Assessment of Autonomic Cardiac Control in Women with Cardiac Syndrome X using Time Related Autonomic Balance Indicator

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Abstract

The various CVD (AH, CHF, IHD) have a different circadian profile of autonomic cardiac control (ACC), compared to the profile in healthy subjects (HS). In this study we analyze the specific abnormalities in ACC circadian changes in women with cardiac syndrome X (CSX).

The results indicated that: i. circadian profile of ACC in women with CSX is similar to that in healthy women; ii. ACC reactivity is suppressed; iii. lower vagal and higher sympathetic activity in comparison with the levels of the autonomic balance in healthy women are the characteristics of the particular disorder in ACC in women with CSX.

1. Introduction

CSX is usually diagnosed in the presence of typical exertional chest pain, a positive response to exercise testing, and normal coronary angiograms. According to J. C. Kaski "Patients with CSX represent a diagnostic and therapeutic riddle" [1].

G. Rosano, P. Ponikowski, St. Adamopoulos, et al [2] note that "Anomalies of autonomic control of the coronary circulation may play a role in the development of syndrome X". The analysis of ACC in patients with CSX in [2-4] suggests two different conclusions about the disorders in the both parts of the autonomous balance. All investigators point out the heterogeneous structure of the group of patients with CSX considering the ground disorder in the autonomous balance. Because of that, patients are divided into two groups- one with reaction to stimulation test with no differences compared with HS; others with particular reaction. In [2] authors find out impaired sympathetic activity with signs of hypersympathicotonia. In [3] in patients with CSX suppressed baroceptor sensitivity comes with low values of PNN50, RMS, HF (parameters which are sensitive to changes of the vagal), in distinction with the values in HS and patients with ICD. In [4] authors find out abnormal regulation with more affected parasympathetic activity in comparison with sympathetic one.

Some studies are focused on the instant state of ACC and do not consider the ground autonomous balance in particular times of the day, when both parts of the balance are with different tonus [5]. In [6] we indicated that the CVD (AH, CHF, IHD) have a different circadian profile of ACC, compared to the profile in HS. In this study we analyze the specific abnormalities in ACC circadian changes in women with CSX. With all that we aim to give more detailed picture of the particular disorder in ACC in those patients.

2. Methods

The study comprised of 25 women (55.4±9.4) with CSX and 22 healthy women (47.3±10.9). All patients are with fulfilled criteria for CSX at the period of pre- or postmenopause and with "clear" coronary arteries verified from angiography or multi-slice CT. Stratification by risk factors, comorbidity and pharmacological management have been done using a standardized protocol. The ACC changes were assessed by HRV indices from ECG recordings in resting state (RS) and by parasympathetic (Valsalva manoeuvre; VM), or sympathetic (handgrip test; HT) stimulation.

In [7] we proposed the Time Related Autonomic Balance Indicator (TRABI) – a non-parametric criterion for estimating the circadian changes of ACC by comparing the values of the HRV indices in RS and by autonomic nervous system stimulation during two intervals – morning (8-9 a.m.) and afternoon (2-3 p.m.). All data is analyzed with StatSoft® product Statistica 7.

3. Results

The main results are represented in a tables and graphics as follows below.

Variable	T-test Marked differences are significant at p < ,05000			
	Mean CSX	p	Mean HS	p
RRSDm	42,48		48,05	
RRSDan	45,72	0,4667	44,82	0,3278
PNN50m	7,20		8,68	
PNN50an	7,32	0,9108	9,68	0,4546
RMSm	33,64		32,59	
RMSan	35,12	0,6750	33,41	0,7714
VLFm	248,16		266,36	
VLFan	197,28	0,2184	219,41	0,2577
LFm	208,52		387,82	
LFan	218,48	0,8222	376,00	0,9223
HFm	173,56		195,59	
HFan	210,76	0,6193	205,91	0,8143

Table 1. Mean values of the HRV indices in patients with CSX and in HS in RS with comparison between morning (m) and afternoon (an) measurements.

