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CLINICAL RESEARCH
Arrhythmia/electrophysiology

Obesity as a risk factor for the progression of paroxysmal to permanent atrial fibrillation: a longitudinal cohort study of 21 years

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Aims Obesity has been shown to be a risk factor for first atrial fibrillation (AF), but whether it is associated with progression from paroxysmal to permanent AF is unknown.

Methods and results In this longitudinal cohort study, Olmsted County, MN residents confirmed to have developed paroxysmal AF during 1980–2000 were identified and followed passively to 2006. The interrelationships of body mass index (BMI), left atrial (LA) size, and progression to permanent AF were analysed. Of a total of 3248 patients (mean age 71 $\pm$ 15 years; 54% men) diagnosed with paroxysmal AF, 557 (17%) progressed to permanent AF (unadjusted incidence, 36/1000 person-years) over a median follow-up period of 5.1 years (interquartile range 1.2–9.4). Adjusting for age and sex, BMI independently predicted the progression to permanent AF (hazard ratio, HR 1.04, CI 1.03–1.06; $P < 0.0001$). Compared with normal BMI (18.5–24.9 kg/m^2), obesity (30–34.9 kg/m^2) and severe obesity ($\geq$35 kg/m^2) were associated with increased risk for progression [HR 1.54 (CI 1.2–2.0; $P = 0.0004$) and 1.87 (CI 1.4–2.5; $P < 0.0001$, respectively)]. BMI remained highly significant even after multiple adjustments. In the subgroup with echocardiographic assessment ($n = 744$), LA volume was incremental to BMI for independent prediction of progression after multiple adjustments, and did not weaken the association between BMI and progression to permanent AF (HR 1.04; CI 1.02–1.05; $P < 0.0001$).

Conclusion There was a graded risk relationship between BMI and progression from paroxysmal to permanent AF. This relationship was not weakened by LA volume, which was independent of and incremental to BMI for the prediction of progression to permanent AF.

Keywords Obesity • Left atrial volume • Atrial fibrillation

Introduction

Obesity and atrial fibrillation (AF) are growing public health problems.[1,2] The prevalence of both has increased over time.[3–8] Prevalence of obesity has increased across all age segments, including the oldest (>70 years)[4,9] who are at greatest risk of AF. Data demonstrating an association between AF and obesity have been discordant. Although a number of studies have demonstrated that greater body mass index (BMI), or obesity, is a risk factor for AF,[10–12] an earlier report from Framingham Heart Study[13] and data from the Cardiovascular Health Study[14] did not support this association. More recently, the Framingham investigators provided convincing data that obesity is indeed associated with excess risk of AF, and that the risk is likely mediated through left atrial (LA) enlargement.[15] As an extension to these studies, we evaluated, as a primary aim, whether obesity is a risk factor for the progression of paroxysmal to permanent AF. We tested the hypothesis that there is a 'dose–response' relationship between BMI and the risk of progression from paroxysmal to permanent AF. Our secondary aim was to evaluate the significance of LA volume, and its interaction with BMI, for the prediction of such progression to permanent AF.

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Methods

Study design and population

This community-based cohort study was approved by the Mayo Foundation Institutional Review Board. Olmsted County, MN, is well suited for the conduction of studies with long-term follow-up because of a number of unique features.[16] Geographically, the community is relatively isolated from other urban centres, and medical care is delivered by only a few health care providers. Most of the Olmsted County residents return to the Mayo Clinic regularly, allowing capture of events. A previous study has shown that 96% of Olmsted County residents aged 65–74 years returned to the Mayo Clinic within a 3-year period.[16] For each patient at the Mayo Clinic, a unified medical record containing details of all inpatient and outpatient encounters is maintained. Within each medical record, diagnoses made during office visits, clinic consultations, emergency room visits, hospital admissions, nursing home care, and autopsy examinations, as well as surgical procedures, are listed on a master sheet and coded. Coded diagnoses are then transferred to a central diagnostic index. This diagnostic index allows all patients with a diagnosis of interest to be readily identified.

