
**Diminished vagal tone is a predictive biomarker of necrotizing enterocolitis-risk in preterm infants.**

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**Abstract**

**BACKGROUND:**
Necrotizing enterocolitis (NEC) is an acute neonatal inflammatory disease which may lead to intestinal necrosis, multisystem failure, and death. Currently, NEC is diagnosed by a combination of laboratory and radiographic tests conducted a posteriori i.e., when NEC is already clinically significant. Given the acute onset and rapid progression of NEC, a non-invasive biomarker that allows early detection of patients at risk is required as a matter of urgency. We evaluated whether the high frequency (HF) component of heart rate variability (HRV), a measure of vagal efferent tonic cholinergic activity may be used as a predictive biomarker for NEC-risk before the onset of clinical disease.

**METHODS:**
In this prospective study, stable preterm (gestational age 28-35 weeks) infants had HRV power spectra analyzed from surface electrocardiogram waveforms taken at rest on day 5-8 of life. We used regression modeling to determine the utility of HF-HRV in predicting NEC.

**KEY RESULTS:**
HF-HRV power was 21.5 ± 2.7 and 3.9 ± 0.81 ms(2) in infants that remained healthy and those that later developed stage 2+ NEC, respectively (p < 0.001). Nine of 70 enrolled infants developed NEC. The ROC discriminated a HF-HRV value of 4.68 ms(2) predictive for developing NEC with a sensitivity and specificity of 89% and 87%, and positive and negative predictive value of 50% and 98%, respectively. With predictive regression modeling, the risk (odds ratio) of developing NEC was 10 per every one SD decrease in HF-HRV.

**CONCLUSIONS & INFERENCES:**
Our preliminary data indicate that HF-HRV may serve as a potential, non-invasive predictive biomarker of NEC-risk in NICU infants.

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**KEYWORDS:**
biomarker; necrotizing enterocolitis; vagal tone

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