

Assessment of cardiac autonomic modulation in the bladder filling process of women with urinary incontinence: the perspective of physiotherapy

Avaliação da modulação autonômica cardíaca no processo de enchimento da bexiga em mulheres com incontinência urinária: perspectiva da fisioterapia

Evaluación de la modulación autonómica cardiaca en el proceso de llenado de la vejiga en mujeres con incontinencia urinaria: perspectiva de la fisioterapia

Juliana Falcão Padilha¹, Melissa Medeiros Braz², Enio Júnior Seidel³, Giovana Zarpellon Mazo⁴, Jefferson Luiz Brum Marques⁵, Cláudia Mirian de Godoy Marques⁶

ABSTRACT | The behavior of the Autonomic Nervous System, through Heart Rate Variability (HRV), during the bladder filling phases of women with and without urinary incontinence (UI) was compared. The International Consultation on Incontinence Questionnaire - Short Form was applied for UI self-diagnosis. For the HRV analysis, electrocardiogram (ECG) records were used, 6 of them were recorded during bladder filling. To quantify HRV, the following methods were used: time domain (milliseconds); frequency (Hertz) and non-linear measurements. Logarithmic transformation (Log) was applied to these parameters. In the comparison of normal data means, the t-test was applied and the Mann-Whitney test was applied for the non-normal data. The participants consisted of 64 women (64.8±6.73 years), 33 with UI and 31 without. The logarithm of the LF and HF ratio (LogLH/HF) was significantly higher (p<0.05) in the continent group at all phases of the bladder filling. Bladder volumetric capacity was significantly higher in the continent women (p=0.0015). Frequency analysis demonstrated a reduction in sympathetic function and an increase in parasympathetic function in incontinent women. The continent women

presented better autonomic balance, during the whole process of bladder filling compared to incontinent ones. The reduction of sympathetic function as well as the increase of the parasympathetic function in the incontinent women could be reported for a decrease of the detrusor relaxation capacity and an increase of the contractions, still in the bladder filling phase, both associated with UI. Keywords | Urinary Incontinence; Heart Rate Variability; Autonomic Nervous System; Physical Therapy; Women's Health.

RESUMO | Comparou-se o comportamento do sistema nervoso autônomo, por meio da variabilidade da frequência cardíaca (VFC), durante as fases de enchimento vesical de mulheres com e sem incontinência urinária (IU). Aplicou-se o International Consultation on Incontinence Questionnaire – Short Form, para autodiagnóstico de IU. Para análise da VFC utilizaram-se registros de eletrocardiograma (ECG), sendo 6 registros durante o enchimento vesical. Para quantificar a VFC utilizaram-se os métodos: domínio do tempo (milissegundos); frequência (Hertz) e medidas não lineares. A estes parâmetros aplicou-se transformação

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²PhD, professor of the Department of Physical Therapy, Universidade Federal de Santa Maria (UFSM) - Santa Maria (RS), Brazil.

Corresponding address: Cláudia Mirian de Godoy Marques - Centro de Ciências da Saúde e do Esporte, Universidade do Estado de Santa Catarina - Rua Paschoal Simone, 358, Coqueiros - Florianópolis (SC), Brazil - Zip Code: 88080-350 - Phone: (48) 3664-8642 - Email: claudia.marques@udesc.br - Finance source: Fundação de Amparo à Pesquisa e Inovação do Estado de Santa Catariana - Conflict os interests: Nothing to declare - Presentation: Ol Apr. 2016 - Accepted for publicatioon: 04 Sept. 2017 - Approved by the Research Ethics Committe of Universidade do Estado de Santa Catarina (Udesc) on advice CAAE No. 25361013.2.0000.0118.

^{&#}x27;Master's degree, Substitute Professor of the Physiotherapy Course of Universidade Federal do Pampa (Unipmpa) – Uruguaiana (RS), Brazil.

