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Correlations between change in neural respiratory drive and heart rate variability in patients submitted to open-heart surgery

Metee Jinakote[1], Karan Pongpanit[2,*]

[1]Faculty of Oriental Medicine, Chiangrai College, Chiang Rai, Thailand
[2]Department of Physiotherapy, Faculty of Allied Health Sciences, Thammasat University, Pathum Thani, Thailand

Respiratory muscle dysfunction after open-heart surgery may influence the cardiopulmonary interactions. The purpose of this study was to examine the correlation between change in the neural respiratory drive (NRD) and change in heart rate variability (HRV) in patients submitted to open-heart surgery. An observational cross-sectional study was conducted among 32 participants. NRD was assessed via a surface electromyogram of the parasternal intercostal muscle (sEMGpara). Polar heart rate monitor was used to measure HRV during the deep breathing maneuver. Evaluations were performed on the day of admission and discharge. There were statistically significant differences in NRD and HRV indices between admission and discharge periods ($P<0.05$). The difference in peak root mean square of sEMGpara recorded during resting (ΔRMS sEMGpara tidal), during maximal inspiratory maneuver (ΔsEMGpara max), and its normalized values (ΔRMS sEMGpara%max) were significantly correlated with the difference in total power (ΔTotal power), mean of heart rate (ΔMeanHR), and mean of R to R intervals (ΔMeanRR) ($r=-0.844$, $P=0.004$, $r=-0.835$, $P=0.005$, and $r=0.643$, $P=0.043$, respectively). It can be concluded that NRD correlated well with HRV in patients who had undergone open-heart surgery.

Keywords: Neural respiratory drive, Heart rate variability, Open-heart surgery

INTRODUCTION

Open-heart surgery, which is performed through a median sternotomy can cause postoperative pulmonary changes by numerous factors including surgical manipulation, anesthetic agents, cardiopulmonary bypass, chest drain, thoracotomy pain, and immobilization (Weissman, 2004; Wynne and Botti, 2004). These changes are associated with respiratory muscle dysfunction and restrictive pulmonary pattern postoperatively (El-Sobkey and Gomaa, 2011; Morsch et al., 2009).

Neural respiratory drive (NRD) is a noninvasive method to measure the neural output of the brainstem respiratory center indirectly by quantifying the electromyogram (EMG) of the parasternal intercostal muscles via surface electrodes (sEMGpara) (Reilly et al., 2011; Reilly et al., 2013). According to previous studies, the sEMGpara has been observed and indicated the load on respiratory muscles in cystic fibrosis (Reilly et al., 2011; Reilly et al., 2012) and chronic obstructive pulmonary disease patients (Jolley et al., 2009; Suh et al., 2015).

Heart rate variability (HRV) is a noninvasive marker used to investigate cardiac autonomic modulations that control the oscillation of instantaneous heart rates (McCraty and Shaffer, 2015). The fluctuation of cardiac rhythm has synchronism with the respiratory cycle, which is known as respiratory sinus arrhythmia (RSA). This phenomenon reflects the parasympathetic integrity markers over the cardiac sinus node. Heart rate was increased during inhalation due to parasympathetic withdrawal to the sinus node and reversed it during exhalation (Grossman and Taylor, 2007). The attenuation of cardiac vagal tone was found in patients who had undergone coronary artery bypass graft (Soares et al., 2005)

*Corresponding author: Karan Pongpanit https://orcid.org/0000-0002-6042-904X
Department of Physiotherapy, Faculty of Allied Health Sciences, Thammasat University, Khlong Nueng, Khlong Luang, Pathum Thani 12120, Thailand
E-mail: karan.p@allied.tu.ac.th
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and cardiac valve surgery (Lakusic et al., 2008).

Although the impact of cardiac surgery on cardiopulmonary functions has been demonstrated, respiratory load and its association with cardiac autonomic function have not been elucidated. Therefore, this study attempted to clarify the correlation between change in NRD and change in HRV among patients submitted to open-heart surgery.

