Trends of Comorbidities in Clinical Trials of Atrial Fibrillation

Atrial Fibrillation (AF) is the most common arrhythmia affecting 2.7 to 6.1 million people in the United States.[1] More than half of patients with AF have comorbidities which can influence the management strategies in AF.[2] Therefore, it is imperative that clinical trials should reflect the clinical complexity seen in routine clinical practice.

Consequently, we reviewed 134 randomized controlled trials ($n = 149,162$) with follow-up of ≥ 3 months using databases of MEDLINE and ClinicalTrials.gov (January 1989 to April 2019) to examine trends of comorbidities in AF trials. Continuous variables were described as mean, standard deviations (SD), median and interquartile range (IQR). Categorical variables were reported as No. (%) and were compared using Chi-square testing. Prevalence of comorbidities across study period were tested using simple linear regression. Statistical significance was set at 5%. SPSS V 24 (IBM Corporation) was used for all analyses.

The median number of participants per trial was 205 (IQR, 729 to 203). Mean age was 64.4 ± 8.4 years, 35.2% were females and mean body mass index (BMI) was 27.6 ± 2.0. The prevalence of comorbidities varied significantly with 13.4% trials reporting smoking, 17.9% BMI, 4.5% obstructive sleep apnea, 35.8% coronary artery disease (CAD), 66.4% diabetes mellitus, 75.4% hypertension, 12.7% dyslipidemia, 9.7% chronic kidney disease (CKD), 44% heart failure (HF), 45.5% cerebrovascular accidents, 9% chronic obstructive pulmonary disease (COPD), and 1.5% venous thromboembolism.

The proportion of smokers (from 11.8% in 1989-1995 to 5.6% in 2014-2019) significantly decreased, while cerebrovascular accident (from 21.0% in 1989-1995 to 53.2% in 2014-2019) significantly increased (Figure 1). The prevalence of diabetes (from 7.3% in 1989-1995 to 25.8% in 2014-2019) and hypertension (from 37.3% in 1989-1995 to 64.7% in 2014-2019) also significantly increased. The representation of patients with CAD, hyperlipidemia, CKD and HF remained consistently low. These trends were similar regardless of the regions of the world. While the recruitment of patients with diabetes, CAD, and COPD was almost similar across government, industry, or academic sponsored trials, the enrollment of patients with CKD (35.5%), hyperlipidemia (41.8%), hypertension (65.3%) and obstructive sleep apnea (28.8%) was higher in industry funded trials, smokers (52.6%) in government funded trials and HF (41.1%) in academic funded trials.

Between 1989 and 2019, the overall reporting on comorbidity varied and was consistently low in AF trials. These trends may reflect the protocols that could limit participation of certain high risk patients to mitigate competing causes of mortality or improve the tolerability of active treatment,[3] or lack of enthusiasm among multimorbid patients.[4,5] These figures call for a more intense and systematic approach to enhance enrollment of multimorbidity patients that can mirror real world population and ensure the generalizability of treatments. In a multilayer framework, involvement of primary care providers, investigators, sponsors, and community members can engage the diverse population; and incentives, such as transportation, access to medical care or childcare can be fruitful. The limitations of this study include lack of access to patient level data, scarce reporting on specific comorbidities across trials subjecting to reporting bias, and heterogeneity in baseline criteria used to define different comorbidities.

In *conclusion*, reporting of comorbid conditions in AF trials remained consistently low over 3 decades. These findings demand innovative strategies to accommodate the multicomplexity of AF population to clinical trials to help inform routine clinical practice.