³PhD, professor of the Department of Statistics, Universidade Federal de Santa Maria (UFSM) – Santa Maria (RS), Brazil. ⁴PhD, rofessor of the Department of Physical Education, Center for Health Sciences and Sports (Céfid), Universidade do Estado de Santa Catarina (Udesc) – Florianópolis (SC), Brazil.

⁵PhD, Professor of the Department of Electrical Engineering, Universidade Federal de Santa Catarina (UFSC), Florianópolis (SC), Brazil. ⁶PhD, Professor of the Department of Health Sciences (DCS), Center for Health Sciences and Sports (Cefid), Universidade do Estado de Santa Catarina (Udesc), Florianópolis (SC), Brazil.

logarítmica (Log). Na comparação de médias de dados normais utilizou-se teste t e para os dados não normais o teste de Mann-Whitney. Participaram 64 mulheres (64,8±6,73 anos), 33 com IU e 31 continentes. A variável logaritmo da razão dos componentes LF e HF (LogLH/HF) foi significativamente maior (p<0,05) no grupo continente em todos os momentos do enchimento vesical. A capacidade volumétrica vesical foi significativamente major nas mulheres continentes (p=0,0015). A análise no domínio da frequência demonstrou redução da função simpática e aumento do parassimpático nas mulheres incontinentes. As mulheres continentes apresentaram melhor balanco autonômico durante todo processo de enchimento vesical, em comparação às incontinentes. A redução da função simpática, bem como o aumento da função parassimpática nas incontinentes, pôde ser reportada para uma diminuição da capacidade de relaxamento do detrusor e um aumento das contrações, ainda na fase de enchimento vesical, ambos associados à IU.

Descritores | Incontinência Urinária; Variabilidade da Frequência Cardíaca; Sistema Nervoso Autônomo; Fisioterapia; Saúde da Mulher.

RESUMEN | Se comparó el comportamiento del sistema nervioso autónomo, a través de la variabilidad de la frecuencia cardíaca (VFC), durante las fases de llenado vesical de mujeres con y sin incontinencia urinaria (IU). Se aplicó el International Consultation on Incontinence Questionnaire – Short Form, para

autodiagnóstico de IU. Para el análisis de la VFC se utilizaron registros de electrocardiograma (ECG), considerándose 6 registros durante el llenado vesical. Para cuantificar la VFC se utilizaron los métodos: dominio del tiempo (milisegundos); frecuencia (Hertz) y medidas no lineales. A estos parámetros se aplicó la transformación logarítmica (Log). En la comparación de promedios de datos normales se utilizó la prueba t y para los datos no normales la prueba de Mann-Whitney. Participaron 64 mujeres (64.8±6.73 años), 33 con IU y 31 continentes. La variable logaritmo de la razón de los componentes LF y HF (LogLH/HF) ha sido significativamente mayor (p<0.05) en el grupo continente en todos los momentos del llenado vesical. La capacidad volumétrica vesical ha sido significativamente mayor en las mujeres continentes (p=0.0015). El análisis en el dominio de la frecuencia demostró reducción de la función simpática y aumento del parasimpático en las mujeres incontinentes. Las mujeres continentes presentaron mejor balance autonómico durante todo el proceso de llenado vesical, en comparación a las incontinentes. La reducción de la función simpática, así como el aumento de la función parasimpática en las incontinentes, pudo ser reportada para una disminución de la capacidad de relajación del detrusor y un aumento de las contracciones, aún en la fase de llenado vesical, ambos asociados a la IU.

Palabras clave | Incontinencia Urinaria; Variabilidad de la Frecuencia Cardiaca; Sistema Nervioso Autónomo; Fisioterapia; Salud de la Mujer.

