that contrasts with observed racial variability in anticoagulation efficacy and practice. Throughout we provide specific strategies for future directions to address gaps in the epidemiology of racial differences and to meet identified racial disparities. We specifically identify areas for further research. We conclude that addressing disparities in prevention and healthcare resource allocation will likely improve AF-related outcomes in minorities.

Keywords

Atrial fibrillation; African-American; Ethnicity; Race; Epidemiology

Introduction

Atrial fibrillation (AF) is the most commonly encountered clinical arrhythmia and is increasing in prevalence. [1] It is associated with significant and heterogeneous adverse outcomes that include stroke, heart failure, and mortality. [2•-5] Population-based studies have consistently reported a lower incidence and prevalence of AF in non-white racial and ethnic groups. Racial and ethnic differences in anticoagulation practices and effectiveness

Corresponding author: Jared W. Magnani, MD, MSc Boston University School of Medicine, Section of Cardiovascular Medicine 88 E. Newton Street, D-8 Boston, MA 02118 Phone: 617-638-8968 Fax: 617-638-8969, jmagnani@bu.edu.

Compliance with Ethics Guidelines

Conflict of Interest

Michael K. D. Amponsah and Emelia J. Benjamin declare no conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

have not been fully explained. The under-recruitment of racial and ethnic minorities in anticoagulation and stroke prevention trials remains a challenge. Race-specific risk factors that may explain racial differences in AF prevalence and AF-related outcomes have had limited investigation. AF remains a disease most studied in developed nations; data from developing nations, where individuals of non-European ancestry are well represented, are strikingly limited. The present review summarizes the significant challenges and objectives for improved understanding of AF in diverse racial and ethnic groups. Examining such differences may inform AF risk stratification and reduce the complications associated with AF in vulnerable and diverse racial and ethnic groups.

The prevalence, lifetime risk, and cost of AF

The epidemiology of AF has been defined primarily in Western countries. In the US and Western Europe, the prevalence of AF is 3.3% in men and 2.4% in women. [6•] In the US, the lifetime risk of AF is one in four in men and women of European ancestry above age 40 years. [7] The cumulative risk of AF at 80 years of age is 21% in white men and 17% in white women. In contrast, by 80 years the cumulative risk of developing AF among African-American men and women has been reported as 11%. [8] The cumulative risk of AF in Hispanics, American-Indians, Asians and Pacific Islanders has not been determined. In a biracial, community-based cohort, blacks had a 41% (95% CI: 8%-62%) lower risk of being diagnosed with AF than whites, following adjustment for age and sex compared to whites. [8] We are unaware of a similar study that compares incident AF in the community between whites and non-black racial minorities. Blacks are less likely than whites to be aware of having AF (OR 0.32, 95% CI: 0.20-0.52), [9••] potentially contributing towards under-ascertainment and the reported incidence of AF.

The epidemiology of AF in non-black racial and ethnic minorities has had limited investigation. Available data from multi-ethnic communities show a consistently lower AF prevalence among minorities compared to whites. In a multi-ethnic United Kingdom city, the sex- and age-adjusted odds ratio of prevalent AF was determined as 0.09 (95% CI: 0.01-0.63; $p=0.02$) in Indo-Asians and 0.27 (95% CI: 0.10-0.75; $p=0.01$) in black Caribbeans compared to whites. [10] AF was similarly less prevalent in South Asians (11.8%; 95% CI: 8.7-14.8; $p < 0.001$) and black Caribbeans (9.0%; 95% CI: 5.7-12.4; $p < 0.001$) than white Europeans (34.8%; 95% CI: 31.9–36.8) in a United Kingdom stroke registry. [11] The multivariable-adjusted odds ratio for AF and concomitant stroke was 0.28 (95% CI: 0.18–0.43; $p < 0.001$) in blacks compared to whites in a hospital-based, prospective analysis. [12] A large survey of male veterans identified the age-adjusted prevalence of AF as 3% in Hispanics, 3.6% in Asians, 5.2% in Pacific Islanders, 5.4% in Native Americans, and 5.7% in whites. [13] The differences in study design, methods of AF ascertainment and demographics of study populations make the comparison of AF incidence and prevalence across diverse racial and ethnic groups suboptimal.

In general, the epidemiology of AF in developing regions beyond the Western world has been limited. The global burden of AF has been reviewed and summarized elsewhere. [6,14] Limited data from Africa suggest that the prevalence of AF is 1% to 4.6%. [15-18] The prevalence of AF in a community-based cohort in China is estimated at 2.8%. [19] The age-adjusted AF prevalence rate in individuals >65 years of age in Brazil has been reported as 2.4%. [20] Most studies outside of Western nations are limited by sample size, study design, and AF ascertainment methods. The heterogeneous nature of ethnic and racial minorities makes regional or trans-continental comparisons a challenge.

In Western nations, AF consumes vast medical and social resources. In the US, the total national incremental cost of AF was estimated at \$26 billion dollars in 2008. [21] The total

cost of AF in five European countries was determined to be \$8.2 billion dollars in 2006 with inpatient and interventional procedures being the main drivers of cost. [22] There have been limited investigations into whether resource allocation and costs differ by race and ethnicity.

Future directions

Obtaining substantive AF data from developing regions of the world will remain a challenge for the foreseeable future. However, designing low-cost cardiovascular surveillance systems in resource poor settings will help track AF incidence and prevalence. The surveillance systems will provide a map for targeted AF research in developing countries. Developing large-sized racial and ethnic minority cohorts and continued diversification of existing cohorts in Western nations will help the scientific community understand the impact of race on AF epidemiology and allow for tailored public health interventions and AF management across different ethnicities and races.

