Baroreflex Sensitivity and Electrophysiological Correlates in Patients After Acute Myocardial Infarction

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Background. Several studies have identified transient disturbances of autonomic function during the acute and recovery phases of myocardial infarction, and it has recently been suggested that survivors of acute myocardial infarction with depressed vagal tone may be at increased risk of sudden or arrhythmic death.

Methods and Results. To investigate this hypothesis, parasympathetic function was assessed by arterial baroreflex sensitivity (BRS) testing (using the phenylephrine method) and by heart rate variability (HRV) analysis from 24-hour Holter recording in 68 patients at day 7–10 after infarction. The relation between autonomic tone and markers of arrhythmic propensity, including programmed ventricular stimulation (PVS) and late potentials in addition to other clinical variables, was examined. BRS for the whole group was 7.0±4.7 msec/mm Hg and was inversely correlated with age (r=0.53, p<0.001) but not with left ventricular ejection fraction (r=0.035, p=NS). In those patients in whom sustained monomorphic ventricular tachycardia (SMVT) was induced, BRS was significantly reduced (p=0.001) as was HRV (p=0.007) and left ventricular ejection fraction (p=0.022). The strongest association between any variable (including HRV, BRS, late potentials, left ventricular ejection fraction, exercise testing, Q waves, and infarct site) and the induction of sustained monomorphic ventricular tachycardia was depressed BRS with a relative risk of 36.28 (95% confidence interval, 5–266).

Conclusions. This study confirms that depressed BRS identifies a subgroup at high risk for arrhythmic events after myocardial infarction and that programmed ventricular stimulation may be safely limited to this group without any loss of predictive accuracy. (Circulation 1991;83:945–952)

Despite considerable improvements in risk stratification after myocardial infarction, the identification of patients who are at risk for sudden or arrhythmic death remains imprecise. Numerous strategies based on indexes including left ventricular function, complex ventricular ectopy, arrhythmias, and coronary artery anatomy have not led to the effective identification of such patients, nor have these strategies suggested a specific mechanism at which treatment can be aimed.

Recent work has drawn attention to autonomic function in postinfarction patients because both depressed baroreflex (BR) sensitivity and heart rate (HR) variability are known to be associated with increased mortality. A possible explanation for this may be that disordered autonomic function facilitates the expression of life-threatening arrhythmias in postinfarction patients.

To investigate this hypothesis, we studied BR sensitivity, HR variability, and markers of arrhythmic propensity including 24-hour electrocardiographic (ECG) recordings, late potentials, and programmed ventricular stimulation (PVS) in 68 postinfarction patients.

Methods

Serial patients less than the age of 70 years who were admitted to St. George’s Hospital with a documented acute myocardial infarction were asked to give written consent to both PVS and BR sensitivity testing. All studies were performed between 7 and 10 days after infarction. Patients with a history of hypertension, insulin-controlled diabetes mellitus, or any severe concomitant disease that may cause mortality were excluded. No patient received β-adrenergic receptor blockers, calcium antagonists, or antiarrhythmic drugs at the time of the investigation. It was

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considered unethical to place restrictions on drug therapy during the follow-up period, and 30% of patients were discharged on a β-blocker and 9% on a calcium antagonist regimen. Revascularization (coronary vein grafting or angioplasty) was performed in 25% of the study group.