INTRODUCTION

Urinary incontinence (UI) is one of the most common chronic diseases in women. It is currently considered a social disease among women in all age groups1. According to the International Continence Society, any involuntary loss of urine is defined as UI, which can generate a social and hygienic problem². UI is a type of lower urinary tract dysfunction that can occur when there is a change in the physiological process of urination or in the structures involved in the support and sustention of the organs responsible for urination³. The lower urinary tract is innervated by an integrated complex of peripheral neural circuits, involving the sympathetic and parasympathetic autonomic nervous system (ANS), and neurons of the somatic nervous system. The sympathetic ANS stimulates the closure of the urethra sphincter as well as relaxation of the detrusor muscle during the bladder filling. The parasympathetic ANS is responsible for the contraction of the detrusor muscle during urination, while simultaneously relaxing the urethral sphincter4. It is believed that the alteration of the ANS may contribute to a voiding dysfunction, since the lower urinary tract is regulated by sympathetic and parasympathetic ANS. The analysis of the Heart Rate Variability (HRV) allows the measurement of the autonomic function⁵ and, therefore, one can relate it to incontinence and urinary continence. Some authors report that there is an intimate relationship between HRV and bladder filling^{6,7}. HRV appears to be an effective tool for the investigation of autonomic activity during bladder filling. Therefore, the applicability of HRV in Urogynecological Physical Therapy is promising because from this assessment it is possible to rethink treatment methods that can modulate ANS more effectively, which has a better treatment success. In view of this, the article aimed to compare the behavior of ANS, through HRV during the bladder filling phases among women with and without UI.

METHODOLOGY

This was a cross-sectional observational study with a quantitative approach8. The article obtained the approval of the Research Ethics Committee of UDESC, under registration CAAE no. 25361013,2,0000,0118. The sample selection was performed intentionally, for convenience8, composed of women living in the cities of Florianópolis - SC and Santa Maria - RS. Women between the ages of 50 and 80 years old who were either menopausal or postmenopausal and who had selfreported UI were included. We excluded women who reported having the following: heart disease; neurological impairment and/or pathologies that interfere in the understanding of the proposed tasks; having had a stroke; being on urge urinary incontinence (UUI) medication and those who did not agree to evaluate bladder filling. Thus, in order to outline the urogynecological profile of the participants, an adapted form of anamnesis was applied^{9,10}. The assessment of voiding dysfunctions was performed by the International Consultation on Incontinence Questionnaire – Short Form (ICIQ-SF) 11, and the zero score was characterized as continent. An 8-minute duration electrocardiogram (ECG) was used to collect HRV. The ECG was obtained through a cardiac monitor and scanned with an analog-to-digital converter, with the resulting signal being digitally filtered (range 5 to 30 Hz) in order to reduce erroneous detection of the QRS complex and RR intervals. For this assessment, the participant was placed in the supine position and asked to remain at rest during the ECG recording. Three disposable electrodes were placed on the thorax, one on the right subclavicular space (negative terminal); another on the 8th left intercostal space (positive terminal), and on the 9th right intercostal space (reference terminal).

ECG signals were digitally processed for HRV analysis, according to Heck et al. 12, using custom software built and developed at Matlab (Mathworks, Natick, Massachusetts, USA). The methods used to quantify the HRV were: time domain; frequency domain and non-linear measurements (Cardiosympathetic Index and Cardiovagal Index). HRV measurements were calculated according to the recommendations of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology¹³.

In the time scope analysis, indexes extracted directly from the temporal variations of the RR intervals in milliseconds were used. The variability signal (RR intervals) was detected by a differentiation process and selected by the mean value of RR intervals, and 2 times the value of the standard deviation. In the frequency scope analysis, the spectral analysis was used, and the method used for the calculation of the Spectral Power Density was the *Fast-Fourie Transformer*. For the nonlinear method, two important parameters were used to characterize the nonlinear fluctuations in the HRV signal: log of the Cardiovagal Index (LogCVI) and the Cardiosympathetic Index (LogCSI), which separately indicated the vagal and sympathetic functions.

The variables analyzed through the ECG recording in the time scope were the logarithm of: Standard Deviation of NN Intervals (LogSDNN), which demonstrated the global variability; Root Mean Square of Successive Differences (LogRMSSD), which represented the parasympathetic activity. In turn, the variables of the frequency domain were: Very Low Frequency (LogVLF); Low Frequency (LogLF), sympathetic expression; High Frequency (LogHF), parasympathetic expression; Ratio of LF and HF (LogLF/HF) components and absolute and relative changes between the sympathetic and parasympathetic components.