AF risk factors in racial and ethnic minorities

Traditional risk factors

The primary risk factors for AF are advanced age, male sex, smoking, diabetes, hypertension, height, obesity, heart failure, valvular heart disease and myocardial infarction. [5,23-25] Racial variations in the prevalence of AF risk factors have been described. Blacks are almost twice likely to have hypertension compared to whites (OR 1.86; 95% CI 1.28-2.94 for men; OR 1.83; 95% CI 1.28-2.62 for women) but the difference in prevalence rates of hypertension between Hispanics and whites was not found to be significant. [26] In contrast, Native Americans have lower rates of hypertension compared to whites and blacks but a higher prevalence of diabetes. [26,27] Generally, obesity is more common in non-Hispanic blacks compared to non-Hispanic whites, Hispanics and Mexican-Americans. [28] Coronary heart disease has been reported by the Center for Disease Control as higher among Native Americans than blacks, Hispanics, whites, or Asians and Pacific Islanders. [29]

“Racial Paradox”

Despite the generally higher burden of most primary AF risk factors in racial and ethnic minorities, epidemiology studies and clinical trials have consistently shown a lower incidence and prevalence of AF in ethnic and racial minorities. [8,10-13,30] In a prospective community cohort study of about 9,000 individuals (67% black; 33% white), the association between primary AF risk factors and AF were generally similar in both whites and blacks. [31] The discordance between the higher AF risk factor burden and the lower incidence and prevalence of AF in blacks has been termed a “racial paradox.” Under-ascertainment and differential mortality may partially contribute towards the apparent lower burden of AF in racial and ethnic minorities. In a prospective, multiethnic study across three continents, AF was ascertained in participants using implanted pacemakers or defibrillators. At 2.5 years of follow up, blacks were noted to have a lower incidence of AF compared to individuals of European ancestry despite a higher burden of AF risk factors. [32] Further investigations are necessary to explain racial differences in the discordance between risk factor burden and AF incidence.

Novel risk factors

Novel risk factors for AF include thyroid disease, alcohol intake, obstructive sleep apnea, P wave indices (PWI, electrocardiographic measures of atrial electrical function), and biomarkers. A linear correlation between declining serum thyroid-stimulating hormone levels and risk of AF has been established. [33] Alcohol intake is associated with an increased risk of AF (RR 1.32; 95% CI: 1.15-1.50 for < 4 drinks/day; RR 1.74; 95% CI: 1.35-2.24 for >8 drinks/day). [34] Obstructive sleep apnea is associated with incident AF.

[35] The contributions of alcohol, hyperthyroidism and obstructive sleep apnea towards the pathogenesis of AF have not been validated in blacks, Hispanics and other racial minorities. P wave duration has been associated with an increased incidence of AF. [36] In a community-based, longitudinal study of ~15,000 participants, blacks had a higher proportion of abnormal PWIs (8.0%-11.3%) compared to whites (2.3%-6.3%; $P<0.0001$ for all comparisons) but markedly limited incidence of AF. [37] The associations of PWI and AF have had limited investigation in individuals not of African or European ancestry.

AF risk prediction

AF risk prediction models provide useful insights to the contribution of the risk factors to AF occurrence and may provide targeted pathways for AF prevention. The development of risk prediction models in racial and ethnic minorities has been challenged by relatively fewer minority cohorts compared to whites. Risk score models have had good generalizability to blacks and an AF risk prediction score that adjusted for race has shown good applicability to blacks.[38•,39] Development of minority cohorts will enhance AF risk prediction in racial minorities.

AF Biomarkers

Biomarkers have the potential to refine AF risk prediction models and further our understanding of the pathogenesis of AF. [40] Biomarkers associated with AF include inflammatory markers, such as Brain Natriuretic Peptide (BNP, including N-terminal proBNP) and C-reactive protein (CRP). N-terminal proBNP has been shown to be an independent predictor of incident AF. [41] BNP also has been associated with a 4-fold increased risk of AF in a longitudinal community-based study. [42] Risk of incident AF is increased with increasing levels of CRP. [43] Blacks are known to have substantially higher levels of CRP. [44] Analyses of ~19,000 individuals in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, showed that 36.0%-61.0% of blacks had higher levels of CRP compared to 27%-40% of whites. [45] The identification of AF biomarkers has been conducted largely in white cohorts. In general, similar investigations have not been undertaken in non-black minorities. Effect modification by race on BNP and CRP, as risk factors for incident AF, has not been reported to our knowledge.

Future directions—Identifying novel risk factors in racial and ethnic minorities may reveal differences that will further refine AF risk prediction in racial and ethnic minorities. Accurate quantification of AF burden in racial minorities will inform preventive measures against such outcomes.

Genetics of Atrial Fibrillation

The hereditary component of AF in cohorts consisting primarily of individuals of European and Asian ancestry has been described elsewhere. [46-49] Genome-wide association studies (GWAS) have facilitated the discovery of multiple genetic loci associated with AF, primarily in individuals of European and Asian ancestry. [50,51•] The loci do not account for the extensive AF heritability that has been identified. The underlying biological mechanisms associated with the identified genetic loci are poorly understood. [2] To the best of our knowledge, AF heritability in individuals of African or Hispanic ancestry/ethnicity has not been defined, primarily because of the unavailability of multigenerational cohorts of minorities. Large GWAS are lacking in blacks, Hispanics, American-Indians and Pacific Islanders and will be essential for our understanding of the genetic associations of AF. GWAS of other races is important because variants observed in multiple races and ethnicities are more likely to represent causal variation. [52]

The emerging field of 'omics' employs varying modalities to uncover the biological system's genomics, epigenomics, RNA, metabolism, and protein expression. Omics are being investigated as a bridge from genetic variants to AF pathogenesis. [2,53] Yet, the discoveries to date are virtually all in European ancestry individuals, with uncertain generalizability to the world's populations.

Genetic variability is an increasingly prominent hypothesis to explain the persistently identified racial differences in AF.[32,54] In U.S. biracial cohorts, a 10% increase in European ancestry was associated with a corresponding 13% rise in incident AF risk (HR 1.13; 95% CI: 1.03-1.23; P=0.007) in both blacks and whites.[54] Identifying unique genetic variants may inform the racial and ethnic variations in AF pathogenesis and facilitate developing race- or ethnic-specific strategies for prevention.

Future directions

Establishing multigenerational cohorts of racial and ethnic minorities will allow for the determination of AF heritability. Including ethnic minorities in GWAS will further understanding of the role of genetics in AF pathogenesis. Inclusion of racial minorities in emerging fields of AF studies such as epigenomics, transcriptomics, proteomics, and metabolomics may uncover distinct racial differences in AF pathogenesis, with implications for prevention and management.

