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Voiding Dysfunction

Autonomous Nervous System Activity in Women with Detrusor Overactivity

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Purpose: To identify autonomic dysfunction among patients with urinary incontinence (UI) with or without detrusor overactivity (DO), we measured and compared heart rate variability (HRV) in these groups.

Materials and Methods: We studied HRV in 12 female UI patients with DO (mean age, 57.3±11.0 years) and 53 female UI patients without DO (mean age, 56.8±9.8 years). HRV parameters were measured by SA-3000P®. Heart rates, the time domain index, and the frequency domain index were compared. To compare time domain indexes, we used the standard deviation of the N-N interval (SDNN), the square root of the mean squared differences of successive N-N intervals (RMSSD), and the frequency domain indexes total power (TP), very low frequency (VLF), low frequency (LF), high frequency (HF), and the low-frequency/high-frequency ratio (LF/HF ratio).

Results: RMSSD values were lower in UI patients with DO than in those without DO, but the values of SDNN and HR showed no significant difference. Whereas the values of LF and HF were lower in UI patients with DO than in those without DO, the LF/HF ratio was higher. TP and VLF were not significantly different.

Conclusions: RMSSD, HF, and LF were lower in DO patients than in controls without DO, but the LF/HF ratio was higher. This suggests that both sympathetic and parasympathetic activity is attenuated in DO, but the autonomic imbalance is higher.

Key Words: *Heart rate; Urinary incontinence*

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INTRODUCTION

Urinary incontinence (UI) is divided into stress urinary incontinence, urge urinary incontinence, and mixed urinary incontinence on the basis of primary symptoms and urodynamic studies [1,2]. UI involves involuntary voiding without the desire to do so. UI is generated from disorders of the bladder itself or neurological conditions, and its main etiology is detrusor overactivity (DO). The etiology and pathology of DO are still unclear. The autonomous nervous system (ANS), which includes the sympathetic and parasympathetic nervous systems, controls the lower urinary tract system and the detrusor muscle [3-5].

The heart rate interval changes even at rest. Heart rate variability (HRV) is a noninvasive quantitative and qualitative tool that shows the balance of the cardiovascular system as controlled by the ANS to the sinoatrial node, allowing study of relationships between the ANS and diseases such as urologic disease, cardiovascular disease, diabetes mellitus, and irritable bowel syndrome [6-9]. In this study, we compared parameters of HRV between UI patients with and without DO, dissected the differences between the groups, and finally investigated the clinical meaning of HRV in DO.

MATERIALS AND METHODS

All processes, procedures, and protocols were evaluated, approved, and monitored by the Institutional Review Board of Ajou University Hospital. We selected 12 women with DO as patients and 53 women without DO as controls after urodynamic studies in patients with UI. DO was diagnosed on the basis of routine chemistry, complete blood count, urine analysis, and uroflowmetry. Women showing signs of dehydration, or a history of neurologic disease, malignancy, coronary heart disease, arrhythmia, diabetes

TABLE 1. Parameters of heart rate variability in patients and controls

	HR (bpm)	SDNN (ms)	RMSSD (ms)	TP (ms^2)	VLF (ms^2)	LF (ms^2)	HF (ms^2)	LF/HF ratio
Controls (n=53)	75.1±10.7	32.0±17.2	24.7±20.0	836.0±1,059.3	437.9±478.0	206.9±331.8	191.1±397.5	1.9±1.9
Patients (n=12)	92.3±56.1	35.3±27.4	18.3±13.6	770.3±943.5	584.0±888.4	111.9±126.3	74.5±140.9	4.3±3.8
p-value	0.475	0.813	0.018	0.182	0.697	0.027	0.002	0.007

Data were presented Mean±SD. HR: heart rate, SDNN: standard deviation of the N-N interval, RMSSD: square root of the mean squared differences of successive N-N intervals, TP: total power, VLF: very low frequency, LF: low frequency, HF: high frequency

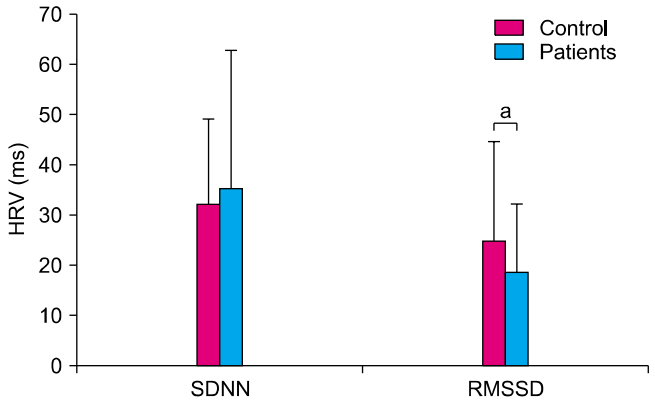

FIG. 1. Mean values of time domain analysis in 12 patients and 53 controls (HRV: heart rate variability, SDNN: standard deviation of the N-N interval, RMSSD: square root of the mean squared differences of successive N-N intervals, [a]: $p < 0.05$).