Variable	T-test Marked differences are significant at p < ,05000			
	Mean CSX	*p*	Mean HS	*p*
RRSDm	*40,72*		39,68	
RRSDan	*32,72*	*0,0318*	41,32	0,6355
PNN50m	7,80		6,77	
PNN50an	5,80	0,2634	7,95	0,4990
RMSm	36,08		30,09	
RMSan	26,80	0,0507	29,86	0,9430
VLFm	96,64		88,68	
VLFan	63,80	0,2017	73,82	0,1986
LFm	71,08		65,45	
LFan	54,04	0,1553	104,18	0,2976
HFm	*57,88*		44,27	
HFan	*35,80*	*0,0387*	59,05	0,4252

Table 2. Mean values of the HRV indices in patients with CSX and in HS by HT stimulation with comparison between morning (m) and afternoon (an) measurements.

Variable	T-test Marked differences are significant at p < ,05000			
	Mean CSX	*p*	Mean HS	*p*
RRSDm	51,75		76,95	
RRSDan	62,67	0,1517	76,55	0,9634
PNN50m	8,17		13,00	
PNN50an	10,67	0,1860	12,41	0,7252
RMSm	36,46		44,73	
RMSan	47,79	0,1130	41,77	0,3718
LFm	89,83		131,14	
LFan	158,50	0,0660	229,68	0,2928
HFm	31,38		61,86	
HFan	41,83	0,2617	49,05	0,2041

Table 3. Mean values of the HRV indices in patients with CSX and in HS by VM stimulation with comparison between morning (m) and afternoon (an) measurements.

Variable	T-test Marked differences are significant at p < ,05000			
	Mean CSX	*p*	Mean HS	*p*
RRSD_r	42,48		*48,05*	
RRSD_ht	40,72	0,6338	*39,68*	*0,0168*
PNN50_r	7,20		8,68	
PNN50_ht	7,80	0,6858	6,77	0,1863
RMS_r	33,64		32,59	
RMS_ht	36,08	0,5481	30,09	0,2226
VLF1_r	*248,16*		*266,36*	
VLF_ht	*96,64*	*0,0149*	*88,68*	*0,0000*
LF_r	*208,52*		*387,82*	
LF_ht	*71,08*	*0,0001*	*65,45*	*0,0001*
HF_r	*173,56*		*195,59*	
HF_ht	*57,88*	*0,0014*	*44,27*	*0,0003*

Table 4. Mean values of the HRV indices in patients with CSX and in HS in RS (r) and by HT stimulation (ht) with comparison between morning measurements.

Variable	T-test Marked differences are significant at p < ,05000			
	Mean CSX	*p*	Mean HS	*p*
RRSD_r	*45,72*		44,82	
RRSD_ht	*32,72*	*0,0040*	41,32	0,0774
PNN50_r	7,32		*9,68*	
PNN50_ht	5,80	0,2557	*7,95*	*0,0359*
RMS_r	*35,12*		*33,41*	
RMS_ht	*26,80*	*0,0321*	*29,86*	*0,0192*
VLF_r	*197,28*		*219,41*	
VLF_ht	*63,80*	*0,0045*	*73,82*	*0,0002*
LF_r	*218,48*		*376,00*	
LF_ht	*54,04*	*0,0026*	*104,18*	*0,0023*
HF_r	210,76		*205,91*	
HF_ht	35,80	0,0707	*59,05*	*0,0002*

Table 5. Mean values of the HRV indices in patients with CSX and in HS in RS (r) and by HT stimulation (ht) with comparison between afternoon measurements.

Variable	T-test Marked differences are significant at p < ,05000			
	Mean CSX	*p*	Mean HS	*p*
RRSD_r	*42,48*		*48,05*	
RRSd1_vm	*50,64*	*0,0459*	*76,95*	*0,0000*
PNN50_r	7,20		8,68	
PNN50_vm	7,92	0,6352	13,00	0,0240
RMS_r	33,64		32,59	
RMS_vm	35,80	0,6180	44,73	0,0004
LF_r	*208,52*		*387,82*	
LF_vm	*86,76*	*0,0006*	*131,14*	*0,0009*
HF_r	*173,56*		*195,59*	
HF_vm	*30,36*	*0,0006*	*61,86*	*0,0012*

Table 6. Mean values of the HRV indices in patients with CSX in RS (r) and by VM stimulation (vm) with comparison between morning measurements.

