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USE OF pNNx STATISTICS IN THE EVALUATION OF HEART RATE VARIABILITY AT REST AND DURING EXERCISE

EL USO DE LOS ESTADÍSTICOS pNNx EN LA EVALUACIÓN DE LA VARIABILIDAD DE LA FRECUENCIA CARDIACA EN REPOSO Y DURANTE EL EJERCICIO

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RESUMEN

El número de diferencias mayores de 50 ms en una serie de latidos cardiacos normales expresada en porcentaje (pNN50) se ha usado ampliamente para medir la Variabilidad de la Frecuencia Cardiaca (VFC). El pNN50 es solo un miembro de una familia general de estadísticos para el análisis de la VFC. El objetivo de este estudio es explorar la potencia de diferentes pNNx para diferenciar sujetos sanos de pacientes cardiacos tanto en reposo como durante un ejercicio aeróbico.
Hemos estudiado a 9 pacientes cardiacos hombres y los resultados fueron comparados con otros 10 hombres sanos y físicamente activos. La señal cardiaca fue registrada latido a latido durante 15 minutos en reposo y otros 15 pedaleando a una intensidad del 60% de la FC máxima teórica. En el momento del estudio cada sujeto del grupo de pacientes había sufrido, al menos, un episodio de infarto agudo de miocardio (IAM) entre 1 y 8 años antes y formaba parte de un programa de rehabilitación cardiaca en fase III. Ningún paciente había sufrido un episodio agudo en el último año.
El pNNx se calculó como el número de diferencias mayores de x ms para valores de x entre 10 y 50 ms.
Todos los valores de pNNx disminuyeron con el ejercicio pero las diferencias son mayores a medida que x es menor. Usando el pNN50 los cardiópatas y sujetos sanos difirieron claramente en reposo (1.71±2.24 y 9.87±5.68, respectivamente) pero no durante el ejercicio (0.48±1.02 y 0.30±0.33, respectivamente). Sin embargo, a medida que se reduce x, las cuatro situaciones van diferenciándose hasta que el pNN10 fue capaz de distinguirlas completamente.
En conclusión, el pNN10 es más sensible que el pNN50 como índice de la VFC en pacientes cardiacos en reposo y ejercicio.

Palabras clave: Variabilidad de la frecuencia cardiaca. pNNx. Ejercicio.

SUMMARY

Number of differences higher than 50 ms in successive normal heartbeats expressed as percent (pNN50) has been widely used to measure the heart rate variability (HRV). But pNN50 is only one member of a general pNNx statistics for HRV. The objective was to assess the power of different pNNx values in distinguishing between healthy people and cardiac patients both at rest and during aerobic exercise.
We studied 9 male cardiac patients and the results were compared to 10 physically healthy active. Heartbeat signal was recorded beat to beat for 15 minutes at rest supine and 15 minutes while pedalling at 60 % of the maximal theoretical HR. At the moment of the study each cardiac patient had suffered at least one episode of acute myocardial infarction (AMI) between 1 and 8 years before the study and he was taking part in the phase III of a cardiac rehabilitation program, so none of the patients have suffered acute episode in the last year.
The pNNx was calculated as the number of differences higher than x ms expressed as percent and for x values from 10 to 50 ms.
All pNNx values decreased with exercise, but the differences increase as "x" values decrease. When using standard pNN50 cardiac and healthy clearly differ at rest (1.71±2.24 and 9.87±5.68, respectively) but not during exercise (0.48±1.02 and 0.30±0.33, respectively). However, at low "x" values these four situations became different and with pNN10 they were completely distinguishable.
In conclusion, pNN10 is more sensible that pNN50 as index of HRV in cardiac patients both at rest and exercise.

Key words: Heart rate variability. pNNx. Exercise.

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INTRODUCTION

Mean number of differences higher than 50 ms in successive normal sinus heart beat intervals (NN_{50}) expressed as percent (pNN_{50})[1] has been widely used to measure the heart rate variability (HRV)[2-6]. This parameter was introduced by Ewing, *et al*[7] to analyze the parasympathetic activity and many works have demonstrated its usefulness both for diagnosis and prognosis in different situations[1,8-16].

