Heart Vessels (2010) 25:410–416
DOI 10.1007/s00380-009-1211-9

ORIGINAL ARTICLE

Koichi Sakabe · Nobuo Fukuda · Yamato Fukuda
Satofumi Morishita · Hisanori Shinohara
Yoshiyuki Tamura

Relation of gender and interatrial dyssynchrony on tissue Doppler imaging to the prediction of the progression to chronic atrial fibrillation in patients with nonvalvular paroxysmal atrial fibrillation

Received: May 10, 2009 / Accepted: September 18, 2009

Abstract This prospective study aimed to identify the relation of gender and interatrial dyssynchrony on tissue Doppler imaging (TDI) to the prediction of the progression to chronic atrial fibrillation (CAF) in nonvalvular paroxysmal AF (PAF) patients. Nineteen consecutive men and 19 women with nonvalvular PAF were prospectively followed after echocardiography. We measured the interval of time from initiation of the P wave on the electrocardiogram until the beginning of the late diastolic TDI signal at the lateral border of the mitral (P-A′(M)) and the tricuspid annulus (P-A′(T)). Interatrial dyssynchrony was defined as the difference between the P-A′(M) and P-A′(T) intervals (A′(M)–A′(T)). The study endpoint was the onset of CAF (>6 months). Six men developed CAF during a follow-up of 32 ± 26 months, and 3 women developed CAF during a follow-up of 25 ± 19 months. Compared to those without CAF, the patients with CAF had significantly longer A′(M)–A′(T) intervals (men: 41 ± 10 vs 27 ± 12 ms, women: 64 ± 4 vs 23 ± 9 ms; $P < 0.01$) in both genders. Kaplan–Meier analysis, using cutoff values determined by analysis of receiver-operating characteristics curves, revealed that the progression to CAF was significantly observed more often when A′(M)–A′(T) interval was >34 ms in men and >43 ms in women. This prospective study suggests that nonvalvular PAF men and women with a high risk of developing CAF have "interatrial dyssynchrony" on atrial TDI, whose cutoff values are shorter and may affect the vulnerability of AF in men.

K. Sakabe (✉) · N. Fukuda · Y. Fukuda · S. Morishita ·
H. Shinohara · Y. Tamura
Department of Cardiology and Clinical Research, National Hospital Organization, Zentsuji National Hospital, 2-1-1 Senyu-cho, Zentsuji, Kagawa 765-8507, Japan
Tel. +81-877-62-2211; Fax +81-877-63-1601
e-mail: ksakabe@jun.ncvc.go.jp

Portions of the results were presented at the 57th Annual Scientific Session, American College of Cardiology 2008, Chicago, USA, March 29–April 1, 2008.

Key words Atrial fibrillation · Gender · Transthoracic echocardiography · Tissue Doppler echocardiography · Interatrial dyssynchrony

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia,[1] and is generally classified as paroxysmal, persistent, or permanent AF.[2] Paroxysmal AF (PAF) often precedes the onset of chronic AF (CAF) (i.e., persistent or permanent AF).[3] Although various echocardiographic and electrocardiographic parameters have been investigated as predictors of atrial function as well as of recurrence and chronicity of AF,[4–9] some authors have questioned their predictive value and have indicated their limitations.[1,10–12] Thus, it remains difficult to predict progression from PAF to CAF.

Recently, atrial electromechanical abnormalities have been reported to promote AF.[13–22] These electromechanical abnormalities have been assessed by determining the time from the onset of the P wave to the beginning of atrial contraction using the electrocardiogram (ECG) and M-mode or Doppler echocardiography. Sequential analysis of atrial electromechanical coupling by tissue Doppler imaging (TDI) allows more precise analysis of atrial electromechanical abnormalities in different regions.[16,18–24] Previously, some gender differences were recognized in atrial remodeling after a second episode of AF, which may be the reason why the prevalence of atrial fibrillation is higher in men than in women.[13,25–28] In the present study, we evaluated interatrial dyssynchrony (defined by the dispersion of right and left atrial electromechanical coupling) by using TDI, and prospectively investigated the relation of gender and interatrial dyssynchrony to the prediction of the transition to CAF in nonvalvular PAF patients.