MATERIALS AND METHODS

Study design and participants

This observational cross-sectional study was accomplished in 32 participants who were undergoing open-heart surgery at Thammasat University Hospital, Thailand within the age of 35–60 years. The participants who had chronic heart failure, cardiac arrhythmia, myocardial infarction, unstable angina, implanted a cardiac pacemaker, uncontrolled diabetes mellitus, uncontrolled blood pressure, pulmonary or neurological diseases, experienced previous cardiac surgery and using mechanical ventilator more than 24 hr after surgery were excluded. This study was approved by the human ethics committee of Thammasat University (152/2560) and all participants have signed written informed consent.

NRD measurement

The sEMGpara was recorded at rest with normal tidal breath using bipolar surface electrodes (Kendall Arbo, Tyco healthcare, Neustadt, Germany) attached at the second intercostal space of both sides, lateral to the sternum for 3 cm. The amplifier and bandpass filter, which were represented as a frequency of EMG, was set at 1 kHz and between 10 Hz–2 kHz using a wireless EMG system (TeleMyo 2400T G2, Noraxon USA Inc., Scottsdale, AZ, USA), respectively. Data were analyzed using MyoResearch XP (ver. 1.07.25; Noraxon USA Inc.). The analog signal was converted to a digital signal at 10 kHz, and peak root means square per breath was calculated and averaged over 1 min (RMS sEMGpara tidal). EMG recordings at rest were normalized to the EMG signal obtained during a maximal static inspiratory pressure (RMS sEMGpara max) and the numerically largest EMG signal from 5 times repeated maneuver was used for normalization (sEMGpara% max).

HRV measurement

RR intervals were recorded using a V800 Polar heart rate monitor (Polar Electro Ltd., Kempele, Finland) at a sampling rate of 1,000 Hz. HRV was recorded during deep breathing maneuver for 4 min in a supine position. Participants were instructed to perform a series of deep and slow inhalation and exhalation to provide a maximal pulmonary volume that varied from total lung capacity to residual volume. Each breathing cycle was performed for 10 sec, divided into 5 sec for inhalation and 5 sec for exhalation, which provides a maximal RSA response (Hayano et al., 1994; Song and Lehrer, 2003). Participants controlled their respiratory cycles via a pointer clock on the computer screen and received verbal feedback from the researcher.

HRV was analyzed in a linear method (time and frequency domains) by Kubios HRV software version 3.0.2 (Biosignal Analysis and Medical Imaging Group, University of Eastern Finland, Kuopio, Finland) following to the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996).

Time-domain analysis was calculated from the mean of the longest RR intervals obtained during the expiratory phase divided by the mean of the shortest RR intervals obtained during the inspiratory phase (expiratory/inspiratory ratio, E/I), the difference between the mean of the highest heart rate obtained during the inspiratory phase and the mean of the lowest heart rate obtained during the expiratory phase (inspiratory-expiratory difference; ΔIE), the mean of RR intervals (MeanRR), the standard deviation of all normal RR intervals (SDNN), and the root mean square of the successive difference (RMSSD). E/I ratio and ΔIE has been indicated cardiac sympathovagal balance, MeanRR and SDNN have been indicated cardiac autonomic modulation, and RMSSD has been indicated cardiac vagal modulation, subsequently.

The fast Fourier transform (FFT) on the time series was utilized as a frequency domain. This FFT algorithm was applied to determine power spectrum density which consisted of low-frequency power (LF: 0.04–0.15 Hz) and high-frequency power (HF: 0.15–0.4 Hz). Spectral components were obtained in normalized units (nu). LF power has been predominantly indicated a sympathetic tone, HF power has been indicated a parasympathetic tone, while the LF/HF ratio has been indicated cardiac sympathovagal balance, respectively.