AF Complications

Stroke

Stroke related to AF contributes significantly to morbidity and medical costs. In a prospective study of a population-based registry, 24.6% of patient with acute stroke were found to have AF. [55] The use of 30-day cardiac event monitors detected paroxysmal AF in 20% of patients who had been diagnosed with cryptogenic stroke. [56] Racial and ethnic minorities have been observed to generally have a higher burden of ischemic stroke risk factors than non-Hispanic whites. [57,58] In blacks the US age-adjusted death rate for stroke is 62.1 per 100,000 in men and 53.4 per 100,000 in women; in contrast the rate in whites is 39.0 per 100,000 in men and 38.6 in women. [59] In general, blacks have more severe and disabling strokes compared to whites. [60] Mexican-Americans have a higher risk (HR 2.46; 95% CI: 1.19-5.11) and severity (P=0.02) of recurrent stroke than non-Hispanic whites. [61]

We speculate that undetected AF may contribute to the increased stroke burden seen in minorities. Hypertension, diabetes, and obesity, are established stroke risk factors, have a higher prevalence in racial and ethnic minorities, and are associated with increased stroke risk. It is important to identify subclinical AF in ethnic and racial minorities and determine its contribution towards stroke risk.

Future directions—Further investigations with enhanced sensitivity for AF ascertainment may provide missing insights into the contribution of AF to stroke in ethnic and racial minorities. Costs and logistics of using sensitive ascertainment methods and recruiting participants willing to undergo extended monitoring is a major challenge. Rigorous studies to define the pathways between AF risk factors and outcomes are essential for developing targeted approaches to prevent strokes related to AF in ethnic and racial minorities.

Heart Failure

AF and heart failure commonly complicate each other's course. The baseline prevalence of AF among New York Heart Association (NYHA) class I and II heart failure patients in a prospective study of over 4,000 individuals was 4%. [62] AF prevalence is approximately

50% in the setting of NYHA class IV heart failure. [63] Determining the causal relation between AF and heart failure is challenging primarily because of the commonality of risk factors and the reciprocal associations between AF and heart failure. [64] The higher heart failure burden in racial minorities compared to whites has been described elsewhere. [65] The exact contribution of AF to heart failure burden in racial and ethnic minorities merits further investigation.

Future directions—Significant minority representation in investigations into the causal relations between AF and heart failure will help define the contribution of AF to heart failure in racial and ethnic minorities. Racial variations in the causal relation between AF and heart failure may exist. Knowledge of the interrelations of AF and heart failure in ethnic and racial minorities may inform prevention strategies for both adverse conditions.

Mortality

AF is an independent risk factor for all-cause mortality. In a white, community-based cohort, AF was associated with an increased risk of death in men (OR 1.50; 95% CI: 1.20-1.80) and women (OR 1.90; 95% CI: 1.50-2.20) after adjusting for age, hypertension, smoking, diabetes, left ventricular hypertrophy, myocardial infarction, congestive heart failure, valvular heart disease, and stroke or transient ischemic attack. [4] In a sub-group analysis of participants without clinically evident cardiovascular disease in the same study, AF mortality more than doubled in both men and women. The association of incident AF and sudden cardiac death was significantly higher in black participants (HR 5.77; 95% CI: 2.96-11.24; $P < 0.001$) than in non-black participants (HR 2.49; 95% CI: 1.49-4.17; $P < 0.001$) in a large community-based cohort (race interaction $P = 0.02$). [66•] We are not aware of studies that have looked at the relation of AF and sudden cardiac death in non-black minorities.

Future directions—The associations of AF and all-cause mortality and sudden cardiac death merit further investigation in racial minorities. There is a potential to reduce AF-related mortality in ethnic and racial minorities by understanding how AF contributes towards mortality risk in these populations.

Cognition

A cross-sectional study of 6,584 mostly white individuals, age greater than 55 years showed an age-adjusted odds ratio for dementia in the setting of AF to be 2.3 (95% CI: 1.4-3.7) and 1.7 (95% CI: 1.2-2.5) after adjusting for sex. [67] A post-hoc analysis of over 1,000 individuals with AF at baseline from two clinical trials showed a 1.13-fold increased risk for a composite of the outcomes of dementia, admission to a long-term care facility, and loss of independence. AF had 1.2-fold increased risk for the same composite outcomes in over 2,000 individuals who developed AF during follow-up in the same study. [68] Validating these findings in other races and ethnicities is essential.

Future directions—Individuals with subclinical cognitive impairment may be less likely to adhere to treatment. [69] Studying AF-related cognitive decline among diverse racial and ethnic groups has the potential to identify individuals at elevated risk for adverse outcomes. Developing interventions to prevent cognitive decline in AF has the potential to reduce the burden of adverse AF outcomes across diverse racial and ethnic groups.

Symptoms and quality of life

The cardinal symptoms of AF are dyspnea and palpitations. Individuals with AF report significantly worse quality of life (QoL) than healthy referents. [70] A subgroup analysis of

716 largely white individuals in a major clinical trial showed a comparable QoL in patients treated with rate control or rhythm control.[71] Similar investigations have generally not been done in racial and ethnic minorities.

Future directions—Since symptoms may lead to the diagnosis of AF, and since symptoms are used in AF treatment guidelines, understanding racial variation in AF symptoms will have diagnostic and therapeutic implications. Accurately assessing the effects of AF on QoL metrics may facilitate developing approaches to improve overall QoL and result in better outcomes.

AF therapies in ethnic and racial minorities

The challenge of anticoagulation in minorities

Warfarin use reduces risk of AF-associated thromboembolism by over 60%. [72] The estimated annual stroke risk without anticoagulation in the setting of AF is 4.5%. [73] Racial differences in anticoagulation are evident: compared to whites blacks require higher and Asians require lower warfarin dose. [74] Beyond increased dosage requirements, the time in therapeutic range (TTR), a measure of warfarin efficacy, has been found to be consistently lower in blacks compared to whites after multivariable adjustment. [75] In contrast, observed TTR in Asians and Hispanics was similar to whites. [76] In an AF Medicare cohort, the stroke rate in blacks was 10.6 per 100 patient-years of warfarin therapy compared to a rate of 5.2 in whites. [77] A GWAS conducted in individuals of African ancestry taking warfarin identified a novel SNP that affects warfarin dose independently of previously reported genotypes. [78••] Considering the extensive racial variability of TTR and stroke risk between blacks and whites, it is essential to determine if inclusion of the identified genotype variants will improve warfarin-dosing algorithms in blacks. Generally, data on warfarin efficacy in Pacific Islanders and Native Americans are lacking.

