CARDIAC PACING

Effect of Ventricular Function on the Exercise Hemodynamics of Variable Rate Pacing

THOMAS A. BUCKINGHAM, MD, FACC, ROBERT C. WOODRUFF, MD, D. GLENN PENNINGTON, MD, ROBERT M. REDD, MD, DENISE L. JANOSIK, MD, FACC, ARTHUR J. LABOVITZ, MD, FACC, ROXANNE GRAVES, RN, HAROLD L. KENNEDY, MD, FACC
St. Louis, Missouri

To determine the effect of ventricular function on the exercise hemodynamics of variable rate pacing, 16 selected patients underwent paired, double-blind, randomized exercise tests in single rate demand (VVI) or variable rate (VVIR) pacing modes. Ejection fraction and cardiac index were determined by two-dimensional and Doppler echocardiography at baseline and during peak exercise.

Baseline ejection fraction ranged from 14 to 73% and was <40% in 6 patients (Group 1) and ≥40% in 10 patients (Group 2). Duration of exercise was longer during the VVIR mode (502 s) than during the VVI mode (449 s) (p < 0.01) and unrelated to baseline ejection fraction. Heart rate during exercise increased 9% in the VVI mode and 35% in the VVIR mode (p < 0.005). Cardiac index increased 49% in the VVI mode and 83% in the VVIR mode. Analysis of variance for repeated measures showed a significant effect of pacing mode (p < 0.01) and exercise (p < 0.001), but not baseline ejection fraction, on cardiac index. Baseline ejection fraction did not correlate with the increase in cardiac index in either pacing mode or with the difference in increase between modes. There was no significant difference between Groups 1 and 2 in exercise duration, peak heart rate-blood pressure (rate-pressure) product, baseline or peak heart rate or baseline or peak cardiac index.

Therefore, in selected patients, VVIR pacing during exercise results in an increase in heart rate, duration of exercise and cardiac index that is unrelated to the degree of baseline left ventricular dysfunction. These data have clinical implications for the use of variable rate pacemakers in patients with abnormalities of ventricular function.

(J Am Coll Cardiol 1988;11:1269-77)

When implantable pacemakers were introduced in 1959, their primary function was to prolong life. As pacemakers became more sophisticated, improving the quality of life became an important goal as well. Studies (1-7) have confirmed that the use of dual chamber pacing, which provides rate variability and atrioventricular (AV) synchrony, increases exercise time and work capacity and provides important benefits for selected patients. However, in patients who have sinus node disease with an inadequate increase in atrial rate during exercise or other times of metabolic need, dual chamber pacing provides AV synchrony but not rate variability. In patients with chronic atrial fibrillation dual chamber pacing is less effective and may deliver an inappropriate rate. In addition, the added costs and problems associated with dual chamber pacemakers have limited their use (8). Furthermore, a variety of studies (9-11) have shown that during exercise, an increase in heart rate is more important than AV synchrony.

These factors have led to the development of single chamber pacemakers with sensors that detect the need for heart rate changes by tracking variables other than atrial function (12-19). Clinical investigators (12-21) using these new devices have reported beneficial effects in selected patients. However, the exact characteristics of patients likely to benefit from these pacemakers have not been precisely defined. Patients who have chronotropic incompetence or atrial fibrillation with high degree AV block (indications for a variable rate pacemaker) may be more likely to have underlying heart disease with coexisting left ventricular
dysfunction (22-24). Few data exist on the hemodynamic benefits of variable rate pacing in patients with poor ventricular function.

The goals of the present study were to determine whether variable rate pacing provides hemodynamic benefit in patients with poor ventricular function and to measure hemodynamic changes during exercise with variable rate pacing.

**Methods**

**Patient selection.** The protocol and consent form used in this study were approved by the Institutional Review Board of St. Louis University on July 12, 1985. Patients were selected for inclusion in the study if they met the following criteria: 1) Implantation of a permanent pacemaker was indicated by criteria from the Joint American College of Cardiology/American Heart Association Task Force (25). 2) Heart rate did not increase adequately during exercise (see later). 3) The patient was able to exercise on a motorized treadmill.

Criterion 2 included patients with chronic atrial fibrillation and high degree AV block as well as patients with chronotropic incompetence. For purposes of this study, chronotropic incompetence was considered present if the maximal heart rate achieved on a treadmill test using a modified Naughton protocol was <75% of that expected for age, gender and level of exercise. Several patients with complete AV block undergoing pacemaker replacement, in whom placement of an additional atrial lead was considered difficult or undesirable, were included despite an adequate atrial response to exercise.