NRD and HRV indices were always evaluated in the afternoon on the day of admission and discharge. All participants were received conventional physiotherapy intervention following the standard cardiac rehabilitation protocol of the hospital including breathing exercises, airway clearance techniques, early mobilization, exercise training, and ambulation training during the postoperative period.

Statistical analysis

Shapiro–Wilk test was used to determine data distribution. Paired *t*-test and Pearson correlation were used for data fitting normal distribution, while the Wilcoxon signed-rank test and Spearman's rank correlation were used for data not consistent with a normal distribution. The statistical significance was considered as $P < 0.05$ using the IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA).

RESULTS

A total of 32 participants, 62.5% male (52.25 ± 5.25 years) were included in the study (Table 1). The comparison of NRD and HRV indices between admission and discharge period are summarized in Table 2. For NRD parameters, RMS sEMGpara tidal and sEMGpara% max were significantly increased, while RMS sEMGpara max was significantly decreased in the postoperative period (all $P < 0.05$). For HRV indices, MeanRR, SDNN, RMSSD, total power, and HFnu were significantly reduced, whereas ΔIE, E/I ratio, mean of heart rate (MeanHR), and LFnu were significantly increased at the discharge period (all $P < 0.05$). There were no significant differenc-

Table 1. Characteristics of the participants

Variable	Value
Age (yr)	52.25 ± 5.25
Male sex	20 (62.5)
Body mass index (kg/m^2)	24.82 ± 4.48
Echocardiography	
Ejection fraction (%)	65.32 ± 7.50
Diagnosis	
Valvular heart disease	16 (50.0)
Coronary artery disease	22 (68.8)
Underlying diseases	
Hypertension	24 (75.0)
Diabetes mellitus	8 (26.7)
Dyslipidemia	18 (60.0)
Spirometrics	
FEV_1 (% predicted)	88.14 ± 10.26
FVC (% predicted)	90.00 ± 9.54
FEV_1/FVC (%)	96.53 ± 9.87
Length of hospital stay (day)	8 (7–9)

Values are presented as mean ± standard deviation, number of participants (%), or median (interquartile range).
FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity.

Table 2. Comparison of neural respiratory drive and change in heart rate variability indices between admission and discharge period

Variable	Admission	Discharge	Difference	*P*-value
Neural respiratory drive				
RMS sEMGpara tidal (μV)[a]	4.44 (3.08–11.30)	13.40 (11.00–16.65)	6.78 (1.70–13.57)	0.012
RMS sEMGpara max (μV)	34.65 ± 14.48	21.97 ± 5.95	-12.68 ± 11.29	0.016
sEMGpara% max (%)[a]	16.70 (8.66–39.66)	61.39 (38.35–83.42)	44.27 (17.80–69.48)	0.012
Time domain of HRV				
ΔIE	9.22 ± 6.11	16.98 ± 8.60	7.76 ± 2.78	<0.001
E/I ratio	1.08 ± 0.06	1.22 ± 0.08	0.15 ± 0.06	<0.001
MeanRR (msec)[a]	756.57 (710.95–896.12)	634.27 (594.53–684.81)	-122.40 (-248.68–[-89.79])	<0.001
MeanHR (beats/min)	79.48 ± 5.87	94.20 ± 5.10	14.72 ± 3.53	0.012
SDNN (msec)	19.78 ± 9.38	9.80 ± 7.66	-9.98 ± 3.77	<0.001
RMSSD (msec)	17.19 ± 7.99	7.15 ± 6.64	-10.04 ± 6.69	0.012
Frequency domain of HRV				
Total power (msec^2)[a]	584.69 (121.20–1143.19)	179.53 (104.24–864.68)	-232.34 (-571.69–[-16.96])	0.012
LFnu	26.13 ± 13.29	53.60 ± 23.11	27.47 ± 24.47	0.016
HFnu	73.87 ± 13.29	46.40 ± 23.11	-27.47 ± 24.47	0.016
LF/HF	0.47 ± 0.32	1.79 ± 1.89	1.32 ± 2.05	0.111

