Heart Rate Variability Analysis in Normal Infants and Infants with Single Ventricle Anatomy Using Power Spectral Density

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Abstract

Heart Rate Variability (HRV) is a measure of the magnitude of autonomic cardiac tone produced by sympathetic and parasympathetic innervations. Power spectral density estimates in adults use traditional low frequency (LF) and high frequency (HF) bands to assess HRV as an indicator of increased risk of cardiac mortality. Studies of altered HRV in infants suggest that classic methods need modification for application in the pediatric population. 24-hour ECG data was collected for 27 normal infants (Group I) and 26 infants with congenital heart defects (Group II) and analyzed in five-minute segments using the Lomb periodogram. Traditional adult frequency ranges were modified for expansion of the HF range and a significant difference was found in Group I and Group II infants. Congenital differences in sympathetic tone remain post-procedure and normal development of parasympathetic tone was not seen in infants with the single ventricle anatomy.

1. Introduction

Heart rate variability (HRV) is a non-invasive technique used to assess cardiac autonomic tone. HRV uses the ECG to derive beat-to-beat intervals, or the time difference between R-R peaks. These intervals show periodic variations over time because the heart does not beat at a constant rate. The heart rate is under control of the autonomic nervous system (ANS) that varies the firing of the sinus node through the modulation of sympathetic and parasympathetic tones.

Spectral analysis has traditionally been used to assess HRV. The power spectral density (PSD) is normally estimated using Fourier Transform methods that require that the time between samples be constant. If however the time series being sampled is the time between R-R intervals, unless the HR is constant, then the time between samples will not be constant, and the signal must then be interpolated. Resampling the time series can introduce artifacts. Interpolation methods underestimate high frequency power and overestimate low frequency power [1]. If the time series contains ectopic beats the PSD estimate can be severely affected because the noise in the time-domain gets converted to broad band clutter in the frequency domain [2].

The Lomb periodogram algorithm estimates PSD with an algorithm that is more robust and not as susceptible to artifacts introduced by non-uniform sampling [2]. The Lomb algorithm weighs the data on a per-data point basis instead of the traditional per time basis as is assumed in a traditional Fourier method. The computation of the Lomb periodogram is equivalent to linear least-square fitting a sinusoid of angular frequency ω to the data [3].

A number of studies demonstrate the risk factors associated with decreased HRV in the adult cohort, including the increased risk of sudden death post myocardial infarction and in other cardiac and non-cardiac conditions. Alterations in HRV are markers of congestive heart failure [4] and multiple organ failure [5], and depressed HRV is associated with an increased risk of cardiovascular mortality in the elderly, as well.

Reduced HRV has been reported in infants with respiratory distress syndrome, reduced gestational age and congenital cardiac abnormalities; however, little data is available to associate HRV with risk factors in the neonate and pediatric populations [6-7]. HRV in infants and children is strongly affected by age due to the maturation of the ANS. HRV is also affected by sleeping position (prone vs. supine) with a reduced sympathetic tone measured in the prone position and sleep state (quiet vs. active) with increased HRV during active sleep [8]. A higher respiratory frequency in infants may alter the frequency components of the heart rate signal.

Congenital heart disease, the most prevalent of birth defects, is defined as gross structural abnormality of the heart or great vessels that causes functional abnormality [6]. Congenital heart disorders characterized by a single ventricle anatomy require reconfiguration of the heart and

vessels to provide systemic and pulmonary circulation with only one functioning pump. Fontan circulation is often used to direct deoxygenated systemic blood to the lungs. Oxygenated blood returning from pulmonary circulation is pumped through the single ventricle into systemic circulation.

Hypoplastic Left Heart Syndrome (HLHS), one example of the single ventricle anatomy, is characterized by an underdeveloped left ventricle, aorta, and aortic valve [7]. Fetal circulation bypasses the pulmonary circuit thus allowing the right ventricle to function as a pump for the systemic circulation. At birth, normal respiration begins, and the foramen ovale and ductus arteriosus close. In the HLHS infants, the underdeveloped left ventricle is unable to support systemic circulation and surgical intervention is necessary [8].