For purposes of analysis, the 16 patients selected for study were classified into two groups: Group 1 consisted of 6 patients with an ejection fraction <40% and Group 2 consisted of 10 patients with an ejection fraction ≥40%.

**Exercise testing.** Symptom-limited paired exercise treadmill tests using a modified Naughton protocol were performed 90 min apart in a double-blind fashion and in random order in the 16 patients who had undergone pacemaker implantation 1 month before. One test was performed in the variable rate pacing mode (VVR) and the other in the single rate, demand pacing mode (VVI). An “R” is added after the three letter code to indicate that the variable rate feature is active. Two physicians were present at each exercise test. One physician, unaware of the programmed pacing mode, supervised each test and encouraged the patient to exercise to maximal capacity. A second physician programmed the patient’s pacemaker before and after each test. The patient was not informed of the pacing mode during either test. After the second and final test, the patient’s pacemaker was reprogrammed to the variable rate pacing mode. Despite these precautions, it is possible that some patients may have been able to determine their pacing mode and “unblind” the study.

**Doppler echocardiographic methods.** Doppler and two-dimensional echocardiographic techniques used by our laboratory have been previously described (26-28). These studies were obtained using a phased-array echo Doppler imaging system (Irex Meridian). Two-dimensional echocardiography was performed using standard parasternal long- and short-axis views and apical two and four chamber views. Still frames of aortic outflow were obtained in the parasternal long-axis view, and the cross-sectional area (A) of the left ventricular outflow tract was calculated from the diameter (D) obtained at rest, at the level of the aortic anulus or above the sinus of Valsalva, using the formula $A = \pi (D/2)^2$. Two-dimensional views were recorded with the patient in the left lateral decubitus or supine position at rest and the optimal transducer locations were marked. Two-dimensional echocardiograms from the same windows were repeated immediately after exercise and were used to determine end-diastolic and end-systolic volumes and ejection fraction. Left ventricular dysfunction was arbitrarily defined as an echocardiographically determined ejection fraction <40%. All calculations were performed by a single observer without knowledge of other data.

**Doppler echocardiography** was performed from the suprasternal notch, interrogating the ascending aorta with an independent Doppler transducer (Pedof). The Doppler unit operates at a frequency of 2.0 MHz in pulsed or continuous wave mode. The maximal velocity limit of the pulsed wave mode is 3.4 m/s at depths of <8 cm and 2.2 m/s at depths of 8 to 13 cm. Pulsed Doppler ultrasound was used for all recordings. Sample volume depth was adjusted until an optimal flow pattern was obtained (highest velocity with least spectral dispersion); sample depth and position in the aortic arch remained constant for the remainder of the examination. Hard copy recordings of the aortic flow were obtained using a paper speed of 50 or 100 mm/s.

At least five consecutive heartbeats of each Doppler tracing were analyzed using a Franklin Quantic 1200 Echo- computer. The darkest part of the tracing was integrated to obtain the flow velocity integral. Stroke volume was calculated from the product of flow velocity integral and aortic cross-sectional area. Cardiac output was obtained from the product of stroke volume and heart rate. Stroke volume index and cardiac index were calculated from the quotient of stroke volume and cardiac output divided by body surface area. Measurements were made before exercise with the patient standing and 30 s before the termination of each stage of exercise. These measurements were repeated at peak exercise, and immediately after exercise while the patient was standing.

**Pacing techniques.** Thirteen patients were implanted with a single chamber, variable rate pacemaker (Medtronic Acti-
We tested variable-rate pacing in each of the patients (VVI and VVIR modes) using chest wall stimulation. The pacemaker can adjust the rate of pacing stimuli in response to low frequency pressure waves generated by muscle movement and propagated through the body. The manner in which the pacemaker responds to activity can be programmed in a variety of different ways (Table 1).

This pacemaker has 3 programmable upper rate limits and 10 rate response settings that govern how high the heart rate peaks in response to exercise. Ten different rate response curves can be programmed. A rate response curve of 1 provides the slowest increase in heart rate to activity and a curve of 10 provides the most rapid increase. In addition, there are three programmable settings of activity threshold that determine the sensitivity of the pacemaker to activity and environmental stimuli. During exercise testing in the VVIR mode, all patients in the study were programmed to a baseline rate of 60 or 70 beats/min, an upper rate limit of 150 beats/min, a rate response curve of 7, and an activity threshold setting of medium.

