Effects of Aerobic Exercise Training on Indices of Ventricular Repolarization in Patients With Chronic Heart Failure*

Arshad Ali, MD; Mandeep R. Mehra, MD, FCCP; Furrukh S. Malik, MD; Carl J. Lavie, MD, FCCP; Donna Bass, RN; and Richard V. Milani, MD

Background: Patients with chronic heart failure (CHF) have a markedly increased incidence of malignant ventricular arrhythmias. QT dispersion (QTd), defined as the difference between maximal and minimal QT intervals, reflects the regional inhomogeneity of ventricular repolarization dispersion and may mark the presence of malignant ventricular arrhythmias.

Purpose: To determine the effects of exercise training on QTd in patients with CHF.

Patients: Fifteen patients with CHF and ejection fractions < 40% (mean, 28 ± 9%) who were on a stable medical regimen.

Design and intervention: Standardized 12-lead surface ECGs were obtained at the beginning and end of the exercise training program, and QT and JT intervals were measured manually and corrected for heart rate by using Bazett’s formula. QTd, heart rate-corrected QTd (QTc-d), JT dispersion (JTd), and heart rate-corrected JTd (JTc-d) were measured in at least eight ECG leads in each patient.

Results: Following the cardiac rehabilitation and exercise training programs, patients with CHF had only slight improvements in exercise capacity (results were not significant). However, these patients had marked improvements in QTd (71 ± 6 to 59 ± 11 ms; p < 0.02), QTc-d (82 ± 28 to 63 ± 17 ms; p < 0.01), JTd (76 ± 19 to 57 ± 18 ms; p < 0.002), and JTc-d (84 ± 23 to 61 ± 18 ms; p < 0.001) following the exercise training programs.

Conclusion: These data indicate that aerobic exercise training significantly reduces the indices of ventricular repolarization dispersion in patients with CHF. Further studies are needed to evaluate how effectively this reduction in ventricular repolarization dispersion decreases the risk of malignant ventricular arrhythmias and sudden death in patients with CHF. (CHEST 1999; 116:83–87)

Key words: arrhythmias; exercise training; heart failure

Abbreviations: CHF = chronic heart failure; JTc = heart rate-corrected JT intervals; JTc-d = heart rate-corrected JT dispersion; JTd = JT dispersion; QTc = heart rate-corrected QT intervals; QTc-d = heart rate-corrected QT dispersion; QTd = QT dispersion

Despite recent pharmacologic advances, chronic heart failure (CHF) remains a highly lethal disease, with annual mortality rates as high as 50%.1,2 Approximately 50% of deaths in patients with mild CHF and 25% of deaths in patients with severe CHF are sudden and unexpected.3,4 Sudden death in these patients is a massive problem with no definitive predictors.5 Studies have suggested that a standard 12-lead surface ECG can provide prognostic information, particularly when related to measurements of ventricular repolarization dispersion. The heterogeneity of ventricular repolarization dispersion, as measured by calculating the QT dispersion (QTd), which is the difference between maximum and minimum QT intervals on a 12-lead surface ECG, has been shown to be a marker of myocardial electrical instability and may predict sudden death.6 More recently, JT dispersion (JTd) has been shown to be a better predictor of sudden death in patients with myocardial infarction.7

The beneficial effects of aerobic exercise training in patients with CHF are well recognized.8,9 There is some evidence that physical training reduces QTd in patients following recent myocardial infarction.10 To our knowledge, however, there are no such data available for patients with CHF.

The purpose of this study was to evaluate any
beneficial effects that aerobic exercise training has on the indices of ventricular repolarization dispersion by measuring QTd and JTd on a 12-lead surface ECG in patients with CHF (ejection fraction, < 40%).

