A Two-step Exercise Test Helps Evaluate the Ventricular Rate Control in Rheumatic Atrial Fibrillation

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Abstract

Background: Rheumatic heart disease is a common cause of atrial fibrillation (AF) in Thailand. Ventricular rate control is an important aspect of the management of rheumatic AF. The criteria for rate control in AF have not been well defined. Adequate rate control was determined by the results of the initial resting heart rate (HR), a standard six-minute walk test or 24-hour ambulatory Holter monitoring. The six-minute walk test and 24-hour ambulatory Holter monitoring have limitations of inconvenience and relatively high costs in the outpatient setting.

Objective: We sought to develop a simple method (two-step exercise test) for evaluating the ventricular rate control in rheumatic AF.

Methods: We studied 21 patients with chronic rheumatic AF. All of them were treated with AV nodal blocking drugs. Each patient was evaluated at baseline for resting HR and blood pressure before a two-step exercise test and a six-minute walk test were performed. The results of these tests were compared to determine rate control during exercise. A 24-hour ambulatory electrocardiogram was obtained to assess the adequacy of ventricular rate control during daily activities.

Results: The two-step exercise test was successfully performed and completed in all patients. A significant correlation was found between the two-step exercise HR and maximal HR during the six-minute walk test ($r = 0.748$, $p < 0.001$, intraclass correlation coefficient $= 0.838$, 95% confidence interval 0.601-0.934). A correlation was also found between the two-step exercise HR and waking-time mean HR ($r = 0.471$, $p = 0.03$).

Conclusions: The two-step exercise test appears to be clinically useful for evaluating the ventricular rate control in rheumatic AF. It is simple and inexpensive and also represents ordinary activity levels similar to the six-minute walk. Exercise HR obtained from the two-step exercise test correlates well with those obtained from the six-minute walk test. Thus, it can be considered as an alternative test to assess the efficacy of ventricular rate control in patients with rheumatic AF.

Key words: Exercise test, Ventricular rate, rheumatic Atrial fibrillation.

Several clinical trials (5-7) comparing the strategies of rhythm control with rate control for AF, as well as meta-analyses (8,9) have shown no significant differences between the two strategies with respect to mortality, major bleeding, and thromboembolic events. A non-significant trend was observed for excess mortality with a rhythm control strategy in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) trial (5). For functional endpoints, three trials have shown some improvement in exercise capacity in the rhythm control group (5-7). The Pharmacological Intervention in Atrial Fibrillation (PIAF) study found no difference in quality of life and symptoms between the rate control strategy and the rhythm control strategy. Those patients on the rhythm control strategy performed better in the six-minute walk test (6).
The issue of rate versus rhythm control has not been critically evaluated in the setting of RHD, and it has been a common belief among clinicians that AF in these patients with fibrosed atria may not be amenable to conversion and sinus rhythm maintenance. Furthermore, whether sinus rhythm improves clinical outcomes in RHD remain questionable.

Ventricular rate control is an important aspect for the management of rheumatic AF. It can improve symptoms, exercise capacity, and cardiac function (6,10,11). In patients with AF, the ventricular rate may accelerate excessively during exercise even when it is well controlled at rest (12). Exercise accelerated HR can further decrease the ventricular filling time resulting in heart failure in some patients. However, the best criteria for rate control in AF, as of yet, have not been well defined. The definition of adequate rate control has been based primarily on short-term hemodynamic benefits. The optimal resting HR has been proposed to be 60-80 bpm (13), and 90-115 bpm with moderate exercise (14). Effectiveness criteria used in the AFFIRM study are based on a consensus of what was considered to be reasonable. The AFFIRM definition of adequate ventricular rate control included an average HR at rest less than 80 bpm and either a maximum HR during a six-minute walk test less than 110 bpm, or an average HR during a 24-hour ambulatory Holter monitoring (ECG) less than 100 bpm (at least 18 h of interpretable monitoring) and no HR > 110% maximum predicted age-adjusted exercise HR (15).

The Master’s two-step exercise test has decreased in popularity. However, it is well known worldwide and is inexpensive. The workload in the Master’s two-step exercise test approximates the daily physiological workload and is similar to the six-minute walk test. It is useful for clinical assessment of the capacity for physical activity of patients with chronic heart failure (16).

Adequate ventricular rate control at rest does not always translate into effective control during activity. The 24–h Holter monitoring or six-minute walk test in the outpatient setting has limitations. This is the first study to investigate a simple method, the two-step exercise test in assessing the adequacy of ventricular rate control during exercise in patients with rheumatic AF. The objective was to study the correlation between the two-step exercise HR, maximal HR during a six-minute walk test, and waking-time mean HR from 24-hour Holter monitoring.

