Original article

Altered trans-mitral flow velocity pattern after exercise predicts development of new-onset atrial fibrillation in elderly patients with impaired left ventricular relaxation at rest: Prognostic value of diastolic stress echocardiography

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Summary

Objective: This study attempted to determine whether exercise induced left ventricular (LV) diastolic dysfunction estimated by altered trans-mitral flow (TMF) velocity pattern after exercise is associated with increased risk of cardiac events including new-onset atrial fibrillation (AF) in elderly patients with impaired LV relaxation at rest.

Background: Diastolic stress echocardiography has been applied to evaluate LV diastolic function during and post-exercise. Prognostic importance of exercise-induced diastolic dysfunction remains uncertain.

Patients and methods: We studied 126 patients (70 ± 5 years; 70 males) who underwent treadmill stress echocardiography. Doppler measurements were done before exercise and immediately after the post-stress image acquisition, and the ratio between early (E) and atrial (A) TMF velocities was measured. Patients with impaired LV relaxation (E/A < 1.0) at rest were studied. Altered TMF velocity pattern was present when patients with E/A < 1.0 at rest developed E/A ≥ 1.0 after exercise.

Primary endpoints for follow-up were combination of major cardiac events and new-onset AF.

Results: There were 42 patients with altered TMF velocity pattern after exercise. During the 5-year follow-up period, there were 30 cardiac events including 13 new-onset AF. Kaplan–Meier

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both positive and negative ExE provide significant prognostic information [1–8].

Diastolic dysfunction has also been recognized as a predictor of clinical outcome. Diastolic dysfunction has been found to be associated with the development of atrial fibrillation (AF) and with cardiac events such as congestive heart failure (CHF), stroke, acute myocardial infarction (MI), and cardiac sudden death [9–15]. Assessment of diastolic function used to be performed at rest. Exertional dyspnea is a common symptom in elderly patients with hypertensive heart disease with preserved left ventricular (LV) ejection fraction (EF). Although elevated LV filling pressure is an important cause of exertional dyspnea in such patients, LV filling pressure is normal at rest and increases only with exertion [16]. Therefore, diastolic stress echocardiography has been utilized to evaluate diastolic function during exercise or post-exercise [17–21]. However, the prognostic importance of exercise-induced LV diastolic dysfunction in elderly patients is undefined.

The purpose of this study was to determine whether exercise-induced diastolic dysfunction estimated by altered trans-mitral flow (TMF) velocity pattern after exercise is associated with increased risk of cardiac events including new-onset AF in elderly patients with impaired LV relaxation at rest.

Methods

Study patients

From September 2001 to May 2004, 209 consecutive patients underwent clinically indicated ExE at Takagi Cardiology Clinic, Kyoto, Japan. Patients with unstable angina, decompensated CHF, or severe chronic obstructive pulmonary disease were not included. All patients were referred for ExE to evaluate known or suspected CAD, and the cause of exertional dyspnea. There were 38 patients with age <60 years. The remaining 171 elderly patients with age ≥60 years were recruited to the present study. We excluded 11 patients because of significant regional or global LV wall motion abnormality (WMA) at rest, 4 patients because of documented history of AF, 6 patients because of more than moderate valvular heart disease, 17 patients because of TMF velocity with early to atrial ratio (E/A ratio) ≥ 1.0 at rest. Finally, 133 elderly patients with impaired LV relaxation at rest were enrolled in the present study. All participants gave informed consent before the examinations.

Clinical variables, body mass index (=body weight (kg)/(height (m))²), and body surface area (m²) were recorded at the time of the treadmill stress echocardiography. Medical treatments and a history of hypertension, diabetes mellitus, lipid disorders, smoking, and CAD were abstracted from the medical record. CAD was defined as previous coronary revascularization or history of MI.

Treadmill stress echocardiography

All patients underwent maximum symptom limited treadmill exercise test by using the standard Bruce protocol or modified Bruce protocol (Fukuda Denshi Co. Ltd., Tokyo, Japan). Beta-blockers and other cardiovascular medication were withheld on the day of testing except for short-acting nitrates. A 12-lead electrocardiography (ECG) was recorded at baseline, every 3 min during the exercise, and every 2 min in recovery. Blood pressure was recorded at the same times as the 12-lead ECG recordings. End points for the treadmill exercise test were significant ST segment depression (≥2 mm in two continuous leads, measured 80 ms after the J point), intolerant symptoms of angina, achieving a target heart rate [=(220 – age) × 0.85 beats/min], systolic blood pressure ≥ 220 mmHg, or exhaustion. Maximal exercise tolerance was defined by the achieved metabolic equivalents (METS).