Racial differences in anticoagulation practice exist. Whites generally are more likely to receive anticoagulation than blacks and other racial and ethnic minorities. A retrospective study of a heart failure database showed that blacks were less likely to receive anticoagulation compared to whites after adjustment for multiple variables including age, sex, history of AF, liver disease, and alcohol use. [79] Analysis of in-hospital mortality among approximately 400,000 patients showed that blacks were less likely to be treated with anticoagulants for AF (OR 0.84; 95% CI: 0.75-0.94). [80] In a population-based study, the odds of blacks being treated with warfarin were only one-fourth as great as whites (OR 0.28; 95% CI: 0.13-0.60). [9] Similarly, Hispanics, Native Americans and Asian/Pacific Islanders were less likely to receive warfarin in an analysis of hospital discharge records across five US states. [81] The racial differences in anticoagulation practice are unexplained and a profound demonstration of racial disparities.

The data from alternative oral anticoagulants are challenging: blacks made up less than 2% of the major trials that resulted in the introduction of novel anticoagulants such as dabigatran, rivaroxaban and apixaban. [82-84] Studies of the efficacy and dose response of anticoagulants were done in populations with little ethnic or racial minority representation. The validity of extrapolating the conclusions to ethnic and racial minorities has not been demonstrated. The lack of successful minority recruitment to clinical AF trials constitutes a major challenge in AF stroke prevention.

Future Directions—Increasing participation of racial and ethnic minorities in anticoagulation trials will allow investigators to identify potential differences in efficacy. Further exploration of genotype variants associated with warfarin metabolism will enhance anticoagulation practice in racial and ethnic minorities. It is imperative to study and

understand the racial disparities in anticoagulation prescription in order to develop measures to mitigate disparities.

Rate vs. rhythm control

There are limited data assessing rate versus rhythm control strategies and outcomes in ethnic and racial minorities. An subgroup analysis of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) found no significant difference in 5-year survival among blacks randomized to rate or rhythm control (69.4% vs. 79.0%; $p=0.22$). [85] In contrast, survival in Hispanics was higher with rate-control (83.9% vs. 66.5%; $p=0.01$). Among whites, overall survival was higher in the rate control group (78.9% vs. 76.4, $p=0.04$). AFFIRM was limited by the small sample size of blacks and Hispanics and variations in baseline characteristics of participants.

Future Directions—Further clinical trials are essential to replicate the findings from AFFIRM in larger minority cohorts. It is imperative to validate effective treatment strategies in ethnic and racial minorities.

Lenient versus strict rate control

Strict rate control in AF (heart rates <80 beats per minute) is not superior to more lenient approaches to rate control (heart rate less than 110). [86] We are unaware of any investigations comparing rate control strategies in racial and ethnic minorities.

Future Direction—The non-inferiority of lenient rate control of AF merits validation across all racial and ethnic groups.

Radiofrequency Ablation (RFA)

RFA has been successfully used in the management of AF. [87] To our knowledge, there have not been reports of variation by race in RFA utilization or outcomes.

Future directions—Data are needed to determine rates of utilization and outcomes of RFA among various ethnic and racial groups.

The persistent problem of racial disparities in healthcare

The National Healthcare and Quality Disparities report highlights persistent racial differences in healthcare access, quality, and outcomes. [88] Despite technological advances in management, in the US, the percentage difference in heart disease mortality rates between blacks and whites increased from 18.5% in 1990 to 27.4% in 2005. [89] Racial and ethnic minorities have less access to preventative and recommended care for heart failure, diabetes, and obesity, despite having higher rates of the conditions. [88] Ethnic and racial minorities are projected to collectively be the majority of the US population in the next few decades. [90] This will have major implications for the overall health of the US population if healthcare racial disparities are not addressed.

Demographic factors contribute to racial disparities in healthcare. Socioeconomic and cultural factors may affect perception of illness and symptom reporting and result in under-diagnoses and sub-optimal care in ethnic and racial minorities. Minorities are less likely to be insured and have primary care providers. [61] Poor health outcomes and racial disparities in healthcare persist even after adjusting for socioeconomic factors. [91] It is likely that minorities' poor access to healthcare contributes to their under-recruitment in clinical trials. [92] The effects of such disparities are noteworthy in terms of the impact on racial and ethnic minorities' perceptions of treatment, clinical trials, and research studies. The

Tuskegee Legacy Project Questionnaire provides another example of a heritage of mistrust. Several decades on, blacks remain apprehensive about participating in biomedical research. [93]

Future Directions

Patient education has been shown to improve recognition of symptoms of heart disease. [94] It is therefore likely that educating racial and ethnic minorities on AF will increase the chances of symptom recognition. Recruiting more ethnic minorities in epidemiological studies and clinical trials will deepen our understanding of racial variations in epidemiology, treatment responses, healthcare utilization and outcomes. Public education on the importance of scientific research and how far science has come in protecting research participants may assist in recruiting racial and ethnic minorities. More epidemiological data on racial minorities will define race-specific risk models that in turn will better inform disease prevention strategies. Increased racial minority AF studies will describe racial and ethnic variations in disease presentation and reduce under-diagnoses and misdiagnoses.

Conclusion

Table 1 outlines the significant domains, challenges and potential areas for discovery of AF in racial minorities. Figure 1 illustrates the racial variations and disparities in AF risk factors, detection and AF-related outcomes. A multi-faceted approach is needed to understand racial variation in AF epidemiology and management. Under-recruitment of racial minorities in epidemiology studies and clinical trials has hampered efforts to identify and address racial disparities. Actively enrolling racial and ethnic minorities in such studies will advance the evidence base for AF management. Genetic studies in racial minorities and improved ascertainment in ethnic minorities will help explain racial differences in AF. An improved public health model targeted at ethnic minorities to recognize and act on symptoms of heart disease and stroke will decrease the burden and complications of AF and lessen the burden on the health system. Potential research participants should be educated on the mechanisms in place to protect them. [95] Minorities must be made aware of the efforts being made to address disparities in healthcare access and outcomes.