**Baroreflex Sensitivity**

BR sensitivity was assessed by a method previously described. All patients were studied in a fasting and supine state between 7 and 10 days (mean, 8.2 days) after acute myocardial infarction. A right femoral line (5F; length, 15 cm) was used to record continuous arterial pressure with simultaneous recording of a single ECG lead at 25 mm/sec. After a period of rest when blood pressure and heart rate were stable, a bolus of phenylephrine was injected during 15 seconds into a peripheral vein. An initial test dose of 0.2 mg was given, which was followed by progressively larger doses until an increase between 15 and 40 mm Hg in systolic blood pressure occurred. The test was then repeated until at least three recordings were made with the optimum bolus dose. BR sensitivity was calculated by plotting the beat-to-beat change in RR intervals against the change in the preceding systolic blood pressure for the first sustained increase in blood pressure (only sinus beats were analyzed). BR sensitivity was then expressed as the slope of the regression line relating RR interval changes to systolic arterial pressure. Only regression lines that had a correlation coefficient greater than 0.80 or that were significant (p<0.05) were used. At least three such slopes were calculated for each patient, and the mean of these was taken as the BR sensitivity and was expressed in milliseconds per millimeters of mercury. As suggested by the larger study of La Rovere et al., a BR sensitivity less than 3.0 msec/mm Hg (mean minus one standard deviation) in postinfarction patients was considered markedly depressed.

**Programmed Ventricular Stimulation**

Programmed ventricular stimulation was performed with the protocol recommended by Wellens et al with a pacing wire placed in the right ventricular apex. In each case, programmed ventricular stimulation was performed 1–2 hours after BR testing. Up to three extrastimuli were introduced at twice diastolic threshold in sinus rhythm and after eight ventricular drive cycles of 600, 500, and 420 msec. The protocol was discontinued on the induction of a sustained ventricular arrhythmia, but only the induction of sustained monomorphic ventricular tachycardia (VT) at a rate less than 270 beats/min was regarded as a positive result. Polymorphic VT, that is, VT with a continuously varying QRS complex configuration in any recorded ECG lead, ventricular fibrillation, or nonsustained arrhythmias were each regarded as nonspecific responses.

**Other Investigations**

Signal-averaged ECG was performed (with the commercially available high-resolution ECG, ART model 1200EPX, Austin, Tex.) at 6–7 days after infarction. The high-pass filter was set at 25 Hz, and 100–200 beats were averaged to achieve a final noise less than 0.3 μV. The presence of late potentials was defined as positive if two of three of Simson’s criteria were met: filtered QRS complex greater than 120 msec, root mean square voltage less than 25 μV during the last 40 msec of the filtered QRS complex, and duration of the filtered QRS complex greater than 40 msec after voltage decreased below 40 μV. A prolonged filtered QRS was not considered a positive criterion if the QRS duration measured from the standard ECG was greater than 120 msec.

At 6–7 days after infarction when the patient was mobile, ambulatory 24-hour ECG recordings were also obtained with the Reynolds Tracker two-channel recorder (Hertford, England) (lead II and CM5) and analyzed with the Pathfinder 3 system, which is an operator–computer interactive device. Each tape was analyzed and was then visually checked for arrhythmia recognition by one of the investigators (T.F.). Recordings were graded for ventricular ectopic frequency greater than 10/hr.

HR variability was calculated by two methods, the standard deviation of successive normal-to-normal RR intervals (SDRR) as described by Kleiger and colleagues and as the HR variability index that we described previously. The whole 24-hour ECG recording was digitized on-line at the analog-to-digital sampling rate of 128 Hz and transferred to a personal computer (IBM PC-AT). With the automatic arrhythmia algorithm standard to the above Holter system (which is based on the matching-pairs principle), each beat was classified as normal (including border patterns) or aberrant. This analysis resulted in the exact timing and classification of each beat as physiological (normal) or aberrant. The frequency distribution of durations of normal-to-normal RR intervals was constructed, and the HR variability index was expressed in milliseconds as the baseline width of the distribution curve measured by the method of the minimum square difference interpolation. In each recording, the mean duration and the SDRR were also computed. The previously described method of expressing HR variability as the SDRR is affected by recording noise and misrecognition artifact, whereas the method of triangular interpolation of the frequency distribution of RR interval duration described above is not. An HR variability index less than 13 (mean minus one standard deviation as in the case of BR sensitivity) was considered markedly depressed and was chosen retrospectively.