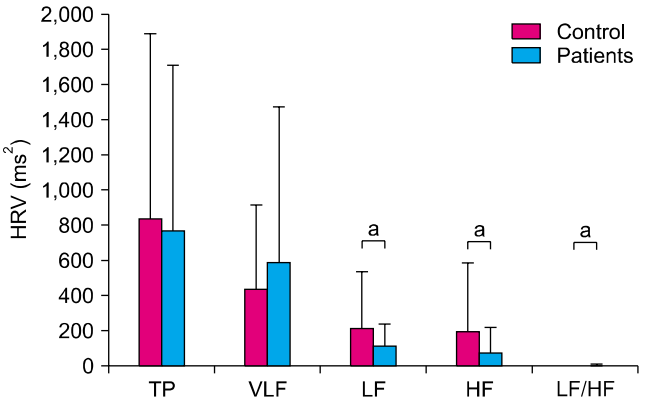

FIG. 2. Mean values of frequency domain analysis in 12 patients and 53 controls (HRV: heart rate variability, TP: total power, VLF: very low frequency, LF: low frequency, HF: high frequency, LF/HF: ratio, [a]: $p < 0.05$ by Mann-Whitney U test).

mellitus, and heart failure, which can influence ANS, were excluded. The parameters of HRV were retrospectively measured. The women did not drink coffee or tea or smoke before the study and were not receiving drugs such as β-receptor agonists or antagonists, angiotensin-converting enzyme inhibitors, anticholinergics, or calcium channel blockers, which can influence ANS. After the women rested for 30 minutes, electrocardiography recording was done for 5 minutes with the women sitting and was then analyzed by SA-3000P® (Medicore Inc., Seoul, Korea). Heart rates, the time domain index, and the frequency domain index were compared. To compare time domain indexes, we used the standard deviation of the N-N interval (SDNN), the square root of the mean squared differences of successive N-N intervals (RMSSD), and the frequency domain indexes total power (TP), very low frequency (VLF), low frequency (LF), high frequency (HF), and the low-frequency/high-frequency ratio (LF/HF ratio). Statistics were performed by using SPSS 12.0.1. (SPSS Inc., Chicago, USA). All results are expressed as Mean±SD values. Comparisons between groups were performed with the Mann-Whitney U test. A p-value less than 0.05 was considered significant.

RESULTS

1. Patient characteristics

Complete blood count, blood chemistry, and general urinary analysis results were normal in both groups, and both groups had a similar average age, 56.8±9.8 years old (range, 42-78 years old) for controls and 57.3±11.0 years old (range, 46-80 years old) for patients (p=0.867), thus indicating no bias in group selection.

2. Analysis of time and frequency domains

For the time domain, SDNN and HR were not statistically significant, but RMSSD was lower in patients than in controls (patients: 18.3±13.6; controls: 24.7±20.0; p=0.018) (Table 1, Fig. 1). For the frequency domain, TP and VLF values were similar, but LF was lower in patients than in controls (patients: 111.9±126.3; controls: 206.9±331.8; p=0.027). HF values were also lower in patients than in controls (patients: 74.5±140.9; controls: 191.1±397.5; p=0.002) and LF/HF values were higher in patients than in controls (patients: 4.3±3.8; controls: 1.9±1.9; p=0.007) (Table 1, Fig. 2).

DISCUSSION

DO is a main cause of UI and reduces quality of life. However, the etiological cause and the pathophysiology of DO are still unclear [10,11]. The lower urinary tract is controlled by the ANS, is innervated by three sets of peripheral nerves (the parasympathetic, sympathetic, and somatic nervous systems), and contains afferent and efferent motor axons. The pelvic parasympathetic nerves from the sacral region (S2-4) control the contraction of the urinary bladder

and the relaxation of the urethra, and the relaxation of the urinary bladder and the contraction of the urethra are controlled by the sympathetic nervous system from the thoracolumbar region (T11-L2) [3,12,13]. Therefore, autonomic dysfunction may contribute to DO.