In 2002, Mietus, *et al*[17] re-examined this standard HRV statistic (pNN_{50}) by determining other thresholds different to 50 ms (pNNx) ranging from pNN_4 to pNN_{100} and comparing them between healthy subjects and patients with congestive heart failure (CHF). They demonstrated that pNN50 is only one member of a general pNNx statistics for HRV and that discrimination between normal and pathological conditions is higher using pNN thresholds as low as 10 or 20 ms rather than the standard 50 ms threshold. However, in reviewing the literature, we have not found any application of these statistics (pNNx) to other groups or situations (such as exercise).

The present work analyses temporal series of NN intervals at rest and during aerobic exercise in healthy subjects and cardiac patients. The objective is to assess the power of different pNNx values in distinguishing between healthy people and cardiac patients both at rest and during aerobic exercise.

MATERIAL AND METHODS

From the records of HRV in our Centre, we looked for those which had been performed both at rest and during exercise. So, we have analyzed retrospectively 10 young, healthy and active men (age 26,5 ± 3,3 years; height 179,3 ± 6,6 cm; weight 80,4 ±11,8 kg) and 9 cardiac patients (age 61,1 ± 4,7 years, height 165,3 ± 5,3 cm; weight 86,9 ± 11,1 kg).

When the heart rate was recorded, each cardiac patient had suffered at least one episode of acute myocardial infarction (AMI) between 1 and 8 years before the study and was included in a phase III of a cardiac rehabilitation program. None of the patients have suffered an acute cardiac episode in the preceding year.

All subjects gave fully informed written consent. This study had the approval of the ethical committee of the Centro Andaluz de Medicina del Deporte (CAMD) according to the ethical guidelines of the 1975 Declaration of Helsinki.

The exercise was an aerobic session in a static bicycle with a constant intensity. The intensity of exercise for the cardiac patients was 75 % of the maximal HR reached in the ergometry according to the discharge information from the hospital (close to 60% of the maximal theoretical HR). That was also the intensity at which the patients exercised in their rehabilitation sessions. Healthy subjects exercised at 60 % of the maximal theoretical HR (calculated as 220-age).

Heart rate recordings, both at rest and during exercise, were 15 minutes, which guaranteed a data sequence long enough for the analysis[1]. Heartbeat signals were recorded using a Polar S810i™ monitor (Kempele, Finlandia) working in a RR mode (beat to beat). Data were incorporated to the computer through an infrared interface (Polar IR), and analysed using the Polar Precision Performance software (version 3). All data were included in a database for statistical and graphic analysis.

For each series, the absolute values of the differences in consecutive NN intervals were obtained. The pNNx was then calculated as the number of differences higher than x ms expressed as percent and for x values of 10, 20, 30, 40 and 50 ms.

The differences were tested using an unpaired Student's t test for the healthy versus patient comparisons (at rest and during exercise) and a paired t test for the rest versus exercise comparisons. Furthermore, we assessed the effect size through a Cohen's d test. Significance was defined by $p < 0.05$.

RESULTS

Table 1 and 2 show the pNNx values (average and standard deviation) for cardiac patients and healthy subjects at rest and during exercise. Data of p and Cohen's d are shown for every value of x.

The differences in pNNx at rest between healthy and cardiac patients are highly significant for any value of "x". However, during exercise only pNN10 shows significant difference between healthy and cardiac patients (p=0,004).

In healthy subjects, pNNx showed significant difference (p<0.0005) between rest and exercise for any value of x. However, cardiac patients didn't show any significant change between these situations. On the other hand, the lower x value, the higher effect size (Cohen's d).

DISCUSSION

The main finding of this work is that lower values of pNNx are more sensitive to characterize the cardiac response to exercise, mainly when heart disease is present.

With these results we agree with Mietus, ~~et al~~[17] about the importance of using thresholds lower than 50 ms and we add the comparison between rest and exercise, both in healthy people and cardiac patients.