Six ECG were performed at 6 different phases of the bladder filling, based on the methodology described by Ben-Dror et al. 14, proceeding as follows: 1st registration, after the volunteer had emptied the bladder. Soon after, water intake was started at a rate of 150 mL every 5 minutes. The volunteers indicated to the evaluator the moment they perceived and felt the urge to urinate, so that the next records could be made. The 2nd registration was performed in the indication of the First Sensations of Bladder Filling (FSF); 3nd Registration – First Urge to Urinate (FUU); 4th Registration – Strong Urge to Urinate (UDF); 5th Registration – Maximum Bladder Capacity (MBC) and, finally, the 6th Registration – after bladder voiding (Figure 1).

After the 5th Registration, the volunteer collected her own urine in a bottle to check the volume (mL) using a graduated cylinder. The data were analyzed with software R, version 2.15.2. Normality of the data was tested using the Shapiro-Wilk Test. For the comparison of means of HRV variables and anamnesis when the normality occurred we used *t-test* and in the data without normality, the Mann-Whitney test was used. For the comparison between CVI and intragroup CSI, the paired t-test and the Wilcoxon test were used, with a significance level of 5%.

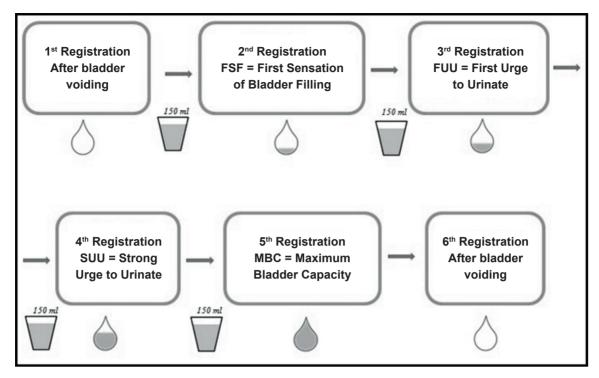


Figure 1. Bladder filling flowchart. FSF = First Sensation of Bladder Filling; FUU = First Urge to Urinate; SUU = Strong Urge to Urinate; MBC = Maximum Bladder Capacity

RESULTS

The sample consisted of 64 women, mean age 64.8±6.73; 33 are incontinent, according to the ICIQ-SF, and 31 are continent (ICIQ-SF zero score). Among the patients with UI, 14 reported stress UI symptoms (SUI); 5 reported UUI, and 14 reported mixed UI (MIU). Table 1 shows the characterization of groups and variables of the anamnesis form.

During the procedure, it was observed that both groups drank approximately the same amount of water, and there was no significant difference between the amount of liquid ingested. However, the volume of urine collected by incontinent women was significantly lower than the continent ones (p=0.001). This may be due to the parasympathetic hyperactivity (Figure 2 (B)) that the UI group presented, causing these women to have decreased continence ability. Table 2 showed the mean values of HRV by time, frequency and non-linear analysis for the 6 stages of process of the bladder filling for the continent and incontinent groups. For the LogLF/HF ratio, which reflected the changes between the sympathetic and parasympathetic components, characterizing the sympathovagal balance, at all phases of bladder filling, the continent group

