

# A Study Protocol on Assessment of Heart Rate Variability as a Prognostic Marker in Critically Ill Patients

## Abstract:

**Background:** Calculation of heart rate variability (HRV) is the most popular approach of actual evaluation of ANS dysregulation, which represents the natural, physiological changes. The natural changes take place in the interim among successive heart beats when sympathetic and parasympathetic expression is balanced on the heart's electrical conduction system. Numerous adult studies have shown that reductions in HRV predate clinical decline, indicate therapy response in correlation with results. Therefore, HRV can be functional as a measure of clinical perceptivity. This study aims to determine role of heart rate variability and other risk factors as a prognostic marker for 90 day survival among patients admitted to critical care unit.

**Methods:** This will be a Observational Cross-sectional Study with Control Group and will include hypertension, diabetes mellitus, Myocardial Infarction, Stroke , Sepsis cases and control cases. The patients admitted in Medicine critical care unit will be included in the study and they will be evaluated for HRV and APACHE IV scoring. Patients demographic profile, anthropometric measurements and history of other comorbid conditions will be documented. Patients outcome indicators like duration of hospital stay, 90 day survival and mortality will be obtained .Data will be analyzed by appropriate statistical tests.

**Expected Results:** Mixed effects models will demonstrate that result of three measurement of HRV will be relatively lower from the starting of day and night compared to the last day and night of MICU admission. Significant relationship between the variability of time from enrollment and log heart rate values, over the last day and night of MICU stay is expected. Also, average HRV is expected to persist significantly higher as compared with that of the first day and night.

**Keywords:** Medical Critical Care Unit, Heart Rate Variability, Critically Ill Patients, APACHE-IV Scoring.

## Introduction:

Heart rate variability is termed as fluctuation in the time interval between adjacent heart beats. The equilibrium among the sympathetic and parasympathetic subgroups of the autonomic nervous system (ANS) is essential for the maintenance of systemic homeostasis and the effective response to external stressors. Loss of normal autonomic function may occur due to swelling and/or injury during chronic disease.(1) The systemic homeostasis disturbance to autonomic nervous system disorder has been resulted and related with organ abnormality to regulate, expanded illness severity, and low result.(2)

Calculation of HRV is the most popular approach of actual evaluation of ANS dysregulation, which represents the natural, physiological changes. The natural changes take place in the interim among successive heart beats when sympathetic and parasympathetic expression is balanced on the heart's electrical conduction system. (3)Numerous adult studies have shown

that reductions in HRV predate clinical decline, indicate therapy response in correlation with cheap results. Therefore, In the MICU, HRV can be functional as a measure of clinical perceptivity. (3)However, it is not yet possible to convert these results into actionable data, accessible in current time to doctors in emergency units.

Given heart rate variability possible applicability to intensive care, review of Heart rate variability will be unusual clinical practice portion. Hence we are going to investigate the function of HRV analysis as a diagnostic marker in critically ill patients.

### **Rationale:**

In 1965, when Hon and Lee observed that fetal distress was accompanied by changes in the interbit interval before any appreciable changes occurred in the heart rate itself, The health significance of the amplitude of the heart rate was measured.

### **Objectives:**

- To determine 24 hours Heart rate variability among patients admitted to critical care unit on admission and one day prior to discharge.
- To determine role of heart rate variability and other risk factors as a prognostic marker for 90 day survival among patients admitted to critical care unit.
- Mortality and Duration of MICU stay.

### **Study Design:**

This will be Observational Cross-sectional Study with Control Group and will include hypertension, DM, CAD, MI, STROKE, SEPSIS cases and control cases.

### **Selection of subjects**

- All cases will be selected from patients admitted for accelerated HTN, DM, CAD, MI, STROKE, SEPSIS uncontrolled Diabetes mellitus matching up with research criteria.

**Controls:** Age and sex matched non obese healthy persons will be taken as control.

### **Exclusion criteria:**

Not giving consent

SAMPLE SIZE = calculated by following formula

Where:

- $Z$  = Z value (e.g. 1.96 for 95% confidence level)
- $p$  = percentage picking a choice, expressed as decimal
- $c$  = confidence interval, expressed as decimal
- prevalence=0.128<sup>(4)</sup>
- Desired Precision=5%

- Sample size =171.51~200

**Methods:**

**Anthropometric measurements:**

Anthropometric features including waist circumference (WC), Hip Circumference, Waist/Hip ratio.

**Waist Circumference:**

The WHO stepwise waist circumference measurement procedure have instructed that the The measurement should be performed at the approximate midpoint between the margin of the last palpable rib and the top of the iliac crest..