Acknowledgments

Jared Magnani received research grants from the American Heart Association and NHLBI/NIH.

References

Papers of particular interest, published recently, have been highlighted as:

• Of importance

••Of major importance

1. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA*. 2001; 285:2370–5. [PubMed: 11343485]
2. Magnani JW, Rienstra M, Lin H, et al. Atrial fibrillation: current knowledge and future directions in epidemiology and genomics. *Circulation*. 2011; 124:1982–93. [PubMed: 22042927] [An in-depth review of the epidemiology, genetics and “omics” of atrial fibrillation, with particular emphasis on the contributions of a systems biology approach to AF pathogenesis, risk stratification, and therapies.]
3. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991; 22:983–8. [PubMed: 1866765]

4. Benjamin EJ, Wolf PA, D'Agostino RB, et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation*. 1998; 98:946–52. [PubMed: 9737513]
5. Stewart S, Hart CL, Hole DJ, et al. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. *Am J Med*. 2002; 113:359–64. [PubMed: 12401529]
6. Ball J, Carrington MJ, McMurray JJ, et al. Atrial fibrillation: Profile and burden of an evolving epidemic in the 21st century. *Int J Cardiol*. 2013
7. Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation*. 2004; 110:1042–6. [PubMed: 15313941]
8. Alonso A, Agarwal SK, Soliman EZ, et al. Incidence of atrial fibrillation in whites and African-Americans: the Atherosclerosis Risk in Communities (ARIC) study. *Am Heart J*. 2009; 158:111–7. [PubMed: 19540400]
9. Meschia JF, Merrill P, Soliman EZ, et al. Racial disparities in awareness and treatment of atrial fibrillation: the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. *Stroke*. 2010; 41:581–7. [PubMed: 20190000] [A large-sized, longitudinal study that demonstrated racial disparities in patient awareness of cardiac conditions and warfarin treatment for AF.]
10. Conway DS, Lip GY. Ethnicity in relation to atrial fibrillation and stroke (the West Birmingham Stroke Project). *Am J Cardiol*. 2003; 92:1476–9. [PubMed: 14675592]
11. Gunaratne A, Patel JV, Potluri R, et al. Secular trends in the cardiovascular risk profile and mortality of stroke admissions in an inner city, multiethnic population in the United Kingdom (1997-2005). *J Hum Hypertens*. 2008; 22:18–23. [PubMed: 17673899]
12. Markus HS, Khan U, Birns J, et al. Differences in stroke subtypes between black and white patients with stroke: the South London Ethnicity and Stroke Study. *Circulation*. 2007; 116:2157–64. [PubMed: 17967776]
13. Borzecki AM, Bridgers DK, Liebschutz JM, et al. Racial differences in the prevalence of atrial fibrillation among males. *J Natl Med Assoc*. 2008; 100:237–45. [PubMed: 18300541]
14. Lip GY, Brechin CM, Lane DA. The global burden of atrial fibrillation and stroke: a systematic review of the epidemiology of atrial fibrillation in regions outside North America and Europe. *Chest*. 2012; 142:1489–98. [PubMed: 22459778]
15. Dewhurst MJ, Adams PC, Gray WK, et al. Strikingly low prevalence of atrial fibrillation in elderly Tanzanians. *J Am Geriatr Soc*. 2012; 60:1135–40. [PubMed: 22646732]
16. Sliwa K, Carrington MJ, Klug E, et al. Predisposing factors and incidence of newly diagnosed atrial fibrillation in an urban African community: insights from the Heart of Soweto Study. *Heart*. 2010; 96:1878–82. [PubMed: 21062777]
17. Zenebe G, Alemayehu M, Asmera J. Characteristics and outcomes of stroke at Tikur Anbessa Teaching Hospital, Ethiopia. *Ethiop Med J*. 2005; 43:251–9. [PubMed: 16523645]
18. Nwosu CM, Nwabueze AC, Ikeh VO. Stroke at the prime of life: a study of Nigerian Africans between the ages of 16 and 45 years. *East Afr Med J*. 1992; 69:384–90. [PubMed: 1396194]
19. Mu HY, Qiu P, Lu WH, et al. [Electrocardiogram Minnesota codings from 30 000 adult cases with Kazakh ethnicity in Xinjiang, China]. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2010; 31:451–4. [PubMed: 20513295]
20. Kawabata-Yoshihara LA, Bensenor IM, Kawabata VS, et al. Prevalence of electrocardiographic findings in elderly individuals: the Sao Paulo aging & health study. *Arq Bras Cardiol*. 2009; 93:602–7. 51–6. [PubMed: 20379640]
21. Kim MH, Johnston SS, Chu BC, et al. Estimation of total incremental health care costs in patients with atrial fibrillation in the United States. *Circ Cardiovasc Qual Outcomes*. 2011; 4:313–20. [PubMed: 21540439]
22. Ringborg A, Nieuwlaat R, Lindgren P, et al. Costs of atrial fibrillation in five European countries: results from the Euro Heart Survey on atrial fibrillation. *Europace*. 2008; 10:403–11. [PubMed: 18326853]
23. Psaty BM, Manolio TA, Kuller LH, et al. Incidence of and Risk Factors for Atrial Fibrillation in Older Adults. *Circulation*. 1997; 96:2455–61. [PubMed: 9337224]