Values are presented as median (interquartile range) or mean ± standard deviation.
sEMGpara, surface parasternal electromyogram; RMS, root mean square; RMS sEMGpara tidal, peak root mean square of sEMGpara recorded during resting; RMS sEMGpara max, peak root mean square of sEMGpara recorded during maximal inspiratory maneuver; sEMGpara% max, resting parasternal EMG activity normalized to the maximal EMG evoked during maximal inspiratory maneuver; ΔIE, inspiratory-expiratory differences; E/I ratio, expiratory/inspiratory ratio; MeanRR, mean of R to R intervals for normal beats; MeanHR, mean of heart rate; SDNN, standard deviation of all R to R intervals; RMSSD, square root of the mean of the sum of the squares of differences between adjacent R to R intervals; LFnu, low frequency power in normalized units; HFnu, high frequency power in normalized units; LF/HF, the ratio between low and high frequency power.
Data analyzed by Paired *t*-test or [a]Wilcoxon signed-rank test.

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Table 3. Correlations between change in neural respiratory drive and change in heart rate variability indices

Variable	ΔRMS sEMGpara tidal (μV)		ΔRMS sEMGpara max (μV)		ΔsEMGpara%max (%)	
	r	*P*-value	*r*	*P*-value	*r*	*P*-value
ΔIE difference	-0.155	0.357	-0.034	0.468	-0.461	0.125
ΔE/I ratio	-0.229	0.292	0.119	0.389	-0.213	0.306
ΔMeanRR (msec)[a]	0.357	0.193	0.595	0.060	0.643	0.043
ΔMeanHR (beats/min)	-0.574	0.068	-0.835	0.005	-0.616	0.052
ΔSDNN (msec)	0.126	0.383	-0.083	0.422	0.132	0.377
ΔRMSSD (msec)	0.253	0.272	-0.116	0.393	0.293	0.241
ΔTotal power (msec^2)	-0.844	0.004	-0.614	0.053	-0.560	0.074
ΔLFnu	-0.535	0.086	-0.464	0.124	-0.269	0.260
ΔHFnu	0.535	0.086	0.464	0.124	0.269	0.260
ΔLF/HF[a]	-0.143	0.368	-0.524	0.091	-0.071	0.433

sEMGpara, surface parasternal electromyogram; RMS, root mean square; ΔsEMGpara tidal, delta change of peak root mean square of sEMGpara recorded during resting; ΔsEMGpara max, delta change of peak root mean square of sEMGpara recorded during maximal inspiratory maneuver; ΔsEMGpara% max, delta change of resting parasternal EMG activity normalized to the maximal EMG evoked during maximal inspiratory maneuver; ΔIE difference, delta change of inspiratory-expiratory differences; ΔE/I ratio, delta change of expiratory/inspiratory ratio; ΔMeanRR, delta change of mean of R to R intervals for normal beats; ΔMeanHR, delta change of mean of heart rate; ΔSDNN, delta change of standard deviation of all R to R intervals; ΔRMSSD, delta change of square root of the mean of the sum of the squares of differences between adjacent R to R intervals; ΔLFnu, delta change of low frequency power in normalized units; ΔHFnu, delta change of high frequency power in normalized units; ΔLF/HF, delta change of the ratio between low and high frequency power.
Data analyzed by Pearson correlation or [a]Spearman rank correlation.

es between time points in the LF/HF ratio. Correlations between change (Δ) in NRD and HRV indices are given in Table 3. There were significant negative correlations between ΔRMS sEMGpara tidal and ΔTotal power ($P < 0.01$), and between ΔRMS sEMGpara max and ΔMeanHR ($P < 0.01$). In contrast, ΔsEMGpara%max was a significantly positive correlation with ΔMeanRR ($P < 0.05$).