**Hip Circumference:**

Surrounding of the broad section of the buttocks will be taken as Hip circumference.

**Waist/Hip Ratio:**

The calculation of waist circumference division by hip circumference is referred to as the waist/hip ratio. We will use stretch resistant tape to wrap adequately throughout the participant, but not to the point of constriction of tape. The tape point will be aligned to the floor at the point of dimension. The participant will upstand during the dimension, with casual state of hand at the side, evenly spread of feet aside and distribution of body weight.

Chart 1. World Health Organization cut off points.

| Indicator       | Cut-off points     | Risk of metabolic Complications |
|-----------------|--------------------|---------------------------------|
| Waist perimeter | >94 cm[M],>80cm[F] | Increased                       |
| Hip perimeter   | >102cm[M],>88cm[F] | Increased significantly         |
| Waist hip ratio | >0.90[M],>0.85[F]  | Increased significantly         |

**Blood pressure:**

We will measure blood pressure by auscultatory method using stethoscope and sphygmomanometer, Riva-Rocci cuffs are positioned around the upper arm at about the same vertical height as the heart, connected to the mercury manometer, which checks the height of a mercury column, giving an accurate result..

**AHA Guidelines For Hypertension:** (Guidelines were published in the Journal of the American College of Cardiology and Hypertension) November 13,2017 (18)

Normal: Less than 120/80 mmHg;

Elevated: Systolic between 120-129 and diastolic less than 80

Stage 1: Systolic between 130-139 or diastolic between 80-90;

Stage 2: Systolic at least 140 or diastolic at least 90mmHg;  
Hypertensive crisis: Medication needs to be modified in patients with systolic over 180 and/or diastolic over 120 although there are no other signs of complications. If signs of organ injury appear, emergency hospitalization will be needed.

### **Discussion:**

Variability in the heart rate is thought to indicate regulation of the sinus node's automaticity by the autonomic nervous system's sympathetic and parasympathetic components. However, the autonomic nervous system (ANS) adapts and controls the heart rate and rhythm continuously. The ability to determine autonomic responses will provide useful information about the pathophysiology, severity and prognosis of these disabilities.(1,2)

In the pathophysiology of illness and prognosis of patients admitted to the intensive care unit (ICU), heart rate variability was a tool for quantifying 'inter-organ contact' and provided useful data.(3)In a patient's presentation, heart rate variability analysis may be able to determine mortality early. A high degree of variability is correlated with wellbeing. Heart rate fluctuations can also be predicted for those patients at risk of impairment and those who can benefit from early ICU admission.(3,4)Inflammation is associated with a host of disorders, such as myocardial infarction, sepsis, systemic inflammatory response syndrome, MODS, and severe trauma.. Heart rate variability (HRV) valued that prediction in clinically relevant results in the intensive care setting has assured by autonomic nervous function; however, there is debate concerning its utility. Heart rate variability (HRV) is a method used for evaluating the autonomic function of the central nervous system, and standards have been in effect for almost 20 years for its use. (3,5)

The purpose of this analysis is to determine the utility of heart rate variability parameters from the start and end of 24 hours of MICU stay to guess the calculation. Heart rate variability is acquiring progressive popularity as a predictor of outcome in different clinical conditions. Depressed heart rate variability in the intensive care unit is indicative of general outcomes. Variability of the heart rhythm adds importance to what remains the most common rating system in the world.. Facing various difficulties with heart rate variability research in the ICU, HRV seems to hold promise as a result predictor. Heart rate (HR) is a dynamic signal that varies with time. The variability in the heart rate may indicate that the current pathological condition is present. The variability in heat rate (HRV), which is characterized as the difference in time between consecutive heartbeats over time, depends mainly on the HR's extra cardiac regulation.

Heart rate variability is a non-destructive and oblique evaluation of the control of cardiac function of the autonomic nervous system and gives an idea of the alignment of activity between the sympathetic and parasympathetic nervous systems. The presence of disease and pathological condition is closely related to changes in HRV, and the degree of alteration of Heart rate variability is a marker of the intensity of the current disease.(4)A high degree of heart rate variability implies a stable individual with a strong autonomic nervous system that works well. An abnormal autonomic system is indicated by a low Heart rate variability. Heart rate variability analysis has been shown to be useful for early diagnosis of infection, particularly in newborns and infants. (4)

In trauma patients, assessment of heart rate variability may provide us with a beneficial effects tool for infection. The extent and intensity of heart rate variability changes can be well associated with the intensity of the disease, suggesting high mortality rates and poor sepsis and viral infection outcomes.(5) The typical method of heart rate variability examination performed by medical professionals is electrocardiography (ECG). Wearable heart rate variability evaluation devices can be a simple, low-cost and convenient alternative. Wearable devices are reliable for dynamic posture heart rate variability analysis. (5). In human response to various internal and external stimuli, the autonomic nervous system (ANS) is a major factor that can affect homeostasis and regulate vital functions such as circulation, ventilation, thermoregulation and hormonal secretion. (5, 6) Heart rate variability (HRV) measurement is a bedside, non-invasive, low-cost and easy-to-perform procedure that involves normal hospital equipment and dedicated software. Heart rate variability (HRV) detects the existence of ANS dysfunction that complicates many diseases by representing the balance of the ANS heart rate control (HR).

