JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 69, NO. 20, 2017

ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jacc.2017.03.558

Lean Body Mass Is the Predominant Anthropometric Risk Factor for Atrial Fibrillation

Morten Fenger-Grøn, MSc,[a] Kim Overvad, MD, PhD,[b,c] Anne Tjønneland, MD, PhD, DMSc,[d] Lars Frost, MD, PhD, DMSc[e]

ABSTRACT

BACKGROUND Obesity is repeatedly emphasized as a risk factor for atrial fibrillation or flutter (AF). However, the underlying evidence may be questioned, as the obvious correlations between various anthropometric measures hamper identification of the characteristics that are biologically driving AF risk, and recent studies suggest that fat carries limited or no independent risk of AF.

OBJECTIVES This study sought to assess mutually adjusted associations among AF risk and height, weight, body mass index, hip and waist circumference, waist-to-hip ratio, and bioelectrical impedance-derived measures of fat mass, lean body mass, and fat percentage.

METHODS Anthropometric measures and self-reported life-style information were collected from 1993 to 1997 in a population-based cohort including 55,273 persons age 50 to 64 years who were followed in Danish registers until June 2013.

RESULTS During a median of 17 years of follow-up, 3,868 persons developed AF. Adjusted hazard ratios per population SD difference (HRs) showed highly statistically significant, positive associations for all 9 anthropometric measures (HRs ranging from 1.08 [95% confidence interval (CI): 1.05 to 1.12] for waist-to-hip ratio to 1.37 [95% CI: 1.33 to 1.42] for lean body mass). Pairwise mutual adjustment of the 9 measures left the association for lean body mass virtually unchanged (lowest HR: 1.33 [95% CI: 1.28 to 1.39] when adjusting for height), whereas no other association remained substantial when adjusted for lean body mass (highest HR: 1.05 [95% CI: 1.01 to 1.10] for height).

CONCLUSIONS Lean body mass was the predominant anthropometric risk factor for AF, whereas no association was observed for either of the obesity-related anthropometric measures after adjustment for lean body mass. (J Am Coll Cardiol 2017;69:2488–97) © 2017 by the American College of Cardiology Foundation.

Atrial fibrillation is estimated to affect up to 1 in 4 persons during a lifespan (1,2), and it is associated with a series of adverse effects, such as lowered health-related quality of life (3), dementia (4), heart failure (5), stroke (6), or death (7), and their implied major human and health-economic costs (8,9). Furthermore, atrial fibrillation is one of the few heart diseases with increasing incidence (10). Thus, identification of modifiable risk factors is highly warranted.

Obesity is modifiable and is repeatedly emphasized as a risk factor for atrial fibrillation (11–17). This is

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From the [a]Research Unit for General Practice and Section for General Medical Practice, Department of Public Health, Aarhus University, Aarhus, Denmark; [b]Section for Epidemiology, Department of Public Health, Aarhus University, Aarhus, Denmark; [c]Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark; [d]Danish Cancer Society Research Center, Copenhagen, Denmark; and the [e]Department of Clinical Medicine, Aarhus University, Silkeborg Hospital, Denmark. The study was supported by the Danish Council for Strategic Research (grant 09-066965). The Diet, Cancer and Health cohort study was funded by the Danish Cancer Society. Mr. Fenger-Grøn is supported by a grant from the Faculty of Health, Aarhus University, Denmark, and from the Lundbeck Foundation, Denmark. Funders had no role in the design and conduct of the study; management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received November 9, 2016; revised manuscript received February 27, 2017, accepted March 14, 2017.

supported by documented associations for a series of obesity-related anthropometric measures including weight, body mass index (BMI), waist and hip circumference, waist-to-hip ratio, fat mass, and fat percentage (11–13,15,18,19). However, associations with atrial fibrillation are also documented for height (13,20–22), and lately even for lean body mass in a large cohort with bioelectrical impedance-derived measures (23). This has raised suspicion that the commonly known association between obesity and atrial fibrillation is largely due to the obvious correlations between the various measures. The suspicion was confirmed by a recent study exploiting dual-energy x-ray absorptiometry measures of body fat and lean body mass in post-menopausal women (24) and, to some extent, by an even newer study on a study group of older adults including men (25), who are at markedly higher risk of atrial fibrillation (10).