Paroxysmal atrial fibrillation cohort

The medical records of Olmsted County, MN adult residents who had AF documented between January 1, 1980 and December 31, 2000, in any of the Mayo administrative and clinical databases [medical index, surgical index, electrocardiographic (ECG), and echocardiographic databases] were reviewed and followed in medical records to March 2004. All diagnoses, covariates, and outcomes were defined a priori, and the same definitions were applied to all patients throughout the 21-year study period. Final inclusion in the study population required ECG confirmation of AF, verification of the AF episode being the first recognized AF event for the person, and that the AF type was paroxysmal.

Definitions

Subjects were categorized as underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2), and obese (BMI ≥ 30 kg/m^2) according to the World Health Organization's definition.[17] In terms of the definition of the subtypes of AF, we followed the criteria as recommended by the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences.[18] Specifically, paroxysmal AF referred to recurrent, intermittent AF that was self-limiting and terminated without specific therapy. Persistent AF was defined by recurrent, sustained AF that had been previously terminated by pharmacological or electrical intervention. Permanent AF referred to continuous AF that could not be converted to normal sinus rhythm by pharmacological or electrical techniques.

Persons who could not be classified according to the definitions above were considered indeterminate, and were excluded from the analyses ($n = 12$). The adjudication of AF types was independently performed by two cardiologists (T.S.M.T. and Y.M.).

Coronary artery disease was defined by angiographic findings of lesions $\geq 50\%$ in any of the three main arterial distributions, angina, or history of myocardial infarction. Myocardial infarction was defined by two or all of the three diagnostic criteria: compatible clinical presentation, diagnostic cardiac enzymes, and consistent ECG changes. Valvular heart disease was defined by echocardiographic confirmation of more than mild degree of valvular stenosis or regurgitation. Carotid artery disease referred to the presence of $\geq 50\%$ stenosis in the carotid arteries by neurovascular imaging, or prior intervention. Stroke was defined by clinical documentation of the diagnosis with or without confirmatory findings on imaging studies. Systemic hypertension was defined by a physician's diagnosis, need for antihypertensive therapy, systolic blood pressure >140 mmHg, or diastolic blood pressure >90 mmHg on two or more occasions that were not associated with acute illness or injury. Diabetes mellitus was defined by physician's diagnosis, and treatment with insulin or oral hypoglycaemic agents. Dyslipidaemia was defined by a total cholesterol ≥ 200 mg/dL, triglycerides ≥ 150 mg/dL, LDL cholesterol ≥ 130 mg/dL, or HDL cholesterol <40 mg/dL on two or more occasions, or treatment with lipid lowering agents. Smoking history was classified as past (>6 months prior) or current smoker. Self-reported use of alcohol of >1 drink per day on a regular basis was recorded. Chronic obstructive pulmonary disease and hyperthyroidism were defined by documented clinical diagnoses. Congestive heart failure was based on the classic Framingham criteria.[19]

Outcome ascertainment

Progression to permanent AF was considered to have occurred if, during follow-up, AF had become continuous and could not be converted to normal sinus rhythm by pharmacological or electrical techniques.[18] We abstracted the data regarding electrical and pharmacological cardioversion from medical records for all persons, and reviewed the ECG series for each. The Mayo ECG database contains all ECGs performed since 1976. Each ECG was read and signed off by a board certified cardiologist. The verified diagnoses were then electronically coded, allowing easy retrieval of the diagnoses for each person. As such, the identification of the rhythm status at the time of each ECG was simple. In addition, for the purpose of this study, we examined each ECG for confirmation of rhythm status for all patients. Since nearly 100% of Olmsted County residents return to the Mayo Clinic over a 3-year period,[16] and the master record documents any diagnoses that have incurred, the review process involving the use of the ECG database and comprehensive evaluation of clinical documentation allowed us to classify AF status. Additionally, we cross-referenced the echocardiographic database which registered the rhythm at the time of any echocardiography study. Ascertainment of death was accomplished through comprehensive review of medical records and the use of the following resources: death certificates, vital status information from Mayo Registration, Minnesota State death tapes, and social security death index.