Three additional patients already had an implanted VVI pacemaker. They underwent testing with a VVIR pacemaker using chest wall stimulation. In this technique, the patient's permanent pacemaker was programmed to a VVT mode (triggered mode), during which the pacemaker paced in response to a sensed electrical event. Electrodes attached to the chest near the implanted pacing system were connected to a VVIR pacemaker programmed to the same settings as those of the implanted VVIR pacemakers described previously. The VVIR pacemaker was strapped securely to the patient's chest using elastic bandages so that the sensor side of the pacemaker was in firm contact with the patient's body. In this manner, the external VVIR pacemaker sensed patient activity and increased the pacing rate. The electrical signals from the external pacemaker were transmitted across the patient's chest and the patient's implanted ventricular pacemaker was "slaved" to the external unit. Subsequent examination of electrocardiographic (ECG) tracings obtained during treadmill testing showed that this method was successful in providing variable rate pacing in each of the patients tested in this manner.

Three types of pacemaker were used in this study. (1) the vitrax Model numbers 8400, 8402 or 8403) at least 1 month before exercise testing. This is a single chamber, demand pacemaker with a piezoelectric crystal bonded to the inside of the pacemaker casing. The pacemaker can adjust the rate of pacing stimuli in response to low frequency pressure waves generated by muscle movement and propagated through the body. The manner in which the pacemaker responds to activity can be programmed in a variety of different ways (Table 1).

This pacemaker has 3 programmable upper rate limits and 10 rate response settings that govern how high the heart rate peaks in response to exercise. Ten different rate response curves can be programmed. A rate response curve of 1 provides the slowest increase in heart rate to activity and a curve of 10 provides the most rapid increase. In addition, there are three programmable settings of activity threshold that determine the sensitivity of the pacemaker to activity and environmental stimuli. During exercise testing in the VVIR mode, all patients in the study were programmed to a baseline rate of 60 or 70 beats/min, an upper rate limit of 150 beats/min, a rate response curve of 7, and an activity threshold setting of medium.

Three additional patients already had an implanted VVI pacemaker. They underwent testing with a VVIR pacemaker using chest wall stimulation. In this technique, the patient's permanent pacemaker was programmed to a VVT mode (triggered mode), during which the pacemaker paced in response to a sensed electrical event. Electrodes attached to the chest near the implanted pacing system were connected to a VVIR pacemaker programmed to the same settings as those of the implanted VVIR pacemakers described previously. The VVIR pacemaker was strapped securely to the patient's chest using elastic bandages so that the sensor side of the pacemaker was in firm contact with the patient's body. In this manner, the external VVIR pacemaker sensed patient activity and increased the pacing rate. The electrical signals from the external pacemaker were transmitted across the patient's chest and the patient's implanted ventricular pacemaker was "slaved" to the external unit. Subsequent examination of electrocardiographic (ECG) tracings obtained during treadmill testing showed that this method was successful in providing variable rate pacing in each of the patients tested in this manner.

Statistical methods. Unless otherwise specified, all variables are presented as mean ± 1 SD. Probability values <0.05 were considered significant. Pearson's correlation coefficient (r) was used to correlate baseline ejection fraction with the percent increase in cardiac index noted during exercise in VVI and VVIR modes as well as with the difference in improvement between these two modes. Comparisons between Groups 1 and 2 were made using a nonpaired Students' t test. The effect of pacing mode and exercise on hemodynamic variables was examined using a two-way analysis of variance with repeated measures. To examine the effect of ventricular function on these variables, baseline ejection fraction was included in the analysis of variance as a covariate.

Results

Patient characteristics (Table 2). Twelve (75%) of the 16 patients were male. The range was 25 ± 24 years (range 7 to 82). Coronary heart disease was present in two patients, valvular heart disease in one, hypertensive cardiomyopathy in one, congestive cardiomyopathy in two and hypertrophic cardiomyopathy in one. Three patients had received a cardiac transplant, two had right ventricular enlargement and chronic obstructive lung disease and four had a structurally normal heart. Thirteen patients had grade AV block alone or associated with a sick sinus node or atrial fibrillation. The latter was present in three patients and sick sinus syndrome or sinus bradycardia in four.