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In the present study, we used updated data from the Danish Diet, Cancer, and Health cohort (23) to depict the correlations between the 9 anthropometric measures, and to assess their associations with risk of atrial fibrillation or flutter (AF) under mutual adjustment. Particularly focusing on the complementary pair comprising fat mass and lean body mass, we further challenge the dogma of fat as the important independent driver of AF risk.

METHODS

DESIGN. We performed a prospective cohort study in which persons recruited for the Danish Diet, Cancer, and Health study (26) were followed in Danish nationwide registers. Information on death or emigration was collected from the Danish Civil Registration System, which was established in 1968, and holds historical and updated electronic records for all persons in Denmark (27).

Information on hospital diagnoses was obtained from the Danish National Registry of Patients, which was founded in 1976. The registry includes dates of all admissions and discharges at nonpsychiatric hospitals in Denmark, as well as a primary discharge diagnosis and possibly 1 or more secondary diagnoses, as coded by the discharging physician (28). Since January 1, 1995, information from outpatient and emergency room visits has also been included. Until 1993, diagnoses were classified according to the Danish version of the International Classification of Diseases-8th Revision (ICD-8) and thereafter according to the national version of the ICD-10.

STUDY GROUP. The Danish Diet, Cancer, and Health study cohort was established between December 1993 and May 1997 through invitation of 80,996 men and 79,729 women who were 50 to 64 years of age (26,29). Eligible cohort members were born in Denmark, were living in the Copenhagen or Aarhus areas, and had no previous cancer diagnosis according to the Danish Cancer Registry (30). For the present study, we excluded participants with an AF event before the date of their recruitment, according to the definition provided later in the text, as well as persons for whom lifestyle-related questionnaire data were missing or insufficient.

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation or flutter

BMI = body mass index

CI = confidence interval

HR = hazard ratio (per sex-specific standard deviation in the population)

ICD = International Classification of Diseases

PRIMARY EXPOSURES. The primary exposures of interest were the anthropometric measures: height, weight, lean body mass (fat-free mass), and waist and hip circumference; as well as the derived measures: fat mass, fat percentage, BMI, and waist-to-hip ratio. Trained laboratory technicians at 2 study clinics in Aarhus and Copenhagen, Denmark, collected all anthropometric measures at the time of enrollment into the study. Fat and lean body mass were estimated using previously developed and validated sex-specific equations on bioelectrical impedance (31), as measured using a BIA 101-F device (Akern/RJL, Florence, Italy). Sensing electrodes were placed over the wrist and ankle, and current electrodes placed over the metacarpals or metatarsals on nonfasting participants lying relaxed, with legs approximately 45° apart and arms 30° from the torso. Further description of the measurements can be found elsewhere (23).

COVARIATES. Comorbidity was assessed using date of first hospital contact that included a primary or secondary diagnosis for hypertension (ICD-8: 400 to 404, 410.09, 411.09, 412.09, 413.09, 414.09, 435.09, 437.00, 437.01, 437.08, 437.09, and 438.09; ICD-10: I10 to I15), diabetes (ICD-8: 249, 250; ICD-10: E10 to E14), ischemic heart disease (ICD-8: 410 to 414; ICD-10: I20 to I25), congestive heart failure (ICD-8: 425.99, 427.09, 427.10, 427.11, 427.19, 427.99, 428.99; ICD-10: I50), or mitral and/or aortic valve disease (ICD-8: 394 to 396; ICD-10: I05, I06, I08, I34, I35). Additional information on diabetes was drawn from the Danish National Diabetes Register (32). These data were supplemented with participants' self-reports of hypertension, hypercholesterolemia, diabetes, and related medical treatment, as well as of menopausal status and hormone replacement therapy for women.

Likewise, we used participants' questionnaire self-reports at recruitment to obtain data on educational level; physical activity during working hours and during leisure time (33); smoking habits; and intake of