HLHS infants typically undergo a 3-stage reconstructive procedure to pump systemic blood through the right ventricle [9]. The first stage, known as the Norwood procedure, is performed in the first days of the neonate's life [10]. During the Norwood procedure the atrial septum is removed, a neoaorta is created, and the pulmonary and brachiocephalic arteries are connected in a procedure known as a Blalock-Taussig (BT) shunt [8,9]. An unexplained high risk of sudden cardiac mortality is associated with the Norwood procedure. Either the Glenn or hemi-Fontan procedure is performed 3-9 months after Norwood, and this is followed by the final stage Fontan procedure typically at 2-3 years of age. HLHS infants undergo the complete Norwood procedure, but infants born with other congenital heart defects may undergo a portion, such as the BT shunt procedure or aortic arch reconstruction.

Only one study to date has evaluated HRV in the population which had previously undergone the Norwood procedure. Davos et al. showed a marked and unusual change in HRV in patients after having undergone the Fontan procedure [11]. Additionally, other studies have shown alterations in HRV in patients with both repaired and unrepaired congenital heart disease [13], though the impact of these alterations have yet to be determined.

In adults, the frequency spectrum is divided into high frequency (0.15 – 0.4 Hz), low frequency (0.04 – 0.15 Hz), and very low frequency (0.0001 – 0.04 Hz) [12]. High frequency power is related to parasympathetic activity. Low frequency is related to primarily sympathetic activity, with some contribution from parasympathetic innervations. There is some evidence that the frequency bands used for assessing HRV in adults must be modified when assessing HRV in infants [14]. A cut-off for the LF band has been proposed at 0.2 Hz, and the upper limit of the HF band has been extended anywhere from 0.8 to 2.0 Hz to capture the respiratory sinus arrhythmia (RSA) in neonates resulting from a higher respiratory frequency.

We postulate that the patients undergoing arch reconstruction, as seen in the Norwood population, may have alterations or interruptions in the cardiac autonomic innervation coursing over the aortic arch. The specific aim of this work is to utilize a Lomb periodogram spectral analysis with modified frequency bands categorized as high frequency (0.2-1.2 Hz) and low frequency (0.04-0.2 Hz) to describe cardiac function in infants born with a single ventricle anatomy before and after reconstructive procedures and in normal infants. The long-term objective is to further the investigation of HRV in the pediatric population to improve understanding and treatment of the single ventricle anatomy characteristic of HLHS infants.

2. Methods

Infants were enrolled at The University of Iowa and at the University of Michigan The infants were enrolled and data were collected only after obtaining IRB approval at each institution, and only after obtaining written consent of each infant's parents.

Thirty-six infants were enrolled at Iowa and 17 infants were enrolled at Michigan. Of these 53 infants, 27 had no cardiac defect and were enrolled as Group I (NN) infants. The remaining 26 infants with congenital heart defects were enrolled as Group II infants. Group II included 15 HLHS infants with a single ventricle anatomy, 5 infants with only the aortic arch reconstruction (AA), and 6 infants who underwent a Blalock-Taussig shunt (BT).

Twenty-four-hour ECG data were collected and analyzed in five-minute segments. Those segments containing artifact were removed from the study. Mean data from each five-minute segment were averaged throughout the 24-hour period. Data were collected for Group II infants at pre-Norwood procedure (pre-procedure), 3-4 weeks post-Norwood procedure (post-procedure1), and at a follow-up time just before the Glenn or hemi-Fontan procedure (post-procedure2). ECG data were obtained for Group I infants at age-matched times. All of the Group II infants were given clinically appropriate medication (such as prostaglandin) as medically indicated. Five of the Group II infants died some time after the Norwood procedure was performed. Not all infants participated in all studies.