Exercise testing. The results of the paired exercise tests are shown in Tables 3 and 4. Intact ventriculoatrial conduc-tion was seen on the surface ECGs in three cases (Cases 8, 12 and 15) during exercise in the VVIR mode. Results of the two-way analysis of variance with repeated measures are shown in Table 5. Duration of exercise was 449 ± 217 s in the VVI mode and 502 ± 245 s in the VVIR mode (p = 0.014). Peak rate-pressure product was higher in the VVIR mode reaching 8.952 ± 2.364 in the VVI mode and 12.330 ± 2.893 in the VVIR mode (p = 0.002). Baseline heart rate was similar at the start of each treadmill test (69 ± 7.6 and 72 ± 9 in the VVI and the VVIR mode, respectively). Heart rate increased to 75 ± 11 in the VVI mode and to 97 ± 12 beats/min in the VVIR mode (p = 0.004). At the start of exercise, baseline ejection fraction was similar in both pacing modes (42 ± 14% in the VVI mode and 42 ± 14% in the VVIR mode). Ejection fraction increased in both pacing modes to a similar extent, reaching 49 ± 11% in the VVI mode and 45 ± 11% in the VVIR mode. Baseline cardiac indexes were similar in both pacing modes (1.91 ± 0.65 in the VVI mode and 1.93 ± 0.7 liters/min per m² in the VVIR mode). However, at peak exercise, cardiac index increased.
significantly more in the VVIR mode reaching 3.07 $\pm$ 1.67 in the VW mode and 3.54 $\pm$ 1.53 liters/min per m$^2$ in the VVIR mode ($p = 0.013$). Exercise had a significant effect on cardiac index and heart rate greater than that of pacing mode (Table 5). Figure 1 shows the mean heart rate and cardiac indexes at each stage of exercise up to stage 4 and during recovery for pacing in the VW and VVIR modes. Figure 2 demonstrates the mean percent increase in heart rate, stroke volume index, cardiac index, ejection fraction and rate-pressure product for each pacing mode. A greater increase in heart rate, cardiac index and rate-pressure product was seen with the VVIR mode. In the VW mode, heart rate increased by 9%, and in the VVIR mode, by 35% ($p < 0.005$). Stroke volume index increased by 32% in the VW mode and by 33% in the VVIR mode ($p = NS$). Cardiac index increased by 4% in the VW mode and by 83% in the VVIR mode ($p = 0.013$). Rate-pressure product increased by 23% in the VW mode and by 63% in the VVIR mode ($p = 0.002$). Ejection fraction increased by 17% in the VVIR mode and 13% in the VWIR mode ($p = NS$).

**Effect of left ventricular function.** There was no significant correlation between baseline ejection fraction and the percent increase in cardiac index in the VI or VVIR mode ($r = 0.25$ and $R = 0.20$) (Fig. 3). In addition, there was no significant correlation between baseline ejection fraction and the difference between the improvement in cardiac index between these pacing modes ($r = 0.06$). Although analysis of variance for repeated measures with an analysis of covariance showed a significant effect of pacing mode on exercise duration, cardiac index, heart rate and rate-pressure product, no significant effect of baseline left ventricular function (as reflected by ejection fraction) was seen on any hemodynamic variable.

**Comparison of patient groups.** There was no significant difference between Groups 1 and 2 with respect to duration of exercise or peak rate-pressure product in either pacing mode (Tables 3 and 4). For example, duration of exercise in the VW mode was 441 $\pm$ 192 s in Group 1 (low ejection fraction) and 455 $\pm$ 228 s in Group 2 (normal ejection fraction). In the VVIR mode, duration of exercise was 491 $\pm$ 192 s in Group 1 and 508 $\pm$ 272 s in Group 2. There also was no significant difference with respect to heart rate at baseline and peak exercise during either pacing mode between groups. Baseline ejection fraction was significantly different between groups ($p < 0.001$); the mean ejection fraction was 28 $\pm$ 9% in Group 1 and 50 $\pm$ 9% in Group 2. At peak exercise, this difference in ejection fraction was no longer present. Peak ejection fraction in the VVI mode was 42 $\pm$ 9.7% in Group 1 and 53 $\pm$ 10% in Group 2 ($p = NS$). In the VVIR mode, peak ejection fraction was 39 $\pm$ 13% in Group 1 and 49 $\pm$ 8.5% in Group 2 ($p = NS$). Cardiac index at baseline and peak exercise in either pacing mode did not significantly differ between groups.
Various studies have demonstrated improvements in patients' exercise capacity with dual chamber pacing (1-3,6). However, patients with sinus node disease with chronotropic incompetence or chronic atrial fibrillation with high degree AV block are unable to achieve this benefit by way of the dual chamber pacing mode. Recent studies (9-11) have shown that increased cardiac output during exercise is related more to an increase in heart rate than to AV synchrony. Dual chamber pacemakers are more expensive than single chamber pacemakers, require the placement of an additional lead, have a higher incidence of complications and require more follow-up care (8,29). Cost containment measures in the United States today make the use of dual chamber pacemakers virtually impossible in some hospitals and limit their use in others. All these factors led to the development of single chamber pacemakers with sensors that detect the need for heart rate variation.