All patients underwent symptom-limited exercise testing with the Bruce protocol. ST segment depression greater than 1.5 mm, chest pain resembling angina, and failure to achieve a 25% or greater increase in systolic
blood pressure were each considered as a positive response. Coronary arteriography was performed in 44 (65%) of the patients on the basis of a positive exercise test. Left ventricular ejection fraction was calculated with the “Mac angio package” (Dodge formula) in the right anterior oblique view. In patients who did not undergo angiography, ejection fraction was calculated with radionuclide scanning.

**Statistical Analysis**

Results were compared with the two-tailed Student's t test or the χ² test with Yates’ correction where appropriate. To assess the relation between BR sensitivity and left ventricular function, simple linear regression was applied. All results are expressed as mean±SD with 95% confidence intervals (CI) where appropriate. Significance was established at a probability value less than 0.05. The standard definitions for sensitivity, specificity, and positive and negative predictive accuracy were used. Relative risk was defined as the event rate in patients with a positive test divided by event rate in patients with a negative test.

**Results**

During the time of study, 68 of a total 170 patients gave their written consent to PVS and BR sensitivity testing. The mean age of the group was 56±10.4 years, and 88% were men. Q wave infarction was present in 46 patients, and the site of infarction was anterior in 34 patients. Mean left ventricular ejection fraction (LVEF) for the whole group was 50.4±15%, and 16 patients (23%) had an impaired LVEF less than 40%. In the 102 patients who refused to participate in the investigation, the mean age was 58±7.5 years, and ejection fraction was 53±15%, neither of which differed significantly from those of the investigated group. The distributions of Q waves and infarction were similar (71 of 102 with Q wave infarction and 65 of 102 patients with anterior infarction).

**Baroreflex Sensitivity**

BR sensitivity was 7.0±4.7 msec/mm Hg, and there was no significant difference in BR sensitivity between groups of patients according to the site of infarct, the presence of Q waves, or positive exercise tests: BR sensitivity was also significantly reduced in patients with late potentials or frequent ventricular ectopics (>10/hr) (Table 1). A weak, but significant, inverse correlation occurred between BR sensitivity and age (p=0.001, r=0.53), but no correlation was noted between BR sensitivity and LVEF (p=NS, r=0.025), the HR variability index (p=NS, r=0.003), or HR variability SDRR (p=NS, r=0.136). In 11 patients, BR sensitivity was judged to be markedly depressed (≤3.0 msec/mm Hg).

**Programmed Ventricular Stimulation**

Sustained monomorphic VT was induced in eight of the 68 patients tested. In seven of these eight patients, induction of sustained monomorphic VT occurred at higher stages of the stimulation protocol with three extrastimuli. An additional 24 patients developed polymorphic VT requiring direct current cardioversion, and the remaining 36 patients had a PVS classified as negative. (This includes patients who developed repetitive responses or nonsustained VT.)

**Electrocardiographic Analysis (24 Hour)**

The HR variability index for the whole group was 24.6±11.4 msec, and the SDRR was 101±60 msec. Eleven patients had a depressed HR variability index (<13 msec), whereas 13 patients had an impaired HR variability SDRR of 50 msec or less. Twenty percent of patients (22 of 68) had a ventricular ectopic frequency greater than 10/hr, and seven patients had nonsustained VT on long-term ECG recordings.

**Exercise Testing and Signal-Averaged Electrocardiogram**

Exercise testing was positive in 44 patients (65%), and 13 patients (19%) had late potentials on the signal-averaged ECG.

**Relation of Baroreflex Sensitivity, Heart Rate Variability, and Other Parameters to Programmed Ventricular Stimulation**

A plot of BR sensitivity in patients according to the results at the time of PVS is shown in Figure 1. For the purpose of this analysis, patients who developed polymorphic VT (a nonspecific response with no prognostic value) and those with a negative response were considered as one group. Other than the polymorphic VT group being older (58.8±10.9 versus 52.2±9.4 years; 95% CI, 1.32–11.9; p=0.016), there were no significant differences between these two groups. BR sensitivity was markedly reduced in those patients who developed sustained monomorphic VT (1.8±1.5 versus 7.8±4.5 msec/mm Hg; 95% CI, 4.2–7.4; p=0.001) (Table 2) as were both measures of HR variability: HR variability index (14.6±5.3 versus 25.8±11.3 msec; 95% CI, 7.04–16.9 msec; p=0.007)

