LOW DIURNAL HEART RATE VARIABILITY INHIBITS EXPERIMENTAL CAROTID STENOSIS

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FLUCTUATION OF HEART RATE (HR) in response to stress is a marker of cardiovascular reactivity and physical fitness and is assessed by measurement of HR variability. Poor physical conditioning increases both diurnal heart rate variability (dHRV) and risk for cardiovascular events.\textsuperscript{1-3} We have previously demonstrated that extrinsic fixed regulation of HR fails to modify the relationship between elevated HR and susceptibility to coronary and peripheral atherosclerosis, suggesting a role of HR variability in plaque formation.\textsuperscript{4,5} In this study we tested the hypothesis that low dHRV retards carotid plaque formation in a non-human primate model of diet-induced atherosclerosis.

MATERIALS AND METHODS

HR was recorded every 20 minutes by an implantable intraaortic sensor/transmitter in 15 unrestricted adult male cynomolgus monkeys. In seven monkeys sinoatrial ablation with electrocautery was employed to lower HR and create a wide range of dHRV for the entire group. Using fast Fourier transform power spectral analysis, dHRV was measured from the HR series of each animal by the power amplitude for the daily HR variability cycle in \( \mu \text{V/Hz} \). All animals were fed an atherogenic diet containing 2\% cholesterol and 25\% peanut oil for 6 months and were thereafter sacrificed. The carotid bifurcations were pressure perfusion fixed and sectioned at five standard levels.

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Summary of heart rate variability measurements

<table>
<thead>
<tr>
<th></th>
<th>Low HRV (n = 7)</th>
<th>High HRV (n = 8)</th>
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</thead>
<tbody>
<tr>
<td>Diurnal HRV (μV/Hz^{0.5})</td>
<td>16.5 ± 4.6</td>
<td>34 ± 6*</td>
</tr>
<tr>
<td>Mean HR</td>
<td>108 ± 7</td>
<td>138 ± 18†</td>
</tr>
<tr>
<td>% Carotid stenosis</td>
<td>34 ± 10</td>
<td>56 ± 17‡</td>
</tr>
<tr>
<td>Total cholesterol (mg%)</td>
<td>744 ± 227</td>
<td>896 ± 239</td>
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</tbody>
</table>

*P < 0.01; †P < 0.006; ‡P < 0.004.

Percent (%) carotid stenosis was quantitated at each level using computer-assisted morphometry.

RESULTS

The 24-hour HR variability cycle was represented by a power peak at 11.5 μHz. dHRV ranged from 7.6 to 42.5 μV/Hz^{0.5} and mean HR from 98 to 173. Sinoatrial node ablation reduced dHRV from 27.7 ± 3.5 to 19.3 ± 6 μV/Hz^{0.5} (P < 0.04) and mean HR from 137 ± 14 to 111 ± 11 (P < 0.02) in 60% of animals. Total mean plasma cholesterol increased from 120 to 825 mg% after diet induction (P < 1 × 10^{-9}). There was a strong positive relationship between % carotid stenosis and both dHRV and mean HR (r = 0.65, P < 0.03). dHRV was a better predictor of carotid stenosis than mean HR; high dHRV animals had almost two times greater carotid stenosis than those with low dHRV (P < 0.004). Total plasma cholesterol was not different for the two groups (P > 0.10) and was not a predictor of the degree of carotid stenosis (Table).

CONCLUSIONS

These findings indicate that dHRV is an important determinant for experimental carotid stenosis. High dHRV is associated with increased susceptibility to carotid bifurcation atherosclerosis. Potential mechanisms for this relationship include HR modulation of the frequency and duration of near wall hemodynamic forces, which are known to influence plaque localization and mural structural composition.6,7 Lowering of dHRV by exercise and stress reduction may help prevent plaque progression and ischemic events in humans and warrants further investigation.

REFERENCES

2. Odemuyiwa O, Malik M, Farrell T, et al: Comparison of the predictive characteristics of heart rate variability index and left ventricular ejection fraction for all-cause mortality,