**Materials and Methods**

**Patient Population**

We retrospectively evaluated 27 patients enrolled in an aerobic exercise training program at our cardiac rehabilitation facility. Entry criteria included the following: (1) the presence of CHF as diagnosed by a clinical presentation along with echocardiographic evidence of depressed left ventricular function (ejection fraction, < 40%); (2) the absence of active ischemia as revealed by a clinical examination or by the exercise testing at the time of enrollment; (3) a stable medical regimen for at least 2 weeks prior to starting exercise training and during the entire training period; (4) the absence of any recent coronary revascularization procedure (≤ 3 months); and (5) no history of myocardial infarction in the 8 weeks prior to enrollment. Exclusion criteria included the following: (1) class IA or III antiarrhythmic medications; (2) the inability to complete the exercise training program; (3) the absence of sinus rhythm at entry or completion of training; and (4) a complete bundle-branch block of either kind.

**Exercise Training Protocol**

All patients completed 12-week (36 exercise sessions), phase II cardiac rehabilitation and exercise training programs as described elsewhere. Each session consisted of approximately 10 min of warm-up exercises, including stretching and calisthenics, followed by 30 to 40 min of continuous upright aerobic and dynamic exercises (various combinations of walking, bicycling, jogging, rowing, etc.), light isometric exercises (hand weights), and approximately 10 min of cool-down stretching and calisthenics. Exercise intensity was prescribed individually so that patients’ heart rates were approximately 70 to 85% of the maximum heart rate. In addition to the supervised exercise sessions, approximately one to three times per week of exercise outside the formal program was encouraged.

Before entering the program, patients underwent symptom-limited exercise testing, which usually consisted of using a ramping treadmill protocol. Breath-to-breath on-line gas analysis was performed by using a metabolic cart (MedGraphics CPX/d; Medical Graphics Corporation; St. Paul, MN), with incremental data collected every 15 s. Maximal oxygen consumption, anaerobic threshold, and metabolic equivalents were determined on the basis of established criteria. After the outpatients’ cardiac rehabilitation exercise training programs, patients underwent protocols similar to the preprogram exercise assessment.

Standard 12-lead surface ECGs were recorded at the beginning of the study at a paper speed of 25 mm/s and an amplification gain of 10 mm/mV. All ECGs were examined by one observer blinded to the clinical status and the follow-up results. Measurements of QT, JT, and RR intervals were performed manually. The QT interval was measured from the beginning of the QRS complex to the end of the T wave at the level of the TP isoelectric baseline. Biphasic T waves were measured to the time of their final return to the TP isoelectric baseline. If U waves were present, the QT interval was measured from the beginning of the QRS complex to the nadir of the curve between the T and U waves. The JT interval was measured from the end of the QRS complex, which was defined as the point at which the QRS complex returns to the TP isoelectric baseline (J point), to the end of the T wave at the level of the TP isoelectric baseline. Extrasystolic and postextrasystolic cycles were excluded from the measurement. If the end of the T wave could not be reliably determined, or if the T waves were isoelectric or of very low amplitude, QT or JT interval measurements were not made, and these ECG leads were excluded from the analysis. In order to get reasonably standardized sets of ECG leads, a lower limit of eight or more technically adequate measurable leads per ECG was set for inclusion into the study. Heart rate-corrected QT (QTc) and JT intervals (JTc) were calculated by using Bazett’s formula (QTc = QT/RR \( \frac{1}{2} \)).

The ventricular repolarization dispersions were determined by calculating the difference between maximum and minimum QT or JT intervals in each ECG, and they were termed QTd, heart rate-corrected QTd (QTc-d), JTd, and heart rate-corrected JTd (JTc-d). ECGs were recorded at the initiation and completion of the training program.

**RESULTS**

**Patient Demographics**

Twelve patients were excluded from the final analyses for various reasons, including a technically poor ECG (n = 7), the presence of ischemia on cardiopulmonary stress testing at the initiation of the study (n = 2), and the development of ischemia at the time of the follow-up ECG (n = 3). Fifteen patients (12 were male) were included in the final analysis (mean age, 68 ± 11 years; ejection fraction, 28 ± 9%). All patients were in the functional class II cardiac and rehabilitation exercise program and remained there until the end of the study. Twelve patients had CHF secondary to ischemic cardiomyopathy, while the other three had CHF secondary to nonischemic dilated cardiomyopathy. All patients were on a stable medical regimen of diuretics, angiotensin-converting enzyme inhibitors, and digoxin. Twelve patients with ischemic cardiomyopathy were also taking aspirin and nitrates. There were no changes made in the dosage of these medications during the training period. As a group, the patients with ischemic cardiomyopathy had a lower ejection fraction than did the patients with nonischemic dilated cardiomyopathy (mean, 26 ± 9% vs 37 ± 6%; p = 0.06).