### Table 1. Summary of Baroreflex Sensitivity Testing (msec/mm Hg) According to Prognostic Variables

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Anterior myocardial infarction</td>
<td>6.8±4.9</td>
<td>7.2±4.6</td>
</tr>
<tr>
<td>Q wave</td>
<td>6.9±4.9</td>
<td>7.2±4.3</td>
</tr>
<tr>
<td>Late potential</td>
<td>5.1±4.9</td>
<td>7.5±4.6</td>
</tr>
<tr>
<td>Ventricular ectopic frequency &gt;10/hr</td>
<td>5.1±5.1</td>
<td>7.7±4.2</td>
</tr>
<tr>
<td>Exercise test positive</td>
<td>6.2±4.7</td>
<td>7.9±4.0</td>
</tr>
</tbody>
</table>
and SDRR (57±25 versus 105±59 msec; 95% CI, 24.9–71 msec; p=0.001).

Other characteristics of patients with inducible sustained monomorphic VT included an impaired LVEF (39.1±13.6% versus 52.2±14.8%; 95% CI, 4.74–21.4; p=0.022), older age (65.3±4.0 versus 54.9±10.0 years; 95% CI, 6.47–14.46; p<0.003), and an increased incidence of late potentials (62.5% versus 13.3%, p=0.005). There were, however, no significant differences in the number of patients with a positive exercise test (87.5% versus 66%), Q wave infarcts (87.5% versus 65%), inferior infarcts (62.5% versus 48.3%), or frequent ventricular ectopics (62.5% versus 28.3%).

In particular, seven of the eight patients who developed sustained monomorphic VT had a profoundly depressed BR sensitivity of 3.0 msec/mm Hg or less, whereas only five of eight such patients had an impaired LVEF (<40%), depressed HR variability index (<13), frequent ventricular ectopics, and late potentials, and only four patients had an HR variability SDRR of 50 msec or less. Of all the variables analyzed, BR sensitivity had the strongest association with the development of sustained monomorphic VT (relative risk, 36.28; 95% CI, 5–266) (Table 3).

Events During Follow-Up

Although the primary concern of this study was the relation between BR sensitivity and the induction of sustained VT at PVS, a number of clinical events have occurred during the limited follow-up period (mean, 9 months; range, 1–15 months). To date, nine events have been recorded (Table 4). Five patients have developed clinical VT (one later dying of cardiogenic shock, one patient dying suddenly, and the remaining three are still alive). Four additional deaths have also occurred, none of which was classified as “arrhythmic” according to the Cardiac Arrhythmia Pilot Study Investigators criteria.9 Two patients died after reinfarction, and one additional patient died of left ventricular failure 9 months after the index infarction. One patient’s death was unwitnessed, the body not discovered until several weeks after the event. In the untreated population, nine deaths and five arrhythmic events have been documented.

From Table 4, it can be seen that all five patients who later developed clinical VT had a profoundly depressed BR sensitivity (0.7, 0.8, 0.6, 2.3, and 0.3 msec/mm Hg) and had inducible sustained monomorphic VT at the time of PVS, whereas in the three patients whose deaths were nonarrhythmia related, BR sensitivity was well preserved (8.1, 10.3, and 8.5 msec/mm Hg), and PVS was negative. In the patient whose death was unwitnessed, BR sensitivity was also well preserved at 9.1 msec/mm Hg, and PVS was negative.

