

Relation of Obesity to New-Onset Atrial Fibrillation and Atrial Flutter in Adults

Andrew J. Foy, MD^{a,b,*}, John Mandrola, MD^c, Guodong Liu, PhD^b, and Gerald V. Naccarelli, MD^a

Prospective cohort studies involving older adults report an association of obesity and new-onset atrial fibrillation and atrial flutter. To assess this relation, we performed a longitudinal cohort study from January 1, 2006 to December 31, 2013, using a national claims database that tracks all inpatient, outpatient, and pharmacy claims data. The primary end point of new-onset atrial fibrillation was compared between obese and nonobese cohorts. We used logistic regression to determine the strength of association between obesity and new-onset atrial fibrillation controlling for age, gender, hypertension, and diabetes. Overall, 67,278 subjects were included in the cohort, divided evenly between those with and without a diagnosis of obesity. Obese subjects were significantly more likely to have hypertension (29.5% vs 14.6%) and diabetes (12.7% vs 5.2%) at study onset. Over 8 years of follow-up, we recorded a new diagnosis of atrial fibrillation in 1,511 (2.2%) subjects. Obesity was strongly associated with a new diagnosis of atrial fibrillation after controlling for age, gender, hypertension, and diabetes (odds ratio 1.4, 95% confidence interval 1.3 to 1.6). In conclusion, this information contributes to the growing evidence supporting the causal relation between obesity and atrial fibrillation, and emphasizes the need of addressing obesity as part of our therapeutic strategy to prevent atrial fibrillation. © 2018 Elsevier Inc. All rights reserved. (Am J Cardiol 2018;■■:■■-■■)

Atrial fibrillation confers significant risk of morbidity and mortality. The global burden of atrial fibrillation is increasing¹ as is the cost of caring for patients with atrial fibrillation.² Obesity represents an increasing global health problem.³ Numerous prospective cohort studies from the United States and Europe have reported an association between new-onset atrial fibrillation and obesity.⁴⁻⁸ These studies primarily included older subjects, and age is a confounding risk factor for atrial fibrillation. Additionally, most of these studies began following up subjects more than 2 decades ago. Although epidemiologic, clinical, and mechanistic evidence support a causative link between obesity and atrial fibrillation,^{9,10} the relation has not been established in a contemporary cohort of young- to middle-aged adults. We, therefore, sought to compare the incidence of new-onset atrial fibrillation in obese and nonobese subjects in a private insurance database called MarketScan using a longitudinal cohort design. Our hypothesis was that new-onset atrial fibrillation would be higher in middle-aged obese subjects. If true, the findings would (1) strengthen the evidence that obesity causes atrial fibrillation, and (2) have important public health implications.

Methods

The study was approved by the institutional review board at Penn State Milton S. Hershey Medical Center. The study

^aDivision of Cardiology, Penn State Heart and Vascular Institute, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania; ^bDepartment of Public Health Sciences, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania; and ^cCardiology Group, Baptist Health Louisville, Louisville, Kentucky. Manuscript received October 19, 2017; revised manuscript received and accepted January 17, 2018.

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*Corresponding author: Tel: (717) 531-5888; fax: (717) 531-4077.

E-mail address: afoy@hmc.psu.edu (A.J. Foy).

used MarketScan Commercial Claims and Encounters data from January 1, 2005 to December 31, 2013. MarketScan is constructed and maintained by Truven Health Analytics and consists of reimbursed health-care claims for employees, retirees, and their dependents of more than 250 medium- and large-sized employers and health plans from across all 50 states and the District of Columbia. The database includes a population of approximately 58 million and captures administrative claims with patient-level de-identified data from inpatient and outpatient visits and filled prescriptions. Diagnosis codes use the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*.

Several filters were applied sequentially to extract our primary cohort for this analysis. First, all subjects who did not maintain continuous enrollment in their insurance plan over the duration of the assessment (January 1, 2005 to December 31, 2005) and follow-up periods (January 1, 2006 to December 31, 2013) were excluded. This was done to ensure complete capture of follow-up data for all subjects. Second, all subjects with a diagnosis of atrial fibrillation and atrial flutter (*ICD-9-CM* code 427.3) during the assessment period were excluded. This was done to maximize the possibility that diagnoses of atrial fibrillation and atrial flutter during the follow-up period represented new diagnoses. Third, all patients with a diagnosis code of obesity (*ICD-9-CM* code 278) during either the assessment or follow-up periods were matched 1:1 on the basis of age and gender with a subject who did not carry the diagnosis code for obesity at any point in the study. This was done to maximize capture of obese subjects as obesity is undercoded in medical encounters.¹ Obesity is a stable trait and therefore, our analysis assumes that all subjects with the diagnosis of obesity, at any point in the study, had obesity at the beginning of the follow-up period.^{2,3} The co-morbid conditions of hypertension (*ICD-9-CM* codes 401.xx, 402, 403.x, 404) and diabetes (*ICD-9-CM* codes

250.xx, 357.xx, 362.0-362.0x, 366.41) were queried for all subjects over the follow-up period.

We determined the unadjusted rates of new-onset atrial fibrillation and atrial flutter (*ICD-9-CM* code 278) for the obese and nonobese cohorts. Multivariate logistic regression analysis was performed to examine the relation between obesity and new-onset atrial fibrillation and atrial flutter adjusting for age, gender, diabetes, and hypertension.