24. Schnabel RB, Sullivan LM, Levy D, et al. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. *Lancet*. 2009; 373:739–45. [PubMed: 19249635]
25. Jabre P, Roger VL, Murad MH, et al. Mortality associated with atrial fibrillation in patients with myocardial infarction: a systematic review and meta-analysis. *Circulation*. 2011; 123:1587–93. [PubMed: 21464054]
26. Sundquist J, Winkleby MA, Pudarc S. Cardiovascular Disease Risk Factors Among Older Black, Mexican-American, and White Women and Men: An Analysis of NHANES III, 1988–1994. *Journal of the American Geriatrics Society*. 2001; 49:109–16. [PubMed: 11207863]
27. Harwell TS, Gohdes D, Moore K, et al. Cardiovascular disease and risk factors in Montana American Indians and non-Indians. *Am J Prev Med*. 2001; 20:196–201. [PubMed: 11275446]
28. Fakhouri TH, Ogden CL, Carroll MD, et al. Prevalence of obesity among older adults in the United States, 2007–2010. *NCHS Data Brief*. 2012:1–8.
29. Prevalence of coronary heart disease--United States, 2006–2010. *MMWR Morb Mortal Wkly Rep*. 2011; 60:1377–81. [PubMed: 21993341]
30. Haywood LJ, Ford CE, Crow RS, et al. Atrial Fibrillation at Baseline and During Follow-Up in ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial). *Journal of the American College of Cardiology*. 2009; 54:2023–31. [PubMed: 19926008]
31. Lipworth L, Okafor H, Mumma MT, et al. Race-Specific Impact of Atrial Fibrillation Risk Factors in Blacks and Whites in the Southern Community Cohort Study. *The American journal of cardiology*. 2012; 110:1637–42. [PubMed: 22922000]
32. Lau CP, Gbadebo TD, Connolly SJ, et al. Ethnic Differences in Atrial Fibrillation Identified Using Implanted Cardiac Devices. *J Cardiovasc Electrophysiol*. 2013; 24:381–7. [PubMed: 23356818]
33. Selmer C, Olesen JB, Hansen ML, et al. The spectrum of thyroid disease and risk of new onset atrial fibrillation: a large population cohort study. *BMJ*. 2012:345.
34. Kodama S, Saito K, Tanaka S, et al. Alcohol Consumption and Risk of Atrial Fibrillation A Meta-Analysis. *Journal of the American College of Cardiology*. 2011; 57:427–36. [PubMed: 21251583]
35. Gami AS, Hodge DO, Herges RM, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. *J Am Coll Cardiol*. 2007; 49:565–71. [PubMed: 17276180]
36. Magnani JW, Johnson VM, Sullivan LM, et al. P wave duration and risk of longitudinal atrial fibrillation in persons ≥ 60 years old (from the Framingham Heart Study). *Am J Cardiol*. 2011; 107:917–21. e1. [PubMed: 21255761]
37. Soliman EZ, Prineas RJ, Case LD, et al. Ethnic distribution of ECG predictors of atrial fibrillation and its impact on understanding the ethnic distribution of ischemic stroke in the Atherosclerosis Risk in Communities (ARIC) study. *Stroke*. 2009; 40:1204–11. [PubMed: 19213946]
38. Alonso A, Krijthe BP, Aspelund T, et al. Simple risk model predicts incidence of atrial fibrillation in a racially and geographically diverse population: the CHARGE-AF consortium. *J Am Heart Assoc*. 2013; 2:e000102. [PubMed: 23537808] [An AF risk prediction model validated across varied racial groups.]
39. Chamberlain AM, Agarwal SK, Folsom AR, et al. A clinical risk score for atrial fibrillation in a biracial prospective cohort (from the Atherosclerosis Risk in Communities [ARIC] study). *Am J Cardiol*. 2011; 107:85–91. [PubMed: 21146692]
40. Hijazi Z, Oldgren J, Siegbahn A, et al. Biomarkers in atrial fibrillation: a clinical review. *European Heart Journal*. 2013
41. Patton KK, Ellinor PT, Heckbert SR, et al. N-terminal pro-B-type natriuretic peptide is a major predictor of the development of atrial fibrillation: the Cardiovascular Health Study. *Circulation*. 2009; 120:1768–74. [PubMed: 19841297]
42. Schnabel RB, Larson MG, Yamamoto JF, et al. Relations of Biomarkers of Distinct Pathophysiological Pathways and Atrial Fibrillation Incidence in the Community. *Circulation*. 2010; 121:200–7. [PubMed: 20048208]
43. Pena JM, MacFadyen J, Glynn RJ, et al. High-sensitivity C-reactive protein, statin therapy, and risks of atrial fibrillation: an exploratory analysis of the JUPITER trial. *Eur Heart J*. 2012; 33:531–7. [PubMed: 22187510]

44. Fearheller DL, Park JY, Sturgeon KM, et al. Racial differences in oxidative stress and inflammation: in vitro and in vivo. *Clin Transl Sci*. 2011; 4:32–7. [PubMed: 21348953]
45. Cushman M, McClure LA, Howard VJ, et al. Implications of increased C-reactive protein for cardiovascular risk stratification in black and white men and women in the US. *Clin Chem*. 2009; 55:1627–36. [PubMed: 19643839]
46. Oyen N, Ranthe MF, Carstensen L, et al. Familial aggregation of lone atrial fibrillation in young persons. *J Am Coll Cardiol*. 2012; 60:917–21. [PubMed: 22726627]
47. Lubitz SA, Yin X, Fontes JD, et al. Association between familial atrial fibrillation and risk of new-onset atrial fibrillation. *JAMA*. 2010; 304:2263–9. [PubMed: 21076174]
48. Christophersen IE, Budtz-Jorgensen E, Olesen MS, et al. Familial atrial fibrillation predicts increased risk of mortality: a study in Danish twins. *Circ Arrhythm Electrophysiol*. 2013; 6:10–5. [PubMed: 23255276]
49. Yang YQ, Zhang XL, Wang XH, et al. Familial aggregation of lone atrial fibrillation in the Chinese population. *Intern Med*. 2010; 49:2385–91. [PubMed: 21088338]
50. Arnar DO, Thorvaldsson S, Manolio TA, et al. Familial aggregation of atrial fibrillation in Iceland. *Eur Heart J*. 2006; 27:708–12. [PubMed: 16428254]
51. Ellinor PT, Lunetta KL, Albert CM, et al. Meta-analysis identifies six new susceptibility loci for atrial fibrillation. *Nat Genet*. 2012; 44:670–5. [PubMed: 22544366] [A genome-wide association study conducted in cohorts of European ancestry that identified six novel genetic loci for AF, four of which were replicated in Japanese cohorts.]
52. Zaitlen N, Pasaniuc B, Gur T, et al. Leveraging genetic variability across populations for the identification of causal variants. *Am J Hum Genet*. 2010; 86:23–33. [PubMed: 20085711]
53. Caglayan AO. Different aspects of atrial fibrillation genetics. *Interact Cardiovasc Thorac Surg*. 2010; 11:779–83. [PubMed: 20696751]
54. Marcus GM, Alonso A, Peralta CA, et al. European ancestry as a risk factor for atrial fibrillation in African Americans. *Circulation*. 2010; 122:2009–15. [PubMed: 21098467]
55. Marini C, De Santis F, Sacco S, et al. Contribution of atrial fibrillation to incidence and outcome of ischemic stroke: results from a population-based study. *Stroke*. 2005; 36:1115–9. [PubMed: 15879330]
56. Eljovich L, Josephson SA, Fung GL, et al. Intermittent atrial fibrillation may account for a large proportion of otherwise cryptogenic stroke: a study of 30-day cardiac event monitors. *J Stroke Cerebrovasc Dis*. 2009; 18:185–9. [PubMed: 19426887]
57. Kurian AK, Cardarelli KM. Racial and ethnic differences in cardiovascular disease risk factors: a systematic review. *Ethn Dis*. 2007; 17:143–52. [PubMed: 17274224]
58. Mathur R, Pollara E, Hull S, et al. Ethnicity and stroke risk in patients with atrial fibrillation. *Heart*. 2013; 99:1087–92. [PubMed: 23720487]
59. Members WG, Roger VL, Go AS, et al. Heart Disease and Stroke Statistics—2012 Update: A Report From the American Heart Association. *Circulation*. 2012; 125:e2–e220. [PubMed: 22179539]
60. Jones MR, Horner RD, Edwards LJ, et al. Racial variation in initial stroke severity. *Stroke*. 2000; 31:563–7. [PubMed: 10700486]
61. Simpson JR, Zahuranec DB, Lisabeth LD, et al. Mexican Americans with atrial fibrillation have more recurrent strokes than do non-Hispanic whites. *Stroke*. 2010; 41:2132–6. [PubMed: 20829515]
62. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. The SOLVD Investigators. *N Engl J Med*. 1991; 325:293–302. [PubMed: 2057034]
63. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). The CONSENSUS Trial Study Group. *N Engl J Med*. 1987; 316:1429–35. [PubMed: 2883575]
64. Shinbane JS, Wood MA, Jensen DN, et al. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies. *J Am Coll Cardiol*. 1997; 29:709–15. [PubMed: 9091514]