Two-dimensional echocardiography was performed using two commercially available ultrasound machines; SSA 350 with 2.5 MHz transducer (Toshiba, Tokyo, Japan), from September 2001 to December 2002, and Vivid FiVe with 2.5 MHz transducer (GE Health Care, Milwaukee, WI, USA), from January 2003 to May 2004. Echocardiographic images using standard apical four-chamber view, apical two-chamber view, and apical long-axis view were acquired at baseline and immediately after peak exercise. Immediate post-exercise images were obtained within 1 min after the termination of exercise. Several successive cardiac cycles were captured and stored in digital image memory. The most satisfactory immediate post-exercise images were selected and compared with the baseline images on a side-by-side quad-screen display using continuous cine loop.

Regional wall motion of the left ventricle was graded according to 16 segments model, in which 1 was considered normal or hyperdynamic, 2 was hypokinetic, 3 was akinetic and 4 was dyskinetic. Wall motion score index (WMSI) was obtained as the average of these segments. Development of new LVWMA was considered as a marker of exercise-induced
myocardial ischemia. As we have previously reported, the sensitivity, specificity, and diagnostic accuracy of the conventional treadmill stress echocardiography for detecting patients with CAD are 87%, 80%, and 84%, respectively, in our clinic [22].

The baseline resting assessment included standard two-dimensional measurements of LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LV end-diastolic dimension (LVED), intraventricular septal thickness (IVS), LV posterior wall thickness (LVPW), and left atrial dimension (LAD). LV volumes were measured using biplane modified Simpson’s method and LVEF was calculated. LAD was normalized for body surface area to obtain LAD index (LADI). LV mass was calculated using the American Society of Echocardiography formula [23] and normalized for body surface area to obtain LV mass index (LVMII).

**Pulsed-wave Doppler echocardiography**

Using above mentioned ultrasound machines, pulsed-wave Doppler echocardiography was performed at baseline and after the treadmill stress subsequently to the acquisition of the two-dimensional echocardiogram. The TMF velocity profile was recorded in the apical four-chamber view or apical long-axis view with the sample volume positioned at the level of the mitral valve tips in diastole. The early (E) and atrial (A) TMF velocities, and deceleration time of early LV filling (E-dct) were measured and averaged over 3 consecutive cardiac cycles. Post-stress Doppler measurements were performed in early recovery following the post-exercise two-dimensional image acquisition (within 3 min of cessation of exercise) at the earliest time that the E and A velocities were sufficiently separated to permit measurement. From TMF velocity profile, diastolic dysfunction was graded as impaired LV relaxation (E/A ratio < 1.0) and elevated LV filling (E/A ratio > 1.0). Because the assessment of E-dct is challenging at high heart rate after exercise, the grading was based only on the E/A ratio. Patients were assigned into 2 groups as shown in Fig. 1, patients with altered TMF velocity pattern after exercise who developed elevated LV filling (E/A ratio > 1.0) after treadmill stress, and patients without altered TMF velocity pattern who remained with impaired LV relaxation (E/A ratio < 1.0) after treadmill stress.

**Patient follow-up**

The follow-up period was initiated on the day of ExE, and serial follow-up was obtained in all patients. Follow-up data were obtained by review of medical records. The primary endpoints for this study were major adverse cardiac events (MACE) such as cardiac death, non-fatal MI, and stroke, cardiac hospitalization (CHF and coronary revascularization) and new-onset AF. We included late coronary revascularization for worsening symptoms at least 3 months after the ExE. Revascularization before 3 months was attributed to the ExE result and not considered as endpoints. New-onset AF was defined by the first presentation of AF that was clinically documented by a physician. The list of patients with the outcome event based on clinical documentation was cross-referenced with the ECG database (Fukuda Denshi Co. Ltd.). All cases of AF had to be confirmed by ECG, and AF was
P-wave

The first 10 regression analysis on the graphic WMA, the variables were investigated to be statistically significant. Differences in categorical variables between two groups were assessed using Fisher's exact test. Differences in continuous variables between two groups were analyzed by Student's t-test. A p-value less than 0.05 was considered to be statistically significant.