Patients and methods

Subjects

We screened 336 consecutive patients with PAF who were referred to Zentsuji National Hospital (Kagawa, Japan) between January 2000 and December 2007. A diagnosis of PAF was established if AF terminated spontaneously and had generally lasted for less than 48 h on standard ECG or 24-h Holter ECG recordings.[6] Only patients with nonvalvular PAF, who had "pure" lone PAF or PAF associated with mild uncomplicated hypertension, were eligible to be enrolled in this study.[6] Patients with a history of cardiovascular, pulmonary, or metabolic diseases were excluded. Other exclusion criteria were the following echocardiographic findings: significant valvular abnormalities, left ventricular hypertrophy (>12 mm) or abnormal wall motion, and left ventricular systolic dysfunction (ejection fraction <50%). Patients were also excluded if their baseline rhythm was not found to be normal sinus rhythm during echocardiographic assessment. As a result, 40 patients with nonvalvular PAF (21 men; mean age: 71 ± 12 years) were enrolled in this study, and were followed prospectively after transthoracic echocardiographic assessment by TDI. The study protocol was approved by the institutional ethics committee, and written informed consent was obtained from all subjects prior to enrollment.

Transthoracic echocardiography and definition of interatrial dyssynchrony

Echocardiographic measurements were carried out prospectively by investigators blinded to clinical data after sinus rhythm had been maintained for at least 1 month.[29] Standard transthoracic echocardiography was performed in the left lateral position with an Acuson Sequoia 512 system (Siemens, Malvern, PA, USA) and a 3.5-MHz transducer.[30,31] The left atrial (LA) and left ventricular (LV) diameters were measured from two-dimensional guided M-mode tracings, according to the recommendations of the American Society of Echocardiography.[31] The LV ejection fraction was calculated by Simpson's method on apical two-dimensional images. The LA volume was calculated by Simpson's method from apical four-chamber views obtained just before mitral valve opening. Pulsed-wave Doppler recordings of transmitral inflow (TMF) were obtained in the apical four-chamber view with the sample volume placed at the orifice of the mitral valve. Then the peak early (E) and late (A) diastolic flow velocity were measured, and the E/A ratio of TMF was calculated.

Pulsed-wave tissue Doppler recordings were obtained in the apical four-chamber view with the sample volume placed at the lateral aspect of the mitral annulus and the tricuspid annulus to measure the peak early and late diastolic mitral (E′(M), A′(M)) and tricuspid (E′(T), A′(T)) annular velocities.[32–34] We also measured the time from initiation of the P wave on the ECG until the beginning of the late diastolic TDI signal at the lateral border of the mitral annulus (P-A′(M)) and the tricuspid annulus (P-A′(T)). Interatrial dyssynchrony was defined as prolongation of the difference between the P-A′(M) and P-A′(T) intervals (A′(M)–A′(T)) (Fig. 1).[19,21,22] All Doppler measurements were calculated as the average over three beats.

Follow-up and study endpoint

All patients were followed as outpatients at our institution every 1–2 months. The study endpoint was defined prospectively as the onset of CAF (persistent or permanent AF) on a standard ECG or 24-h Holter ECG during the follow-up period. A diagnosis of CAF was established if AF did not terminate spontaneously and had generally lasted for more than 6 months.[35] Patients in whom drug therapy was changed during the follow-up period were excluded from this study.

Statistical analysis

Continuous variables are expressed as the mean ± SD and were assessed by analysis of variance (ANOVA) followed by post hoc multiple comparison. Comparisons between clinical variables were done by the chi-squared test. The time until the onset of CAF was estimated by the Kaplan–Meier method, and comparisons between two indices were done by the log-rank test. For these analyses, $P < 0.05$ was considered to indicate statistical significance.

Results

Patients' characteristics

Two men were excluded from follow-up evaluation because of changes in antiarrhythmic drugs due to side effects or lack of detailed follow-up data. Table 1 summarizes the clinical characteristics of the remaining 38 patients (mean age: 71 ± 11 years; 19 men) for whom follow-up data were available. During an average follow-up period of 32 ± 26 months (range: 3–94 months), 6 of these 19 men (31.6%) developed CAF, and 3 of these 19 women (15.7%) developed CAF during a follow-up period of 25 ± 19 months (range: 2–68 months). Follow-up period was not statistically different between men and women. In both genders, there were no significant differences between the patients with or without progression to CAF with respect to age or use of antiarrhythmic agents and other drugs.