Conflict of Interest

The authors declare that they have no known competing financial interests
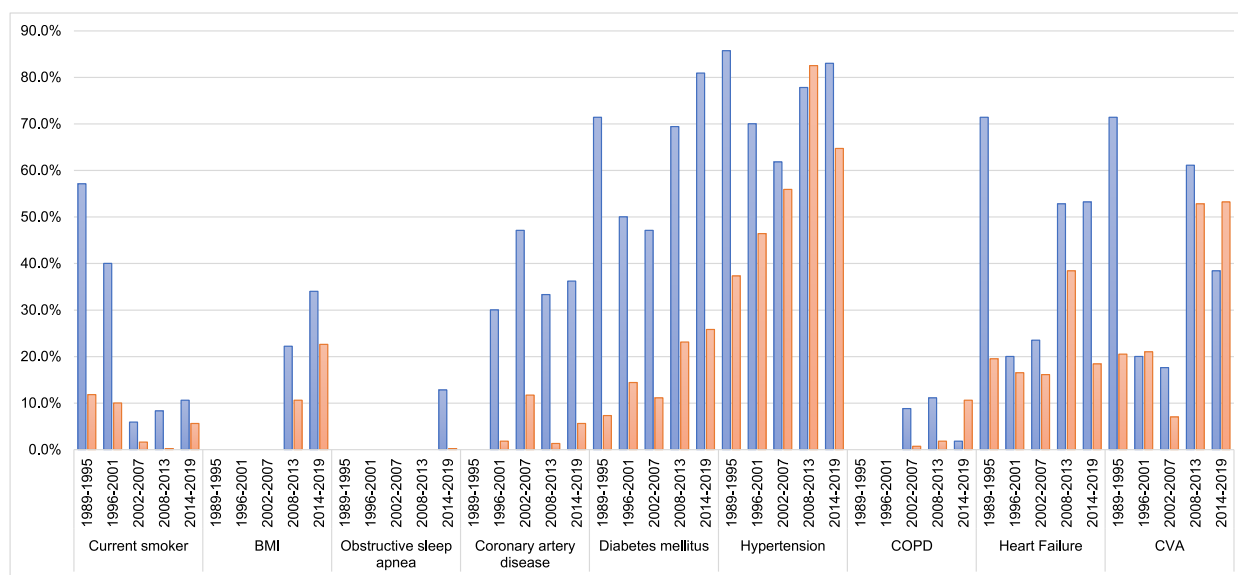

Figure 1. Trends of comorbidities in clinical trials of atrial fibrillation.
BMI = Body Mass Index; COPD = Chronic Obstructive Pulmonary Disease; CVA = Cerebrovascular Accident. Blue bar represents proportion of trials reporting comorbidities. Red bar represents proportion of participants with comorbidities. (Color version available online.)

or personal relationships that could have appeared to influence the work reported in this paper.

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Is Increased Sleep Responsible for Reductions in Myocardial Infarction During the COVID-19 Pandemic?

The COVID-19 pandemic caused by the highly contagious SARS-CoV-2 virus has had devastating consequences across the globe. However, multiple clinics and hospitals have experienced a decrease in rates of acute myocardial infarction and corresponding cardiac catheterization lab activations, raising the question: Has the risk of myocardial infarction decreased during COVID? Sleep deprivation is known to be an independent risk factor for myocardial infarction, and sleep has been importantly impacted during the pandemic, possibly due to the changes in work-home life leading to a lack of structure. We conducted a social media-based survey to assess potential mechanisms underlying the observed improvement in risk of myocardial infarction. We used validated questionnaires to assess sleep patterns, tobacco consumption and other important health outcomes to test the hypothesis that increases in sleep duration may be occurring which have a beneficial impact on health. We found that the COVID-19 pandemic led to shifts in day/night rhythm, with subjects waking up 105 minutes later during the pandemic (p <0.0001). Subjects also reported going to sleep 41 minutes later during the pandemic (p <0.0001). These shifts led to longer duration of sleep during the COVID-19 pandemic. Before the pandemic, subjects reported sleeping 6.8 hours per night, which rose to 7.5 hours during the pandemic, a 44 minute or 11% increase (p <0.0001). We acknowledge the major negative health impact of the global pandemic but would advocate for using this crisis to improve the work and sleep habits of the general population, which may lead to overall health benefits for our society. © 2020 Elsevier Inc. All rights reserved. (Am J Cardiol 2020;131:127−140)

The COVID pandemic has had devastating consequences globally including impact on health and economics. However, some hospitals have seen a 38-49% decrease in presentations of acute myocardial infarction (MI).[1−3] Whether this finding represents patients' avoiding medical care due to COVID, which would lead to greater numbers of cardiovascular deaths and higher rates of post-MI complications, versus a true reduction in incidence of MI via unknown mechanisms is unclear.[1−4] Sleep deprivation is common in today's 24/7 society and has been independently associated with risk of incident MI. Furthermore, sleep has been importantly impacted during the pandemic, perhaps due to a lack of regular daily structure, and sleep deprivation is an independent risk factor for MI.[5] We conducted a social media survey to assess potential mechanisms underlying observed reductions in MI. We used validated questionnaires to assess sleep patterns, inhalant use, anxiety and depression. We sought to test the hypothesis that sleep duration has increased in the time of COVID and may beneficially impact overall health.

Methods

Participants were recruited to participate in online surveys through widespread Twitter, Facebook, Craigslist and Reddit advertisements. Participants were incentivized to complete both pre- and during-pandemic online surveys based on random lottery. We received