Echocardiographic predictors of frequency of paroxysmal atrial fibrillation (AF) and its progression to persistent AF in hypertensive patients with paroxysmal AF: Results from the Japanese Rhythm Management Trial II for Atrial Fibrillation (J-RHYTHM II Study)

Takeki Suzuki, MD, MPH,* Tsutomu Yamazaki, MD, PhD,† Satoshi Ogawa, MD, PhD,‡ Ryozo Nagai, MD, PhD,* Takeshi Yamashita, MD, PhD,¶ and the J-RHYTHM II Investigators

*From the *Department of Cardiovascular Medicine, University of Tokyo Graduate School of Medicine, Tokyo, Japan, †Department of Clinical Epidemiology & Systems, University of Tokyo Graduate School of Medicine, Tokyo, Japan, ‡Division of Cardiology, International University of Health and Welfare, Mita Hospital, Tokyo, Japan, and ¶Department of Cardiovascular Medicine, Cardiovascular Institute, Tokyo, Japan.*

BACKGROUND Little is known about associations among echocardiographic variables, frequency of atrial fibrillation (AF), and progression from paroxysmal to persistent AF.

OBJECTIVE The purpose of this study was to investigate echocardiographic predictors of frequency of paroxysmal AF and its progression to persistent AF in hypertensive patients with paroxysmal AF.

METHODS We used data from 286 patients with paroxysmal AF and hypertension in the Japanese Rhythm Management Trial II for Atrial Fibrillation (J-RHYTHM II Study). Echocardiographic evaluation was performed at baseline. Endpoints were (1) percent of AF days measured daily by transtelephonic monitoring over 1 year and (2) development of persistent AF, defined as incidence of AF lasting for longer than 7 days and/or need for electrical cardioversion. Univariate and multivariate linear regression analysis was performed to evaluate the association between echocardiographic variables and percent of AF days. Cox proportional hazards analysis was used to examine the association between echocardiographic variables and development of persistent AF.

RESULTS Among echocardiographic variables, increased left atrial dimension (LAD) was associated with more AF days and development of persistent AF: a 10-mm increase in LAD was associated with a 6.5% increase in AF days (95% confidence interval 2.7%–10.3%) and an 84% increased risk of developing persistent AF (hazard ratio 1.84, 95% confidence interval 1.28–2.67). These associations remained significant after adjustment for age, sex, and other potential confounding factors.

CONCLUSION Increased LAD is associated with more AF days and progression from paroxysmal to persistent AF in patients with paroxysmal AF and hypertension. Increased LAD may be a good echocardiographic predictor of AF frequency and progression.

KEYWORDS Arrhythmia; Atrial fibrillation; Hypertension; Echocardiography; Left atrial dimension; Transtelephonic electrocardiographic monitoring

ABBREVIATIONS **AF** = atrial fibrillation; **CI** = confidence interval; **ECG** = electrocardiogram; **HR** = hazard ratio; **IVS** = interventricular septum; **J-RHYTHM II Study** = Japanese Rhythm Management Trial II for Atrial Fibrillation Study; **LA** = left atrium; **LAD** = left atrial dimension; **LV** = left ventricle; **LVDd** = left ventricular end-diastolic diameter; **LVDs** = left ventricular end-systolic diameter; **LVPW** = left ventricular posterior wall; **sBP** = systolic blood pressure

(Heart Rhythm 2011;8:1831–1836)

Introduction

Atrial fibrillation (AF) is one of the most common arrhythmias in clinical practice.[1,2] It is estimated that 2.2 million people in America and more than 6 million in Europe suffer from this arrhythmia.[2,3] Being a strong risk factor for stroke, AF itself can cause severe devastating symptoms, resulting in impaired quality of life.[4]

Hypertension is a well-known AF comorbid condition. More than half of AF patients have hypertension as an underlying condition.[5,6] Furthermore, hypertension is known to be a risk factor for AF.[7,8] Hypertension results in left ventricular (LV) hypertrophy, reduced LV diastolic function, and left atrial (LA) enlargement.[9,10]

Address reprint requests and correspondence: Dr. Takeki Suzuki, Department of Cardiovascular Medicine, University of Tokyo Graduate School of Medicine, 7-3-1 Hongo Bunkyo-ku, Tokyo, Japan 113-8655. E-mail address: suzukit-tky@umin.ac.jp. (Received June 17, 2011; accepted July 28, 2011.)

1547-5271/$ -see front matter doi:10.1016/j.hrthm.2011.07.035

Previous studies have evaluated associations between echocardiographic variables and AF.[11–13] It has been shown that left atrial dimension (LAD) is associated with AF prevalence[11] and incidence.[12,13] However, these studies have not specified patterns of AF, such as paroxysmal, persistent, and permanent forms,[1] and whether LAD is associated with frequency of paroxysmal AF remains unknown. Furthermore, little is known about the association between echocardiographic variables and progression from paroxysmal to persistent AF. Transtelephonic electrocardiographic (ECG) monitoring has enabled us to examine daily cardiac rhythm at home and, therefore, the frequency of paroxysmal AF. The purpose of this study was twofold: first, to examine the association between LAD and AF frequency; and second, to examine the association between echocardiographic variables and progression from paroxysmal to persistent AF in patients with paroxysmal AF and hypertension.