Transthoracic echocardiographic parameters and interatrial dyssynchrony

The transthoracic echocardiographic data obtained at baseline are summarized in Table 2. There were no significant differences between patients with or without progression to CAF with respect to LA and LV morphologic parameters (LA diameter, LA volume, LV end-diastolic diameter, and

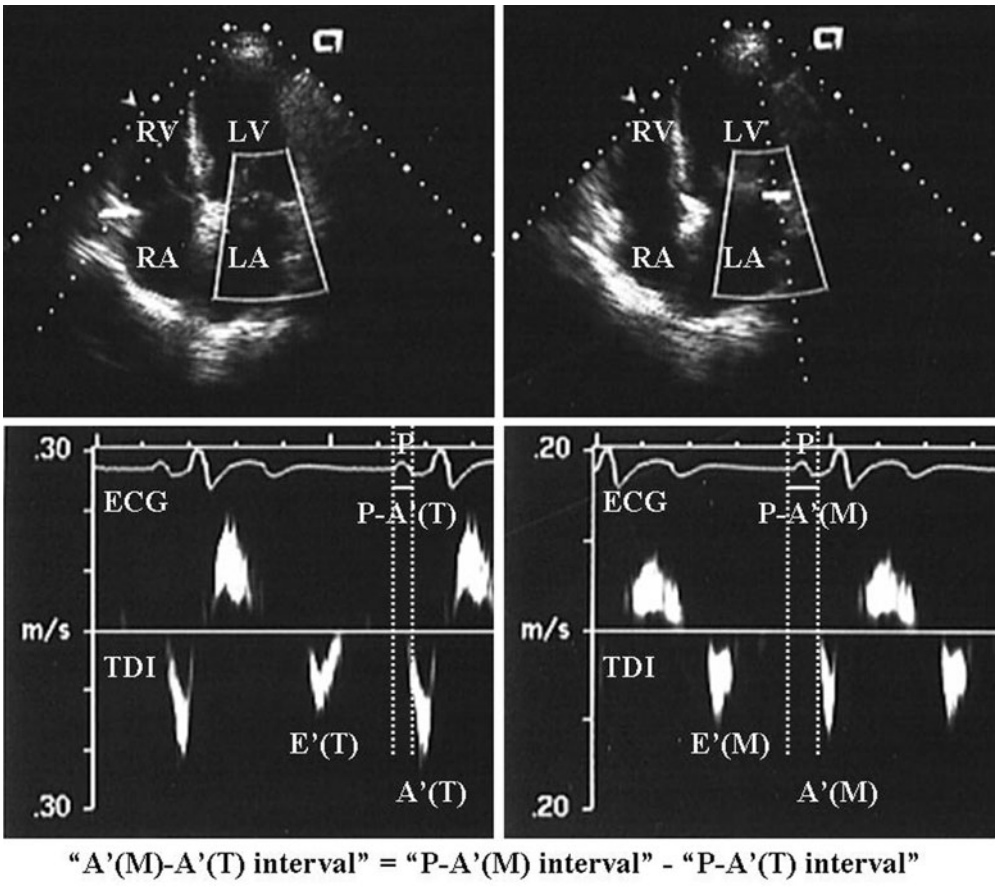

Fig. 1. The P-A′(M) and P-A′(T) intervals were measured as the time from initiation of the P wave on the electrocardiogram (*ECG*) until the beginning of the late diastolic tissue Doppler imaging (*TDI*) signal at the lateral border of the mitral annulus (*P-A′(M)*) and tricuspid annulus (*P-A′(T)*). Interatrial dyssynchrony was defined as prolongation of the difference between the P-A′(M) and P-A′(T) interval (A′(M)–A′(T)). *LA*, left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle

Table 1. Clinical characteristics of the subjects

	Overall		Men		Women	
	Men	Women	CAF	Not CAF	CAF	Not CAF
No. of patients	19	19	6 (31.6%)	13	3 (15.7%)	16
Age (years)	65 ± 10	76 ± 9**	67 ± 8	65 ± 11	78 ± 5	76 ± 10
BSA (m^2)	1.7 ± 0.1	1.5 ± 0.2**	1.7 ± 0.1	1.7 ± 0.1	1.3 ± 0.1	1.4 ± 0.1
Antiarrhythmic drugs	6 (32%)	6 (32%)	2 (33%)	4 (31%)	1 (33%)	5 (31%)
Cibenzoline	1	1	0	1	0	1
Pirmenol	2	2	1	1	1	1
Pilsicainide	3	3	1	2	0	3
None	13	13	4	9	2	11
ACE inhibitors	3	2	1	2	0	2
ARB	1	1	0	1	0	1
β-Blockers	1	1	1	0	1	0
Diuretics	2	1	1	1	0	1

Values are mean ± SD or n (%)
CAF, chronic atrial fibrillation; BSA, body surface area; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers
**$P < 0.01$ vs men. There were no significant differences between the patients with and without the transition to CAF in men and women

LV end-diastolic volume) or LV systolic function (LV ejection fraction) in both genders. Regarding pulsed-wave Doppler parameters of TMF, the peak E-wave velocity did not differ between patients with or without progression to CAF in both genders. However, in our relatively elderly patients (mean age: men, 65 ± 10 years, women, 76 ± 9 years), men and women who developed CAF had a significantly higher peak E/A velocity ratio of transmitral inflow such as "pseudonormalization pattern" (men: 1.45 ± 0.56 vs 0.97 ± 0.32, $P < 0.05$; women: 1.27 ± 0.25 vs 0.89 ± 0.23, $P < 0.05$) than those without CAF.

