Background: We previously proposed heart rate complexity (HRC) as a "new vital sign" suitable for assessment of the need to perform lifesaving interventions (LSIs) in trauma patients. We explored the feasibility of performing HRC analysis of the EKG in combat casualties in the theater.
Methods: A total of 800-beat ectopy-free sections of electrocardiographs from 11 combat casualties were analyzed off-line using nonlinear methods: sample entropy (SampEn), detrended fluctuation analysis (DFA), and point correlation dimension (PD2i).
Results: See Table 1. All casualties survived their injuries.
Conclusions: Casualties demonstrated abnormal HRC. Those requiring LSIs had Min PD2i values of less than 1. These findings suggest the potential utility of HRC is as a tool for diagnosis of the need for LSIs in combat casualties.

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Early detection of infection with continuous heart rate variability analysis in neutropenic patients

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Hypothesis: Infection leading to organ failure kills more critically ill patients than any other cause. Early diagnosis of infection leading to timely antibiotics and resuscitation saves both patient lives and costs of care; however, current techniques to diagnose infection are imprecise, insensitive, and frequently show late manifestations of infection. To address this problem, our aim was to uncover hidden information contained within cardiac interbeat-interval time series using advanced mathematical analysis rooted in complex systems science. Previous work has demonstrated altered heart rate variability (HRV) in patients with infection (more regular, less complex cardiac variation); not only is HRV altered with infection, the degree of HRV alteration also correlates with its severity. Building upon these results, our principal objective was to perform *continuous HRV monitoring* in adult patients at high risk for infection and evaluate the hypothesis that change in HRV precedes traditional markers of infection.
Methods: In a consecutive observational trial, ambulatory patients undergoing bone marrow transplantation (BMT) for hematological malignancy underwent continuous Holter heart rate monitoring, starting the day before BMT and continuing until recovery. Demographic, clinical, microbiological data, daily symptoms, and patient temperature were recorded; HRV analysis was performed and displayed with *continuous individualized variability analysis* software that performs multiparameter characterization of variability (including time-domain, frequency-domain, scale-invariant, and complexity measures of variability), using a smoothed, overlapping, iterative, interval-in-time analysis algorithm (interval and step size, 1200 and 200 heart beats).
Results: A total of 10 patients have completed this pilot investigation to date, undergoing monitoring for 12 ± 3 days (range, 5-15 days). All 10 patients became neutropenic, and all were diagnosed and treated for infection. The clinical diagnosis of infection was made owing to fever (core temperature, >38.0°C) in 8 patients and to symptoms in 2 (mucositis, diarrhea). Baseline HRV was defined as the average HRV during the first 24 hours of observation (before BMT); reproducible reduction in baseline variability was present in all patients in association with infection (100%), as well as with severe symptoms (30%) such as recurrent diarrhea or vomiting. A 10% and 20% decrease in baseline HRV occurred 41 ± 45 and 33 ± 45 hours before antibiotic administration. No patient required intensive care unit admission, and recovery of HRV was observed in 70% patients.
Conclusions: These descriptive preliminary data support the feasibility of continuous HRV monitoring in ambulatory patients. Given that changes in HRV occur in association with symptoms and infection, and occur earlier than traditional clinical markers of infection, further investigation is warranted to define accuracy, sensitivity, and specificity of change in variability as a tool for early detection of infection.

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Relation of heart rate variability to serum levels of C-reactive protein in patients with severe sepsis and septic shock

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Objective: Recent experimental data in patients with cardiovascular diseases have suggested that depressed heart rate variability (HRV) is associated with increased markers of inflammation. Whether such a relation also exists in critically ill patients is unknown. In this study, we tried to quantify the instantaneous and longitudinal correlations between different HRV indices and daily measured C-reactive protein (CRP) serum levels in a cohort of patients with severe sepsis and septic shock.
Methods: We assessed HRV daily in the time domain (standard deviation of RR intervals [SDNN]) and in the frequency domain (low frequency [LF], high frequency [HF] [ms^2/Hz]), the 2 values of standard deviation (SD1 and SD2), as indicators of the dispersion of RR points obtained from the Poincaré plot and measured CRP levels, in 20 patients admitted to our intensive care unit with a primary diagnosis of severe sepsis or septic shock. Acute Physiology and Chronic Health Evaluation II score of admission was 18 ± 5.6. Patients with a previous history of atrial flutter or fibrillation, trauma brain injury, and acquired immunodeficiency were excluded from the study. The electrocardiogram signal was recorded for 10 minutes and sampled at 250 Hz, under sedation and mechanical ventilation. Linear regression and correlation analysis with Pearson's test was performed on log-transformed HRV data and CRP levels to assess whether HRV variables were independent predictors of CRP and for evaluation of trends over time. Differences between survivors and nonsurvivors were evaluated by analysis of variance.
Results: C-Reactive protein blood levels exhibited significant negative correlations with LF ($r =)0.78$, $P < .01$), HF ($r =)0.80$, $P < .01$), LF/HF ($r =)0.61$, $P < .05$), and SDNN ($r =)0.79$, $P < .01$), and a positive correlation with SD1/SD2 ($r = 0.66$, $P < .05$). SDNN, LF, and HF power values were the most significant predictors of increasing C-reactive protein levels ($P < .01$ for the 3 comparisons) and proved to be significantly different between survivors and nonsurvivors ($P < .01$ for the 2 comparisons).