When clinical arrhythmic events were considered, BR sensitivity remained significantly reduced (0.9±0.8 versus 7.4±4.5 msec/mm Hg; 95% CI, 5.15–7.83; p=0.0001) as was the HR variability index (12.7±4.0 versus 25.6±11.2 msec; 95% CI, 9.7–18.1; p=0.0001) and SDRR (45±20 versus 104±58 msec; 95% CI, 35.8–82.2; p=0.0001) (Table 5). Again, patients with clinical arrhythmic events had a lower LVEF (33±10% versus 52±14%; 95% CI, 5.1–15.6; p=0.01), were older (66±4.2 versus 55±10 years; 95% CI, 9.9–23.9; p=0.0001), and also had an in-

Table 2. Summary of Investigations According to Results at Programmed Ventricular Stimulation

<table>
<thead>
<tr>
<th></th>
<th>SMVT at PVS</th>
<th>PVS negative</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baroreflex sensitivity (msec/mm Hg)</td>
<td>1.85±1.5</td>
<td>7.8±4.5</td>
<td>0.001</td>
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<tr>
<td>Heart rate variability index (msec)</td>
<td>14.6±5.3</td>
<td>25.8±11.3</td>
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<td>Heart rate variability SDRR (msec)</td>
<td>57±25</td>
<td>105±59</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>65.3±4.0</td>
<td>54.9±10.0</td>
<td>0.003</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>39.1±13.6</td>
<td>52.2±14.8</td>
<td>0.022</td>
</tr>
<tr>
<td>Late potential positive (%)</td>
<td>62.5</td>
<td>13.3</td>
<td>0.005</td>
</tr>
<tr>
<td>Ventricular ectopic frequency &gt;10/hr (%)</td>
<td>62.5</td>
<td>28.3</td>
<td>NS</td>
</tr>
<tr>
<td>Exercise test positive (%)</td>
<td>87.5</td>
<td>66</td>
<td>NS</td>
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SMVT, sustained monomorphic ventricular tachycardia; PVS, programmed ventricular stimulation; SDRR, standard deviation of normal RR intervals.
creased prevalence of late potentials (80% versus 14.3%, \( p=0.003 \)) and frequent ventricular ectopics (100% versus 28.6%, \( p=0.05 \)). When all-cause mortality was considered for all the variables, only LVEF was significantly reduced (41±16% versus 52±14%; 95% CI, 10–21; \( p=0.02 \)).

Selection of Patients for Programmed Ventricular Stimulation

If PVS had been limited to those patients with depressed BR sensitivity (<3.0 msec/mm Hg), then only 11 of 68 patients would have required PVS, identifying seven of the eight patients who developed sustained monomorphic VT. All five patients having arrhythmic events would also have been identified. Only two of the 11 patients tested would have gone on to develop polymorphic VT that would have required cardioversion (compared with 24 patients above), and the positive predictive accuracy of the test would have been considerably improved without altering the sensitivity of the test (Table 3). These data are represented in Figures 2 and 3, which illustrate a comparison of impaired LVEF (<40%) and depressed BR sensitivity (<3.0 msec/mm Hg) in the selection of patients for PVS. Using impaired LVEF, we would have identified four of five clinical arrhythmic events and only five of the eight patients who developed sustained monomorphic VT. The use of alternative indexes such as depressed HR variability, late potentials, ventricular ectopic frequency, exercise testing, Q waves, or infarct site in the selection of patients for PVS proved inferior.

Discussion

The results of this study add further support to the theory that depressed autonomic function identifies a subgroup of patients at risk for sudden or arrhythmic death after myocardial infarction. Both BR sensitivity and HR variability were markedly reduced in those patients developing sustained monomorphic VT at PVS and later clinical arrhythmic events. When all-cause cardiac mortality was considered, only LVEF was a significant predictor of mortality. Thus, autonomic function tests such as BR sensitivity and HR variability may be of particular value in the prediction of arrhythmic or sudden death.

Why Should Altered Autonomic Function Predispose to the Genesis of Arrhythmias?