Kaplan–Meier event-free survival analysis with log-rank test was used for graphic display of relationships of exercise-induced myocardial ischemia and diastolic dysfunction to the first cardiac events. For the event-free survival analysis, the patients with non-cardiac death were censored at the time of death but not included as cardiac death.

The association of clinical, exercise, and echocardiographic variables with time to first cardiac event was investigated with multivariate Cox proportional hazards regression analysis. Variables selected for entry into multivariate analysis were those with p < 0.10 on Cox univariate analysis. Despite having univariate p > 0.10, LVEF, LADI, WMA, and exercise capacity (METs) were forced to multivariate analysis, because they are reported as important variables pertinent to cardiac outcome.

All analyses were performed using Stat View J-5.0 (SAS Institute, Inc., Cary, NC, USA).

### Table 1: Comparison of patient characteristics and treatments between two groups.

<table>
<thead>
<tr>
<th></th>
<th>Patients with altered TMF after exercise n = 42</th>
<th>Patients w/o altered TMF after exercise n = 84</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>71 ± 5</td>
<td>70 ± 5</td>
<td>0.1736</td>
</tr>
<tr>
<td><strong>Male (%)</strong></td>
<td>26 (62%)</td>
<td>44 (52%)</td>
<td>0.3459</td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td>23.2 ± 2.8</td>
<td>23.8 ± 2.8</td>
<td>0.2838</td>
</tr>
<tr>
<td><strong>Body surface area (m²)</strong></td>
<td>1.62 ± 0.17</td>
<td>1.61 ± 0.16</td>
<td>0.7780</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>40 (95%)</td>
<td>72 (86%)</td>
<td>0.1392</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>22 (52%)</td>
<td>43 (51%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>12 (29%)</td>
<td>25 (30%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>3 (8%)</td>
<td>8 (10%)</td>
<td>0.7505</td>
</tr>
<tr>
<td>History of CAD (%)</td>
<td>15 (36%)</td>
<td>22 (26%)</td>
<td>0.3028</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI and/or ARB</td>
<td>16 (38%)</td>
<td>30 (36%)</td>
<td>0.8456</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>29 (69%)</td>
<td>47 (56%)</td>
<td>0.1799</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>23 (55%)</td>
<td>26 (31%)</td>
<td>0.0121</td>
</tr>
<tr>
<td>Diuretics</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>4 (10%)</td>
<td>2 (2%)</td>
<td>0.0948</td>
</tr>
<tr>
<td>Nicorandil</td>
<td>11 (26%)</td>
<td>10 (12%)</td>
<td>0.0734</td>
</tr>
<tr>
<td>Nitrate</td>
<td>8 (19%)</td>
<td>11 (13%)</td>
<td>0.4320</td>
</tr>
<tr>
<td>Aspirin</td>
<td>25 (59%)</td>
<td>39 (46%)</td>
<td>0.1890</td>
</tr>
<tr>
<td>Statins</td>
<td>18 (43%)</td>
<td>29 (35%)</td>
<td>0.4353</td>
</tr>
<tr>
<td>Anti-diabetic agents</td>
<td>7 (17%)</td>
<td>10 (12%)</td>
<td>0.5819</td>
</tr>
</tbody>
</table>

TMF, trans-mitral flow; CAD, coronary artery disease; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

defined as an episode of irregular rhythm with no visible P-wave on the documented ECG recording lasting more than 10 s.

### Statistical analysis

Categorical variables are expressed as absolute value and percentage (%). Continuous variables are reported as the mean value ± standard deviation (SD).

Differences in categorical variables between two groups were assessed using Fisher's exact test. Differences in continuous variables between two groups were analyzed by Student's t-test. A p-value less than 0.05 was considered to be statistically significant.

Kaplan–Meier event-free survival analysis with log-rank test was used for graphic display of relationships of exercise-induced myocardial ischemia and diastolic dysfunction to the first cardiac events. For the event-free survival analysis, the patients with non-cardiac death were censored at the time of death but not included as cardiac death.