MATLAB code was used to calculate the Lomb periodogram of a non-uniformly sampled signal. The power in the LF and HF bands and the LF/HF ratio was calculated using both the traditional adult (Trad) frequency bands (LF: 0.04-0.15 Hz, HF: 0.15-0.4 Hz) and the modified (Mod) frequency bands (LF: 0.04-0.2 Hz, HF: 0.2-1.2 Hz)

Statistical analyses were performed using paired t-tests with significance being defined at the α=0.05 level.

3. Results

Table 1 shows the average heart rate for all infants in the study. The pre-procedure HR for normal infants was significantly lower than HLHS, AA, and BT infants. The HR for HLHS infants was higher than the HR for AA and BT infants.

Table 1 – Average heart rate for NN, HLHS, AA and BT infants for pre-procedure, post-procedure1, and post-procedure2 times. * indicates difference between Group I and Group II infants. ** indicates difference between HLHS infants, and AA and BT infants at pre-procedure time.

Group	Procedure	N	Mean ± SEM
NN	Pre-procedure	27	123.9 ± 1.6*
	Post-procedure1	19	141.4 ± 2.2
	Post-procedure2	15	130.0 ± 2.9
HLHS	Pre-procedure	13	161.9 ± 2.3**
	Post-procedure1	9	142.9 ± 2.6
	Post-procedure2	6	120.2 ± 5.2
AA	Pre-procedure	5	155.0 ± 4.2
	Post-procedure1	4	144.5 ± 3.2
	Post-procedure2	2	136.1 ± 8.7
BT	Pre-procedure	6	146.4 ± 2.2
	Post-procedure1	6	142.6 ± 4.3
	Post-procedure2	5	114.0 ± 8.3

Figure 1 shows the HF power using both the traditional and modified frequency bands for Group I and Group II infants. There was a significant difference between the traditional and modified frequency bands for Group I and Group II infants at the pre- and post-procedure times.

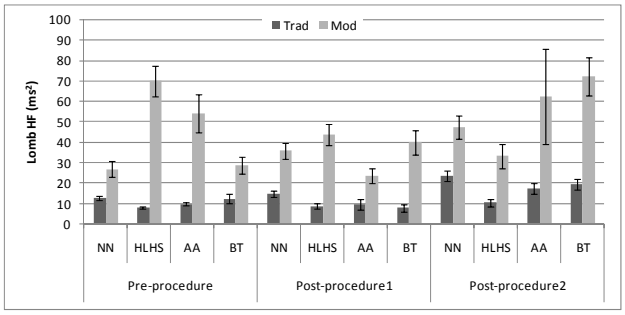

Figure 1 – HF power for the traditional adult (Trad) and modified (Mod) frequency bands for all infants at three data collection times. There is a significant difference between traditional and modified frequency bands for Group I and Group II infants at the pre- and post-procedure times.

Figure 2 shows the results of LF power for Group I and Group II infants. There was a significant difference between Group I and Group II infants at the pre-procedure, post-procedure1 and post-procedure2 times. No significant difference was found between the NN and AA infants.

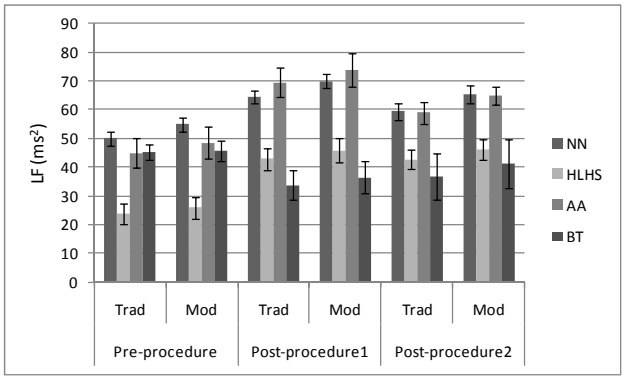

Figure 2 – LF power for all infants at three data collection times. There is a significant difference between Group I and Group II infants at the pre-procedure, post-procedure1 and post-procedure2 times.

