Rate Dependent Ventricular Ectopia Following Acute Coronary Occlusion

The Concept of An Optimal Antiarrhythmic Heart Rate

By Kul D. Chadda, M.D., Vidya S. Banka, M.D., and Richard H. Helfant, M.D.

SUMMARY
Recent reports have indicated that tachycardia as well as bradycardia may be arrhythmogenic in acute myocardial infarction. The present experimental study was designed to systematically evaluate the arrhythmogenic and antiarrhythmic effect of heart rate over a wide spectrum using sinus node crush and atrial pacing. Serial recordings of the surface electrocardiograms and local electrograms for a maximum period of three hours were taken at rates of 60-200 beats/min before and after ligation of the left anterior descending coronary artery in 24 open chested dogs. Immediately following coronary occlusion, the incidence of ventricular ectopic complexes was 7.6 ± 1.6/min at a rate of 60, and gradually decreased to 2.5 ± 0.4/min at a rate of 90 (P < 0.01). At rates of 110-150 ≤ 1 ventricular ectopic complex/min was noted. However, at rates of 180 and above, the incidence of ventricular ectopic complexes dramatically increased with frank ventricular tachycardia and/or fibrillation being provoked on seventeen occasions. Similarly, at rates of 60-90, ventricular tachycardia and/or fibrillation was exhibited on sixteen occasions, but never at rates between 110-150. Local electrograms exhibited marked ST segment elevation with higher heart rates compatible with increased local ischemia. It is concluded that ventricular ectopia is more common at rapid as well as slow heart rates after acute coronary occlusion. There appears to be an optimal intermediate rate for maximal antiarrhythmic effect.

Additional Indexing Words:
Bradycardia Tachycardia Ventricular tachycardia Overdrive Myocardial infarction Ventricular fibrillation Atrial pacing

SEVERAL EXPERIMENTAL1, 2 and clinical3, 4 reports have indicated that bradycardia predisposes the heart to ventricular ectopia in the course of acute myocardial infarction. By increasing the temporal dispersion of refractoriness, bradycardia has also been found to lower the threshold for ventricular fibrillation.5 However, more recent studies have indicated that rapid heart rates may also be arrhythmogenic under these circumstances. These latter studies have emphasized that in situations of acute ischemia, tachycardia may indeed have more deleterious effects than bradycardia in producing ventricular ectopia.6 Conversely, it has also recently been shown that lowering heart rate may decrease ventricular ectopia following coronary occlusion.7

To date the effects of a wide range of heart rates have not been systematically studied in relation to the development and frequency of ventricular ectopia. The present experimental study was designed to evaluate the arrhythmogenic and antiarrhythmic effects of heart rate following acute coronary occlusion and to further investigate the concept of overdrive from the standpoint of an optimal heart rate.

Material and Methods
Experiments were performed on 24 mongrel dogs weighing 15-30 kg, anesthetized with sodium pentobarbital (30 mg/kg intravenously). The trachea was intubated and positive pressure respiration was employed using a Harvard pump. The chest was opened in the midline and the pericardium incised to form a pericardial cradle. The left anterior descending coronary artery was dissected approximately 3 cm from its origin and a silk ligature was placed loosely around the vessel.

Local bipolar electrograms were recorded from

From the Division of Cardiology, Presbyterian-University of Pennsylvania Medical Center, Philadelphia, Pennsylvania.
Address for reprints: Richard H. Helfant, M.D., Chief, Division of Cardiology, Presbyterian-University of Pennsylvania Medical Center, 51 North 39th Street, Philadelphia, Pennsylvania 19104.
Received June 20, 1973; revision accepted for publication November 12, 1974.
potentially ischemic and nonischemic myocardium by inserting two pairs of fine teflon coated stainless steel wires, one in each zone. A pair of additional wires was inserted into the right atrial appendage and atrial pacing was performed with a battery powered Medtronic Model 5837 pacemaker.

The sinus node was crushed with a clamp. Only those experiments were included in the study in which a heart rate of 60 was achieved with sinus node crush alone. This was achieved in 16 of the 24 experiments. Lead II of the surface ECG was continuously monitored and all records were taken on a multichannel recorder at paper speeds of 10 and 25 mm/sec.

Control recordings were obtained at heart rates of 60, 70, 80, 90, 110, 120, 150, 180 and 200 beats/min using right atrial pacing. The coronary artery was ligated and continuous recordings of the incidence of ventricular ectopic complexes/minute were obtained at each heart rate. Atrial pacing was performed in random sequence for a period of two minutes at each heart rate. Data was collected for three hours following coronary occlusion. For purposes of statistical analysis, each episode of ventricular tachycardia or fibrillation was given an arbitrary score of 10 ventricular ectopic complexes/minute.