There is ample clinical and experimental evidence that the electrical stability of the myocardium is dependent on the normal synergistic influences of both divisions of the autonomic nervous system. The detrimental effects of elevated sympathetic activity and the powerful protective effects of vagal reflexes, such as baroreceptor-induced heart rate changes, in

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Event</th>
<th>BRS (msec/mm Hg)</th>
<th>HRV index (msec)</th>
<th>HRV SDRR (msec)</th>
<th>SMVT (Y/N)</th>
<th>EF (%)</th>
<th>LP (Y/N)</th>
<th>VE10 (Y/N)</th>
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<tr>
<td>1</td>
<td>61</td>
<td>VT</td>
<td>0.6</td>
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<td>39</td>
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<tr>
<td>2</td>
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<tr>
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</tr>
<tr>
<td>4</td>
<td>62</td>
<td>VT+D</td>
<td>0.3</td>
<td>10.8</td>
<td>50</td>
<td>Y</td>
<td>22</td>
<td>Y</td>
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<tr>
<td>5</td>
<td>68</td>
<td>VT+SD</td>
<td>0.7</td>
<td>12.1</td>
<td>47</td>
<td>Y</td>
<td>35</td>
<td>Y</td>
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</tr>
<tr>
<td>6</td>
<td>37</td>
<td>RI+D</td>
<td>10.3</td>
<td>29.3</td>
<td>142</td>
<td>N</td>
<td>59</td>
<td>N</td>
<td>N</td>
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<tr>
<td>7</td>
<td>70</td>
<td>RI+D</td>
<td>8.1</td>
<td>14.2</td>
<td>64</td>
<td>N</td>
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<td>N</td>
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<tr>
<td>8</td>
<td>57</td>
<td>UWD</td>
<td>9.1</td>
<td>20.7</td>
<td>80</td>
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<td>45</td>
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<tr>
<td>9</td>
<td>70</td>
<td>LVF+D</td>
<td>8.5</td>
<td>7.6</td>
<td>41</td>
<td>N</td>
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BRS, baroreflex sensitivity; HRV, heart rate variability; SDRR, standard deviation of normal RR intervals; SMVT, sustained monomorphic ventricular tachycardia; EF, ejection fraction; LP, late potential positive; VE10, greater than 10 ventricular ectopics in any 1 hour; CAD, number of diseased coronary arteries; VT, ventricular tachycardia; D, death; SD, sudden death; RI, reinfarction; UWD, unwitnessed death; LVF, left ventricular failure; Y/N, yes or no.
maintaining myocardial electrical stability during acute myocardial ischemia are well recognized.10-14 Myocardial infarction may distort autonomic interaction through several mechanisms. Local areas of myocardial denervation (sympathetic and parasympathetic) may arise after infarction that lead to catecholamine hypersensitivity.15-17 Such autonomic heterogeneity may then predispose to the genesis of local arrhythmias. Alternatively, the destruction of local ventricular chemoreceptors and mechanoreceptors may alter neural feedback to the higher centers, resulting in impaired autonomic regulation and inappropriate autonomic tone (particularly excessive sympathetic or impaired vagal discharge) that may predispose to the genesis of arrhythmias. Reduced HR variability and BR sensitivity would then be seen as markers of this autonomic disarray.

Is Abnormal Autonomic Tone the Sole Requirement for the Genesis of Arrhythmias?

Abnormal autonomic tone per se is probably not the sole requirement for the development of life-threatening arrhythmias in postinfarction patients. Presumably, an abnormal myocardial substrate is also required, autonomic tone having a permissive role for the expression of arrhythmias. Late potentials that represent disordered and inhomogenous conduction through surviving Purkinje fibers are thought to indicate a substrate for reentrant tachycardias.18 In this study, as in others,19,20 a significant correlation was found between the presence of late potentials and the inducibility of sustained monomorphic VT, and four of the five patients classified as having arrhythmic events had positive late potentials. The combination of disordered autonomic function and late potentials may be very specific for arrhythmic propensity.