The variable rate pacemaker. The variable rate pacemaker (Medtronic) used in this study contains a piezoelectric crystal that detects low frequency pressure waves generated by muscle activity. Preliminary studies demonstrated the feasibility of this approach (14,30) and a subsequent large multicenter clinical trial demonstrated its safety and efficacy (20,21). Results from the multicenter trial conducted by the manufacturer, which showed improvement in exercise capability in selected patients, led to the release of this pacemaker by the Food and Drug Administration in June 1986. A variety of other sensors have been used in pacemaker systems to detect the need for an increased heart rate. These include central venous temperature, respiratory rate, stimulus-T interval and oxygen saturation (15,16,18,19). Other sensors are being developed for this purpose.

Table 3. Results of Exercise Testing in 16 Patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>VVI</th>
<th>VVIR</th>
<th>VVI</th>
<th>VVIR</th>
<th>VVI</th>
<th>VVIR</th>
<th>VVI</th>
<th>VVIR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>480</td>
<td>600</td>
<td>7,200</td>
<td>16,400</td>
<td>64</td>
<td>63</td>
<td>90</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>421</td>
<td>480</td>
<td>5,600</td>
<td>10,800</td>
<td>71</td>
<td>79</td>
<td>70</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>272</td>
<td>233</td>
<td>9,100</td>
<td>11,200</td>
<td>69</td>
<td>70</td>
<td>70</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>300</td>
<td>12,300</td>
<td>14,200</td>
<td>69</td>
<td>69</td>
<td>99</td>
<td>116</td>
</tr>
<tr>
<td>5</td>
<td>840</td>
<td>840</td>
<td>5,200</td>
<td>7,360</td>
<td>71</td>
<td>69</td>
<td>69</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>320</td>
<td>432</td>
<td>8,300</td>
<td>20,900</td>
<td>60</td>
<td>96</td>
<td>83</td>
<td>122</td>
</tr>
<tr>
<td>Mean</td>
<td>441</td>
<td>491</td>
<td>8,146</td>
<td>13,298</td>
<td>57</td>
<td>74</td>
<td>72</td>
<td>100</td>
</tr>
<tr>
<td>SD</td>
<td>196</td>
<td>192</td>
<td>2,491</td>
<td>4,281</td>
<td>4.0</td>
<td>11</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>317</td>
<td>309</td>
<td>9,840</td>
<td>12,040</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>91</td>
</tr>
<tr>
<td>8</td>
<td>645</td>
<td>630</td>
<td>9,000</td>
<td>10,200</td>
<td>61</td>
<td>65</td>
<td>90</td>
<td>102</td>
</tr>
<tr>
<td>9</td>
<td>240</td>
<td>245</td>
<td>9,750</td>
<td>11,480</td>
<td>74</td>
<td>69</td>
<td>75</td>
<td>82</td>
</tr>
<tr>
<td>10</td>
<td>490</td>
<td>690</td>
<td>9,400</td>
<td>10,450</td>
<td>72</td>
<td>70</td>
<td>70</td>
<td>95</td>
</tr>
<tr>
<td>11</td>
<td>764</td>
<td>964</td>
<td>7,170</td>
<td>11,640</td>
<td>60</td>
<td>61</td>
<td>67</td>
<td>97</td>
</tr>
<tr>
<td>12</td>
<td>330</td>
<td>354</td>
<td>12,300</td>
<td>14,016</td>
<td>62</td>
<td>62</td>
<td>89</td>
<td>96</td>
</tr>
<tr>
<td>13</td>
<td>120</td>
<td>73</td>
<td>10,050</td>
<td>12,000</td>
<td>61</td>
<td>79</td>
<td>70</td>
<td>111</td>
</tr>
<tr>
<td>14</td>
<td>811</td>
<td>840</td>
<td>7,960</td>
<td>10,400</td>
<td>82</td>
<td>79</td>
<td>84</td>
<td>104</td>
</tr>
<tr>
<td>15</td>
<td>800</td>
<td>644</td>
<td>13,200</td>
<td>11,610</td>
<td>81</td>
<td>79</td>
<td>86</td>
<td>96</td>
</tr>
<tr>
<td>16</td>
<td>240</td>
<td>334</td>
<td>7,930</td>
<td>13,659</td>
<td>60</td>
<td>63</td>
<td>61</td>
<td>91</td>
</tr>
<tr>
<td>Mean</td>
<td>455</td>
<td>508</td>
<td>9,436</td>
<td>11,749</td>
<td>69</td>
<td>71</td>
<td>77</td>
<td>96</td>
</tr>
<tr>
<td>SD</td>
<td>228</td>
<td>272</td>
<td>2,144</td>
<td>1,221</td>
<td>9.0</td>
<td>7.5</td>
<td>9.7</td>
<td>8.2</td>
</tr>
</tbody>
</table>