Results

A total of 67,278 subjects were included in the cohort; 33,639 with obesity and 33,639 without. The average age of both cohorts was 43.8 years and 76.9% were women. Subjects in the obese cohort were significantly more likely to have hypertension (29.5% vs 14.6%; $p < 0.0001$) and diabetes (12.7% vs 5.2%; $p < 0.0001$) compared with controls.

Over 8 years of follow-up, a new diagnosis of atrial fibrillation was recorded in 1,511 (2.2%) subjects; 915 (2.7%) in the obese cohort and 596 (1.8%) in the nonobese cohort. In both groups, yearly cases of new-onset atrial fibrillation increased steadily over time (Table 1). The cumulative incidence of atrial fibrillation also increased steadily in both groups (Figure 1). The absolute difference in the incidence of atrial fibrillation for the obese compared with the control cohort was 0.1% after 1 year of follow-up and diverged steadily, reaching 0.9% by the end of the follow-up period.

Obesity was strongly associated with new-onset atrial fibrillation after controlling for age, gender, hypertension, and diabetes (odds ratio [OR] 1.40, 95% confidence interval [CI]

1.26 to 1.56). Other variables independently associated with new-onset atrial fibrillation included age (OR 1.08, 95% CI 1.07 to 1.09), male gender (OR 1.96, 95% CI 1.76 to 2.18), baseline hypertension (OR 1.45, 95% CI 1.29 to 1.62), and diabetes (OR 1.51, 95% CI 1.31 to 1.73).

Discussion

The main finding was that obesity is strongly associated with new-onset atrial fibrillation in a nationally representative, privately insured cohort of middle-aged adults in the United States. After adjusting for known atrial fibrillation risk factors, such as age, gender, hypertension, and diabetes, obese subjects were 40% more likely to develop new-onset atrial fibrillation. We observed a steady increase in absolute difference in the incidence of atrial fibrillation over time in the obese cohort compared with the controls. Adding confidence to the association is the high specificity of the obesity code in similar studies using administrative claims data.¹¹

The observed increased risk of new-onset atrial fibrillation in obese subjects extends the findings of older US and European cohort studies³⁻⁷, which included older-aged subjects recruited during a different era of medicine (Table 2). The incidence of new-onset atrial fibrillation in our exposed and unexposed cohorts was similar to that found in the Women's Health Study, which followed up patients for 12.9 years.⁶ Surprisingly, participants in our study were, on average, more than 10 years younger at baseline. However, the difference in male participants in our study, compared with the Women's Health Study (23% vs 0%), may explain why the incidence rates in the 2 studies are similar despite the shorter duration of follow-up and younger age of participants in ours.⁶ Male gender is highly associated with new-onset atrial fibrillation. Compared with the other studies in Table 1, our analysis included younger adults from a contemporary sampling of typical US subjects. Also, our cohort included a far greater number of exposed subjects' mitigating concerns related to undersampling. The signal of increased risk of new-onset atrial fibrillation in middle-aged obese subjects lends further support to the causal relation between obesity and atrial fibrillation.

These findings have significant public health implications. Based on our results, in middle-aged adults, obesity confers an independent risk of new-onset atrial fibrillation (40%) that is nearly equal to that of hypertension (45%) and diabetes (51%). Thus, prevention of obesity would reduce the burden of atrial fibrillation, which is increasing in Western countries. And once obesity is established, weight loss has been shown to not only reduce atrial fibrillation symptoms and episodes, but also to improve cardiac risk factors such as blood pressure, glycemic indices, and lipid profiles.^{12,13} A focus on obesity prevention and treatment should be an important focus of public health.

This analysis has limitations. Administrative claims data lack precise information on body mass index (BMI), both at study onset and over time. Two previous reports suggest that undercoding of obesity in our analysis is likely. Stephens¹⁴ reported that of 482,628 patients in a military database with a BMI exceeding 30, only 16% had an associated *ICD-9* code for obesity. In a linkage study, Kuhle et al¹¹ found that using

Table 1
Cases per year of new-onset atrial fibrillation

	2006	2007	2008	2009	2010	2011	2012	2013
Control	69	60	59	63	59	86	95	105
Obesity	107	100	99	176	93	127	151	125

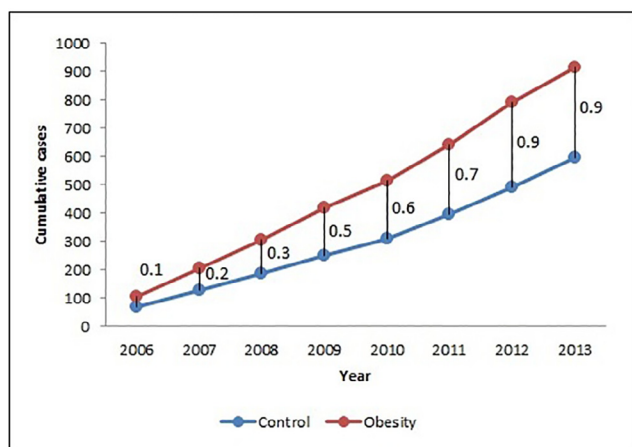


Figure 1. Cumulative cases of new-onset atrial fibrillation over time. The absolute percentage difference in cumulative atrial fibrillation incidence is represented by the vertical lines.

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