

Body Mass Index and Adverse Events in Patients with Incident Atrial Fibrillation

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ABSTRACT

BACKGROUND: Obesity is associated with the development of atrial fibrillation and may impact atrial fibrillation-related outcomes. To date, no anthropometric measure is included in any risk stratification scheme for stroke and death in atrial fibrillation patients.

METHODS: The prospective Danish Diet, Cancer and Health study is a cohort including 57,053 participants (27,178 men and 29,875 women) aged between 50 and 64 years. The study population for this study included the 3135 patients (2025 men and 1110 women) who developed incident atrial fibrillation during follow-up.

RESULTS: Of the subjects with atrial fibrillation, 1414 (45%) had a body mass index (BMI) in the overweight category (BMI 25 to <30 kg/m²) and 767 (24%) were categorized as obese (BMI ≥30 kg/m²). During a median follow-up of 4.9 years, 609 deaths and 216 thromboembolic events (98% ischemic strokes) occurred. Using normal-weight patients as reference, the risk of a composite end point of “ischemic stroke, thromboembolism, or death” was significantly higher in overweight (crude hazard ratio [HR] 1.31; 95% confidence interval [CI], 1.09-1.56) and obese patients (crude HR 1.55; 95% CI 1.27-1.90). After adjustment for CHADS₂ and CHA₂DS₂-VASc scores, the HRs for the composite end point were 1.21 (95% CI 1.02-1.45) and 1.31 (95% CI 1.10-1.56), respectively, for overweight and 1.25 (95% CI 1.03-1.53) and 1.36 (95% CI 1.11-1.65), respectively, for obese. Continuous analyses of BMI stratified by sex identified obese men and normal-weight women as the sex-specific “high-risk” categories.

CONCLUSION: Overweight and obesity are risk factors for “ischemic stroke, thromboembolism or death” in patients with atrial fibrillation, even after adjustment for CHADS₂ and CHA₂DS₂-VASc scores. The association between BMI and outcomes among atrial fibrillation patients may be modified by sex.

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Atrial fibrillation is the most common sustained cardiac rhythm disorder. It affects 1%-1.5% of the population in the developed world,^{1,2} and the prevalence is expected to increase due to an aging population and an increase in the prevalence of established risk factors for incident atrial fibrillation, for example, diabetes mellitus.³ Atrial fibrillation entails a substantial risk of mortality and morbidity from often-fatal stroke and thromboembolism.^{4,5} Furthermore, health care costs related to atrial fibrillation are increasing.⁶

The risk of stroke in atrial fibrillation is not homogeneous. Several well-established risk factors^{7,8} have been used to formulate stroke risk-stratification schema, such as

the Cardiac failure, Hypertension, Age ≥ 75 , Diabetes, Stroke [Doubled] (CHADS₂) score.⁹ A refinement of the CHADS₂ score has since been introduced, the CHA₂DS₂-VASc score, which gives extra weight to age ≥ 75 years [doubled], and includes vascular disease, age 65-74 years, and female sex as risk factors.¹⁰

Thus far, no anthropometric variable has been included in any clinical risk stratification schema for stroke in atrial fibrillation.

Obesity has reached pandemic proportions,¹¹ and body mass index (BMI), a proxy measure of obesity, is associated with higher overall mortality^{12,13} and a higher risk of, especially, ischemic stroke.¹⁴ In recent years, obesity has been established repeatedly as an independent predictor of incident atrial fibrillation,¹⁵⁻¹⁸ including in the present cohort.¹⁹ Despite the overwhelming amount of research linking obesity and the *development* of atrial fibrillation, the *prognostic impact* of obesity on outcomes among atrial fibrillation patients is sparsely investigated, and the studies thus far have revealed inconsistent results.²⁰⁻²³

As obesity often coexists with established risk factors for ischemic stroke among atrial fibrillation patients as well as the general population, we hypothesized that obesity would be associated with the risk of stroke and death among patients with atrial fibrillation. To test this hypothesis, we analyzed data from a large Danish prospective cohort—the Diet, Cancer and Health study—to assess the risk of ischemic stroke, thromboembolism, and death according to BMI among patients with incident atrial fibrillation.

METHODS

The Diet, Cancer and Health study cohort was established between 1993 and 1997. The study design has been reported in detail elsewhere.²⁴ The primary objective of this prospective study was to investigate the etiologic role of diet and lifestyle in the development of cancer, and 57,053 participants were enrolled (27,178 men and 29,875 women). The study participants were aged between 50 and 64 years and without a cancer diagnosis registered in the Danish Cancer Registry²⁵ at entry into the Diet, Cancer and Health cohort. Participants were, for this study, followed from time of first diagnosis of atrial fibrillation (not earlier than January 1995) until December 2009.

The cohort subjects were linked to the National Patient Register²⁵ using a unique, national identification number, which is part of the personal information stored in the Civil Registration System. Exclusion criteria are listed in **Figure 1**. Codes from the International Classification of Dis-

eases (ICD-10) were used to extract hospital discharge admissions for atrial fibrillation. Atrial fibrillation and atrial flutter have one ICD-10 code (I48). Therefore, a small number of atrial flutter cases also would have been included.

Exposure Variable

The exposure variable studied was BMI. Anthropometric data were collected at the time of entry into the Diet, Cancer and Health cohort by trained laboratory technicians. Height

CLINICAL SIGNIFICANCE

- Obesity and atrial fibrillation are common and often coexist, but the prognostic impact of obesity on outcomes among patients with atrial fibrillation is sparsely investigated.
- Several risk stratification schemes useful for predicting stroke and death among atrial fibrillation patients exist, but none include anthropometric measures.
- Overweight and obese represent “high-risk” atrial fibrillation patients, even after adjustments for CHADS₂ and CHA₂DS₂-VASc, but the associations are modified by sex.

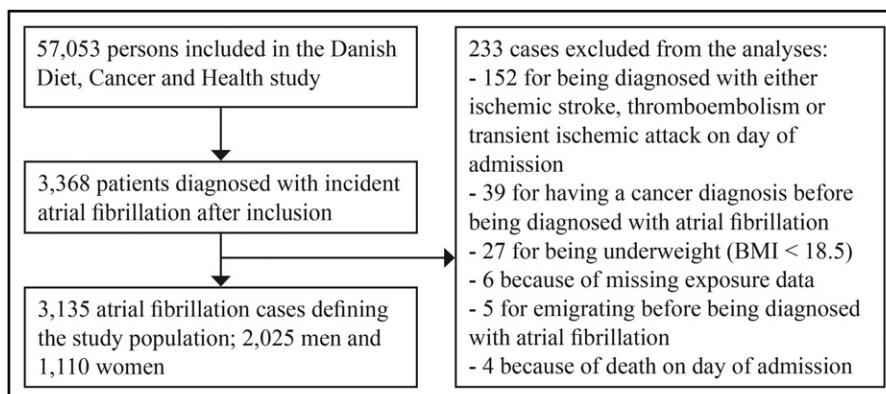


Figure 1 Flow diagram of how the study population was arrived at.

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