Comparison Between Groups

<table>
<thead>
<tr>
<th>p Value</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>For All Patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>448</td>
<td>502</td>
<td>9,893</td>
<td>12,330</td>
<td>69</td>
<td>72</td>
<td>75</td>
<td>97</td>
</tr>
<tr>
<td>SD</td>
<td>217</td>
<td>245</td>
<td>3,964</td>
<td>2,893</td>
<td>2.6</td>
<td>9.0</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

VVI = single rate pacing mode; VVIR = variable rate pacing mode.
Patients with high degree AV block and either atrial fibrillation or chronotropic incompetence are more likely than other pacemaker patients to have left ventricular dysfunction (22-24). The patients in the present study demonstrated a beneficial effect from the variable rate pacing mode despite poor ventricular function. The current study was limited to 16 patients of whom only 6 had an ejection fraction <40%. Nonetheless, ejection fraction had a broad range (14 to 73%) and failed to correlate with exercise outcome in either pacing mode. The percent improvement in cardiac index in either pacing mode or between pacing modes was not related to baseline ventricular systolic function. These data demonstrate the utility of variable rate pacing in carefully selected patients despite poor ventricular function.

Prior studies. Several previous studies (14,16,18,19,30) have also shown a beneficial effect of variable rate pacing on exercise ability in selected patients. Humen et al. (14) conducted early hemodynamic studies using this pacemaker in six patients (five with a history of congestive heart failure) and demonstrated an improvement in exercise capacity, anaerobic threshold, heart rate response and cardiac output. Ryden et al. (30) noted improved exercise ability in three patients who received an implanted activity-responsive pacemaker and underwent treadmill testing and bicycle ergometry. Using the respiration-dependent pacemaker, Rossi et al. (19) studied 25 patients and noted a 25%
improvement in exercise performance with variable rate pacing compared with VVI pacing. They examined hemodynamic variables in a subset of nine patients from their study and noted a peak cardiac output of 10.2 liters/min in VVI mode significantly different from 12.6 liters/min in respiratory-dependent pacing mode (VVIR) (p < 0.05). In 15 patients who received the stimulus-T-sensitive pacemaker, a significant increase in exercise ability and a 40% increase in cardiac output were noted with variable rate pacing compared with VVI pacing by Donaldson and Rickards (16). Wirtzfeld et al. (18) conducted studies in 10 patients using a central venous oxygen saturation-sensitive pacemaker system during bicycle ergometry. They noted an 18% improvement in cardiac output during exercise with variable rate

Figure 1. Mean heart rate (A) and cardiac index (B) observed at baseline (B), during each stage of exercise, in the recovery phase immediately after exercise (R) and 5 and 10 minutes later (R5 and R10) in 16 patients. Values ± 1 SD are shown only through stage 4 for the single rate mode (VVI) and the variable rate mode (VVIR) of pacing.

Figure 2. Percent change in heart rate (HR), stroke volume index (SVI), cardiac index (CI), ejection fraction (EF), and rate-pressure (double) product (DP) from rest to peak exercise in VVI and VVIR pacing modes in 16 patients. Other abbreviations as in Figure 1.

