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Letters

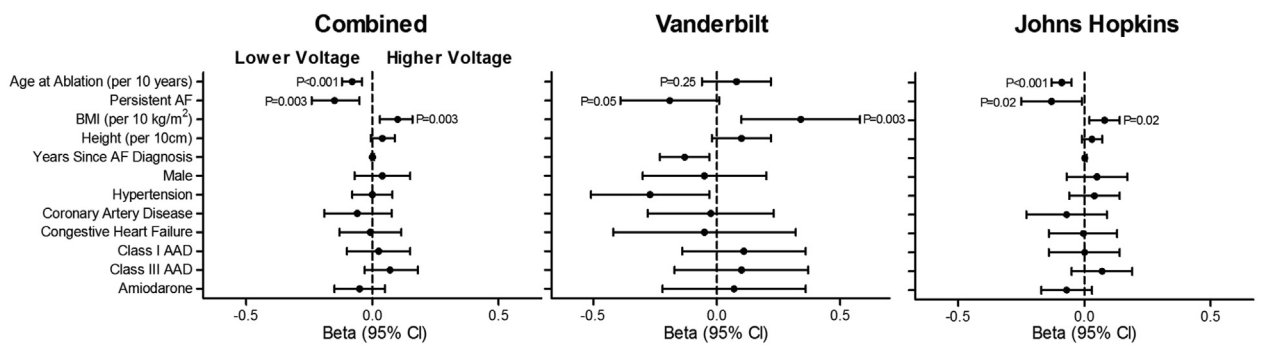
Association of Body Mass Index With Intracardiac Left Atrial Voltage in Patients With Atrial Fibrillation

Obesity is a global epidemic and the strongest clinical predictor for development of atrial fibrillation (AF) (1). Obesity-related AF is emerging as a unique subgroup for which specific therapeutic strategies are being successfully developed (2). Obesity contributes to a complex atrial cardiomyopathy. In general, atrial cardiomyopathies begin with atrial hypertrophy without tissue fibrosis and progress to atrial hypertrophy with progressive accumulation of collagen fibrosis and/or adipose tissue, inflammatory cells, or amyloid deposits (3). Prior research has demonstrated that obesity is associated with many atrial interstitial changes, including fibrosis, fatty infiltration, and inflammation (4); however, evidence to demonstrate that myocyte hypertrophy is part of an obesity-related atrial cardiomyopathy is currently lacking. Given that obesity is associated with elevated atrial pressure and results in significant hypertrophy in the ventricle, we sought to test the idea that, similar to other atrial cardiomyopathies, atrial hypertrophy was present in obese patients with AF. Accordingly, we analyzed the association between body mass index (BMI) and global left atrial (LA) voltage in patients referred for ablation.

Patients referred for first-time AF ablation at Johns Hopkins Hospital or Vanderbilt University Medical Center from 2010 to 2016 were enrolled and provided informed consent. Patients were in sinus rhythm and a 3-dimensional voltage map (CARTO-III, Biosense-Webster Inc., Irvine, California) of the LA was created. Bipolar voltage was $\log_{10}$ transformed and analyzed using multivariable generalized estimating equations. An autoregressive working correlation matrix was used to adjust for the correlation within individual patients and between closely spaced points. Because of potential differences in the study population and data collection between centers, the cohorts were analyzed independently and the overall results were obtained using inverse variance weighted, fixed-effects meta-analysis.

The study cohort consisted of 342 patients (age 64 years; interquartile range [IQR]: 56 to 70 years), 72% male, 47% persistent AF, BMI 29 kg/m^2 (IQR: 25.5 to 33.3 kg/m^2), with 161 participants (15,996 LA points; 92 LA points/subject [IQR: 61 to 127]) and 181 participants (20,601 LA points; 64 LA points/subject

FIGURE 1 Predictors of Global LA Voltage: Results of Multivariable Analysis



BMI is independently associated with increased LA voltage, whereas age and persistent AF are associated with decreased LA voltage. AAD = antiarrhythmic drug; AF = atrial fibrillation; BMI = body mass index; LA = left atrial.

[IQR: 50 to 93]) from Johns Hopkins and Vanderbilt, respectively. In multivariable analysis, predictors of lower LA voltage were age (per 10 years: beta = -0.08; 95% confidence interval [CI]: -0.12 to -0.04; $p < 0.001$) and persistent AF (beta = -0.14; 95% CI: -0.24 to -0.05; $p = 0.003$), whereas the predictor of higher voltage was BMI (per 10 kg/m^2: beta = 0.10; 95% CI: 0.03 to 0.16; $p = 0.003$), with height being nearly significant (per 10 cm: beta = 0.04; 95% CI: -0.006 to 0.09; $p = 0.086$). The remaining covariates in the multivariable model demonstrated nonsignificant associations (**Figure 1**).

The main finding of this study was that increasing BMI was associated with a higher global LA voltage, which was observed in 2 large, independent cohorts. An important distinction between the analysis method used in this paper and prior research using electroanatomic voltage mapping is that we analyzed voltage measurements as a continuous variable, which provided greater statistical power. Prior studies analyzing atrial voltage collected in patients undergoing AF ablation have used semiquantitative assessments based on the presence of contiguous low voltage points visually detected using the color display on an electroanatomic map (5). That method allows for detection of patchy fibrosis. Consistent with the current conceptual framework of atrial cardiomyopathies, we believe our finding that BMI is associated with increased global LA voltage provides evidence to support the idea that obesity also results in atrial hypertrophy; this complements rather than challenges the results of prior studies that found evidence to support the presence of patchy fibrosis.

A limitation of our study was that voltage points were not categorized according to specific sites in the LA. In an ovine model of obesity, Mahajan et al. found that the posterior wall in obese sheep had lower voltage than lean controls (4). Our current analysis cannot define the association between BMI and voltage in specific regions of the LA, or exclude the possibility that higher BMI is associated with lower voltage in the posterior wall in obese patients with AF. Also, our study population was limited to patients referred for ablation, which may represent patients at an earlier stage in the natural history of AF compared with the overall population. Finally, in addition to wall thickness and cellular hypertrophy, many other factors that influence atrial electrogram amplitude were not assessed in this study, including factors determining conduction velocity, such as cell-to-cell conduction, and fibrosis, which would be expected to decrease electrogram amplitude.

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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

REFERENCES

1. Magnussen C, Nijranen TJ, Ojeda FM, et al. Sex differences and similarities in atrial fibrillation epidemiology, risk factors, and mortality in community cohorts. Circulation 2017;17:1588–97.

2. Abed HS, Wittert GA, Leong DP, et al. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation. JAMA 2013;310:2050–60.

3. Goette A, Kalman JM, Aguinaga L, et al. EHRA/HRS/APHRS/SOLAECE expert consensus on atrial cardiomyopathies: definition, characterization, and clinical implication. Europace 2016;18:161.

4. Mahajan R, Lau DH, Brooks AG, et al. Electrophysiological, electroanatomical, and structural remodeling of the atria as consequences of sustained obesity. J Am Coll Cardiol 2015;66:1–11.

5. Dinov B, Kosiuk J, Kircher S, et al. Impact of metabolic syndrome on left atrial electroanatomical remodeling and outcomes after radiofrequency ablation of nonvalvular atrial fibrillation. Circ Arrhythm Electrophysiol 2014;7:483–9.