**Methods**

All patients with RHD with AF, were selected from the outpatient section of King Chulalongkorn Memorial Hospital. Patients were eligible to enter into the study if they had had another ECG done at least 3 months earlier that also showed the presence of AF. All patients were treated with AV nodal blocking drugs. Exclusion criteria were patients with hemodynamic compromise necessitating surgery or balloon valvulotomy, valvular surgery or balloon valvulotomy in the previous 2 months, pregnancy, and physical inability to perform the two-step exercise test.

We conducted a cross-sectional descriptive study in 21 patients with rheumatic AF. After enrollment, patients had to take the AV nodal blocking drugs for 2 weeks before the tests and were instructed not to consume xanthine containing products, sympathomimetic drugs, or tobacco for 24 hours before the tests. Each patient had a physical examination and was evaluated for resting HR and BP at baseline. Instruction for the two-step exercise test was given to all patients. Patients were required to walk up and over a device that consisted of three steps; two steps were 7 inches above the floor separated by a top step 14 inches high. One trip consists of walking up, over and down the device. The patients turned and repeated the procedure for 90 seconds. The two-step exercise test and six-minute walk test were performed under a AV nodal blocking drug effect. After both tests, maximal dyspnea was self-rated using a score in the range of 0-10 according to the visual analog Borg scale.(17) ECG was continuously monitored. The tests and measurements were taken after > 10 minutes at rest. HR was recorded immediately, and at 2, 4, 6 minutes after the two-step exercise test. 24-h Holter monitoring was obtained after the two-step exercise test in order to record HR during the six-minute walk test and then patients returned to their normal daily activities.

All data are presented as mean ± standard deviation (SD). The correlation between the two-step exercise HR, maximal HR during the six-minute walk test, and waking-time mean HR from the 24-hour Holter monitoring were examined by the Pearson’s correlation coefficient method. To compare the effect of different treatments on mean
HR from 24-h Holter monitoring, an unpaired t-test was used. A p-value < 0.05 was considered statistically significant. SPSS for windows (version 13) statistical package was used for data analysis.

Results
A total of 21 selected patients who consented to participate in the study were recruited. There were 16 women and 5 men, with a mean age of 48.6 years (range 32-68 years). All patients were in New York Heart Association (NYHA) functional class I or II, and had rheumatic mitral valve disease. There were 4 patients with mild mitral stenosis, 13 patients with moderate mitral stenosis, and 4 patients with a prosthetic mitral valve. The mean left atrial dimension was 5.1 cm (SD 0.7, range 4.4-7.3) and the mean left ventricular ejection fraction (LVEF) was 56.6 ± 9.0%. All patients were treated with AV nodal blocking drugs, including digoxin alone (n = 7), a combination of digoxin and beta-blocker (n = 6), a beta-blocker alone (n = 7), and a combination of digoxin and diltiazem (n = 1). Table 1 shows baseline patient characteristics. All patients were able to perform the two-step exercise test for 90 seconds. The mean step was 20.1 ± 3.5 trips. The Borg score ranged from 2-7 (median 3, mean 3.3 ± 1.2). There was a correlation between the two-step exercise Borg score and six-minute walk Borg score (r = 0.676, p = 0.001). A strong correlation was observed between the two-step exercise HR and the maximal HR during the six-minute walk test with r = 0.748 and p < 0.001. The intraclass correlation coefficient was 0.838 with 95% confidence interval (CI) 0.601-0.934 (Figure 1). The two-step exercise HR and waking-time mean HR also had some degree of significant correlation (r = 0.471, p = 0.03).

Results from 24-hour Holter monitoring showed that all patients had a 24-hour average HR lower than 90 bpm. Eighteen of 21 patients (86%) had adequate ventricular rate control following the AFFIRM definition. There were no significant differences of 24-hour mean HR, waking-time mean HR, and sleep-time mean HR in patients receiving a beta-blocker compared to those who did not receive a beta-blocker (Table 2).