presented values significantly higher in relation to the UI group. The continent group pointed higher mean values for LogSDNN (it represents the global variability), except in the UDF. However, only in the 6th Registration this comparison was statistically significant. These results demonstrated that, in general, the continent group presented better autonomic balance during bladder filling. In the non-linear analysis, the variable LogCSI, although not significant for some moments, presented higher mean values in the continent women throughout the bladder filling. Therefore, it was observed that there was a tendency for sympathetic ANS to be less activated in incontinent women. Figure 2 illustrates the results of ANS behavior during bladder filling, intragroup (continent and incontinent) for LogCSI and LogCVI variables. In Figure 2 (A), the continent group, the sympathetic ANS had a tendency to decrease, alongside the increase of the parasympathetic ANS. The bladder filling could be divided into two phases, the first phase, of slow and progressive filling "Initial Stage of Filling", which represented greater sympathetic activation, "1st Registration" to "FSF". The second stage corresponded to the "Pre-Urination" that went from "FSF" to "MBC", with greater parasympathetic activation, presenting significant values in the three Registrations (FUU, SUU, MBC) (p<0.05), causing the urge to urinate. Regarding the incontinent group (Figure 2 (B)), the comparisons of LogCVI values were significantly higher than LogCSI (p<0.01), except in the 1st Registration,

however, the LogCVI still presented higher values. Thus, parasympathetic hyperactivity could be observed in the incontinent group, observing that parasympathetic ANS remained more activated throughout the process.

Table 1. Comparison of the means of the variables of the continent and incontinent groups

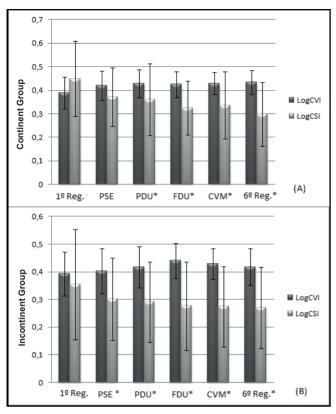
	Continents	Incontinents	– p value	
Variables	Mean (±SD)	Mean (±SD)		
Age (years)	62.4 (±6.09)	67.1 (±6.67)	0.0038*	
Weight (kg)	67.1 (±11.24)	69.3 (±12.32)	0.4630	
Height (m)	1.6 (±0.07)	1.4 (±0.05)	0.5932	
Índice de Massa Corporal	27.5 (±3,85)	28.8 (±5.10)	0.2538	
How often they urinate per day	6.6 (±3.28)	8 (±4.16)	0.1060	
Amount of urine (mL)	530.7 (±196.29)	384.2 (±142.49)	0.0015*	
Amount of ingested water (mL)	1558.1 (±356.40)	1386.4 (±335.47)	0.0520	

^{*} Significant values p<0.05. For variables with normality, the t test was used; without normality, the Mann-Whitney test. SD: standard deviation

Table 2. Comparison of means of HRV parameters in the sequence of bladder filling records. Continent Group (CG) and Incontinent Group (IG)

Mandalidas	1st Registration			FSF			FUU		
Variables —	CG	IG	p value	CG	IG	p value	CG	IG	p value
LogSDNN	1.348	1.337	0.7268	1.408	1.345	0.1524	1.428	1.382	0.0560
LogRMSSD	1.166	1.228	0.8719	1.295	1.285	0.3825	1.322	1.331	0.3645
LogCVI	0.389	0.392	0.7268	0.421	0.402	0.1948	0.428	0.416	0.1175
LogCSI	0.449	0.355	0.0419*	0.371	0.301	0.0456*	0.361	0.291	0.0684
LogVLF	1.998	1.853	0.2452	2.104	1.788	0.0012*	2.060	1.889	0.0607
LogLF	1.678	1.508	0.1696	1.839	1.538	0.0054*	1.775	1.603	0.0338*
LogHF	1.600	1.759	0.7068	1.876	1.840	0.3899	1.944	1.948	0.3540
LogLH/HF	0.078	-0.251	0.0008*	-0.036	-0.310	0.0194*	-0.170	-0.345	0.0394*
	SUU			MBC			6 th Registration		
		SUU			MBC		6 th	Registration	
_	CG	SUU	p value	CG	MBC IG	p value	CG	Registration IG	p value
LogSDNN	CG 1.402		p value 0.9144	CG 1.420		p value 0.2506			
LogSDNN LogRMSSD		IG			IG		CG	IG	p value
, i	1.402	IG 1.447	0.9144	1.420	I G 1.409	0.2506	CG 1.426	IG 1.371	p value 0.0401*
LogRMSSD	1.402 1.327	1.447 1.405	0.9144 0.7117	1.420 1.333	1.409 1.370	0.2506 0.9037	CG 1.426 1.369	IG 1.371 1.339	p value 0.0401* 0.1662
LogRMSSD LogCVI	1.402 1.327 0.424	1.447 1.405 0.440	0.9144 0.7117 0.8141	1.420 1.333 0.429	1.409 1.370 0.430	0.2506 0.9037 0.4437	1.426 1.369 0.434	1.371 1.339 0.417	p value 0.0401* 0.1662 0.0489*
LogRMSSD LogCVI LogCSI	1.402 1.327 0.424 0.325	1.447 1.405 0.440 0.277	0.9144 0.7117 0.8141 0.1690	1.420 1.333 0.429 0.336	1.409 1.370 0.430 0.274	0.2506 0.9037 0.4437 0.0897	1.426 1.369 0.434 0.298	1.371 1.339 0.417 0.269	p value 0.0401* 0.1662 0.0489* 0.4291
LogCVI LogCSI LogVLF	1.402 1.327 0.424 0.325 2.014	1.447 1.405 0.440 0.277 2.019	0.9144 0.7117 0.8141 0.1690 0.9578	1.420 1.333 0.429 0.336 1.999	1.409 1.370 0.430 0.274 1.951	0.2506 0.9037 0.4437 0.0897 0.5556	1.426 1.369 0.434 0.298 2.064	1.371 1.339 0.417 0.269 1.817	p value 0.0401* 0.1662 0.0489* 0.4291 0.0315*

