Frequency of Left Ventricular Hypertrophy in Non-Valvular Atrial Fibrillation

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Left ventricular hypertrophy (LVH) is significantly related to adverse clinical outcomes in patients at high risk of cardiovascular events. In patients with atrial fibrillation (AF), data on LVH, that is, prevalence and determinants, are inconsistent mainly because of different definitions and heterogeneity of study populations. We determined echocardiographic-based LVH prevalence and clinical factors independently associated with its development in a prospective cohort of patients with non-valvular (NV) AF. From the "Atrial Fibrillation Registry for Ankle-brachial Index Prevalence Assessment: Collaborative Italian Study" (ARAPACIS) population, 1,184 patients with NVAF (mean age 72 ± 11 years; 56% men) with complete data to define LVH were selected. ARAPACIS is a multicenter, observational, prospective, longitudinal on-going study designed to estimate prevalence of peripheral artery disease in patients with NVAF. We found a high prevalence of LVH (52%) in patients with NVAF. Compared to those without LVH, patients with AF with LVH were older and had a higher prevalence of hypertension, diabetes, and previous myocardial infarction (MI). A higher prevalence of ankle-brachial index ≤0.90 was seen in patients with LVH (22 vs 17%, p = 0.0392). Patients with LVH were at significantly higher thromboembolic risk, with CHA_2DS_2-VASc ≥2 seen in 93% of LVH and in 73% of patients without LVH (p <0.05). Women with LVH had a higher prevalence of concentric hypertrophy than men (46% vs 29%, p = 0.0003). Logistic regression analysis demonstrated that female gender (odds ratio [OR] 2.80, p <0.0001), age (OR 1.03 per year, p <0.001), hypertension (OR 2.30, p <0.001), diabetes (OR 1.62, p = 0.004), and previous MI (OR 1.96, p = 0.001) were independently associated with LVH. In conclusion, patients with NVAF have a high prevalence of LVH, which is related to female gender, older age, hypertension, and previous MI. These patients are at high thromboembolic risk and deserve a holistic approach to cardiovascular prevention. © 2015 Elsevier Inc. All rights reserved. (Am J Cardiol 2015;■:■−■)

Atrial fibrillation (AF) is the most prevalent supraventricular tachyarrhythmia [1,2] associated with high risk of death and stroke.[3] Hypertension is the most frequent cardiovascular risk factor in AF and recognized as a predictor of new onset AF.[4−6] One of the hypertension-related target organ damage is left ventricular hypertrophy (LVH).[7−10] Data on gender differences in development of LVH have been reported in hypertensive patients with[11] or without concomitant heart failure.[10] Notwithstanding different definitions and threshold criteria, LVH prevalence ranges widely in the general population.[10] Nonetheless, LVH is an independent risk factor for major cardiovascular events and all cause death.[12−15] Also, left ventricular remodeling has been identified as an independent risk factor for stroke and mortality in patients with AF.[16] The aim of our study was to determine LVH prevalence, using well-defined echocardiographic criteria based on left ventricular mass (LVM) indexed by body surface area (BSA) in a cohort of patients with non-valvular (NV) AF. Second, we aimed to identify the clinical factors independently associated with LVH in our patients with NVAF. Third, we conducted a gender-stratified analysis to investigate relevant gender differences in LVH in patients with NVAF.

Methods

We performed a cross-sectional analysis on the "Atrial Fibrillation Registry for Ankle-brachial Index Prevalence

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See page 5 for disclosure information.

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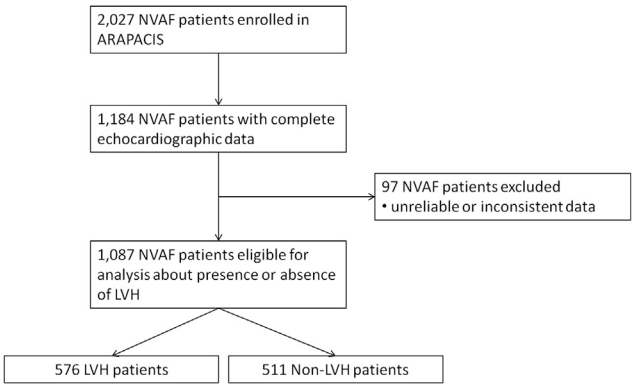

Figure 1. Flow diagram of NVAF patient selection.

Assessment: Collaborative Italian Study" (ARAPACIS), a multicenter, observational, prospective on-going study designed to estimate prevalence of ankle-brachial index (ABI) $\leq$0.90 in patients with NVAF and its influence on cardiovascular and cerebrovascular events incidence over a 3-year follow-up.[17,18]

Details on standard study procedures have been previously reported.[18] In addition, a standard transthoracic echocardiography[19] was performed where feasible. Even if a central analysis of echocardiographic images was not performed, an experienced cardiologist in echocardiography performed a blinded evaluation of measurements for consistency and reliability.