Figure 3 shows the results of HF for Group I and Group II infants. A significant different was found between Group I and Group II infants pre-procedure using both traditional and modified frequency bands. A significant difference was found at the post-procedure times using the traditional frequency bands, but not the modified frequency bands. Using the modified frequency bands there is a significant difference between HLHS and BT infants pre-procedure and between HLHS and AA infants post-procedure1.

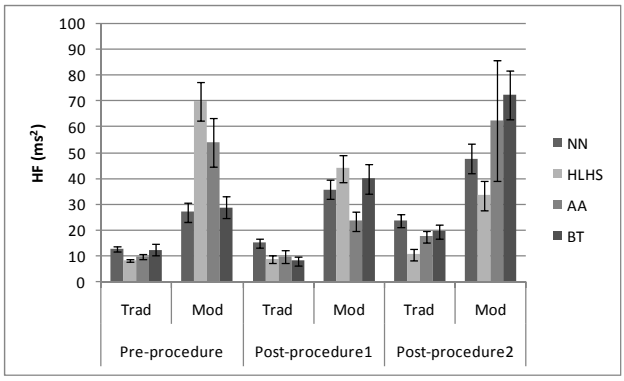

Figure 3 – HF power for all infants at three data collection times. There is a significant difference between Group I and Group II infants pre-procedure with both frequency bands, but post-procedure only with traditional frequency bands. Modified frequency bands show a significant difference between HLHS and BT infants pre-procedure and HLHS and AA infants post-procedure1.

Figure 4 shows the results of LF/HF for Group I and Group II infants. There is no significant difference between Group I and Group II infants using traditional frequency bands. When using modified frequency bands, however, there is a significant difference between Group

I and Group II infants at the pre-procedure and post-procedure1 times. There is a significant difference between HLHS and AA infants pre-procedure and post-procedure1, and between HLHS and BT infants pre-procedure and post-procedure2.

There was no difference in LF, HF, or LF/HF at the pre-procedure time between the HLHS infants who died post-Norwood procedure and the infants who survived.

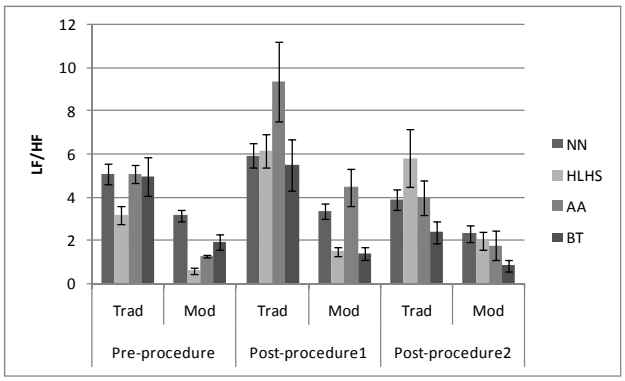

Figure 4 – LF/HF for all infants at three data collection times. There is a significant difference between Group I and Group II at the pre-procedure and post-procedure1 times using modified frequency bands.

4. Discussion and conclusions

We found (Figure 1) a pre-procedure difference in HF power between normal and HLHS and AA infants only when the modified frequency band is used; the difference was not seen using the traditional (adult) frequency band. Pre-procedural differences in HF power suggest increased parasympathetic tone in HLHS and AA infants at birth. Increase in HF power over time in Group I infants indicates that these infants developed increasing parasympathetic cardiac tone with age. In contrast, HLHS infants show continued decrease in HF power over time, which may indicate innervations are missing due to the single ventricle anatomy or damaged due to the Norwood procedure. Reduced LF power of HLHS and BT infants pre- and post-procedure suggests differences in sympathetic activity are due to the single ventricle anatomy and may not be attributed to the Norwood procedure.

We found no difference in LF, HF, or LF/HF in HLHS infants who died post-Norwood and HLHS infants who survived in spite of cardiac deaths. Spectral analysis may not adequately describe cardiac function in the single ventricle anatomy. Non-linear techniques may better quantify HRV in the pediatric population.

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