65. Gupta DK, Shah AM, Castagno D, et al. Heart Failure with Preserved Ejection Fraction in African-Americans - The Atherosclerosis Risk in Communities (ARIC) Study. *JACC Heart Fail.* 2013; 1:156–63. [PubMed: 23671819]
- 66 ••. Chen LY, Sotoodehnia N, B žková P, et al. Atrial fibrillation and the risk of sudden cardiac death: The atherosclerosis risk in communities study and cardiovascular health study. *JAMA Internal Medicine.* 2013; 173:29–35. [PubMed: 23404043] [This study demonstrated the association between AF and sudden cardiac death.]
67. Ott A, Breteler MMB, de Bruyne MC, et al. Atrial Fibrillation and Dementia in a Population-Based Study: The Rotterdam Study. *Stroke.* 1997; 28:316–21. [PubMed: 9040682]
68. Marzona I, O'Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *CMAJ.* 2012; 184:E329–36. [PubMed: 22371515]
69. Hawkins LA, Kilian S, Firek A, et al. Cognitive impairment and medication adherence in outpatients with heart failure. *Heart Lung.* 2012; 41:572–82. [PubMed: 22784869]
70. Dorian P, Jung W, Newman D, et al. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: implications for the assessment of investigational therapy. *J Am Coll Cardiol.* 2000; 36:1303–9. [PubMed: 11028487]
71. Jenkins LS, Brodsky M, Schron E, et al. Quality of life in atrial fibrillation: the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J.* 2005; 149:112–20. [PubMed: 15660042]
72. Hart RG, Benavente O, McBride R, et al. Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. *Ann Intern Med.* 1999; 131:492–501. [PubMed: 10507957]
73. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Arch Intern Med.* 1994; 154:1449–57. [PubMed: 8018000]
74. Dang MT, Hambleton J, Kayser SR. The influence of ethnicity on warfarin dosage requirement. *Ann Pharmacother.* 2005; 39:1008–12. [PubMed: 15855242]
75. Shen AY-J, Chen W, Yao JF, et al. Effect of Race/Ethnicity on the Efficacy of Warfarin: Potential Implications for Prevention of Stroke in Patients with Atrial Fibrillation. *CNS Drugs.* 2008; 22:815–26. [PubMed: 18788834]
76. Shen AY-J, Yao JF, Brar SS, et al. Racial/Ethnic Differences in Ischemic Stroke Rates and the Efficacy of Warfarin Among Patients With Atrial Fibrillation. *Stroke.* 2008; 39:2736–43. [PubMed: 18635860]
77. Birman-Deych E, Radford MJ, Nilasena DS, et al. Use and effectiveness of warfarin in Medicare beneficiaries with atrial fibrillation. *Stroke.* 2006; 37:1070–4. [PubMed: 16528001]
- 78 ••. Perera MA, Cavallari LH, Limdi NA, et al. Genetic variants associated with warfarin dose in African-American individuals: a genome-wide association study. *The Lancet.* 2013 [A GWAS of African-Americans that discovered a novel single nucleotide polymorphism affecting warfarin metabolism.]
79. Ibrahim SA, Kwok CK, Harper DL, et al. Racial differences in the utilization of oral anticoagulant therapy in heart failure: a study of elderly hospitalized patients. *J Gen Intern Med.* 2000; 15:134–7. [PubMed: 10672118]
80. Schwamm LH, Reeves MJ, Pan W, et al. Race/ethnicity, quality of care, and outcomes in ischemic stroke. *Circulation.* 2010; 121:1492–501. [PubMed: 20308617]
81. Christian JB, Lapane KL, Toppa RS. Racial disparities in receipt of secondary stroke prevention agents among US nursing home residents. *Stroke.* 2003; 34:2693–7. [PubMed: 14551402]
82. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. *New England Journal of Medicine.* 2009; 361:1139–51. [PubMed: 19717844]
83. Granger CB, Alexander JH, McMurray JJV, et al. Apixaban versus Warfarin in Patients with Atrial Fibrillation. *New England Journal of Medicine.* 2011; 365:981–92. [PubMed: 21870978]
84. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. *New England Journal of Medicine.* 2011; 365:883–91. [PubMed: 21830957]