Regarding the pulsed-wave tissue Doppler parameters recorded at the mitral and tricuspid annulus, the peak E′(M), A′(M), E′(T), and A′(T) velocity and E/E′(M) ratio did not differ between patients with or without progression to CAF in both genders. However, with respect to interatrial

Table 2. Comparisons of echocardiographic parameters and interatrial dyssynchrony between the groups with and without progression to CAF

	Overall		Men		Women	
	Men	Women	CAF	Not CAF	CAF	Not CAF
No. of patients	19	19	6 (31.6%)	13	3 (15.7%)	16
LAD (mm)	44 ± 6	44 ± 7	44 ± 5	43 ± 6	51 ± 1	43 ± 7
LAV (ml)	108 ± 24	115 ± 33	114 ± 25	106 ± 24	138 ± 23	111 ± 34
LVDD (mm)	48 ± 5	48 ± 4	47 ± 5	49 ± 5	52 ± 1	47 ± 4
LVEDV (ml)	87 ± 22	68 ± 16**	78 ± 14	92 ± 24	66 ± 14	68 ± 16
LVEF (%)	63 ± 7	67 ± 7*	66 ± 5	61 ± 8	60 ± 1	68 ± 7
TMF						
E velocity (cm/s)	67 ± 16	70 ± 13	73 ± 8	65 ± 19	75 ± 1	69 ± 14
A velocity (cm/s)	65 ± 18	77 ± 19*	56 ± 22	69 ± 16	61 ± 12	80 ± 19
E/A ratio	1.12 ± 0.45	0.95 ± 0.27	1.44 ± 0.56†	0.97 ± 0.32	1.27 ± 0.25†	0.88 ± 0.22
TDI						
E′(M) velocity (cm/s)	9.9 ± 2.3	8.2 ± 2.2*	11.2 ± 1.8	9.3 ± 2.3	9.5 ± 1.5	8.0 ± 2.3
A′(M) velocity (cm/s)	10.3 ± 3.0	9.7 ± 3.0	8.0 ± 1.5	11.4 ± 2.9	7.0 ± 2.0	10.2 ± 2.9
E′(T) velocity (cm/s)	11.6 ± 3.0	10.9 ± 2.9	11.2 ± 2.9	11.8 ± 3.2	10.5 ± 3.5	10.9 ± 3.0
A′(T) velocity (cm/s)	15.5 ± 5.6	16.1 ± 4.5	11.8 ± 3.5	17.0 ± 5.7	15.5 ± 2.1	16.2 ± 4.8
E/E′(M) ratio	7.1 ± 2.1	9.4 ± 4.9	6.7 ± 1.3	7.4 ± 2.4	8.1 ± 1.3	9.6 ± 5.4
P–A′(T) interval (ms)	137 ± 26	137 ± 25	139 ± 36	136 ± 21	115 ± 35	141 ± 22
P–A′(M) interval (ms)	169 ± 32	166 ± 21	180 ± 39	163 ± 27	178 ± 38	164 ± 18
A′(M)–A′(T) interval (ms)	31 ± 13	29 ± 17	41 ± 10††	26 ± 11	64 ± 4††	23 ± 9

Values are mean ± SD
CAF, chronic atrial fibrillation; LAD, left atrial diameter; LAV, left atrial volume; LVDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; TMF, transmitral inflow; TDI, tissue Doppler imaging
* $P < 0.05$, ** $P < 0.01$ vs men. † $P < 0.05$, †† $P < 0.01$ vs not CAF