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Variables</th>
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<tr>
<td>Number</td>
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<tr>
<td>Mean age (year)</td>
<td>48.6 (32-68)</td>
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<tr>
<td>Gender (Male : Female)</td>
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<tr>
<td>NYHA functional class</td>
<td></td>
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<tr>
<td>I</td>
<td>9</td>
</tr>
<tr>
<td>II</td>
<td>12</td>
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<tr>
<td>Prosthesis</td>
<td>4</td>
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<tr>
<td>LA dimension (cm)</td>
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<tr>
<td>LVEF (%)</td>
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<tr>
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<td>Digoxin and diltiazem</td>
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</tr>
</tbody>
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MS = mitral stenosis; LVEF = Left ventricular Ejection Fraction
Figure 1. Relation between the post two-step exercise HR and maximal HR during a six-minute walk test (6MWT)

Table 2. Comparison of ventricular rate variation on 24 h-Holter monitoring

<table>
<thead>
<tr>
<th></th>
<th>Regimen with beta-blocker (n=13)</th>
<th>Regimen without beta-blocker (n=8)</th>
<th>P-value</th>
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<tr>
<td>24 h-mean HR</td>
<td>70.1 ± 9.7</td>
<td>73.9 ± 6.9</td>
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<tr>
<td>Awake-time mean HR</td>
<td>75.2 ± 10.7</td>
<td>81.6 ± 9.1</td>
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<tr>
<td>Sleep-time mean HR</td>
<td>61.0 ± 9.0</td>
<td>60.6 ± 6.5</td>
<td>0.91</td>
</tr>
</tbody>
</table>

Discussion

What might constitute an “adequate” ventricular rate control in all patients with AF remains undefined. It’s not known whether indices of adequate control should now include patterns of change in the circadian rhythmicity of ventricular rate, mean HR from 24-hour Holter recordings or a defined reduction in the peak HR during a standardized exercise test.

Current guidelines state that in patients who experience symptoms related to AF during activity, the adequacy of HR control should be assessed during exercise, adjusting pharmacological treatment as necessary, to keep the rate in the physiological range (18). The present study indicates that the two-step exercise test can assess ventricular rate control during exercise in patients with rheumatic AF and provide results that strongly correlate with those obtained from the six-minute walk test. Thus, it may be most suitable for serial monitoring. The workload in the two-step exercise test has been shown to represent ordinary activity level, similar to the six-minute walk test. The six-minute walk test requires a large corridor and a longer testing time. Moreover, 24-h Holter monitoring is relatively inconvenient and costly. The two-step exercise test has the advantage of being inexpensive and simple to perform, particularly in the outpatient setting. In our study, we used 2 pieces of a two-step ladder which was available at the outpatient department to construct the two-step exercise device. The measurement of HR by ECG monitoring can be inconvenient. A stethoscope for listening to the HR immediately after the exercise test is recommended.

Interestingly, all patients had a reduction in HR of greater than 20% within 2 minutes after the two-step exercise test, suggesting that all patients were effectively treated with AV nodal blocking agents. Marked bradycardia or pauses were absent in all patients. Our observations in patients with rheumatic AF from this study are in contrast to those from previous studies (15,19, 20). Digoxin alone, even in a low dose, was able to control HR with the same efficacy as that obtained from a beta-blocker regimen, indicating that the effect of augmented vagal tone is important for ventricular rate control. In addition, patients in this study were in NYHA functional class I or II. Therefore their catecholamine states might not be high. However, this study was not designed as a treatment trial. There was no plasma drug level data. Thus, we did not make it for the final conclusion about the effect of digoxin. It might be a new data for further investigation.

Study limitations

All patients were in NYHA functional class I or II with rheumatic MS and were able to complete the two-step exercise test for 90 seconds. This may not be applicable to patients with a poorer functional class. Rapid ventricular response of AF more adversely affects the hemodynamics...
in MS than other valvular heart diseases. The exercise protocol should be validated for other rheumatic valvular heart diseases. The different speeds of exercise may impact the workload, however, the mean step was 20.1 ± 3.5 trips, indicating all patients had similar levels of speed.

Conclusions
The two-step exercise test appears to be clinically useful for evaluating the ventricular rate control in rheumatic AF. It is simple and inexpensive and also represents ordinary activity levels, similar to the six-minute walk. Exercise HR obtained from the two-step exercise test correlates well with those obtained from the six-minute walk test. Thus, it can be considered as an alternative test to assess the efficacy of ventricular rate control in patients with rheumatic AF.

Acknowledgement
The authors acknowledge Dr. Wacin Buddhari for many helpful comments on an earlier draft of the paper.