The association of clinical, exercise, and echocardiographic variables with time to first cardiac event was investigated with multivariate Cox proportional hazards regression analysis. Variables selected for entry into multivariate analysis were those with p < 0.10 on Cox univariate analysis. Despite having univariate p > 0.10, LVEF, LADI, WMA, and exercise capacity (METs) were forced to multivariate analysis, because they are reported as important variables pertinent to cardiac outcome.

All analyses were performed using Stat View J-5.0 (SAS Institute, Inc., Cary, NC, USA).

### Results

A total of 126 of the 133 patients (95%) completed 5 years of follow-up. A measurement of post-exercise E/A ratio was feasible in all patients. There were 42 patients (33.3%) with altered TMF velocity pattern after exercise, and 84 patients (66.7%) without altered TMF velocity pattern after exercise, respectively.

### Patient characteristics

Clinical characteristics of the study patients in two groups are shown in Table 1. There were no significant differences between the two groups in age, gender, body size, and coronary risk factors. There were no significant differences between the two groups in the medical treatments at the time of ExE, except usage of beta-blockers was much more frequent in patients with altered TMF velocity pattern after exercise.

### Treadmill stress

Hemodynamic variables during treadmill stress are shown in Table 2. Maximal exercise tolerance defined by the achieved METs was reduced in patients with altered TMF velocity pattern after exercise. Heart rate, systolic blood pressure, and double products at peak stress were significantly smaller in patients with altered TMF velocity pattern after exercise.
Resting and post-stress echocardiographic variables are shown in Table 2.

There were no significant differences between the two groups in LV volumes, LVEF, LVMi, and LADI. E/A ratio at rest was significantly greater in patients with altered TMF velocity pattern after exercise, and E-dct at rest was significantly shorter in patients with altered TMF velocity pattern after exercise. There were no significant differences between the two groups in WMSi at rest and post-exercise. Incidence of inducible myocardial ischemia was equivalent in the two groups.

Outcomes

During the 5-year follow-up period, 30 cardiac events occurred (Table 3). As shown in Fig. 2, altered TMF velocity pattern after exercise was associated with increased risk of total cardiac events \((p<0.0001)\), however, inducible myocardial ischemia was not associated with increased risk of total cardiac events \((p=0.1395)\). As shown in Fig. 3, altered TMF velocity pattern after exercise was associated with late coronary revascularization \((p=0.0204)\) and new-onset AF \((p=0.0003)\). Exercise-induced myocardial ischemia was also associated with increased risk of late coronary revascularization \((p=0.0010)\); however, inducible myocardial ischemia was not associated with increased risk of new-onset AF \((p=0.0896)\).

As shown in Fig. 4, patients with both altered TMF velocity pattern after exercise and inducible myocardial ischemia had the most unfavorable prognosis. Patients with isolated altered TMF velocity pattern after exercise also had unfavorable prognosis.

As shown in Table 4, univariate Cox proportional hazards regression analysis demonstrated that, higher age, male gender, history of CAD, greater LVMi, and altered TMF velocity pattern after exercise were associated with increased risk of total cardiac events. Conversely, usage of angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, beta-blocker, nicorandil, and aspirin were associated with reduction of the cardiac events. Multivariate Cox proportional hazards regression analysis demonstrated that altered TMF velocity pattern after exercise was the best predictor of cardiac events including new-onset AF. Multivariate analysis also demonstrated that usage of aspirin was associated with reduction of cardiac events.

Discussion

This retrospective observational study has demonstrated that new-onset AF developed significantly more frequently in patients with exercise-induced diastolic dysfunction estimated by altered TMF velocity pattern after exercise, which is in accord with previous studies on diastolic dysfunction at rest and risk of AF [9–11,15].
Table 3  Cardiac events during five years follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Patients with altered TMF after exercise</th>
<th>Patients w/o altered TMF after exercise</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cardiac events</td>
<td>20 (48%)</td>
<td>10 (12%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sudden death + MI</td>
<td>3 (7%)</td>
<td>2 (2%)</td>
<td>0.3323</td>
</tr>
<tr>
<td>Sudden death</td>
<td>2 (5%)</td>
<td>0 (0%)</td>
<td>0.1093</td>
</tr>
<tr>
<td>MI</td>
<td>1 (2%)</td>
<td>2 (2%)</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Late PCI</td>
<td>7 (17%)</td>
<td>4 (5%)</td>
<td>0.0411</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>10 (24%)</td>
<td>3 (4%)</td>
<td>0.0009</td>
</tr>
<tr>
<td>CRT</td>
<td>0 (0%)</td>
<td>1 (1%)</td>
<td>&gt;0.9999</td>
</tr>
</tbody>
</table>

TMF, trans-mitral flow; MI, myocardial infarction; PCI, percutaneous coronary intervention; CRT, cardiac resynchronization therapy.