Figure 3. Panels A and B show the relation between the percent increase in cardiac index (CI) in each pacing mode and baseline ejection fraction (EF) in 16 patients. Panel C shows the difference in the percent increase in cardiac index (CI) between pacing modes versus baseline ejection fraction (EF). Pearson's correlation coefficient (r), shown for each graph, failed to reach statistical significance in any of the three correlations. Other abbreviations as in Figure 1.
pacing compared with fixed rate pacing. These results are all consistent with those of the current study.

Effect of ventriculoatrial conduction. Single chamber, single rate ventricular pacemakers may cause "pacemaker syndrome," particularly in patients with intact VA conduction (31,32). The mechanisms of pacemaker syndrome may include loss of AV synchrony, valvular incompetence and inadequate circulatory reflexes (32). In the present study, the lack of a beneficial response to exercise in three subjects (Cases 8, 12 and 15) with intact VA conduction suggests the possibility that this may be a factor in variable rate pacing and that the lack of hemodynamic benefit in these cases may have been due to VA conduction. Interestingly, no adverse effects of intact VA conduction were seen in this study, and it may be that the beneficial effect of variable rate pacing counteracted to some extent the negative effects of VA conduction. Although "pacemaker syndrome" was not noted in this series of patients, this does not mean that this problem is nonexistent with the VVIR pacing mode.

Long-term effects and prognosis. Alpert et al. (7) compared the survival of 132 patients with a VVI pacemaker with that of 48 patients with a dual chamber pacemaker and showed that the 5 year cumulative predicted survival rate was better in patients with pre-existing congestive heart failure who received a dual chamber pacemaker (7). Using a crossover design, Kruse et al. (6) examined the effect of 3 month periods of pacing in the VVI and VDD modes in 16 patients. They noted that mean heart size was significantly smaller after 3 months of VDD pacing. These studies show that there are long-term benefits associated with dual chamber pacing for patients with poor ventricular function. It is not known whether the AV synchrony or the rate variability provided by these devices is more important in producing these long-term benefits. Similar long-term studies have not yet been performed for variable rate pacemakers. For this reason, caution is indicated in the use of VVIR pacemakers in patients with sinus node disease and congestive heart failure.

Limitations. 1) The study population was a select group of patients with specified types of conduction disorders. The conclusions drawn here should not be generalized to all pacemaker patients. 2) Ejection fraction in this study was measured with the patient in the supine or the left lateral decubitus position, whereas cardiac index was measured with the patient upright. This makes correlations between these measurements difficult to interpret. 3) The cardiac index in this study tended to be lower than normal in many instances. We believe that this is related to the technique used to measure cardiac index. Doppler-derived cardiac output correlates only moderately well with cardiac output by other methods, but changes in cardiac output in a given patient can be measured accurately (33).

Clinical Implications. Preoperative exercise testing can assist in selecting the proper pacemaker for a patient and is particularly useful in the patient with sinus node disease. If preoperative exercise testing shows a heart rate increase during exercise, than a variable rate pacemaker is less likely to improve exercise ability. In patients who already have an implanted pacemaker and replacement is being considered, preoperative exercise testing with chest wall stimulation and an external VVIR pacemaker can determine whether a patient will benefit. Although this type of testing will show whether benefit occurs with exercise, the long-term effects of variable rate pacing are still unknown.

In patients with atrial fibrillation and poor ventricular function, these data are encouraging for the use of this new pacing modality. The results of our study are also encouraging for the use of VVIR pacing in patients who are pacemaker dependent and in whom an atrial lead is undesirable or impossible to place. The multicenter clinical study (20,21) of the activity-responsive pacemaker also showed a greater improvement in exercise ability for pacemaker dependent patients.

In patients with sinus node disease and congestive heart failure who are not pacemaker dependent, restoration or maintenance of AV synchrony provides a significant benefit at rest. In addition, many patients with sick sinus syndrome do not have chronotropic incompetence and may not require a sensor-controlled pacemaker. In patients with sinus node disease and congestive heart failure, concerns regarding the use of variable rate pacing in the ventricle include the possible adverse role of VA conduction (if present), competition with an intrinsic heart rate increase and the long-term effects of the lack of AV synchrony on heart size and survival. It should be noted that many patients with sinus node disease have normal AV conduction and could be treated with variable rate pacing to the atrium with maintenance of AV synchrony.

We express our gratitude for the expert secretarial assistance of Gloria Skelton.

References