DISCUSSION

The finding of the present study was showed the correlation between the alteration of both NRD and HRV indices indicates that increased a load of respiratory muscle after open-heart surgery was associated with the attenuated of cardiac vagal control.

This study demonstrated postoperative hyperactivation of NRD which was detected by measuring neural control of parasternal intercostal muscle via surface EMG. Although the study of sEMGpara in patients who had undergone cardiac surgery is still lacking, the purpose mechanisms of this phenomenon may be involved in respiratory muscle workload and could be explained by physiological responses. The phasic mode of parasternal intercostal muscle plays a role in the thoracic expansion and increase lung volume during inspiration (De Troyer et al., 2005). It was possible that a load of parasternal intercostal muscle was increased due to respiratory muscle dysfunction and restrictive pulmonary pattern postoperatively (El-Sobkey and Gomaa, 2011; Morsch et al., 2009). The worsening of these respiratory functions is related to the surgical manipulation, anesthetic agents, thermal damage, cardiopulmonary bypass, chest drain, thoracotomy pain, and immobilization that lead to altering the respiratory mechanic and pulmonary compliance (Weissman, 2004; Wynne and Botti, 2004).

HRV indices obtained during deep breathing maneuver provided a marker of vagal integrity over the cardiac sinus node (McCraty and Shaffer, 2015). This study revealed a decrease in postoperative cardiac vagal control and reaffirmed with the previous study that showed a significant HRV reduction after coronary artery bypass graft (Soares et al., 2005) and cardiac valve surgery (Lakusic et al., 2008). Sinus arrhythmia is modulated by the synchronicity between the cardiovascular and respiratory system (Grossman and Taylor, 2007). In this context, alteration of respiratory variables can alter this phenomenon. Because the breathing frequency was controlled during deep breathing maneuver, it possible that lower HRV values are a result of the reduction of tidal volume. Altered pulmonary compliance may be the primary mechanism to explain this phenomenon. As a result of the postoperative restrictive pulmonary pattern, the vital capacity was decreased, thus reducing the range of the tidal volume displacement (El-Sobkey and Gomaa, 2011). So, although the patients were instructed to take deep and slow breathing during deep breathing maneuver, the tidal volume assembled could have been minimal due to the decreased lung capacity.

The correlation between alteration of NRD and HRV indices as a result of this study indicated that modifications of the respiratory

muscle workload could profoundly influence the RSA magnitude and HRV behavior; slow and deep breathing will amplify RSA magnitude and HRV behavior, whereas fast and shallow breathing may contribute to reduced RSA magnitude and HRV behavior (Grossman and Taylor, 2007). Assuming that respiratory muscle weakness with restrictive pulmonary pattern leads to shallow breathing and considering that the neural output of the brainstem respiratory center drive to the respiratory muscles was shown to be increased, the baroreceptor and pulmonary stretch receptor may be early activated and may consequently be responsible for the fast central response in cardiac autonomic modulation (Yasuma and Hayano, 2004).

This study has some limitations which have to be pointed out. First, this study was not measured and controlled tidal volume and end-tidal of carbon dioxide during deep breathing protocol, but we instructed the participants to breathe as deep and slow as they can follow the pointer clock to provide a maximum lung volume that varied from total lung capacity to the residual volume also with monitored pulse oxygen saturation. Second, the RMS sEMGpara max was conducted in one maximal volitional maneuver, so normalized to the EMG signal at rest may not be the most value. Furthermore, all participants were received beta-blockers, which could influence on HRV, however, this study intended to investigate the real-life situations.

In conclusion, this study revealed that the patients who had undergone open-heart surgery were increased NRD that measured by sEMGpara and it was correlated to altering cardiac autonomic function, which was characterized by a decrease in HRV. This finding could provide the rehabilitation targets to restore respiratory workload and improve cardiac vagal tone.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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