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A Novel Heart Rate Variability Index of Cardiac Vagal Outflow Predicts Sudden Cardiac Death after an Acute Myocardial Infarction

Category: 10 Ambulatory ECG/Heart Rate Variability/QT Interval

Presentation Time: Friday, 9:30 a.m. - 9:45 a.m.

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Presentation Number: AB27-6

Cardioprotective role of vagal activity is well documented in experimental animal models. However, vagally mediated high-frequency (HF, 0.15-0.4 Hz) oscillation of R-R intervals (RRi) has failed to provide prognostic information on the risk of sudden cardiac death (SCD) in clinical studies. We describe a novel method of quantifying the vagal activity (V_{index}), which eliminates the potential biases of measurements of HF oscillations from ambulatory recordings, such as effects of saturation or physical activity on heart rate variability (HRV).

PURPOSE: To study whether V_{index} provides prognostic information on SCD. **METHODS:** Ambulatory 24-h RRi were recorded for 590 patients 5-14 days after an acute myocardial infarction (AMI). V_{index} was calculated from the linear portion of the regression line between the average RRi and the HF power. The upper RRi limit was defined by the deflection point of the quadratic regression curve between the HF power and RRi (lower bound of 99% CI: 92% of the maximum RRi), and the lower limit was defined as 82% of maximum RRi to equalize the range of relative RRi and to eliminate the effects of physical activity on HRV. Other traditional and newer HRV indexes, such as heart rate turbulence (HRT) and fractal scaling exponent (α_1), were calculated by standard methods. **RESULTS:** During the mean follow-up of 39 ± 14 months, total mortality was 13% (n=74), and SCD occurred in 3% (n=17) of the patients. In univariate analysis, $V_{index} < 4.45 \text{ ms}^2$ (RR: 5.9, 95% CI: 1.7-20.7, $p < 0.01$) and HRT slope $< 1.9 \text{ ms/RRi}$ (RR: 4.4, 95% CI: 1.6-12.0, $p < 0.01$) were the most powerful predictors of SCD. After adjustment with age, ejection fraction and diabetes mellitus, both V_{index} and HRT remained as independent predictors of SCD (RR: 4.3, 95% CI: 1.2-15.4, $p < 0.05$ and RR: 3.0, 95% CI: 1.1-8.4, $p < 0.05$, respectively). Other HRV indexes did not predict SCD in multivariate analysis. **CONCLUSIONS:** A novel index quantifying cardiac vagal activity from the 24-hour ECG recordings is a powerful predictor of SCD in post-AMI population, confirming the experimental data on importance of cardiac vagal outflow in prevention of fatal arrhythmic events in humans.

Commercial Relationship: A.M. Kiviniemi, None; M.P. Tulppo, None; A.J. Hautala, None; T.H. Mäkilä, None; T. Seppänen, None; H.V. Huikuri, None.

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