^{*} Significant values p<0.05; for normal variables t-test was used; without normality Mann-Whitheny test. LogSDNN: logarithm Standard Deviation of NN Intervals; LogRMSSD: logarithm Root Mean Square of Successive Differences; LogCVI: logarithm of Cardiovagal Index; LogCSI: logarithm of the Cardiosympathetic Index; LogVLF: logarithm of Very Low Frequency, LogLF; logarithm of Low Frequency; LogLF/HF: logarithm of the ratio of LF and HF components



* Significant differences (p<0.05). Logarithm of the Cardiovagal Index (LogCVI); Cardiosympathetic Index Logarithm (LogCSI)

Figure 2. Comparison between LogCVI and LogCSI during the process of bladder filling for each group. (A) Continent Group; (B) Incontinent Group. Values expressed as mean and standard deviation

DISCUSSION

The incontinent group was significantly older than the continent group, suggesting that advanced age is a facilitating factor for UI development, as a recently reported study¹⁵. The volume of urine collected was significantly lower in the UI group; this may be related to the autonomic imbalance, mainly related to the increase of the parasympathetic function.

In this study, the IU group presented the worst autonomic balance compared to the control group. Blanc et al. 16 compared the ANS activity in the different types of UI by means of HRV analysis. The comparison was performed among 11 incontinent women without Idiopathic Detrusor Instability (IDI) and with 14 incontinent women with IDI. The overall ANS activity of IDI patients was significantly lower (p<0.05) than those with UUI, but sympathovagal balance was not significantly different between groups. The researchers pointed out that IDI instability was associated with an

overall reduction in ANS activity compared to that of patients without IDI.

In this study, the variable LogRMSSD, which represented the parasympathetic activity, was not significant in most registrations, but the incontinent group presented higher values of the LogRMSSD than the control, except for the FSF and the 6th Registration. These results were not similar to those of another study6, which evaluated 12 women with Overactive Bladder Syndrome (OAB) and 53 women in a control group. The variable RMSSD was lower in the patients than in the control (p=0.018). On the other hand, the LF/HF values were higher in patients than in controls (p=0.007), which is not in accordance with this study, in which, for all phases assessed, the control group had higher values of LF/HF than the UI group (p<0.05).