Assessment of elevated left ventricular filling pressure

For the purpose of present study, the definition of elevated LV filling was based only on the E/A ratio and therefore too simplistic. The E/A ratio ≥ 1.0 was graded as elevated LV filling, which is thought to consist of pseudo-normal filling and restrictive filling. However, differentiation of pseudonormal from normal filling is a significant problem of TMF velocity assessment, especially in patients with preserved LV systolic function. The group of patients with E/A ratio ≥ 1.0 may include patients with high filling pressure and also some normal subjects. To solve this problem, the ratio of trans-mitral E to peak early diastolic mitral annular velocity (E') assessed by tissue Doppler imaging has been widely utilized at rest [12–15] and during exercise or post-exercise [17–21]. Unfortunately, however, we did not do routine E'/E assessment at the time of the present study. And not using E'/E was the major limitation of the present study. To minimize this problem, we excluded patients with E/A ratio ≥ 1.0 at rest. We hypothesized that patients with altered TMF velocity pattern after exercise (E/A < 1.0 at rest, E/A ≥ 1.0 after exercise) had worse diastolic function than patients who remained with impaired LV relaxation after exercise (E/A < 1.0 at rest, E/A < 1.0 after exercise). It has been reported that there was a significant increase in TMF E and A velocities during exercise, and because of proportional increases in these values, E/A ratio was unchanged during exercise in middle-aged healthy subjects [24]. Peteiro et al. have demonstrated that patients with altered TMF velocity pattern after exercise (E/A < 1.0 at rest, E/A ≥ 1.0 after exercise) had the highest E/E' values after exercise [25]. However, they reported that the sensitivity of TMF velocity pattern assessment for detection of exercise-induced elevated LV filling was lower than that of E/E'. Therefore, there is some possibility of underestimating the presence of exercise-induced elevated LV filling in our study.

It has been reported that left atrial (LA) size reflects the chronicity and magnitude of elevated LV filling pressure and provides significant prognostic value. Bangalore et al. reported that enlarged LA defined as LADI ≥ 2.4 cm/m² was a significant predictor of cardiac events independent of LV systolic function and myocardial ischemia [26]. In the present study, however, LADI did not provide significant prognostic value. Relatively small LADI (2.2 ± 0.3 cm/m² in patients with altered TMF velocity pattern after exercise and 2.1 ± 0.3 cm/m² in patients without altered TMF velocity pattern after exercise, respectively) in the present study is thought to be a reason for the discrepancy between the two studies. Because we measured LADI, not LA volume index in this study, there is some possibility of underestimating the prognostic value of LA size [27,28].

Figure 2  Kaplan–Meier survival curves showing the prognosis associated with the altered trans-mitral flow (TMF) velocity pattern after exercise (left) and inducible myocardial ischemia (right). Altered TMF velocity pattern after exercise is associated with increased risk of the total cardiac events including new-onset atrial fibrillation, however, inducible myocardial ischemia was not associated with increased risk of the total cardiac events. WMA, wall motion abnormality.
Exercise-induced diastolic dysfunction predicts new-onset atrial fibrillation in elderly patients

Myocardial ischemia and left ventricular filling pressure

It has been reported that exercise-induced myocardial ischemia could influence LV filling pattern. Presti et al. reported that E/A ratio was increased from rest to post-exercise in patients with inducible myocardial ischemia [29]. In the present study, prevalence of patients with exercise-induced LV WMA was equivalent in the two groups (Table 2). We did not find significant difference in post-exercise E/A value between patients with inducible myocardial ischemia and patients without it (post

Figure 3  Kaplan–Meier survival curves showing the prognosis associated with the altered trans-mitral (TMF) velocity pattern after exercise (left) and inducible myocardial ischemia (right). Both parameters are not associated with increased risk of sudden death or myocardial infarction (top panels). Altered TMF velocity pattern after exercise is associated with increased risk of late coronary revascularization (left middle) and new-onset atrial fibrillation (left bottom). Inducible myocardial ischemia was also associated with increased risk of late coronary revascularization (right middle), however, inducible myocardial ischemia was not associated with increased occurrence of new-onset AF (right bottom). WMA, wall motion abnormality.