The ANS affects sinus node rhythm on the basis of the body and the environment, resulting in a cyclic variation of the heartbeat called HRV. A stable condition generally produces a complicated HRV, whereas exercise or stress normalizes HRV.

HRV depends on the influence of sympathetic and vagal activity on the sinus node, and variability reflects spontaneous changes in autonomic activity. HRV is an important tool for studying autonomic control of the heart and autonomic dysfunction. Many commercial devices now provide automated HRV measurement, providing a simple tool for both research and clinical studies. The clinical relevance of HRV was first appreciated in 1965, when Hon and Lee noted that fetal distress manifested itself as alterations in interbeat intervals before any appreciable change occurred in the heart rate itself, which was the first indication that HRV indicates body changes or pathology [14].

The Joint Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology established the measurement tool of HRV, pathological analysis, and standard of clinical use in 1996 [12]. HRV reflects the function of intra-body ANS function. HF and RMSSD are predominantly a response to changes in parasympathetic tone, whereas LF and SDNN are dually influenced by cholinergic and adrenergic activities, as well as by other physiologic inputs. TP values are similar to SDNN; they affect control of the autonomous nervous system.

Efferent vagal activity is a major contributor to the HF component, as is seen in clinical and experimental observations of autonomic maneuvers such as electrical vagal stimulation, muscarinic receptor blockade, and vagotomy (especially when expressed in normalized units) and includes both sympathetic and vagal influences. HRV parameters are divided into two parts: time domain analysis and frequency analysis. Time domain includes average heart rate, SDNN, and RMSSD, and frequency domain involves TP (total power for 5 minutes, including VLF, LF, and HF), VLF (frequency strength of 0-0.04 Hz for test times $>$5 min), LF (frequency strength of 0.04-0.15 Hz), and HF (frequency strength of 0.15-0.4 Hz). LF reflects the regulation of the sympathetic nerve system in the sinus node. HF reflects the regulation of the vagal nerve of the sinus node and electronic stability and thus can predict heart function during aging and sudden death from heart failure. The LF/HF ratio indicates autonomic balance. Patients with diarrhea during irritable bowel syndrome show decreased HF and an increased LF/HF ratio, indicating activation of the sympathetic system. Patients with constipation show higher HF values and a decreased LF/HF ratio, indicating parasympathetic activation. SDNN represents a change of all factors for HRV, and its reduction is associated with less left ventricle function. RMSSD represents heart control of the parasympathetic system [15]. VLF represents the regulation of body temperature, renin-angiotensin activity, peripheral chemical receptor function, vascular system stress, and the stress of the whole body [16-20]. Women have lower LF, VLF, SDNN, and LF/HF ratio values than men but have higher HF and RMSSD. Age decreases HF, RMSSD, SDNN, and LF in both genders [21]. Heart rate values in the afternoon (13:00-16:00) are significantly higher than in the morning (08:30-11:00); the values of SDNN, RMSSD, TP, and HF are significantly lower, but LF and the LF/HF ratio do not change [22].

HRV has been measured in heart diseases such as cardiac infarction, heart failure, arrhythmia, and syncope. HRV also reflects autonomic function in diabetic autonomic neuropathy, irritable bowel syndrome, Parkinsonism, multiple sclerosis, Guillain-Barre syndrome, and Shy-Dragger type postural hypotension [23]. In urologic disease, SDNN, RMSSD, TP, VLF, and HF in overactive bladder are lower than in healthy women [24]. Bladder overfilling in overactive bladders decreases HF and increases LF values, indicating an autonomic imbalance [4]. HF values in men with lower urinary tract symptoms are low, indicating abnormal parasympathetic activity [25]. TP and HF in women with urgency are remarkably lower than in normal women, indicating lower autonomic activity [26]. In this study, RMSSD, HF, LF, and the LF/HF ratio of UI patients with DO were different than in patients without DO, indicating imbalanced autonomic activity.

This study has several limitations. First, the sample size of both groups was small. Second, despite exclusion criteria for drugs such as smoking, coffee, tea, angiotensin-converting enzyme inhibitor, and β-blockers that affect autonomic activity, we could not control individual emotion and mental state. Last, we only compared patients with and without DO, limiting the dose-response activity. However, this study is the first report to show that autonomic variability occurs with DO.

CONCLUSIONS

RMSSD, HF, and LF were lower in DO patients than in controls without DO, but the LF/HF ratio was higher. This suggests that both sympathetic and parasympathetic activity re attenuated in DO, but the autonomic imbalance is higher. Despite the small scale and use of a single center, this study increases our understanding of the etiology and pathophysiology of DO.

Conflicts of Interest

The authors have nothing to disclose.

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