Echocardiographic data

Two-dimensional left ventricular (LV) dimensions were used for calculation of ejection fraction [LV ejection fraction (%) = (LV end-diastolic dimension^2 − LV end-systolic dimension^2)/LV end-diastolic dimension^2].[20] We calculated LA volume using a validated formula:[21] (LA volume) = 3.7 (LA dimension)$^{1.8}$. Indexed LA volume was calculated by dividing LA volume by body surface area.

Statistical methods

Baseline characteristics were summarized using frequencies and percentages for categorical data, and mean ± SD for continuous data. Cox proportional hazards regression models were used to examine the relation between each risk factor and progression to permanent AF, where age and sex remained in the models throughout. BMI was modelled both as a continuous and a categorical variable. Since increased BMI might exert its effect on progression to permanent AF via its association with multiple other comorbidities, we performed

multivariable analyses, which adjusted for relevant baseline covariates in addition to age and sex. Specifically, we included the risk factors that emerged as significant ($P < 0.05$) after age and sex adjustment: history of hypertension, valvular heart disease, myocardial infarction, congestive heart failure, smoking, chronic pulmonary disease, systolic and diastolic blood pressures at baseline AF diagnosis. In addition, we adjusted for interim myocardial infarction or congestive heart failure, which were considered as time-dependent covariates. Persons who were underweight ($n = 146$, 4%) or did not have BMI documented ($n = 34$, 1%) were excluded from the primary analyses. We did, however, perform supplemental analyses of the relationship between BMI and risk of progression to permanent AF without excluding the underweight group.

The development of multivariable adjustment models for the prediction of permanent AF was done first, for all patients; and second, for the subset with echocardiographic assessment. Using all patients, a set of baseline clinical variables were identified by fitting the Cox proportional model with backward elimination process. The process was repeated in the subgroup analyses of those who had echocardiogram performed ($n = 744$) within 30 days of AF diagnosis. LA volume and LV ejection fraction were entered into these models and evaluated for their incremental value for the prediction of permanent AF. The effect of LA size on prediction was assessed in three ways: absolute LA volume, indexed LA volume, as well as by M-mode LA dimension. The possibility of multiplicative interaction effect between indexed LA volume and BMI was tested by adding the product term to the model with indexed LA volume and BMI.

Assumptions of linearity were assessed by adding a quadratic term for each continuous variable in the model. Although age demonstrated non-linearity, the coefficient for BMI remained unchanged after these additions. To assess proportional hazards assumptions, the model was adjusted to include each variable and log follow-up time term in a time-dependent proportional hazards model. Of all the continuous variables, none showed any significance and the coefficient for BMI remained unchanged.

We also plotted the hazards of progression by BMI categories. Kaplan–Meier curves showing cumulative risk for progression by BMI categories were provided. Finally, the age- and sex-adjusted hazards of progression by BMI and LA volume were depicted. In all cases, statistical significance was defined as 2-tailed $P < 0.05$. Age- and sex-adjusted hazard ratios (HR) by BMI and LA volume categories were displayed in graphics.

Results

Baseline characteristics of patients by body mass index

Of the 3248 persons (1745 men; 1503 women) whose paroxysmal AF was first documented in 1980–2000, 492 (15%) had become persistent and 557 (17%) permanent AF over a median follow-up time of 5.1 years (interquartile range 1.2–9.4 years). Mean age of the cohort was 71 ± 15 years. Electrical cardioversion was performed in 445 persons (initially successful in 418), with or without attempt at pharmacological cardioversion; while only pharmacological conversion was used in 276 (initially successful in 259). The majority of those who initially were cardioverted to sinus rhythm had progressed to permanent AF by last follow-up (513/677; 75%). The unadjusted incidence of progression from paroxysmal to permanent AF was 36 per 1000 person-years overall. The age- and sex-adjusted incidence of progression per 1000 person-years was as follows: normal BMI 33; overweight 35; obesity 43; and severe obesity 47 ($P < 0.0001$). The baseline characteristics for the entire study population, and for the subgroup with echocardiography studies, are shown in *Table 1*.