Methods

Study patients

The Japanese Rhythm Management Trial II for Atrial Fibrillation (J-RHYTHM II Study) is a randomized clinical trial examining the effect of calcium channel blocker (amlodipine) and angiotensin receptor blocker (candesartan) in Japanese patients with paroxysmal AF and hypertension. Details of the study design are described elsewhere.[14,15] In brief, patients were enrolled in the study if they met both of the following criteria: (1) history of paroxysmal AF within the preceding 6 months, and (2) hypertension, defined as systolic blood pressure (sBP) ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Patients were excluded if they met any of the following criteria: (1) history of vasospastic angina pectoris; (2) persistent AF with duration ≥1 week and/or permanent AF; (3) AF that had occurred within 1 month of onset of myocardial infarction; (4) transient AF

Table 1 Basic characteristics of the cohort according to LAD quartile*

	LAD quartile				
	Quartile 1 (LAD ~34 mm)	Quartile 2 (LAD 35~38 mm)	Quartile 3 (LAD 39~42 mm)	Quartile 4 (LAD 43 mm~)	*P* value
N	65	73	78	70	
Male gender (%)	43 (65)	47 (71)	49 (74)	56 (84)	NS
Angiotensin receptor blocker use (randomization) (%)	32 (48)	39 (59)	40 (60)	33 (50)	NS
Age (y)	66.7 ± 9.0	65.0 ± 10.5	65.2 ± 10.2	64.2 ± 8.8	NS
Systolic blood pressure (mmHg)	141 ± 17	139 ± 14	140 ± 14	142 ± 16	NS
Diastolic blood pressure (mmHg)	83 ± 12	84 ± 11	79 ± 12	83 ± 9	NS
Heart rate (bpm)	68 ± 11	69 ± 14	71 ± 11	71 ± 15	NS
Duration of atrial fibrillation					NS
<1 y (%)	20 (31)	19 (26)	22 (28)	12 (17)	
≤1 y and <5 y (%)	21 (32)	35 (48)	27 (35)	32 (46)	
≥5 y (%)	16 (25)	14 (19)	25 (32)	21 (30)	
Unknown (%)	8 (12)	5 (7)	4 (5)	5 (7)	
Antihypertensive medication (%)	50 (76)	58 (88)	58 (88)	55 (83)	NS
Antiarrhythmic drug treatment (except pill-in-pocket use) (%)	43 (65)	51 (77)	60 (90)	54 (81)	NS
Prior embolism (%)	7 (11)	6 (9)	4 (6)	5 (8)	NS
Heart failure (%)	1 (2)	3 (5)	1 (2)	3 (5)	NS
Old myocardial infarction (%)	1 (2)	2 (3)	0 (0)	1 (2)	NS
Angina pectoris (%)	2 (3)	0 (0)	2 (3)	2 (3)	NS
Dilated cardiomyopathy (%)	0 (0)	1 (2)	0 (0)	0 (0)	NS
Hypertrophic cardiomyopathy (%)	0 (0)	3 (5)	0 (0)	2 (3)	NS
Valvular heart disease (%)	5 (8)	2 (3)	8 (12)	8 (12)	NS
Cardiac surgery (%)	0 (0)	1 (2)	0 (0)	3 (5)	NS
Pacemaker implantation (%)	3 (5)	7 (11)	10 (15)	5 (8)	NS
Stroke/systemic embolism (%)	5 (8)	5 (8)	3 (5)	1 (2)	NS
Transient ischemic attack (%)	1 (2)	1 (2)	2 (3)	1 (2)	NS
Diabetes mellitus (%)	3 (5)	8 (12)	13 (20)	4 (6)	NS
Hyperlipidemia (%)	20 (30)	16 (24)	28 (42)	23 (35)	NS
LVDd (mm)	45.7 ± 5.5	47.1 ± 4.4	48.3 ± 4.3	49.5 ± 4.8	<.001
LVDs (mm)	28.3 ± 4.9	29.2 ± 4.3	30.2 ± 4.9	31.2 ± 4.9	<.005
LVEF (%)	68.4 ± 8.2	68.7 ± 7.7	67.3 ± 6.7	66.2 ± 10.0	NS
LAD (mm)	31.1 ± 3.5	36.6 ± 1.1	40.4 ± 1.2	47.8 ± 5.5	<.001
IVS (mm)	9.3 ± 1.6	9.6 ± 1.6	10.0 ± 1.5	10.9 ± 2.4	<.001
LVPW (mm)	9.3 ± 1.7	9.7 ± 1.4	9.7 ± 1.4	10.4 ± 1.9	<.005

IVS = interventricular septum; LAD = left atrial dimension; LVDd = left ventricular end-diastolic diameter; LVDs = left ventricular end-systolic diameter; LVEF = left ventricular ejection fraction; LVPW = left ventricular posterior wall.

*For continuous variables, mean ± SD is shown.