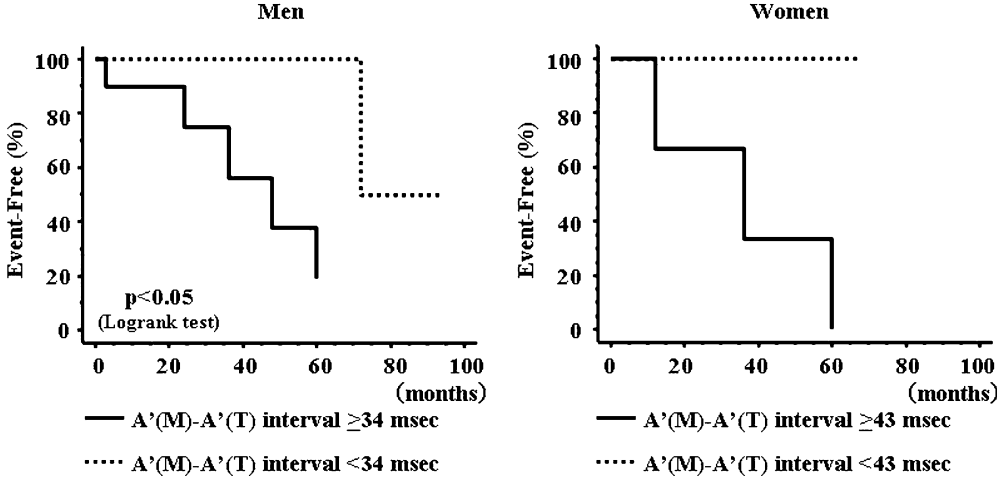

Fig. 2. Kaplan–Meier event-free curves for progression to chronic atrial fibrillation (CAF) in men and women based on interatrial dyssynchrony. Progression to CAF was more frequent when A′(M)–A′(T) interval was >34 ms in men ($P < 0.05$) and >43 ms in women

dyssynchrony, men and women with CAF had a significantly longer A′(M)–A′(T) interval than those without CAF (men: 41 ± 10 vs 27 ± 12 ms, $P < 0.01$; women: 64 ± 4 vs 23 ± 9 ms, $P < 0.01$). The A′(M)–A′(T) interval tended to correlate with the LA dimension in women (left atrial diameter: $r = 0.53$, $P < 0.05$; left atrial volume: $r = 0.44$, $P = 0.06$). Kaplan–Meier event-free curves for progression to CAF in men and women based on interatrial dyssynchrony are shown in Fig. 2. Kaplan–Meier analysis with the log-rank test, using cutoff values determined by analysis of receiver-operating characteristics curves, revealed that progression to CAF was more frequent when the A′(M)–A′(T) interval was >34 ms in men ($P < 0.05$) and >43 ms in women. Considering gender differences, cutoff values of A′(M)–A′(T) interval for predicting the progression to CAF were shorter in men than in women (34 vs 43 ms).

Discussion

Atrial fibrillation is the most common sustained arrhythmia, and the prevalence of AF is increasing with an increase in the size of the elderly population.[1,36] Atrial fibrillation may be paroxysmal or persistent and permanent, and it is well known that PAF often precedes the development of chronic (persistent or permanent) AF.[2,3] In this study, during an average follow-up period of 32 ± 26 months, 6 of 19 men (31.6%) developed CAF, and 3 of 19 women (15.7%) developed CAF during a follow-up period of 25 ± 19 months. The probability of progression to CAF (permanent AF) has been reported to be about 8.6% after 1 year, 21% after 2 years, and 24.7% after 5 years in PAF patients.[4,37] Considering that the prevalence of AF is higher in men than in

women,[26] our results are consistent with these probabilities.[4,37] In previous studies, several echocardiographic and electrocardiographic parameters (such as the left atrial dimension, pulsed-wave Doppler parameters of TMF and pulmonary venous flow, and P-wave parameters) were investigated as predictors of AF, but it still remains difficult to predict progression from PAF to CAF.[4–9]

In this study, men and women who developed CAF had a significantly higher peak E/A velocity ratio of transmitral inflow such as "pseudonormalization pattern" than those without CAF. The E/A ratio of TMF has been used as a surrogate marker of LA contractile function.[7,8] It has been reported that a "pseudorestrictive pattern" of the E/A ratio occurs as a result of functional impairment of the LA after AF develops.[7] These Doppler parameters of TMF, which reflect LA contractile function, were useful for predicting progression from PAF to CAF in both genders.[7,8] However, these Doppler parameters can be influenced by factors such as the heart rate, preload, and afterload, which limits their value as predictors.[1]

Atrial conduction delay is one of the important features of AF.[17] Recently, atrial electromechanical abnormalities caused by atrial conduction abnormalities have been reported as a risk factor for AF.[13–22,38] In this study, we used TDI to evaluate interatrial dyssynchrony, which was defined by the dispersion of right and left atrial electromechanical coupling. Men and women with CAF had prolonged interatrial dyssynchrony compared to those without CAF. Thus, we demonstrated for the first time that interatrial dyssynchrony is useful for predicting progression from PAF to CAF in both genders. Dispersion of interatrial electromechanical coupling has been reported in patients with PAF, mitral stenosis, scleroderma, and heart failure.[19,21,22,38] Cui et al. reported that the interatrial electromechanical delay was about 25 ms in patients with PAF, which is consistent with our results in the PAF men and women without CAF,[21] while men and women with CAF showed more prolonged interatrial electromechanical delay. Progression of interatrial conduction abnormalities may be associated with nonhomogeneity of atrial conduction and perpetuation of AF.[4,13–22,38]