**Changes in Metabolic Parameters**

Table 1 shows the changes in exercise capacity that occurred during the exercise training program in terms of the metabolic equivalents, maximum oxygen consumption, and anaerobic threshold. There was only a modest increase in exercise capacity and peak oxygen consumption, which did not reach statistical significance, whereas there was no change in the anaerobic threshold.
**Table 1—Changes in Metabolic Parameters and Exercise Capacity Associated With Exercise Training in Patients With CHF**

<table>
<thead>
<tr>
<th>Exercise Status</th>
<th>Exercise Capacity, METs</th>
<th>Anaerobic Threshold, mL O₂/kg/min</th>
<th>VO₂ max, mL O₂/kg/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preexercise training</td>
<td>4 ± 1</td>
<td>12 ± 2</td>
<td>15 ± 4</td>
</tr>
<tr>
<td>Postexercise training</td>
<td>5 ± 2</td>
<td>12 ± 4</td>
<td>16 ± 6</td>
</tr>
</tbody>
</table>

*p = 15. Values are expressed as mean ± SD. METs = metabolic equivalents; VO₂ max = maximal oxygen consumption; NS = not significant.

**ECG Analysis**

Table 2 shows paired t test results from the QTd, QTc-d, JTd, and JTc-d. Although parameters of exercise capacity showed no significant increases, there were statistically significant decreases in all intervals at the completion of the exercise training programs. The greatest decrease was seen in JTc-d, which had an absolute average reduction of 23 ms.

**Repolarization Dispersion and Etiology of Heart Failure**

As shown in Table 3, we analyzed the differences between the indices of ventricular repolarization dispersion before and after exercise training, and we divided the results according to the etiology of heart failure. At the TP isoelectric baseline, QTd, QTc-d, JTd, and JTc-d were higher in patients with nonischemic dilated cardiomyopathy (n = 3) than they were in patients with ischemic cardiomyopathy, but statistical significance was not reached. This difference persisted following exercise training when the magnitude of change in patients with nonischemic dilated cardiomyopathy was much more pronounced (Fig 1); however, statistically significant improvements were noted in the 12 patients with ischemic cardiomyopathy.

**Discussion**

Although the patients in this cohort had only modest improvements in exercise capacity following the exercise training program, our data demonstrate that their indices of ventricular repolarization dispersion were markedly reduced; hence, the patients’ risk of having malignant ventricular dysrhythmias or experiencing sudden cardiac death should have been reduced as well.

The precise mechanism behind the increases in the homogeneity of ventricular repolarization dispersion remains elusive. The duration of the action potential is primarily responsible for the time span of the repolarization. Cells isolated from failing human and animal hearts reveal action potentials that have a significantly longer prolongation than the action potentials in normal hearts, an effect that is independent of the underlying cause of CHF.18 If the prolongation of action potential were homogeneous, it would not necessarily produce an arrhythmogenic milieu.19 But variations in the duration of the action potential would create a ventricular repolarization dispersion that could be arrhythmogenic.20 Regional differences in the density of potassium currents have been demonstrated in human hearts.21 It is conceivable that the reductions in the densities of currents generated by repolarization in the failing heart are nonuniform, thus creating regional differences in repolarization.20

Influences of the autonomic nervous system on QT dispersion are well demonstrated.22 The heterogeneity of sympathetic innervation is well described in patients with heart failure and may contribute to the heterogeneity of repolarization.23,24 Patchy myocardial fibrosis causing local disturbances in repolarization may also be a contributing factor in some cases.6

Aerobic exercise training restores the heart rate variability, increases the vagal tone, and reduces the sympathetic tone in patients after myocardial infarction.25 This beneficial effect of aerobic exercise is also demonstrated in patients with CHF.8,26 In addition, the favorable effect that exercise training has in reducing QT dispersion has been demonstrated in patients following myocardial infarction.10 This improvement in the autonomic profile may be one of the mechanisms responsible for reducing the ventricular repolarization dispersion, as measured by QTd and JTd in our study group of patients with CHF.