Relationship between body mass index and progression from paroxysmal to permanent atrial fibrillation

There was a graded risk relationship between BMI and progression to permanent AF: the greater the BMI at baseline, the higher the likelihood of progression from paroxysmal to permanent AF (*Figure 1*, *Table 1*). Age- and sex-adjusted Cox models showed that BMI, as a categorical or continuous variable, was strongly associated with progression to permanent AF, even after adjusting for multiple baseline clinical risk factors, and additionally for interim myocardial infarction and congestive heart failure (*Table 2*). Relative to normal BMI, the hazards for age- and sex-adjusted risk for progression from paroxysmal to permanent AF for overweight, obesity, and severe obesity were 1.1 ($P = 0.24$), 1.54 ($P = 0.0004$), and 1.87 ($P < 0.0001$), respectively.

In a multivariable model, BMI $\geq$30 kg/m^2 was associated with a >1.5 fold increase in risk of converting to permanent AF (*Table 2*). As a continuous variable, BMI (per kg/m^2), was associated with progression to permanent AF [HR 1.03 (1.01–1.04), $P < 0.0001$], adjusting age, sex, and multiple clinical risk factors. Neither the use of beta-blockers nor calcium channel blockers nor antiarrhythmic drugs was associated with status of permanent AF at follow-up. Kaplan–Meier analyses showed that the progression to permanent AF progressively increased with time for all groups, with the gradient of risk predicted by BMI categories (*Figure 2*).

In the supplemental analysis without exclusion of the underweight group, the hazard for risk of progression for BMI <18.5 kg/m^2, relative to normal BMI, was 0.96 ($P = 0.68$) when age- and sex-adjusted. When further adjusted for other covariates, the risk of progression remained non-significant.

Effects of left artrial size and obesity on the progression to permanent atrial fibrillation

Among those who had an echocardiogram performed within 30 days of the diagnosis of paroxysmal AF ($n = 744$), baseline characteristics are detailed in *Table 1*. The significance of BMI as a predictor of progression did not appear attenuated when adjusted for LA size, measured as LA volume, indexed LA volume, or M-mode LA dimension.

LA size was independently predictive of progression to permanent AF. LA size remained independently predictive of progression to permanent AF, after adjusting for age, sex, BMI, other baseline clinical factors, and interim myocardial infarction and congestive heart failure. When adjusted for all these factors in a multivariable model, LA volume remained highly predictive of progression to permanent AF (HR 1.04 (1.02–1.05; $P < 0.0001$). The level of significance was similar whether LA size was measured as LA volume or M-mode LA dimension. Age- and sex-adjusted risk of progression increased with higher BMI and larger LA volume.

Table 1 Baseline characteristics and associated age- and sex-adjusted risks for progression to permanent atrial fibrillation