Variable	T-test Marked differences are significant at p < ,05000			
	Mean CSX	*p*	Mean HS	*p*
RRSD_r	45,00		*44,82*	
RRSD_vm	62,67	0,0532	*76,55*	*0,0014*
PNN50_r	*7,38*		9,68	
PNN50_vm	*10,67*	*0,0273*	12,41	0,0508
RMS_r	35,25		*33,41*	
RMS_vm	47,79	0,0825	*41,77*	*0,0400*
LF_r	226,13		376,00	
LF_vm	158,50	0,3186	229,68	0,3058
HF_r	216,88		*205,91*	
HF_vm	41,83	0,1101	*49,05*	*0,0035*

Table 7. Mean values of the HRV indices in patients with CSX in RS (r) and by VM stimulation (vm) with comparison between afternoon measurements.

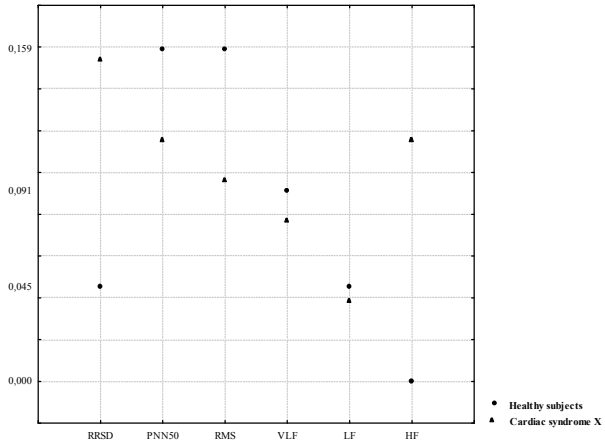

Figure 1. Values of TRABI for the HRV indices in healthy woman and in woman with CSX with comparison between morning and afternoon measurements in RS and by HT stimulation.

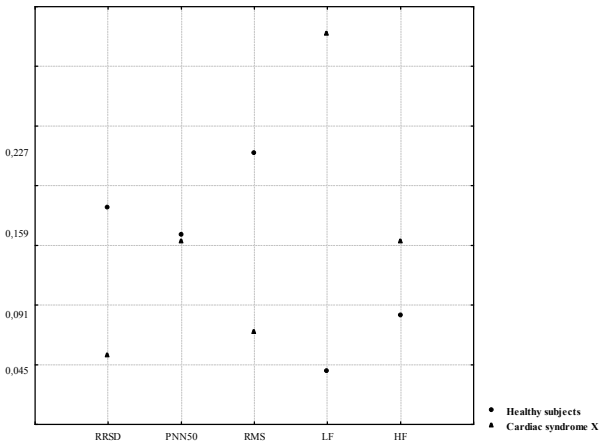

Figure 2. Values of TRABI for the HRV indices in healthy woman and in woman with CSX with comparison between morning and afternoon measurements in RS and by VM stimulation.

4. Discussion and conclusions

Results shown in table 1, 2 and 3 demonstrate that there is no significant difference in the parameters of HRV in HS compared with patients with CSX when comparing measured values in the morning and in the afternoon in all three measurements: in RS and after stimulation with HT and VM. Only in stimulation with HT there is a significant decrease in the total variability predominantly because of the reduction of the parasympathetic activity (RRSDm and HFm > RRSDan and HFan; $p < 0,05$).

Comparative studies at rest and with HT stimulation in the morning and in the afternoon (table 4 and 5), demonstrate unidirectional reaction at stimulation in patients and HS in the morning as well as in the afternoon: to decrease the total activity (RRSD) as well as the parameters describing the both parts of the autonomous balance (VLF and LF, respectively PNN50, RMS and HF). This trend in the both groups is more marked in the afternoon. We explain these results with the higher activity of the autonomous system in the morning in reaction to the sympathetic stimulation and that reaction decreases in the afternoon, in HS as well as in women with CSX. The smaller number of the significant changes in the parameters in women with CSX is because of the higher tonus of the sympathetic nervous system in those patients as demonstrating the results in table 2.