Several other factors, including left ventricular function and continuing ischemia, might have influenced the development of sustained monomorphic VT at PVS. Although ejection fraction was lower in the sustained monomorphic VT group, no direct correlation was found between BR sensitivity and LVEF in the population examined. This may appear surprising, but previous studies of BR sensitivity in postinfarction patients have also failed to show such a relation, and prior reports of an inverse correlation between BR sensitivity and LVEF have been limited to patients with overt congestive cardiac failure that...
was not present in any of the patients at the time of investigation.\textsuperscript{1,21} Age also appeared to be of relevance because the group developing sustained monomorphic VT was significantly older (\(p<0.005\)). Autonomic function and BR sensitivity are known to become impaired with increasing age, and this was confirmed in this study.\textsuperscript{1} But if the premise that impaired autonomic tone predisposes to ventricular arrhythmias is correct, an increased incidence of inducible ventricular arrhythmias in older patients would be a reasonable expectation. Whether depressed BR sensitivity is an independent predictor of sudden death or is dependent on other variables will have to be determined by multivariate analysis in a larger group of patients. However, in this study, both PVS and BR sensitivity appeared to be sensitive markers of arrhythmic risk.

Depressed BR sensitivity was also a more sensitive predictor of arrhythmic events than was the impaired HR variability index. Although both BR sensitivity and HR variability are accepted markers of vagal tone, BR sensitivity testing may be a more specific measure of the maximum ability of the vagal reflexes to respond, whereas HR variability (measured in the convalescent phase) may be a specific measure of resting vagal tone. Also of note, the two estimates of HR variability, particularly the SDRR measures used in this study, may not be the best measures of vagal activity; the root mean square difference of successive RR intervals and the proportion of successive RR intervals greater than 50 msec in difference may be superior.\textsuperscript{21} Bigger et al\textsuperscript{21} in a collaborative study found only a moderate correlation between HR variability and BR sensitivity and suggested that these values may measure differing but complementary components of vagal tone.

Clinical Implications and Scheme for Stratification

Tables 4 and 5 indicate that depressed BR sensitivity and PVS were the most sensitive predictors of future arrhythmic events. PVS has the advantage that it probably identifies a specific mechanism for sudden death at which treatment can be aimed. It would not be appropriate or practical to perform PVS in all postinfarction patients, instead it would be preferable to limit PVS to a high-risk group. Limiting PVS to those patients with evidence of impaired autonomic function may prove to be a method of selecting patients superior to methods used at present. Despite the greater predictive value of BR sensitivity in this study a noninvasive method such as HR variability may be of more value in larger populations (and this will require investigation in a larger prospective trial).

Criticism

This study by its nature has involved a small number of patients and events, and care should be taken in drawing conclusions from these results and applying them to clinical situations. It will be necessary to prospectively test the value of our results in a larger group before confirming BR sensitivity as an independent predictor of arrhythmic events. The selection of dichotomy points, although retrospective, is based on the previous observations of La Rovere et al,\textsuperscript{1} and the points were chosen to gain the maximum sensitivity and specificity. Although all patients were tested in a drug-free state, it is impossible at present to exclude the effects of drug therapy and revascularization on survival during the follow-up period.

Last, BR sensitivity was assessed by a standard method in a resting supine state, but care must be taken in extrapolating these results to clinical practice, particularly because BR control in ambulant humans is not static, and dynamic Resetting of the threshold setting point and gain occurs.\textsuperscript{22}

Conclusion

We suggest that all postinfarction patients undergo an assessment of autonomic function (preferably BR sensitivity measurement) or HR variability analysis before hospital discharge. Patients with depressed BR sensitivity or HR variability should be considered at high risk for future arrhythmic events and will require further investigations including programmed ventricular stimulation. Specific treatments such as PVS-directed drug therapy or the implantation of automatic defibrillators may then be considered in patients developing sustained monomorphic VT at PVS.

References


**KEY WORDS**
- autonomic function
- baroreceptor function
- sudden death
- myocardial infarction
Baroreflex sensitivity and electrophysiological correlates in patients after acute myocardial infarction.
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