HEART RATE AND EXPERIMENTAL CAROTID
ATHEROSCLEROSIS

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RESTING HEART RATE is a recognized independent risk factor associated with cardiovascular disease.1 Previous experiments from our laboratory have demonstrated that lowering the heart rate retards coronary atherogenesis.2 It is not clear whether a similar relationship exists between heart rate and carotid atherosclerosis. We examined the effect of heart rate and controlled modification of heart rate on the severity of carotid bifurcation atherosclerosis in a primate model of diet-induced atherosclerosis.

MATERIALS AND METHODS

Adult male cynomolgus monkeys (n = 18) underwent continuous 24-hour electrocardiogram telemetry for two months to determine the pattern of intrinsic heart rate. The basal heart and its range (maximum — basal heart rate) was determined from the frequency distribution heart rate histogram of each animal. Using cluster analysis, animals were divided into two groups: 7 animals (Group I) had a low basal heart rate (94 ± 12) and high range (33 ± 6), while 11 animals (Group II) had a higher basal heart rate (128 ± 7) and lower range (22 ± 5) (P < 0.01). To assess the effect of low and high fixed controlled heart rate on carotid atherosclerosis, all animals underwent chemical atrioventricular node ablation with 40% formalin and placement of a left ventricular epicardial pacemaker. They were randomly assigned to continuous pacing at either 80 or 130 beats per minute (bpm) for a period of six months during which time they were fed an atherogenic diet containing 2% cholesterol and 25% peanut oil. After sacrifice, the carotid bifurcations were pressure perfusion fixed and sectioned at six standard levels. Carotid lesion area, percent stenosis, and maximum lesion thickness at each level were quantitated using computer-assisted morphometry.

RESULTS

There was significantly more plaque in high heart rate (Group II) animals compared with low heart rate (Group I) animals (Table 1). Mean plasma cholesterol levels were not different between the two groups (401 vs. 493 mg%, P > 0.5). Fixed controlled pacing resulted in a

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<thead>
<tr>
<th>Measurement</th>
<th>Intrinsic HR</th>
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<th>Paced HR</th>
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<tbody>
<tr>
<td></td>
<td>Group I (n = 7)</td>
<td>Group II (n = 11)</td>
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<tr>
<td></td>
<td>(↓ HR, ↑ HR range)</td>
<td>(↑ HR, ↑ HR range)</td>
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<td>Lesion area (mm²)</td>
<td>0.20 ± 0.05</td>
<td>0.45 ± 0.10*</td>
<td>0.38 ± 0.08</td>
<td>0.32 ± 0.06</td>
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<td>Stenosis (%)</td>
<td>4.5 ± 0.82</td>
<td>11 ± 1.72*</td>
<td>8.7 ± 1.3</td>
<td>7.8 ± 1.2</td>
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<td>Maximum less thickness (μm)</td>
<td>125 ± 21</td>
<td>191 ± 26*</td>
<td>174 ± 22</td>
<td>169 ± 21</td>
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Values are expressed as mean ± SEM. HR = heart rate; bpm = beats per minute.

*P < 0.01.

**P < 0.001.
moderate degree of carotid atherosclerosis with no difference between low and high heart rate paced animals (Table 1).

DISCUSSION

Low and oscillatory wall shear stress have been implicated in the pathogenesis of early carotid bifurcation lesions.\(^3\) The frequency and duration of these near wall flow patterns are heart rate dependent. The findings of this study indicate a clear association between intrinsic heart rate and susceptibility/resistance to carotid atherosclerosis with low heart rate protecting against and high heart rate enhancing carotid bifurcation lesions. Extrinsic fixed regulation of the heart rate failed to modify this relationship. Further studies are needed to elucidate the effect of exercise and pharmacological alterations of heart rate and its variability on carotid and peripheral atherosclerosis.

REFERENCES