HRV-Derived Autonomic Responses to Noradrenaline Differentiate ICU Mortality Outcomes

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Critically ill patients in the Intensive Care Unit (ICU) often require noradrenaline (NE) to maintain hemodynamic stability in states of vasodilatory hypotension and circulatory failure. The inter-individual variability in physiological response to NE may carry prognostic information. This study investigates whether autonomic response phenotypes, quantified via heart rate variability (HRV), are associated with ICU mortality.

RR intervals were extracted from ECG signals recorded by ICU monitors of patients receiving NE therapy and combined with clinical data from the MIMIC-III database. HRV was analysed across four temporal stages relative to infusion: pre-infusion (−70 to −10 min), early infusion (+10 to +70 min), late infusion (−70 to −10 min before cessation), and post-infusion (+10 to +70 min). Patients with atrial fibrillation or poor-quality ECG signals were excluded. We stratified patients into two groups: (1) those who died in the ICU after the post-infusion stage, and (2) those discharged after this stage.

A total of 252 patients (mean age 62.6 ± 14.7 years; 24% mortality) were included in the analysis. Significant differences in HRV features between groups were observed at all stages except pre-infusion. The largest divergences occurred during late and post-infusion periods. Survivors exhibited a significantly higher level of HRV features related to complexity, particularly in detrended fluctuation analysis metrics such as DFA alpha2 ($p<0.01$ for late and post-infusion stages) and scale-dependent DFA exponents across a wide range of scales (45-94 for early infusion, 16–100 for late infusion, and 19-55 for post-infusion).

These findings suggest that late-stage and recovery-phase autonomic dynamics reflect physiological resilience and the capacity to restore coordinated control following hemodynamic stress. HRV-derived response phenotypes to NE may provide clinically relevant prognostic markers and support more personalised management strategies in critically ill patients.

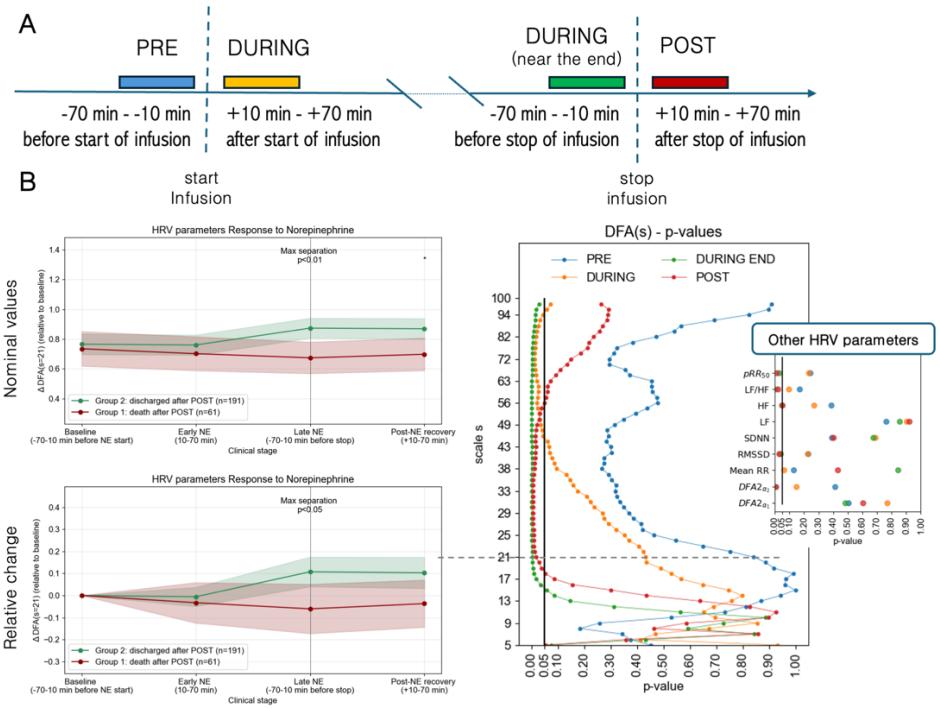

Figure: A) Data preparation: HRV features extracted from 4 stages during the noradrenaline (NE) therapy. B) The comparison between study groups showing significant differences in a wide range of scales in DFA(s) (example result for s=21) and other HRV parameters.