Considering gender differences, the interatrial electromechanical delay tends to be shorter in CAF men than CAF women. Cutoff values of A′(M)–A′(T) interval for predicting the progression to CAF were shorter in men than in women (34 vs 43 ms), which might be associated with the vulnerability of AF in men.[13,25–28] Historically, gender difference was recognized in atrial remodeling after a second episode of atrial fibrillation, which may be the reason why the prevalence of atrial fibrillation is higher in men than in women.[27,28]

Previous studies have shown that prolonged right and left atrial electromechanical intervals also promote AF.[18–22,38] However, we could not find any significant differences of the P-A′(M) and P-A′(T) intervals between our patients with or without CAF in both genders. Our patients were relatively elderly, and both the P-A′(M) and P-A′(T) intervals were longer in the patients without CAF than were previously reported for patients with PAF.[18–22,38] This might have led to the lack of a difference in intra-atrial dyssynchrony.[21] Van Beeumen et al. evaluated intra-atrial and interatrial dyssynchrony in patients with heart failure by color tissue Doppler imaging.[38] Their method might evaluate interatrial dyssynchrony more precisely than our TDI method.[19,21,22,38] However, our method is simple, fast, and sufficiently reliable for clinical use.[19,21,22]

The LA dimension tended to be enlarged in men and women with CAF and it showed a positive correlation with interatrial electromechanical delay (A′(M)–A′(T)), but this association was not statistically significant. This suggests that interatrial dyssynchrony is not only explained by LA enlargement, but also by the time of dispersion from electrical activation in the atrium to atrial myocardial contraction.[39] Some authors have reported that the LA structural remodeling (i.e., altered atrial tissue architecture or interstitial fibrosis) is important for predicting the restoration of sinus rhythm.[7,40] Progressive histopathological changes that occur in AF, such as atrial fibrosis and loss of atrial muscle mass, may lead to nonhomogeneity of atrial conduction and perpetuation of AF.[4,41]

Atrial fibrillation was classified as paroxysmal or chronic AF in our study, according to the time when it was performed. Recently, AF has been classified as paroxysmal, persistent, and permanent, so using a different classification of AF is a limitation.[2] In addition, the exclusion criteria for the study limited our sample size and the number of patients who developed CAF. The A′(M)–A′(T) interval tended to be an independent predictor of CAF on multivariate Cox proportional hazard analysis, but this might not have been statistically significant because of our small CAF group. Our small sample size also limited the age-matched comparison for predicting CAF. Further prospective studies involving more patients are needed to address this subject. Another limitation was that we could not characterize the episodes of PAF (duration, frequency, and symptoms) before and after enrollment, factors that could also influence the development of CAF, and this could have been helpful to establish the influence of clinical parameters on echocardiographic findings.

In conclusion, this prospective study suggested that men and women with nonvalvular PAF at high risk for progression to CAF have "interatrial dyssynchrony" on atrial TDI, whose cutoff values were shorter and might affect the vulnerability of AF in men. Transthoracic echocardiography with TDI may be useful for identifying men and women with a high risk for progression from nonvalvular PAF to CAF, and has the advantages of being an inexpensive and accessible method. Our study provides a basis for further prospective trials involving larger numbers of men and women.

References

1. Nishimura RA, Abel MD, Hatle LK, Tajik AJ (1989) Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography. Part II. Clinical studies. Mayo Clin Proc 64:181–204

2. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Halperin JL, Hunt SA, Nishimura R, Ornato JP, Page RL, Riegel B, Priori SG, Blanc JJ, Budaj A, Camm AJ, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Tamargo JL, Zamorano JL; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; European Society of Cardiology Committee for Practice Guidelines; European Heart Rhythm Association; Heart Rhythm Society (2006) ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation 114: e257–e354
3. Jahangir A, Lee V, Friedman PA, Trusty JM, Hodge DO, Kopecky SL, Packer DL, Hammill SC, Shen WK, Gersh BJ (2007) Long-term progression and outcomes with aging in patients with lone atrial fibrillation: a 30-year follow-up study. Circulation 115: 3050–3056
4. Kerr CR, Humphries KH, Talajic M, Klein GJ, Connolly SJ, Green M, Boone J, Sheldon R, Dorian P, Newman D (2005) Progression to chronic atrial fibrillation after the initial diagnosis of paroxysmal atrial fibrillation: results from the Canadian Registry of Atrial Fibrillation. Am Heart J 149:489–496
5. Tsang TS, Gersh BJ, Appleton CP, Tajik AJ, Barnes ME, Bailey KR, Oh JK, Leibson C, Montgomery SC, Seward JB (2002) Left ventricular diastolic dysfunction as a predictor of the first diagnosed nonvalvular atrial fibrillation in 840 elderly men and women. J Am Coll Cardiol 40:1636–1644
6. Lindgren KS, Pekka Raatikainen MJ, Juhani Airaksinen KE, Huikuri HV (2003) Relationship between the frequency of paroxysmal episodes of atrial fibrillation and pulmonary venous flow pattern. Europace 5:17–23
7. Yamada H, Donal E, Kim YJ, Agler DA, Zhang Y, Greenberg NL, Mazgalev TN, Thomas JD, Grimm RA (2004) The pseudorestrictive pattern of transmitral Doppler flow pattern after conversion of atrial fibrillation to sinus rhythm: is atrial or ventricular dysfunction to blame? J Am Soc Echocardiogr 17:813–818
8. Verma A, Kilicaslan F, Adams JR, Hao S, Beheiry S, Minor S, Ozduran V, Claude Elayi S, Martin DO, Schweikert RA, Saliba W, Thomas JD, Garcia M, Klein A, Natale A (2006) Extensive ablation during pulmonary vein antrum isolation has no adverse impact on left atrial function: an echocardiography and cine computed tomography analysis. J Cardiovasc Electrophysiol 17:741–746
9. Fukunami M, Yamada T, Ohmori M, Kumagai K, Umemoto K, Sakai A, Kondoh N, Minamino T, Hoki N (1991) Detection of patients at risk for paroxysmal atrial fibrillation during sinus rhythm by P wave-triggered signal-averaged electrocardiogram. Circulation 83:162–169
10. Kiès P, Leclercq C, Bleeker GB, Crocq C, Molhoek SG, Poulain C, van Erven L, Bootsma M, Zeppenfeld K, van der Wall EE, Daubert JC, Schalij MJ, Bax JJ (2006) Cardiac resynchronization therapy in chronic atrial fibrillation: impact on left atrial size and reversal to sinus rhythm. Heart 92:490–494
11. Brodsky MA, Allen BJ, Capparelli EV, Luckett CR, Morton R, Henry WL (1989) Factors determining maintenance of sinus rhythm after chronic atrial fibrillation with left atrial dilatation. Am J Cardiol 63:1065–1068
12. Hakala T, Hedman A (2003) Predicting the risk of atrial fibrillation after coronary artery bypass surgery. Scand Cardiovasc J 37: 309–315
13. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG (1995) Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. Arch Intern Med 155:469–473
14. Fuenmayor AJ, Ramírez L, Fuenmayor AM (2002) Validation of inter-atrial conduction time measurement by means of echo-Doppler. Arch Cardiol Mex 72:125–128
15. Chen MC, Guo GB, Chang HW (2002) Atrial electrophysiological properties evaluated by right and left atrial pacing in patients with or without atrial fibrillation. Jpn Heart J 43:231–240
16. Rein AJ, O'Donnell CP, Colan SD, Marx GR (2003) Tissue velocity Doppler assessment of atrial and ventricular electromechanical coupling and atrioventricular time intervals in normal subjects. Am J Cardiol 92:1347–1350
17. Daubert JC, Pavin D, Jauvert G, Mabo P (2004) Intra- and inter-atrial conduction delay: implications for cardiac pacing. Pacing Clin Electrophysiol 27:507–525
18. Merckx KL, De Vos CB, Palmans A, Habets J, Cheriex EC, Crijns HJ, Tieleman RG (2005) Atrial activation time determined by transthoracic Doppler tissue imaging can be used as an estimate of the total duration of atrial electrical activation. J Am Soc Echocardiogr 18:940–944
19. Ozer N, Yavuz B, Can I, Atalar E, Aksöyek S, Ovünç K, Ozmen F, Kes S (2005) Doppler tissue evaluation of intra-atrial and inter-atrial electromechanical delay and comparison with P-wave dispersion in patients with mitral stenosis. J Am Soc Echocardiogr 18:945–948
20. Roshanali F, Mandegar MH, Yousefnia MA, Rayatzadeh H, Alaeddini F, Amouzadeh F (2007) Prediction of atrial fibrillation via atrial electromechanical interval after coronary artery bypass grafting. Circulation 116:2012–2017
21. Cui QQ, Zhang W, Wang H, Sun X, Wang R, Yang HY, Meng XQ, Zhang Y, Wang H (2008) Assessment of atrial electromechanical coupling and influential factors in nonrheumatic paroxysmal atrial fibrillation. Clin Cardiol 31:74–78
22. Can I, Onat AM, Aytemir K, Akdogan A, Ureten K, Kiraz S, Ertenli I, Ozer N, Tokgozoglu L, Oto A (2007) Assessment of atrial conduction in patients with scleroderma by tissue Doppler echocardiography and P wave dispersion. Cardiology 108:317–321
23. Garcia MJ, Rodriguez L, Ares M, Griffin BP, Klein AL, Stewart WJ, Thomas JD (1996) Myocardial wall velocity assessment by pulsed Doppler tissue imaging: characteristic findings in normal subjects. Am Heart J 132:648–656
24. Edvardsen T, Urheim S, Skulstad H, Steine K, Ihlen H, Smiseth OA (2002) Quantification of left ventricular systolic function by tissue Doppler echocardiography: added value of measuring pre- and postejection velocities in ischemic myocardium. Circulation 105: 2071–2077
25. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA (1994) Independent risk factors for atrial fibrillation in a population based cohort. The Framingham Heart Study. JAMA 271:840–844
26. Larsen JA, Kadish AH (1999) Effects of gender on cardiac arrhythmias. J Cardiovasc Electrophysiol 9:655–664
27. Tada H, Sticherling C, Chough SP, Baker RL, Wasmer K, Daoud EG, Oral H, Pelosi F Jr, Knight BP, Strickberger SA, Morady F (2001) Gender and age differences in induced atrial fibrillation. Am J Cardiol 88:436–438
28. Tse HF, Oral H, Pelosi F, Knight BP, Strickberger SA, Morady F (2001) Effect of gender on atrial electrophysiologic changes induced by rapid atrial pacing and elevation of atrial pressure. J Cardiovasc Electrophysiol 12:986–989
29. Khan IA (2003) Atrial stunning: basics and clinical considerations. Int J Cardiol 92:113–128
30. Henry WL, DeMaria A, Gramiak R, King DL, Kisslo JA, Popp RL, Sahn DJ, Schiller NB, Tajik A, Teichholz LE, Weyman AE (1980) Report of the American Society of Echocardiography Committee on nomenclature and standards in two-dimensional echocardiography. Circulation 62:212–217
31. Sahn DJ, DeMaria A, Kisslo J, Weyman A (1978) Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 58: 1072–1082
32. Severino S, Caso P, Galderisi M, De Simone L, Petrocelli A, de Divitiis O, Mininni N (1998) Use of pulsed Doppler tissue imaging to assess regional left ventricular diastolic dysfunction in hypertrophic cardiomyopathy. Am J Cardiol 82:1394–1398
33. Quinones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA (2002) Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force