Criteria for ventricular ectopic beats were as follows:
1) fixed coupling time with compensatory pause (unpaced);
2) independence of atrial activity;
3) presence of fusion beats;
4) rapid degeneration of the ectopy to ventricular fibrillation.

The number of episodes of ventricular ectopia were calculated according to the following classification to evaluate the severity of arrhythmia.
Class I = less than six ventricular ectopic complexes/minute.
Class II = greater than six ventricular ectopic complexes/minute.
Class III = greater than six ventricular ectopic complexes/minute plus two successive ventricular ectopic complexes and/or multifocal ventricular ectopic complexes.
Class IV = ventricular tachycardia (including runs of three or more ventricular ectopic complexes in a row) or ventricular fibrillation.

For purposes of tabulation the most severe arrhythmia was classified during atrial pacing at each heart rate.

During the first six experiments it was noted that class III or IV arrhythmia invariably precipitated ventricular fibrillation at either the 60-90 or 180-200 rate ranges. Hence, when class III or IV arrhythmia occurred in these rate ranges, the pacing rate was abruptly changed to a higher or lower level. Thus, in these experiments the effects of increasing or decreasing the heart rate could also be studied. For purposes of tabulation heart rates were grouped into three categories: 60-90, 110-150 and 180-200.

Results

Frequency of Ventricular Ectopia

Figure 1 illustrates the frequency of ventricular ectopic complexes with respect to heart rate. Ventricular ectopic complexes occurred most frequently at a heart rate of 60 and this incidence was significantly higher \( P < 0.01 \) than that which occurred at a heart rate of 90. The frequency of ventricular ectopic complexes further decreased as the heart rate was increased, with a minimum of ventricular ectopia \( (<1/min) \) at heart rates of 110, 120, and 150 (fig. 1). However, ventricular ectopic complexes occurred more frequently as the heart rate was further increased to 180 and 200. The increase in frequency at 200/min was statistically significant compared to the 110-150 rates \( P < 0.001 \).

Severity of Ventricular Ectopia

Table 1 shows the effect of heart rate on the total number of instances of ventricular ectopia class I to IV. Maximum episodes of class IV ectopia were noted at extremes of heart rate, i.e., the 60-90 and 180-200 groups. Sixteen such episodes occurred at heart rates of 60-90; and seventeen were exhibited at rates of 180-200. In contrast, there was a dramatic absence of such arrhythmias at intermediate rates. All sixteen episodes of ventricular tachycardia which occurred in the 60-90 group followed class I, II or III arrhythmias (fig. 2). In contrast, 7 of 17

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-90</td>
<td>24</td>
<td>7</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>110-150</td>
<td>14</td>
<td>1</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>180-200</td>
<td>7</td>
<td>0</td>
<td>2</td>
<td>17</td>
</tr>
</tbody>
</table>

Table 1

Relationship of heart rate to total episodes of ventricular ectopia.

Figure 1

Frequency of ventricular ectopia with respect to heart rate.

Circulation, Volume XLIX, April 1974

Figure 2

Ventricular ectopic complexes followed by an episode of ventricular fibrillation at a heart rate of 60. Note the elevated ST segments in the local electrogram from the ischemic zone.
episodes of ventricular tachycardia occurring at heart rates of 180-200 were not preceded by any ventricular ectopic complexes and thus were of sudden onset (fig. 3). In addition, none of the nine episodes of class III arrhythmias in the 110-150 group progressed to ventricular tachycardia and fibrillation (table 1).

All eight episodes of ventricular fibrillation were preceded by either class I, II, or III ventricular ectopia or ventricular tachycardia. Three episodes of ventricular fibrillation occurred at heart rates of 60-90, while five episodes occurred at heart rates of 180-200.

Figure 4 shows the distribution of class I-IV ventricular arrhythmia at various heart rates. Total number of class I arrhythmia is highest in the slow rate range, i.e. 60-90, while class IV arrhythmia predominated in the 180-200 rate range. It is interesting to note that although the total instances of class I-III arrhythmias diminished gradually with increase in heart rate with a minimum at the faster rate ranges, class IV arrhythmia occurs commonly at the rapid rates as at the slow ones.

Effects of Change in Pacing Rate
The effect of change in pacing rate was particularly apparent when class III and IV ventricular ectopia occurred at both the slow and the high rate ranges. Ventricular tachycardia or fibrillation was invariably provoked if the same pacing rate was continued under these circumstances. On the other hand, thirteen episodes of class III or IV arrhythmias were terminated by increasing the pacing rate in the 60-90 group (fig. 5).