Variables	Overall	Cox age and sex adjusted *P*-value	Hazard ratio (95% CI)
Entire study population ($n = 3248$)			
Age, years	71 ± 15	<0.0001	1.034 (1.027–1.041)
Male, *n* (%)	1745 (54)	0.3489	1.087 (0.913–1.293)
BMI, kg/m^2	27 ± 6	0.0268	1.005 (1.001–1.009)
Normal BMI, *n* (%)	1233 (38)	0.0030	0.756 (0.629–0.909)
Overweight, *n* (%)	1211 (37)	0.2245	0.898 (0.755–1.068)
Obesity, *n* (%)	521 (16)	0.0051	1.337 (1.091–1.639)
Severe obesity, *n* (%)	283 (9)	0.0004	1.608 (1.236–2.093)
Systolic blood pressure, mm Hg	138 ± 21	0.0002	1.016 (1.007–1.024)
Diastolic blood pressure, mm Hg	77 ± 11	<0.0001	1.042 (1.028–1.057)
History of CHF, *n* (%)	866 (27)	<0.0001	1.568 (1.286–1.911)
History of hypertension, *n* (%)	2577 (79)	0.0026	1.439 (1.136–1.824)
History of valvular heart disease, *n* (%)	598 (18)	<0.0001	1.590 (1.296–1.951)
Current or past smoker, *n* (%)	1907 (59)	0.0174	1.250 (1.040–1.503)
Chronic pulmonary disease, *n* (%)	713 (22)	0.0463	1.231 (1.003–1.511)
Angina/any CAD/prior MI, *n* (%)	1377 (42)	0.6919	0.965 (0.812–1.149)
History of coronary revascularization, *n* (%)	491 (15)	0.5109	0.924 (0.730–1.169)
Peripheral vascular disease, *n* (%)	434 (13)	0.6712	1.060 (0.810–1.388)
History of diabetes mellitus, *n* (%)	621 (19)	0.1660	1.172 (0.936–1.468)
History of dyslipidaemia, *n* (%)	1349 (42)	0.3197	1.090 (0.920–1.293)
Regular alcohol use, *n* (%)	389 (12)	0.3330	1.135 (0.878–1.468)
Renal disease, *n* (%)	591 (18)	0.1549	1.193 (0.935–1.522)
History of obstructive sleep apnoea, *n* (%)	73 (2)	0.1598	1.512 (0.849–2.693)
History of malignant disease, *n* (%)	910 (28)	0.5451	0.938 (0.763–1.154)
Antiarrhythmic use (Class I and Class III)	61 (2)	0.1738	1.514 (0.833–2.751)
Betablocker/calcium channel blocker use	923 (28)	0.1413	1.149 (0.955–1.381)
Echo subgroup ($n = 744$)			
Age, years	69 ± 15	<0.0001	1.049 (1.033–1.066)
Male, *n* (%)	411 (55)	0.0167	1.549 (1.083–2.217)
Systolic blood pressure, mm Hg	136 ± 19	0.0944	1.008 (0.999–1.017)
Diastolic blood pressure, mm Hg	76 ± 11	0.0147	1.020 (1.004–1.037)
History of hypertension, *n* (%)	585 (79)	0.0256	1.840 (1.077–3.143)
History of valvular heart disease, *n* (%)	216 (29)	0.0361	1.48 (1.026–2.137)
History of obstructive sleep aponea, *n* (%)	28 (4)	0.0123	2.568 (1.228–5.373)
Current or past smoker, *n* (%)	431 (58)	0.0278	1.512 (1.046–2.185)
Chronic pulmonary disease, *n* (%)	139 (19)	0.0403	1.534 (1.019–2.309)
Left atrial diameter, mm	45 ± 8	<0.0001	1.056 (1.031–1.08)
Left atrial volume, mL/m^2	36 ± 11	<0.0001	1.001 (1.000–1.002)
Left ventricular ejection fraction	55 ± 14	0.9529	1.000 (0.987–1.012)
Angina/any CAD/prior MI, *n* (%)	270 (36)	0.5242	0.888 (0.615–1.281)
History of coronary revascularization, *n* (%)	137 (18)	0.5379	0.865 (0.545–1.373)
History of CHF, *n* (%)	182 (24)	0.4189	1.190 (0.780–1.816)
Peripheral vascular disease, *n* (%)	92 (12)	0.2837	0.721 (0.397–1.311)
History of diabetes mellitus, *n* (%)	137 (18)	0.5157	0.845 (0.507–1.406)
History of dyslipidaemia, *n* (%)	403 (54)	0.2679	1.216 (0.861–1.717)
Regular alcohol use, *n* (%)	85 (11)	0.3745	1.276 (0.745–2.184)
Renal disease, *n* (%)	126 (17)	0.3520	1.252 (0.780–2.010)
History of malignant disease, *n* (%)	204 (27)	0.3820	1.183 (0.812–1.725)
Antiarrhythmic use (Class I and Class III)	9 (1)	0.9402	1.078 (0.150–7.744)
Beta-blocker/calcium channel blocker use	229 (31)	0.3364	1.196 (0.831–1.721)

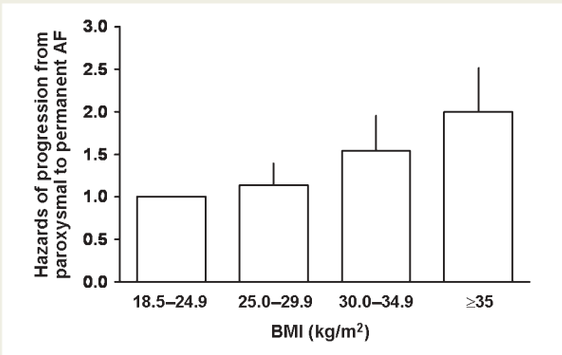

Figure 1 Age- and sex-adjusted hazards of progression from paroxysmal to permanent atrial fibrillation by body mass index.

