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Original Contributions

HEART RATE VARIABILITY ANALYSIS IN PATIENTS WHO HAVE BRADYCARDIA PRESENTING TO THE EMERGENCY DEPARTMENT WITH CHEST PAIN

Jeffrey Tadashi Sakamoto, MD,* Nan Liu, PHD,†‡ Zhi Xiong Koh, BENG,§ Dagang Guo, PHD,§ Micah Liam Arthur Heldeweg, MMED,‖ Janson Cheng Ji Ng, BSC,§ and Marcus Eng Hock Ong, MBBS, MPH§#

*Duke University School of Medicine, Durham, North Carolina, †Health Services Research Centre, Singapore Health Services, Singapore, ‡Centre for Quantitative Medicine, Duke-NUS Medical School, Singapore, ‖Department of Emergency Medicine, Singapore General Hospital, Singapore, §Faculty of Medical Sciences, University of Groningen, Netherlands, and #Health Services and Systems Research, Duke-NUS Medical School, Singapore

Reprint Address: Nan Liu, PHD, Health Services Research Centre, Singapore Health Services, Academia Level 6, 20 College Road, Singapore 169856, Singapore

☐ **Abstract—Background: Heart rate variability (HRV) is a noninvasive method to measure the function of the autonomic nervous system. It has been used to risk stratify patients with undifferentiated chest pain in the emergency department (ED). However, bradycardia can have a modifying effect on HRV. Objective: In this study, we aimed to determine how bradycardia affected HRV analysis in patients who presented with chest pain to the ED. Methods: Adult patients presenting to the ED at Singapore General Hospital with chest pain were included in the study. Patients with non-sinus rhythm on electrocardiogram (ECG) were excluded. HRV parameters, including time domain, frequency domain, and nonlinear variables, were analyzed from a 5-min ECG segment. Occurrence of a major adverse cardiac event ([MACE], e.g., acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft, or mortality) within 30 days of presentation to the ED was also recorded. Results: A total of 797 patients were included for analysis with 248 patients (31.1%) with 30-day MACE and 135 patients with bradycardia (16.9%). Compared to non-bradycardic patients, bradycardic patients had significant differences in all HRV parameters suggesting an increased parasympathetic component. Among non-bradycardic patients, comparing those who did and did not have 30-day MACE, there were significant differences predominantly in time domain variables, suggesting decreased HRV. In bradycardic patients, the same analysis revealed significant differences in predominantly frequency-domain variables suggesting decreased parasympathetic input. Conclusions: Chest pain patients with bradycardia have increased HRV compared to those without bradycardia. This may have important implications on HRV modeling strategies for risk stratification of bradycardic and non-bradycardic chest pain patients.** © **2017 Elsevier Inc. All rights reserved.**

Nan Liu and Marcus Eng Hock Ong have a patent filing related to heart rate variability that is not directly related to this study (System and method of determining a risk score for triage, Application Number: US 13/791,764). Marcus Eng Hock Ong has a similar patent filing unrelated to this study (Method of predicting acute cardiopulmonary events and survivability of a patient, Application Number: US 13/047,348). Marcus Eng Hock Ong also has a licensing agreement with ZOLL Medical Corporation for the above patented technology. There are no further patents, products in development or marketed products to declare. The remaining authors disclose no conflicts.

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INTRODUCTION

Heart rate variability (HRV) is a well-studied, noninvasive measure of autonomic nervous system function and has been used for a wide range of clinical applications ranging from cardiology to psychiatry (1). In the emergency department (ED), HRV has been utilized for identification of critically ill patients and for risk stratification of patients presenting with sepsis, trauma, or chest pain (2–7).

Measurements of HRV are collected using continuous cardiac monitoring to measure consecutive R-R intervals. This series of R-R intervals can then be analyzed for variability in multiple ways, which have been defined previously and are listed in Table 1 (8). Using these parameters, HRV can provide insights into the balance between sympathetic and parasympathetic nervous inputs. This balance has been shown to be clinically relevant for risk stratifying chest pain patients in the ED. Works by Ong et al., Heldeweg et al., and Liu et al., have shown that decreased HRV and increased sympathetic tone are associated with adverse cardiac outcomes in patients who present to the ED with chest pain (7,9–11).

Increased sympathetic tone and less variability can be signs of a stressed or failing heart (12). Early in the physiologic progression of heart failure, patients may present with normal vital signs due to compensatory mechanisms. Therefore, HRV measurements may be helpful in early identification of chest pain patients who are more critically ill and in need of a higher level of care necessitating acute interventions.

The effect of heart rate on HRV has been studied in ambulatory patients as well as athletes, with both studies concluding that bradycardia was associated with increased HRV (13,14). Tsuji et al. identified heart rate as an important determinant for HRV (13). Despite these findings, ED risk-stratification strategies employing HRV typically use equivalent analyses for bradycardic patients and patients with normal heart rates, as there has been no data in the literature to suggest a definite difference in HRV variables between bradycardic and non-bradycardic patients.

Therefore, in a population of patients presenting to the ED with undifferentiated chest pain, we aimed to determine whether or not bradycardia (< 60 beats/min) had an effect on HRV analysis. Prior studies using HRV for chest pain risk stratification do not use separate analyses for bradycardic patients (7,9–11). If bradycardia does impact analysis, this may imply that different HRV risk-stratification strategies should be used for bradycardic versus non-bradycardic chest pain patients.

MATERIALS AND METHODS

Adult patients (> 20 years old) who presented to Singapore General Hospital ED with undifferentiated chest pain were conveniently and prospectively recruited between September 2010 and July 2015. Patients diagnosed with obvious noncardiac chest pain (e.g., trauma, pneumonia, and pneumothorax) by the emergency physician were excluded. Patients with irregular/non-sinus rhythm on electrocardiogram (ECG) or extensive artifact/ectopic beats (> 5%) preventing appropriate HRV analysis were also excluded. SingHealth's Centralized Institutional Review Board (ref: 2014/584/C) approved this study with a waiver of patient consent, as there was no associated therapeutic intervention. Part of this patient

Table 1. Measures of Heart Rate Variability

Variable	Type	Measure
aRR (s)	Time	Average of the R-R intervals
sdRR (s)	Time	Standard deviation of R-R intervals
RMSSD (s)	Time	Square root of the mean squared differences between R-R intervals
NN50 (count)	Time	The number of times that the absolute difference between 2 successive R-R intervals exceeds 50 ms
pNN50 (%)	Time	NN50 divided by the total number of R-R intervals
LF power (ms2)	Frequency	Low-frequency power (sympathetic and a component of parasympathetic tone)
HF power (ms2)	Frequency	High-frequency power (parasympathetic tone)
LF power norm (n.u.)	Frequency	Normalized low-frequency power
HF power norm (n.u.)	Frequency	Normalized high-frequency power
LF/HF ratio	Frequency	Ratio between low- and high-frequency power
Poincare plot SD1 (ms)	Nonlinear	Graphical representation of R-R interval correlation
Poincare plot SD2 (ms)	Nonlinear	Graphical representation of R-R interval correlation
Approximate entropy	Nonlinear	R-R interval irregularity
Sample entropy	Nonlinear	R-R interval irregularity
DFA (α1)	Nonlinear	Detrended fluctuation analysis: fractal organization within the R-R interval series
DFA (α2)	Nonlinear	Detrended fluctuation analysis: fractal organization within the R-R interval series

n.u. = normalized units.