Figure 4  Kaplan–Meier survival curves depicting the prognosis associated with the 4 groups of classification based on altered trans-mitral flow (TMF) velocity pattern after exercise and inducible ischemia. Patients with both altered TMF velocity pattern after exercise and inducible myocardial ischemia had most unfavorable prognosis (closed circle). Patients with isolated altered TMF velocity pattern after exercise also had unfavorable prognosis (open circle). WMA, wall motion abnormality.
exercise E/A was 0.95 ± 0.29 in patients with new LVWMA and 0.98 ± 0.33 in patients without new LVWMA, respectively, \( p = 0.6386 \). Because the study patients were older in the present study, contribution of exercise-induced diastolic dysfunction without myocardial ischemia might be greater.

Recently, Holland et al. have reported that exercise E/E' > 14.5 is associated with cardiovascular hospitalization, independent of and incremental to inducible ischemia [30]. They demonstrated that prognosis was similar in patients with isolated raised exercise E/E’ and those with ischemia and normal E/E’. Similarly, patients with isolated altered TMF’ velocity pattern after exercise had unfavorable prognosis in this study (Fig. 4). Holland reported that 90% of the cardiac events were coronary events, however, in the present study, coronary events were only half of the cardiac events, and most of the remaining events were new-onset AF. Difference in the patients’ age between the two studies may be the reason of this discrepancy. Nevertheless, the present study is unique in demonstrating the independent prognostic value of altered TMF’ velocity pattern for predicting new-onset AF in elderly patients with impaired LV relaxation at rest.

### Study limitations

Because this is a study from a single institution, and a relatively small study, the results should be interpreted carefully. Further studies are necessary for evaluating prognostic value of the exercise-induced diastolic dysfunction.

A physician was present to encourage maximal exercise, however, sub-maximal exercise in elderly patients with musculoskeletal problems may be associated with inadequate measurement of post-exercise E/A value. Different exercise stress, such as bicycle stress may attenuate this limitation.

Although the authors are experienced with stress echocardiography, altered TMF’ velocity pattern after exercise can be an expression of myocardial ischemia, not detected by conventional visual wall motion assessment [22,31]. Further studies using new techniques such as strain assessment are required to test this hypothesis.

Baseline E/A ratio was significantly greater in patients with altered TMF’ velocity after exercise, and more close to 1 in this study. Therefore, there was some possibility that these patients had more impaired diastolic function compared to patients without altered TMF. However,
differentiation of these patients is a significant problem of TMF velocity assessment as discussed previously. Utilizing E' or E/E' may allow differentiation of patients with relatively more impaired diastolic function from patients with relatively less impaired diastolic function at baseline.

Finally, although patients were carefully followed up, it cannot be ruled out that some of those who were classified as having stable sinus rhythm had episodes of undocumented AF. A recent study using implantable cardiac monitor in post MI patients with LV systolic dysfunction demonstrated a much higher incidence of AF [15] than previous studies using conventional ECG at clinical follow-ups to diagnose AF. However, it is difficult to use implantable cardiac monitor in patients with normal LV systolic function and no history of syncope attack as we studied.

Clinical implications

AF is the most common form of cardiac arrhythmia in clinical practice, and its prevalence increases over time as the population ages [32].

Although new-onset AF is not acutely life-threatening, increased risk of heart failure and stroke associated with AF cause severe morbidity and mortality, especially among the elderly people in the community.

Over several years, primary and secondary prevention of AF have become subject to intense investigation, due to its clinical importance. As shown in this study, patients with altered TMF velocity pattern after exercise have a significant risk of new-onset AF. Therefore, these patients should be considered as candidates for the prospective study to evaluate whether intensive medical treatments can reduce new-onset AF in elderly hypertensive patients.

Conclusion

In elderly patients with impaired LV relaxation (E/A < 1.0) at rest, one third of the patients developed E/A ≥ 1.0 after treadmill stress. This altered TMF velocity pattern after exercise is associated with increased risk of cardiac events including new-onset AF independent of inducible myocardial ischemia.

Conflict of interest

None.

References