To confirm the diagnosis and Assess the severity of failure of the ANS, heart rate variability (HRV) is used. This shows that HR signal power spectral analysis can be used in the ICU as a complementary prognostic method for outcome prediction. (7)

As critical illness resolves, improvements in heart rate variability (HRV) may be observed by comparing HRV from the time of admission to the medicine critical care unit with heart rate variability instantly earlier to dispense.(6,7)

Heart rate variability in this population can be a functional marker of clinical vision, although confirmation in a larger subset of patients is needed. Via continuous HRC surveillance, their follow-up randomized managed test revealed a decrease in death rate in neonates. (8) The capacity to quantify accurate minute changes in real-time is basic factor for the effectiveness of HRV as a clinical perceptivity marker. Although data were analyzed retrospectively in this report, all HRV data were measured in current-time prospectively and processed for analysis. (9)

The effect of the undulating sympathetic and parasympathetic tones is highly affected by the heart rate and rhythm. For heart disorders, information on heart rate variability is plentiful. Stressed heart rate variability predicts death rate after myocardial infarction and arrhythmic complications. Heart rate variability evaluation should be carried out 1 week after such a case, best using time domain measures that provide better prognostic details.

In order to evaluate the sympathetic and parasympathetic effect on variations in heart rate, two analysis methods were developed. The measurements for the time domain are easy to use but mostly needs a longer recording time (24 hours). Heart rate variability in healthy subjects and critically ill patients is a promising method for assessing inter-organ communication and can be acquired consistently and safely.

#### **Limitations:**

- It is important to note the backdated extant of present research and limitation for patient sample size without stable control group.
- Normal considerations is that treatment of all cardiac failure patients were within 4 days of admission, but not on the same day.

- The circadian variability and CRP measurement restricts the important relationship between heart rate variability as an indicator of critical disease and CRP as a marker of inflammatory activity.(10)

Distinction between subgroups of the autonomic nervous system and evaluation of the autonomic nervous modulation of critically ill patients was acknowledged by spectral HRV analysis. Spectral HRV analysis was basic factor to distinguish the guessing ability of heart rate variability measures of ill patients in the ICU for in-hospital mortality. Short-term spectral heart rate variability analysis in the ICU may achieved early recognition of all ill patient at risk of in-hospital mortality. Furthermore, ICU patients with death-risk disease had reduced cardiac variability (decreased SDNN or TP) and tilted sympathovagal function towards sympathetic repression (decreased LFP/HFP and LFP) relative to patients with lower in-hospital mortality rates.. Every patient with illness visiting the ICU should carry out Spectral HRV analysis, so that the risk of in-hospital death rate in the future can knowledgeable to the clinicians treating the patients.

Complex network of mediators and toxins is a characteristic of illness that might affect cardiovascular reflexes, cause to happen disability in the autonomic nervous modulation.

A common response to systemic inflammation is shown by rise in regularity or reduced variability of organ functions. This common reaction seems in large different systems during endotoxemia. Speculation is that a host reaction for counter equilibrium of the endotoxin caused systemic inflammation can derived as elevated vagal tone and forward outcome is decreased sympathovagal balance (11). Articles from GBD study reflect on the problem of critical illnesses (12-14). Few of the related studies on critically ill patients and hypertension were reviewed (16-26).

#### **Expected Results:**

The outcomes of this study will prove that, comparison to the time just before MICU discharge, HRV will be lower within the first 24 hours of MICU stay, confirming its capability to adapt as a clinical acuity marker. The outcome of this analysis is consistent with the above findings and also shows that patients with disease at risk of death have diminished cardiac variability and reduced sympathovagal balance, frequently tending towards relative sympathetic inhibition, compared with survivors.

#### **Conclusion:**

Heart rate variability was slightly lower in the first 24 hours relative to the previous MICU release, after determination of critical sickness. This shows possibility to investigate changes in heart rate variability using mechanical framework for steaming analytics. With patients who need prompt care if there are no other indications of problems, changes in medication.

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