85. Bush D, Martin LW, Leman R, et al. Atrial fibrillation among African Americans, Hispanics and Caucasians: clinical features and outcomes from the AFFIRM trial. *J Natl Med Assoc.* 2006; 98:330–9. [PubMed: 16573295]
86. Van Gelder IC, Groenveld HF, Crijns HJ, et al. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med.* 2010; 362:1363–73. [PubMed: 20231232]
87. Wazni OM, Marrouche NF, Martin DO, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA.* 2005; 293:2634–40. [PubMed: 15928285]
88. United States. Agency for Healthcare R, Quality. [July 1, 2013] National healthcare disparities report 2010. 2011. Available at <http://www.ahrq.gov/research/findings/nhqrdr/nhqrdr10/qdr10.html>.
89. Orsi JM, Margellos-Anast H, Whitman S. Black-White health disparities in the United States and Chicago: a 15-year progress analysis. *Am J Public Health.* 2010; 100:349–56. [PubMed: 20019299]
90. Frey, WH. [July 1, 2013] America Reaches Its Demographic Tipping Point . Available at <http://www.brookings.edu/blogs/up-front/posts/2011/08/26-census-race-frey>.
91. Thomas J, Thomas DJ, Pearson T, et al. Cardiovascular disease in African American and white physicians: the Meharry Cohort and Meharry-Hopkins Cohort Studies. *J Health Care Poor Underserved.* 1997; 8:270–83. discussion 84. [PubMed: 9253218]
92. Zhang T, Tsang W, Wijeyesundera HC, et al. Reporting and representation of ethnic minorities in cardiovascular trials: A systematic review. *Am Heart J.* 2013; 166:52–7. [PubMed: 23816021]
93. Katz RV, Green BL, Kressin NR, et al. Willingness of minorities to participate in biomedical studies: confirmatory findings from a follow-up study using the Tuskegee Legacy Project Questionnaire. *J Natl Med Assoc.* 2007; 99:1052–60. [PubMed: 17913117]
94. Bell M, Lommel T, Fischer JG, et al. Improved recognition of heart attack and stroke symptoms after a community-based intervention for older adults, Georgia, 2006-2007. *Prev Chronic Dis.* 2009; 6:A41. [PubMed: 19288984]
95. Quinn SC. Ethics in public health research: protecting human subjects: the role of community advisory boards. *Am J Public Health.* 2004; 94:918–22. [PubMed: 15249289]
96. Mbewu, A.; Mbanya, JC. Cardiovascular Disease.. In: Jamison, DT.; Feachem, RG.; Makgoba, MW., et al., editors. *Disease and Mortality in Sub-Saharan Africa*. The International Bank for Reconstruction and Development/The World Bank; Washington DC: 2006.
97. Deswal A, Petersen NJ, Urbauer DL, et al. Racial variations in quality of care and outcomes in an ambulatory heart failure cohort. *Am Heart J.* 2006; 152:348–54. [PubMed: 16875921]

Figure 1.

Figure 1 summarizes racial differences and disparities in traditional and novel risk factors; genetic studies, AF detection and symptom recognition; and AF-related outcomes. The role of novel risk factors in AF pathogenesis in minorities has had limited investigation. The contributions of traditional risk factors to AF pathogenesis merits further study. Racial differences in the pattern of AF occurrence may exist but have not been well characterized. Intermittent or paroxysmal AF may be more common in minorities and potentially under diagnosed. Racial and ethnic minorities are less likely to recognize symptoms of AF. Racial variations in warfarin use and efficacy have had limited study. The effectiveness of novel anticoagulants has not been validated in clinical trials enrolling substantive numbers of racial and ethnic minorities. Limited access to care, barriers to trial recruitment, and long-standing racial disparities may be contributing to higher rates of heart failure, ischemic stroke and overall cardiovascular mortality in minorities. Quality of life and mortality related to AF have had markedly limited investigations in ethnic and racial minorities.

Table 1
The significant domains, challenges and potential areas for discovery of AF in racial minorities

Domain	Challenge	Example of Challenge	Areas for potential discovery, scientific advancement or improvement
Epidemiology	AF global burden	Absent cardiovascular surveillance systems and limited studies from resource-poor settings. [96]	Low cost cardiovascular surveillance systems in resource-poor settings for targeted AF research.
	'Racial Paradox'	Lower age- and sex-adjusted risk of AF in blacks compared to whites despite higher risk factor burden.[8]	Cost-effective sensitive methods of AF ascertainment and quantification of unrecognized AF burden.
	Limited studies of novel risk factors and AF biomarkers in racial and ethnic minorities	Novel risk factors: TSH, obstructive sleep apnea, PWI, Alcohol, obesity AF biomarkers: BNP, CRP.	Investigations in racial and ethnic minorities to validate novel risk factors and AF biomarkers.
Genetics	Heritability of AF and GWAS	No reported studies of AF heritability in individuals of non-European and non-Asian ancestry. Current GWAS limited to largely white cohorts.	GWAS in non-European ancestry cohorts to understand racial variations in AF and AF heritability.
AF outcomes	Adverse outcomes	Higher ischemic stroke death rate and heart failure hospitalization rates in racial minorities. [59], [97]	Risk factor quantification, AF ascertainment and consistent adherence to scientific guidelines in stroke and heart failure treatment in minorities.
	AF QoL and cognitive decline	Current studies of AF QoL and AF-related cognitive decline consist primarily of white participants. [71]	AF QoL and AF-related cognitive decline analyses in racial and ethnic minorities
Anticoagulation	Anticoagulation practice	Racial minorities less likely to receive anticoagulation after multivariable adjustment. [9,79,81]	Research barriers to adherence to anticoagulation. Improve implementation of scientific guidelines for AF management in ethnic and racial minorities.
	Efficacy of Warfarin	Decreased warfarin TTR in blacks. [75]	Incorporating recently identified genetic variants in African-Americans associated with warfarin dosage in pharmacogenetic dosing algorithms.[78]
	Efficacy of oral alternatives to warfarin	Efficacy of oral alternatives to warfarin not validated in racial and ethnic minorities. [82-84]	Validate efficacy of novel anticoagulants in racial and ethnic minorities

AF indicates atrial fibrillation; GWAS, genome-wide association study; TTR, time in therapeutic range; QoL, quality of life.