Another study¹⁷ aimed to evaluate the ANS function, using HRV, of 40 OAB patients compared to 131 healthy volunteers. The results showed that the SDNN variable of OAB patients was significantly lower than in the control groups. This result is similar to that of another study¹⁸, which investigated the HRV of 33 women with OAB and 176 controls. The evaluation consisted of ECG recording from the onset of urinary urge and 5 minutes after urination. SDNN values were also significantly lower in the OAB group. These results corroborated the ones of this study: although not significant, the control group presented mostly higher values for the LogSDNN in relation to the UI group.

Other results of the study¹⁷ showed that the VLF variable of patients with OAB were significantly lower than in the control group. This outcome was similar to the one in this study: although it did not present significant difference at all phases, the control group reported higher values of LogVLF in most cases. In turn, the LF/HF variable did not show a significant difference¹⁷, which differed from this study, where LogLF/HF was significant in all registrations. This divergence may have happened because the authors did not standardize the bladder filling. In another investigation¹⁴ the ANS function was compared among 9 women with OAB and 15, without OAB, during bladder filling. ECG signals were used to evaluate HRV. The analyzed variables were RMSSD, LF and HF to evaluate the autonomic sympathetic and parasympathetic function, respectively. For RMSSD and HF, no significant difference was observed between groups. This fact was similar to his study, in which there was also no significant difference between the groups studied. Analyses revealed that LF values were significantly lower throughout the

bladder filling in women with OAB than in the control. These results were close to those obtained in this study. Although there was no significant difference in the LogLF variable between the groups, the continent group had higher values of LogLF during filling compared to the UI group.

In a few studies^{7,14,18} an increase in sympathetic ANS was observed during bladder filling sensations in the control groups, since the authors defended the theory that a continuous increase in sympathetic activity was required during bladder filling, to allow the bladder to expand without contraction of the detrusor. However, in this study there was a decline in sympathetic activation, with a significant difference (p<0.02) between LogLF and LogHF for FUU, SUU and MBC. This suggested the overlap of the parasympathetic to the sympathetic, and there was some contraction of the detrusor, due to the UDF as well as the MBC. This causes us to reflect on the neurophysiology of continence, which reaches the SNC afferently, signals returning efferent signals that regulate the ANS to maintain continence or to the onset of urination. Based on a systematic review¹⁹ in Brazilian journals, it was observed that HRV is used in the scope of Physical Therapy as a resource for the evaluation of physiotherapeutic interventions, as a way of investigating pathological conditions common to clinical practice and for the interpretation of physiological conditions. Its use is made, mainly, by the cardiorespiratory specialty. However, few studies discuss and address this issue in the field of physiotherapy in the area of women's health.

Another scientific literature review²⁰, which addresses the subject of HRV and UI, found that although there are researches that use HRV as an important tool in Physical Therapy, few studies are focused on the analysis of ANS dysfunction in patients with UI.

Knowing HRV in the field of Physical Therapy is of fundamental importance, since it is possible to observe in more detail the behavior of the ANS of the studied population. The usefulness of this tool, regarding the treatment, requires more research regarding the applicability and efficiencies of techniques with purpose in modulating the ANS, with consequent inhibition of the parasympathetic hyperactivity, of incontinent women.

This study had as a limitation the non-performance of the comparison of HRV parameters in the different types of UI. It is also suggested that the investigation of sympathetic and parasympathetic activation should be conducted in an isolated way for the detrusor and urethral sphincter.

CONCLUSION

This study evidenced that the continent women presented a better autonomic balance in comparison to the incontinent ones during the whole process of bladder filling. It was observed that incontinent women presented higher values of parasympathetic function, even before filling, as in the continents there was no such behavior, initiating the procedure with greater bladder relaxation.

The reduction of the sympathetic function (LogCSI) and the increase of the parasympathetic function (LogCVI), in the UI group, could report a decrease of the relaxation capacity and increase of the contractions of the detrusor, still in the filling phase. As a result, the bladder capacity decreased, since the continents presented greater volumetric capacity than incontinent ones.

It can also be verified that HRV has proved to be an effective tool for the investigation of sympathetic and parasympathetic Autonomic Nervous System activity during bladder filling.

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