Table 2 Models for prediction of progression to permanent atrial fibrillation: role of body mass index and left atrial size

Entire population (n = 3,248)	HR (95% CI)	*P*-Value
BMI as continuous variable (per kg/m^2 increase)		
Adjusted for age and sex	1.04 (1.03-1.06)	<0.0001
Adjusted for clinical variables	1.04 (1.02-1.05)	<0.0001
Adjusted for clinical variables[a] and interim MI/CHF	1.03 (1.01-1.04)	0.0003
BMI as a categorical variable (per level increase)		
Adjusted for age and sex		
Normal BMI	1.000	
Overweight	1.13 (0.92–1.39)	0.2415
Obese	1.54 (1.21–1.95)	0.0004
Severely obese	1.87 (1.40–2.51)	<0.0001
Adjusted for age, sex, and other clinical variables[a]		
Normal	1.000	
Overweight	1.11 (0.90–1.37)	0.3482
Obese	1.39 (1.09–1.79)	0.0084
Severely obese	1.66 (1.21–2.24)	0.0015
Adjusted for clinical variables[a] and interim MI/CHF		
Normal	1.000	
Overweight	1.09 (0.88–1.35)	0.4147
Obese	1.30 (1.01–1.66)	0.0408
Severely Obese	1.48 (1.08–2.01)	0.0134
Subgroup with echo parameters (n = 744)	HR (95% CI)	*P*-Value
BMI as continuous variable (per kg/m^2 increase)		
Adjusted for age, sex and LA volume	1.05 (1.02–1.07)	<0.0001
Adjusted for age, sex, other clinical variables[a], and LA volume	1.05 (1.02–1.08)	0.0015

Continued

Table 2 ***Continued***

Entire population (n = 3,248)	HR (95% CI)	*P*-Value
Adjusted for age, sex, other clinical variables[a], and interim MI/CHF	1.03 (1.01–1.06)	0.0206
BMI as a categorical variable (per level increase)		
Age, sex, and LA volume adjusted		
Normal	1.000	
Overweight	0.77 (0.50–1.19)	0.2416
Obese	1.42 (0.89–2.26)	0.1370
Severely obese	1.89 (1.11–3.21)	0.0193
Adjusted for age, sex, other clinical variables[a], and LA volume		
Normal	1.000	
Overweight	0.71 (0.45–1.12)	0.1413
Obese	1.15 (0.70–1.88)	0.5915
Severely obese	1.59 (0.89–2.83)	0.1152
Adjusted for age, sex, other clinical variables[a], interim MI/CHF and LA volume		
Normal	1.000	
Overweight	0.68 (0.42–1.08)	0.0985
Obese	1.04 (0.64–1.71)	0.8679
Severely obese	1.39 (0.78–2.49)	0.2659

[a]Clinical variables adjusted for include history of hypertension, valvular heart disease, myocardial infarction, congestive heart failure, smoking, chronic pulmonary disease, systolic and diastolic blood pressures at baseline AF diagnosis (see section Methods for details). History of CHF, valvular heart disease, hypertension, and diastolic blood pressure remained significant as predictors in all the above multivariable models adjusting for clinical covariates.

The risk was greatest for those with both BMI and LA volume in the highest tertile (*Figure 3*). We also assessed for the possibility of a joint effect of LA size and obesity by adding a multiplicative interaction term to the model with indexed LA volume and BMI as continuous variables, and no significant interaction was evident.

Discussion

This study represents an extension of prior studies showing a relationship between obesity and AF. Unlike previous studies demonstrating an association between obesity and first AF, we report the new finding of obesity being a risk factor for progression of paroxysmal to permanent AF. The data also suggested a dose–response relationship between BMI and progression. When age- and sex-adjusted, or adjusted for other factors including interim myocardial infarction and congestive heart failure, obesity remained associated with a >1.5 fold increase in risk of progression. This level of hazard was similar to that observed for the relationship between obesity and development of first AF.[15]

LA enlargement was proposed as the mediating factor for obesity being a risk factor for incident AF in the Framingham Study.[15] In our study, obesity remained significantly associated with progression to permanent AF, after adjusting for LA size.