of the Nomenclature and Standards Committee of the American Society of Echocardiography. J Am Soc Echocardiogr 15:167–184
34. Hirono K, Konishi T, Origasa H, Ichida F, Miyawaki T (2009) Echocardiographic and electrocardiographic analyses of patients with severe motor and intellectual disabilities. Heart Vessels 24: 46–53
35. Paraskevaidis IA, Theodorakis GN, Katritsis DG, Tsiapras DP, Livanis EG, Kremastinos DT (1999) Pulmonary vein flow analysis by transoesophageal echocardiography in patients with chronic atrial fibrillation; 1 year follow-up after cardioversion. Eur Heart J 20:375–385
36. Suzuki S, Yamashita T, Otsuka T, Sagara K, Uejima T, Oikawa Y, Yajima J, Koike A, Nagashima K, Kirigaya H, Ogasawara K, Sawada H, Yamazaki T, Aizawa T (2009) Treatment strategy and clinical outcome in Japanese patients with atrial fibrillation. Heart Vessels 24:287–293
37. Budeus M, Felix O, Hennersdorf M, Wieneke H, Erbel R, Sack S (2007) Prediction of conversion from paroxysmal to permanent atrial fibrillation. Pacing Clin Electrophysiol 30:243–252
38. Van Beeumen K, Duytschaever M, Tavernier R, Van de Veire N, De Sutter J (2007) Intra- and interatrial asynchrony in patients with heart failure. Am J Cardiol 99:79–83
39. Omi W, Nagai H, Takamura M, Okura S, Okajima M, Furusho H, Maruyama M, Sakagami S, Takata S, Kaneko S (2005) Doppler tissue analysis of atrial electromechanical coupling in paroxysmal atrial fibrillation. J Am Soc Echocardiogr 18:39–44
40. Fleg JL, Shapiro EP, O'Connor F, Taube J, Goldberg AP, Lakatta EG (1995) Left ventricular diastolic filling performance in older male athletes. JAMA 273:1371–1375
41. Allessie M, Ausma J, Schotten U (2002) Electrical, contractile and structural remodeling during atrial fibrillation. Cardiovasc Res 54:230–246