In a study of 163 patients with CHF due to ischemic cardiomyopathy and nonischemic dilated cardiomyopathy, Fu et al27 found that JTc-d is a powerful independent predictor of sudden cardiac death. A cut-off value of 85 ms for JTc-d had a 74% positive and a 98% negative predictive accuracy in identifying risk for sudden cardiac death. The mean
The value of JTc-d in our study group was 84 ms, which is quite similar to that of the cohort in the study by Fu et al.27

There were differences between patients with ischemic cardiomyopathy and patients with nonischemic dilated cardiomyopathy in that their indices of ventricular repolarization dispersion differed at the TP isoelectric baseline and following exercise. Patients with nonischemic dilated cardiomyopathy seemed to have more pronounced improvements following exercise in QTc-d and JTc-d than did patients with ischemic cardiomyopathy; however, the small number of patients with nonischemic dilated cardiomyopathy in our study group (n = 3) makes interpretation of these findings difficult.

Measurements of QTd may provide an advantage over those of heart rate variability in clinical settings. A limitation in using heart rate variability as an index of the effect of the autonomic nervous system on the ventricle is that it is indirect, reflecting changes in the RR interval by way of reflex mechanisms mediated by the sinus node. The QT interval is an index of ventricular repolarization dispersion that is directly influenced by myocardial health and autonomic nervous system activity. Therefore, variability of the QT interval should predict cardiac risk more directly and accurately than variability of the RR interval does.20

Table 3—Repolarization Dispersion in Ischemic Cardiomyopathy and Nonischemic Dilated Cardiomyopathy, Before and After an Exercise Training Program

<table>
<thead>
<tr>
<th>Cardiomyopathy</th>
<th>QTd Pre</th>
<th>QTd Post</th>
<th>QTc-d Pre</th>
<th>QTc-d Post</th>
<th>JTd Pre</th>
<th>JTc-d Pre</th>
<th>JTc-d Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic (n = 12)</td>
<td>69 ± 12</td>
<td>62 ± 15</td>
<td>81 ± 31</td>
<td>67 ± 16</td>
<td>75 ± 21</td>
<td>58 ± 19</td>
<td></td>
</tr>
<tr>
<td>Nonischemic dilated (n = 3)</td>
<td>77 ± 6</td>
<td>47 ± 21</td>
<td>85 ± 13</td>
<td>46 ± 16</td>
<td>80 ± 10</td>
<td>53 ± 15</td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td>0.3</td>
<td>0.1</td>
<td>0.8</td>
<td>0.06</td>
<td>0.7</td>
<td>0.6</td>
<td></td>
</tr>
</tbody>
</table>

*Values are expressed as mean ± SD. Pre = before exercise training; Post = after exercise training.

Figure 1. Improvements in ventricular repolarization in patients with ischemic cardiomyopathy (ICM; n = 12) and dilated nonischemic cardiomyopathy (DCM; n = 3).

CONCLUSION

Following a formal cardiac rehabilitation and aerobic exercise training program, JTc-d decreased by an average of 23 ms, with other indices of ventricular repolarization dispersion significantly improving as well. These marked improvements may translate into substantial clinical benefits, but prospective data in a large patient population are needed to confirm this.

Our study adds to the evidence of the beneficial effects of exercise training in patients with CHF. Measurement of QTd and JTd on a surface ECG is a noninvasive technique that seems to reflect the risks of malignant ventricular dysrhythmias and sudden cardiac death. Although marked improvements were noted in indices of ventricular repolarization dispersion following exercise training in patients with CHF, large-scale prospective trials are needed to validate these findings and to determine whether these improvements translate into significant reductions in major cardiac events.

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