References
การออกกำลังกายโดยใช้บันไดสองขั้นเพื่อประเมินความสามารถควบคุมการเต้นของหัวใจในผู้ป่วยโรคหัวใจรูหัวใจรูปที่มีการเต้นผิดจังหวะชนิดเอเตรียลฟิบริลเลชั่น

วรวุฒิรุ่งแสงมนูญ น.บ., สมชายปรีชาวัฒน์ น.บ.
สาขาวิชาโรคหัวใจและหลอดเลือด ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

บทคัดย่อ
วัตถุประสงค์ ศึกษาความสัมพันธ์ของอัตราการเต้นของหัวใจหลังการออกกำลังกายโดยใช้บันไดสองขั้นกับอัตราการเต้นของหัวใจสูงสุดขณะเดินพื้นราบเป็นเวลา 6 นาที และค่าเฉลี่ยอัตราการเต้นของหัวใจตลอด 24 ชั่วโมง โดยมุ่งหวังว่าการออกกำลังกายด้วยบันไดสองขั้นสามารถใช้ประเมินความสามารถควบคุมการเต้นของหัวใจในผู้ป่วยหัวใจรูหัวใจรูปที่มีการเต้นผิดจังหวะชนิดเอเตรียลฟิบริลเลชั่นได้ใกล้เคียงกับตัวที่ทดสอบโดยการเดินพื้นราบเป็นเวลา 6 นาที และการบันทึกอัตราการเต้นของหัวใจตลอด 24 ชั่วโมง

ความสำคัญและที่มาของปัญหาการวิจัย โรคหัวใจรูหัวใจรูปที่มีการเต้นผิดจังหวะชนิดเอเตรียลฟิบริลเลชั่นเป็นสาเหตุสำคัญของการเต้นผิดจังหวะในประเทศไทย การควบคุมอัตราการเต้นของหัวใจเป็นการรักษาที่สำคัญในโรคหัวใจรูหัวใจรูปที่มีการเต้นผิดจังหวะชนิดเอเตรียลฟิบริลเลชั่น ปัจจุบันยังไม่มีมาตรฐานการควบคุมอัตราการเต้นของหัวใจในผู้ป่วยเอเตรียลฟิบริลเลชั่น ในการศึกษา AFFIRM ได้ให้นิยามเกณฑ์สำหรับการควบคุมอัตราการเต้นของหัวใจในผู้ป่วยเอเตรียลฟิบริลเลชั่นซึ่งเป็นที่ยอมรับโดยทั่วไป โดยอาศัยอัตราการเต้นของหัวใจขณะพักขณะเดินทดสอบบนพื้นราบเป็นเวลา 6 นาที และการบันทึกอัตราการเต้นของหัวใจตลอด 24 ชั่วโมง ซึ่งในเวชปฏิบัติผู้ป่วยอาจไม่สะดวกและมีข้อจำกัดในการใช้งาน

วิธีการวิจัย ทำการศึกษาในผู้ป่วยโรคหัวใจรูหัวใจรูปที่มีการเต้นผิดจังหวะชนิดเอเตรียลฟิบริลเลชั่นจำนวน 21 คน โดยที่ผู้ป่วยทุกคนได้รับยาควบคุมการเต้นของหัวใจ (AV nodal blocking drugs) ผู้ป่วยแต่ละคนจะได้รับการประเมินอัตราการเต้นของหัวใจและความดันโลหิตขณะพักจากนั้นผู้ป่วยจะถูกทดสอบโดยการออกกำลังกายด้วยบันไดสองขั้นและการเดินพื้นราบเป็นเวลา 6 นาที การบันทึกอัตราการเต้นของหัวใจตลอด 24 ชั่วโมงโดยจะแนะนำให้ผู้ป่วยปฏิบัติวิธีวิจัยตามปกติ

ผลการวิจัย อัตราการเต้นของหัวใจหลังการออกกำลังกายโดยใช้บันไดสองขั้นมีความสัมพันธ์กับอัตราการเต้นของหัวใจสูงสุดขณะเดินพื้นราบเป็นเวลา 6 นาทีอย่างมีนัยสำคัญทางสถิติ (r = 0.748, p < 0.001, intraclass correlation coefficient = 0.838, 95% confidence interval 0.601-0.934) พบความถี่สัมพันธ์ระดับปานกลางระหว่างอัตราการเต้นของหัวใจหลังการออกกำลังกายโดยใช้บันไดสองขั้นและค่าอัตราการเต้นของหัวใจขณะเดินบน (r = 0.471, p = 0.03)

ข้อสรุป การออกกำลังกายด้วยบันไดสองขั้นสามารถใช้ประเมินความสามารถควบคุมการเต้นของหัวใจในผู้ป่วยโรคหัวใจรูหัวใจรูปที่มีการเต้นผิดจังหวะชนิดเอเตรียลฟิบริลเลชั่นได้ใกล้เคียงกับการทดสอบโดยการเดินพื้นราบเป็นเวลา 6 นาที สามารถทำได้ง่าย ไม่เสียค่าใช้จ่ายเพิ่ม และเหมาะสมสำหรับการปฏิบัติในผู้ป่วยนอก