Enhanced sympathetic activity at the ventricular myocardium can destabilize repolarization, increasing the risk of death. Sympathetic activity is known to cluster in low-frequency bursts; therefore, we hypothesized that sympathetic activity induces periodic low-frequency changes of repolarization. We developed a technique to assess the sympathetic effect on repolarization and identified periodic components in the low-frequency spectral range ($\leq 0.1$ Hz), which we termed periodic repolarization dynamics (PRD). We investigated the physiological properties of PRD in multiple experimental studies, including a swine model of steady-state ventilation ($n=7$) and human studies involving fixed atrial pacing ($n=10$), passive head-up tilt testing ($n=11$), low-intensity exercise testing ($n=11$), and beta blockade ($n=10$). We tested the prognostic power of PRD in 908 survivors of acute myocardial infarction (MI). Finally, we tested the predictive values of PRD and T-wave alternans (TWA) in 2,965 patients undergoing clinically indicated exercise testing. PRD was not related to underlying respiratory activity ($P<0.001$) or heart-rate variability ($P=0.002$). Furthermore, PRD was
enhanced by activation of the sympathetic nervous system, and pharmacological blockade of sympathetic nervous system activity suppressed PRD (P<=0.005 for both). Increased PRD was the strongest single risk predictor of 5-year total mortality (hazard ratio 4.75, 95% CI 2.94-7.66; P<0.001) after acute MI. In patients undergoing exercise testing, the predictive value of PRD was strong and complementary to that of TWA. We have described and identified low-frequency rhythmic modulations of repolarization that are associated with sympathetic activity. Increased PRD can be used as a predictor of mortality in survivors of acute MI and patients undergoing exercise testing.ClinicalTrials.gov NCT00196274. This study was funded by Angewandte Klinische Forschung, University of Tübingen (252-1-0).