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Anish Sanjay Shah, MD

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Date

**Approval Sheet**

Stress Reactivity

Disturbances of the Neurocardiac Axis

By

Anish Sanjay Shah, MD

Master of Science

Clinical Research

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Disturbances of the Neurocardiac Axis

By

Anish Sanjay Shah

M.D., Texas A&M University, 2016

B.S. Emory University, 2011

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An abstract of

A thesis submitted to the Faculty of the

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Master of Science in Clinical Research

2021

Abstract

Stress Reactivity

Disturbances of the Neurocardiac Axis

By

Anish Sanjay Shah, MD

Stress, both physiological and psychological, serve as triggers for cardiovascular events in those with a damaged cardiac substrate, such as ischemic heart disease. The physiological reaction to stress is mediated through the autonomic nervous system, which can be quantified through heart rate variability (HRV).

We measured HRV in three cohorts that had varying burdens of ischemic heart disease, from no known disease, high risk of disease, and known disease after myocardial infarction. Each cohort also had varying types of HRV, from short-term recordings during acute psychological and physiological stress, to longer, diurnal recordings. Two of these cohorts were followed longitudinally to assess for cardiovascular outcomes and mortality. Short-term and cosinor HRV metrics served as the exposure and psychological stress, myocardial ischemia, and major adverse cardiovascular events (MACE) served as outcomes in logistic regression modeling and survival analysis.

Autonomic dysfunction was robustly associated with psychological stress, myocardial ischemia, and MACE. We found a significant relationship between circadian autonomic variability and depression and posttraumatic stress disorder. We found that autonomic dysfunction was also strongly related to mental stress-induced myocardial ischemia. We found that autonomic dysfunction, both to circadian changes and acute mental stress, was associated with an increased, independent risk for MACE.

This suggests that autonomic dysfunction, measured by HRV, plays an important, independent role in the additional cardiovascular risk seen in patients with psychological disease. This association highlights neurocardiac mechanisms as a not yet understood pathological process in both psychiatric and cardiovascular disease that may have implications in diagnosis and therapy.

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