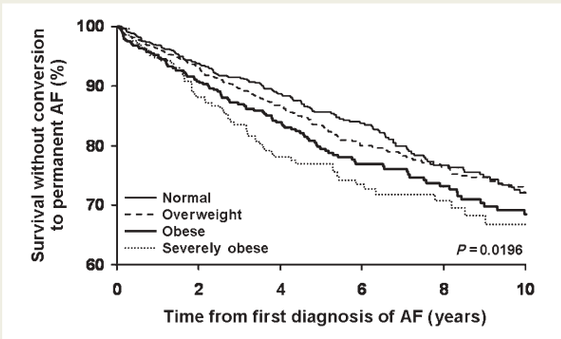

Figure 2 Survival without conversion to permanent atrial fibrillation.

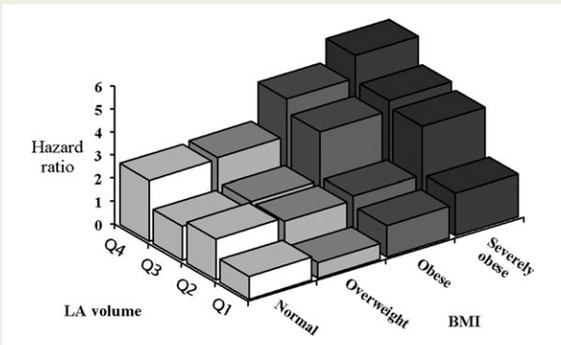

Figure 3 Age- and sex-adjusted hazards of progression to permanent atrial fibrillation stratified by body mass index categories and LA volume quartiles. LA, left atrial.

Neither LA volume nor M-mode LA dimension significantly attenuated the hazard of progression associated with BMI. In our study, the presence of a larger sized left atrium augmented the independent risk of obesity for the progression to permanent AF.

After accounting for LA size, the residual, minimally attenuated risk of obesity may reflect unmeasured effects frequently associated with obesity which could have an impact on LA structural and electrical remodelling. For instance, obesity is associated with systemic inflammation, as is evident by the increased levels of inflammatory markers, such as C-reactive protein, and interleukins in obese persons.[22–25] Inflammation has in fact been touted as a causative factor for AF development and recurrence.[26–29] Obesity is also associated with changes in neurohormonal activation,[30–33] which in turn affect sodium and fluid homeostasis, culminating in increased LV diastolic filling pressures. Larger BMI is associated with increased arterial stiffness[34] which correlates with levels of free oxygen radicals[35] that may perpetuate atrial arrhythmia.[36] Finally, obesity is a well-known risk factor for obstructive sleep apnoea, which has been increasingly linked to incident AF and its recurrence.[37] We were not able to precisely delineate the contribution from these various factors to the excess risk of progression associated with obesity.

The retrospective nature of the study was a limitation in terms of classification of AF status. However, we took precautions to assure that the adjudication of the AF type followed the criteria as defined by the most recent consensus guideline.[18] Despite BMI was found to be an independent risk factor for progression to permanent AF in this study, we did not have data regarding the modifying effects of diet, physical activity, or interim weight changes. Data from the subgroup analyses of patients who underwent a clinically indicated echocardiogram within 30 days of AF diagnosis cannot be extrapolated to AF patients in general. The lack of ethnic diversity is typical of studies confined to Olmsted County, MN, residents; and whether the interaction of BMI, LA size, and AF progression occurs in the same direction and magnitude in other racial ethnic groups could not be determined.

Conclusion

This study extends our understanding of the relationship between obesity/LA size and AF. Specifically, there was a graded risk relationship between BMI and progression from paroxysmal to permanent AF, and larger LA size augmented the risk of such progression. BMI and LA volume were independent predictors of progression to permanent AF. Studies of weight reduction, and of reversal of LA enlargement, may provide insight as to whether these interventions may lower the risk for the development of first AF, and reduce or delay the progression from paroxysmal to permanent AF.

Conflict of Interest: none declared.

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