Comparative studies at rest and with VM in the morning and in the afternoon– table 6 and 7, also demonstrate unidirectional reaction to stimulation in patients and in HS in the morning as well as in the afternoon. In the same time, results of the parameters reacting to particular part of the autonomous balance (LF, respectively PNN50, RMS and HF; the duration of the measurement with the Valsalva maneuver does not allow the determination of the VLF) demonstrate different ground level of the sympathetic and parasympathetic tone in HS and in patients with CSX, although the reactivity of the autonomous control to be with the same profile. Parasympathetic activity is higher in the morning in both groups, but in patients with CSX the reaction to parasympathetic stimulation is weaker.

In maintenance of the mentioned results are the circadian profiles of the sympathetic and parasympathetic components in ACC, composed from the assessment of parameters for HRV by TRABI – fig. 1 and 2.

At HT stimulation the difference between changes in the morning and in the afternoon compared those parameters at rest, assessed by LF and VLF is not significant: TRABI values are 0,038 and 0,096 (n.s.) in patients with CSX respectively 0,045 and 0,091 (n.s.) in HS (fig. 1). In the same time, the difference in the variability among patients with CSX increases significantly (TRABI assessment for RRSD is 0,154 respectively 0,045 in HS, $p<0,05$). This difference obviously is due to the higher possibility of the parasympathetic activity to vary from the ground levels at rest, because of relatively low tone (and there for high elasticity) in comparison with the sympathetic activity (assessment for HF is 0,115 relative unites in patients with CSX and assessment 0,0 in HS, $p<0,05$).

Comparative study with VM (fig. 2), confirms conclusions above. TRABI assessment of HF point out that this parameter reflects relative changes in parasympathetic tone at stimulation in comparison with it's tone at rest in the morning and in the afternoon (0,154 respectively 0,091 in HS, $p<0.05$). In the same time, slighter affected sympathetic activity at that test demonstrates considerable elasticity, because of the mentioned previously decrease of the sympathetic tone in patients with CSX in the afternoon compared with that in the morning (TRABI assessments of LF are respectively 0,327 and 0,045, $p<0,05$).

In conclusion we could generalize that: i. circadian activity of ACC in women with CSX is similar to that in healthy women; ii. Autonomous balance reactivity is suppressed; iii. lower level of the parasympathetic tone and higher of the sympathetic tone in comparison with the levels of the autonomous balance in healthy women, are the characteristics of the particular disorder of the ACC in women with CSX.

Acknowledgements

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References

[1] Kaski JC. Pathophysiology and Management of Patients with Chest Pain and Normal Coronary Arteriograms (Cardiac Syndrome X). Circulation 2004;February 10:568-72.

[2] Rosano GMC, Ponikowski P, Adamopoulos S, Collins P, Poole-Wilson P, Coats AJS and Kaski JC. Abnormal autonomic control of the cardiovascular system in syndrome X. The American J. of Cardiol. 1994;73(16):1174-9.

[3] Adamopoulos S, Rosano GMC, Ponikowski P, et al. Impaired baroreflex sensitivity and sympathovagal balance in syndrome X. The American J. of Cardiol. 1998;82(7):862-8.

[4] Gulli G, Cemin R, Pancera P, et al. Evidence of parasympathetic impraiment in some patients with cardiac syndrome X. Cardiovascular Research 2001;52:208-16.

[5] Wennerblum B, Lurje L, Karlsson T, et al. Circadian Variations of Heart Rate Variabilty and the role of autonomic change in morning hours in Healthy subjects and angina patients. Int J Cardiol 2001;79(1): 61-69.

[6] Matveev M, Prokopova R. Normal and abnormal circadian profiles of heart autonomic balance, evaluated by time-ralated common indicator of heart rate variability. The Anatolian J Cardiol 2007;7/S1:125-9.

[7] Matveev M, Prokopova R, Nachev Ch. Time-Related Heart Vegetative Balance Characteristics. Computers in Cardiology 2003;30:457-60.

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