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CORRESPONDENCE

Research Correspondence

Prevalence of Peripheral Artery Disease by Abnormal Ankle-Brachial Index in Atrial Fibrillation

Implications for Risk and Therapy

To the Editor: Nonvalvular atrial fibrillation (NVAF) is the most common sustained arrhythmia encountered in clinical practice and is associated with a 5-fold increased risk for stroke (1).

Moreover, patients with NVAF often suffer from atherosclerotic complications such as acute myocardial infarction (AMI) (2). Peripheral artery disease (PAD) is an established marker of systemic atherosclerosis but its prevalence in NVAF is still unclear. We reasoned that inclusion of ankle-brachial index (ABI), which is an established tool for diagnosis of PAD (3), in the CHA_2DS_2-VASc (4) score would better define the prevalence of vascular disease.

To address this issue, the Italian Society of Internal Medicine (SIMI) established an Italian registry documenting ABI in NVAF patients.

The Atrial Fibrillation Registry for the ARAPACIS (Ankle-brachial Index Prevalence Assessment: Collaborative Italian Study) study is an independent research project involving all Regional Councils of SIMI. The first objective of the study was to estimate the prevalence of ABI ≤0.90 in NVAF patients.

Consecutive patients with NVAF referred to internal medicine wards were eligible for the enrollment. Enrollment started in October 2010 and continued until October 30, 2012. Patients were enrolled if they were 18 years or older and had a diagnosis of NVAF, recording during the qualifying admission/consultation or in the preceding 12 months, and if it was possible to obtain the ABI measurement. Exclusion criteria included the following: acquired or congenital valvular AF, active cancer, disease with life expectancy <3 years, hyperthyroidism and pregnancy.

We initially planned to include 3,000 patients. The Data and Safety Monitoring Board (Online Appendix) decided to perform an interim analysis to assess the prevalence of ABI in the enrolled populations—as a higher than expected prevalence of low ABI was detected—and decided to interrupt the patients' enrollment. The sample size was amended as follows: a sample of 2,027 patients leads to the expected prevalence of 21% with a 95% confidence interval width of 3.5% (StataCorp LP, College Station, Texas).

Among the 2,027 NVAF patients included in the study, hypertension was detected in 83%, diabetes mellitus in 23%, dyslipidemia in 39%, metabolic syndrome in 29%, and smoking in 15%. At least 1 atherosclerotic risk factor was detected in 90% of patients.

The NVAF population was at high risk for stroke, with only 18% having a CHA_2DS_2-VASc score of 0 to 1, while 82% had a risk ≥2. Despite this, 16% were untreated with any antithrombotic drug, 19% were treated with antiplatelet drugs (APs), and 61% with oral anticoagulants (OAC); 4% of patients were treated with both APs and OAC.

Among the AF population, 428 patients (21%) had ABI ≤0.90 compared with 1,381 patients, who had an ABI of 0.91 to 1.39 (69%); 204 patients (10%) had ABI ≥1.40 (Fig. 1). ABI recorded only in 1 leg was excluded from the analysis (n = 14). ABI ≤0.90 progressively increased from paroxysmal to permanent NVAF (18%, 21%, 24%; p = 0.0315).

NVAF patients with ABI ≤0.90 were more likely to be hypertensive (88% vs. 82%; p = 0.032), diabetic (34% vs. 20%; p < 0.0001), or smokers (20% vs. 14%; p = 0.0008), or to have experienced transient ischemic attack or stroke (17% vs. 10%; p < 0.001). NVAF patients with ABI ≤0.90 had a higher percentage of CHA_2DS_2-VASc score ≥2 compared with those with ABI >0.90 (93% vs. 82%; p < 0.0001).

Logistic regression analysis demonstrated that ABI ≤0.90 was significantly associated with a smoking habit (odds ratio [OR]: 1.99; 95% confidence interval [CI]: 1.48 to 2.66; p < 0.0001), diabetes (OR: 1.93; 95% CI: 1.51 to 2.46; p < 0.0001), age class 65 to 74 years (OR: 2.05; 95% CI: 1.40 to 3.07; p < 0.0001), age class ≥75 years (OR: 3.12; 95% CI: 2.16 to 4.61; p < 0.0001), and history of previous transient ischemic attack/stroke (OR: 1.64; 95% CI: 1.20 to 2.24; p = 0.002).