Patients were consecutively recruited, both as inpatients or outpatients, if they were aged $\geq$18 years and had NVAF diagnosis recorded in the preceding 12 months. Enrollment was performed in 136 facilities belonging to the Italian Internal Medicine Society network from October 2010 and continued until 30 October 2012. All patients signed a written informed consent. The study was conducted in accordance with the EU Note for Guidance on Good Clinical Practice CPMP/ECH/135/95 and the Declaration of Helsinki.

LVM estimation was calculated according to American Society of Echocardiography (ASE) and European Association of Echocardiography (EAE) joint recommendations.[19] LVM values have been indexed by BSA, calculated with the Dubois and Dubois formula (BSA = 0.007184 $\times$ weight $[Kg]^{0.425}$ $\times$ height $[cm]^{0.725}$). Thus, we defined the presence of LVH for an LVM indexed by BSA (LVMI-BSA) >95 g/m^2 for women and an LVMI-BSA >115 g/m^2 for men.[19]

The definition of LV remodeling was assessed calculating the relative wall thickness (RWT). In accordance to ASE/EAE recommendations,[19] RWT $\geq$0.42 defined a concentric remodeling, otherwise an RWT <0.42 defined an eccentric remodeling. All patients were then categorized into 4 categories of cardiac remodeling: (1) no remodeling, that is, patients without LVH and with an RWT <0.42; (2) concentric remodeling, that is, patients without LVH and with an RWT $\geq$0.42; (3) eccentric hypertrophy, that is, patients with LVH and an RWT <0.42; and (4) concentric hypertrophy, that is, patients with LVH and an RWT $\geq$0.42.

According to Shapiro–Wilk normality test, variables with a normal distribution were tested for differences by the Student *t* test and reported as mean $\pm$ standard deviation. Variables with nonhomogeneous variances were tested by the Mann–Whitney *U* test and reported as median and interquartile range. Categorical variables, expressed as counts and percentages, were analyzed by a chi-square test. A gender-stratified analysis was also conducted. Finally, a multivariate regression analysis was performed to establish LVH determinants in patients with NVAF. To reduce interobserver variability, the regression analysis was corrected for enrolling centers. The probability values were 2 sided; a p value <0.05 was considered statistically significant. All analyses were carried out with SPSS version 20 (IBM, NY, USA).

Results

Among a total of 2,027 patients enrolled in ARAPACIS, echocardiographic data were available for 1,184 subjects (59%). After data revision, 1,087 patients (72 $\pm$ 11 years; 56% men) were eligible for analysis (Figure 1). Clinical and demographic variables in nonincluded patients were similar to those analyzed (Table 1).

Previous cardiovascular disease was recorded for about 1/4 of patients. Among classic cardiovascular risk factors, hypertension was the most prevalent (82%). The mean LVMI-BSA was 112 $\pm$ 31 g/m^2. Values of LVMI-BSA were greater in permanent NVAF compared to those with persistent AF (p = 0.0107) or paroxysmal AF (p = 0.0023). LVMI-BSA progressively increased with higher CHA_2DS_2-VASc risk classes (p <0.0001; Figure 2).

LVH was recorded in 52% of patients. Clinical and demographic characteristics in the groups are reported in Table 1. Patients with LVH were older, had a higher prevalence of hypertension, diabetes, and previous myocardial infarction (MI) compared to those without. ABI $\leq$0.90 was prevalent in patients with LVH. CHA_2DS_2-VASc $\geq$2 class was recorded more frequently in patients with LVH.

Table 2 summarizes echocardiographic characteristics of the 2 groups. Patients with LVH had poorer ventricular function compared to those without LVH. In 59% of patients with LVH, there was a concentric hypertrophy pattern.

Pharmacologic treatments distribution in the 2 groups are reported in Table 3. Patients with LVH were more likely treated with oral anticoagulants (OAC) and angiotensin-converting enzyme inhibitors than those without LVH.

Final forward logistic model showed that female gender (odds ratio [OR] 2.808, 95% confidence interval [CI] 2.152 to 3.664, p <0.001), age (OR per year 1.035, 95% CI 1.021 to 1.048, p <0.001), hypertension (OR 2.302, 95% CI 1.606 to 3.299, p <0.001), diabetes (OR 1.623, 95% CI 1.169 to 2.253, p = 0.004), and previous MI (OR 1.964, 95% CI 1.328 to 2.903, p = 0.001) were independently associated with LVH. No influence of enrolling centers was evident.

LVH was detected in 67% of NVAF women compared to 42% in men. Number of atherosclerotic risk factors was greater in male patients with LVH compared to those without (2.04 $\pm$ 1.20 vs 1.76 $\pm$ 1.02, p = 0.0041). Similar data were recorded in female patients with LVH compared to those without (1.92 $\pm$ 1.12 vs 1.70 $\pm$ 1.10, p = 0.0434). Concentric hypertrophy was more common in female