However, this overdrive effect was not beneficial in two instances of sustained ventricular tachycardia which progressed to ventricular fibrillation despite increasing the pacing rate. Similarly at the 180-200 rates, eleven episodes of class III and IV arrhythmia were abolished by decreasing the pacing rate to the 110-150 rate range (fig. 6).

Relation of Ventricular Tachycardia and Fibrillation to Duration of Ischemia
Figure 7 shows the temporal relationship of the episodes of class IV arrhythmia to time from coronary occlusion. It is evident that class IV arrhythmia frequently occurs after the initial hour of ischemia and its relationship to underlying heart rate (i.e., occurrence at the extremes of rate) persisted throughout the three hour period of the study.

Discussion
The relationship between ventricular ectopia and underlying heart rate has evoked considerable controversy.6, 8, 9, 10 The arrhythmogenic effects of bradycardia in circumstances of both experimental1, 2 and clinical3-4 myocardial ischemia or infarction have been widely accepted. The mechanism of the slow rate induced ectopia has been attributed to increased dispersion of refractoriness.5 Scherlag et al.7 have more recently shown that rapid heart rates following coronary occlusion are also arrhythmogenic. These latter findings have been supported by
Redwood et al.\(^8\) as well as Zipes and Knöbelsmith.\(^11\) It has also been shown that rapid heart rates increase non-homogeneity of refractory periods in contiguous areas of myocardium and increase the vulnerability to fibrillation.\(^12\)

The results of the present study indicate that both slow and rapid heart rates are arrhythmogenic during acute ischemia. A total of 33 instances of ventricular tachycardia and eight of fibrillation occurred with equal frequency at extremes of heart rates. In contrast, ventricular tachycardia and ventricular fibrillation were strikingly absent throughout the three-hour period of study (fig. 7) in the intermediate rate range (table 1, fig. 4). It is of interest that this relationship of class IV arrhythmia to heart rate persisted throughout the study. This observation indicates that the rate relationship is not solely an acute phenomenon, but persists throughout the period of ischemia studied.

In addition, the effects of increasing or decreasing the heart rate in the low and high rate groups respectively, also resulted in marked changes in frequency and severity of ventricular ectopia. Thirteen instances of ventricular tachycardia at the 60-90 rate range were terminated by increasing the paced rate (fig. 5). Conversely, eleven instances of ventricular tachycardia were controlled in the 180-200 group by decreasing the rate to the intermediate range (fig. 6). These findings indicate that there are beneficial antiarrhythmic effects of “underdrive” as well as “overdrive” at the extremes of heart rate.

A gradual decline in the occurrence of class I, II and III arrhythmias was noted as the heart rate was increased, although somewhat paradoxically the incidence of class IV arrhythmia was highest in the 180-200 rate range (fig. 4). Several investigators, including our group have noted increased ischemia in the local electrogram ST segment exhibited with the higher heart rates.\(^7,\,8\) It has also been demonstrated that the size of the ischemic area is increased at higher heart rates.\(^18\) It is probable that in circumstances of increased ischemia a concomitant increase in vulnerability to ventricular tachycardia or fibrillation exists. Therefore, even though the actual number of ventricular ectopic beats decreases at the high rate range, they have more malignant potential. This is borne out by the finding that although all sixteen instances of class IV arrhythmias in the 60-90 group were preceded by class I-III arrhythmias (fig. 2), this was true in only ten of seventeen class IV episodes in the 180-200 group. The remaining seven episodes were abrupt in onset and presumably were precipitated by the initial ventricular ectopic beat.

In summary, the findings of the present study indicate that the incidence and severity of ventricular ectopia is highest at the extremes of heart rates. Thus there appears to be an optimum intermediate rate range at which ventricular ectopia are at a minimum. In the presence of significant ventricular ectopia associated with myocardial ischemia this intermediate rate is “antiarrhythmic” when achieved by either “overdriving” or “underdriving” the pre-existing arrhythmogenic heart rate.

Acknowledgment

The authors wish to thank Mrs. Joan Wachlin and Mr. Joseph Lewandowski for their technical assistance, and Mrs. Eileen McCrudden for her assistance in preparing the manuscript.

References

10. EPSTEIN SE, REDWOOD DR, SMITH ER: Atropine and
acutely myocardial infarction. Circulation 47: 430, 1973
12. Kent KM, Smith ER, Redwood DR, Epstein SE:
Rate Dependent Ventricular Ectopia Following Acute Coronary Occlusion: The Concept of An Optimal Antiarrhythmic Heart Rate
KUL D. CHADDA, VIDYA S. BANKA and RICHARD H. HELFANT

Circulation. 1974;49:654-658
doi: 10.1161/01.CIR.49.4.654

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1974 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/49/4/654

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/