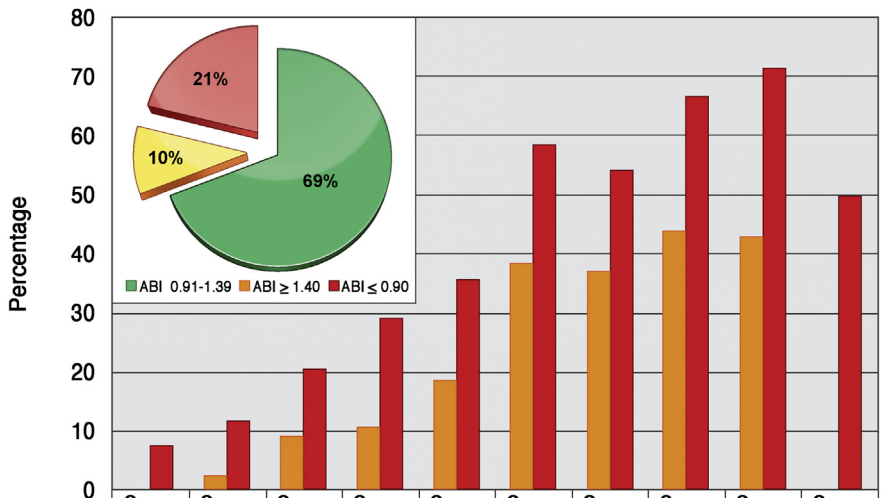
Vascular disease, as assessed by the history elements of CHA_2DS_2VASc score, was recorded in 17.3% of patients; inclusion of ABI ≤0.90 in the definition of vascular disease yielded a total prevalence of 33%. A higher prevalence of vascular disease was detected if ABI ≤0.90 was included in the CHA_2DS_2VASc score (Fig. 1). CHA_2DS_2VASc including ABI ≤0.90 was more associated with previous stroke (43%; OR: 1.85; 95% CI: 1.41 to 2.44; p < 0.0001) compared to CHA_2DS_2VASc with ABI 0.91 to 1.39 (23%; OR: 1.52; 95% CI: 1.10 to 2.11; p = 0.0117).

To the best of our knowledge, there is no large-scale study that specifically examined the prevalence of ABI ≤0.90 in NVAF. In our population, 21% had ABI ≤0.90 indicating that NVAF is often associated with systemic atherosclerosis.

The $CHADS_2$ has been recently refined with the CHA_2DS_2-VASc score, which includes vascular disease as documented by a history of AMI, symptomatic PAD, or detection of atherosclerotic plaque in the aortic arch (4).

Comparison of vascular prevalence as assessed by CHA_2DS_2-VASc score and/or ABI ≤0.90 is of interest to define the potentially positive impact of measuring ABI in the management of NVAF patients. Inclusion of ABI ≤0.90 in the definition of vascular disease greatly increased the prevalence of vascular disease, which increased from 17.3% (based on history alone) to 33% (based on ABI) in the entire population. If ABI ≤0.90 was encompassed in the definition of vascular disease of CHA_2DS_2-VASc score the prevalence of vascular disease increased in every risk class.

Inclusion of ABI ≤0.90 in the CHA_2DS_2-VASc score allowed us to better define the risk profile of NVAF patients with an up-grading of the risk score in each CHA_2DS_2-VASc score category. This may have important therapeutic implications if the new score could be tested prospectively, as a higher number of NVAF patients would



	Score 0	Score 1	Score 2	Score 3	Score 4	Score 5	Score 6	Score 7	Score 8	Score 9
VASc	0	2.56	9.19	10.79	18.65	38.49	37.14	43.94	42.86	0
VASc + ABI	7.69	11.97	20.73	29.26	35.73	58.58	54.29	66.67	71.43	50

Figure 1 **ABI Distribution of Any Category and CHA2DS2-VASc Score Including ABI ≤0.90**

C = congestive heart failure (or left ventricular systolic dysfunction) (Points: 1), H = hypertension (Points: 1), A_2 = Age ≥75 years (Points: 2), D = diabetes mellitus (Points: 1), S_2 = prior stroke or transient ischemic attack or thromboembolism (Points: 2); V = vascular disease (previous acute myocardial infarction, peripheral arterial disease, or aortic plaque) (Points: 1); A = age 65 to 74 years (Points: 1); Sc = sex category (female) (Points: 1). ABI = ankle brachial index.

potentially be candidates for an anticoagulant treatment by measuring ABI. A prospective study is, therefore, necessary to validate the risk score of this new definition of vascular disease.

In conclusion, this study provides the first evidence that one-fifth of NVAF patients had an ABI ≤0.90, indicating that it may represent a simple and cheap method to better define the prevalence of vascular disease in NVAF.

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REFERENCES

1. Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the Management of Atrial Fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J 2012;33:2719–47.
2. Violi F, Lip GY, Basili S. Peripheral artery disease and atrial fibrillation: a potentially dangerous combination. Intern Emerg Med 2012;7:213–8.
3. Aboyans V, Criqui MH, Abraham P, et al. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. Circulation 2012;126:2890–909.
4. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor based approach: the euro heart survey on atrial fibrillation. Chest 2010;137:263–72.

APPENDIX

For a listing of the ARAPACIS collaborators, please see the online version of this article.