One aspect that may be criticized in this work is the different age in both groups (26,5 ± 3,3 vs 61,1 ± 4,7 years), because aging is one factor influencing HRV. However, we believe that this could be a problem comparing both groups at rest but not when we compare the differences from rest to exercise in every group. Cardiac patients clearly differ from healthy subjects but due to the difference in age we can not say if the differences should be attributed to age, cardiac disease or both but it is clear that for any group, pNNx values are always lower in exercise compared to the rest value (Table 1 and 2). And we can also state that the differences are higher as "x" value is lower. During exercise, only pNN_{10} is able to distinguish between healthy people and

			REST			
	CARDIAC	PATIENTS	HEALTHY	SUBJECTS		
pNNx	Mean	SD	Mean	SD	p	Cohen's d
pNN_{50}	1,71	2,24	9,87	5,68	0,001	-1,89
pNN_{40}	3,96	4,7	15,94	8	0,001	-1,82
pNN_{30}	9,3	9,41	25,72	9,96	0,007	-1,69
pNN_{20}	21,28	15,24	42,28	10,6	0,002	-1,6
pNN_{10}	48,49	18,37	67,31	8,27	0,02	-1,32

TABLE 1. Average and standard deviation for the pNNx values in cardiac patients and healthy subjects at rest. P values and Cohen's d are shown for every value of x

			EXERCISE			
	CARDIAC	PATIENTS	HEALTHY	SUBJECTS		
pNNx	Mean	SD	Mean	SD	p	Cohen's d
pNN_{50}	0,48	1,02	0,3	0,33	0,64	0,24
pNN_{40}	1,5	3,76	0,44	0,44	0,42	0,39
pNN_{30}	3,55	7,85	0,58	0,5	0,34	0,53
pNN_{20}	10,1	14,03	1,21	1,15	0,09	0,89
pNN_{10}	36,04	21,51	7,93	10,75	0,004	1,65

TABLE 2. Average and standard deviation for the pNNx values in cardiac patients and healthy subjects during exercise. P values and Cohen's d are shown for every value of x

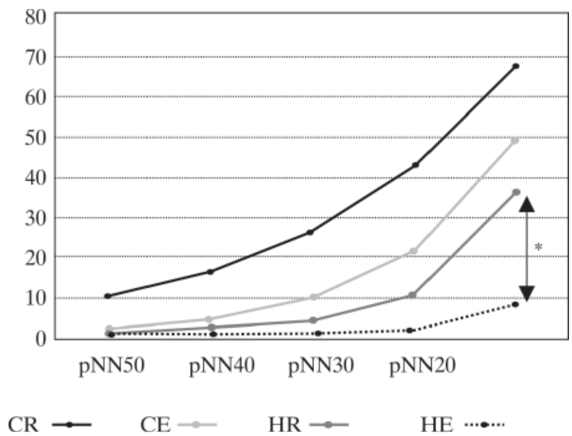

FIGURE 1. Mean values of pNN_{50}, pNN_{40}, pNN_{30}, pNN_{20} and pNN_{10} (HR: healthy subject at rest, HE: healthy subject during exercise, CR: cardiac patients at rest, CE: cardiac patien ts during exercise). Significant differences: (*) $p<0.05$

cardiac patients. Even if aging would be influencing the differences during exercise, it is clear that these differences are not significant with any pNN, except for pNN_{10}.

When we use the standard pNN50 we observe that it decreases in healthy people[14] from a high value at rest (around 10%) to a value lower than 3% during exercise and that cardiac patient have this low value both at rest and during exercise. So, we can difference between healthy (younger) and pathologic (older) people at rest but we can not do it during exercise. Figure 1 shows that as "x" value is decreasing, the four situations became different in such a way that for pNN_{20} and pNN_{10} they are completely distinguishable.

CONCLUSIONS

Although more reports are needed using pNNx less than 50 ms, we believe that lower values (as pNN_{20} or pNN_{10}) are more sensitive for statistical analysis of HRV in different physiological or pathological situations. This is an outstanding observation from the work of Mietus, *et al*[17] but it has been barely explored. Our work adds the comparison between rest and exercise, both in healthy people and cardiac patients, and opens the way to use it in the exercise prescription for cardiac patients and in their control during cardiac rehabilitation.

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BIBLIOGRAPHY

1. **Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996).** Heart rate varibaility: standars of measurement, physiological interpretation and clinical use. *Circulation* 1996;93:1043-65.

2. **Bigger JT Jr, Kleiger RE, Fleiss JL *et al.*** Components of heart rate varibaility measured during healing of acute myocardial infarction. *Am J Cardiol* 1988;61:208-215.

3. **Nolan J, Batin PD, Andrews R *et al.*** Prospective study of heart rate variability and mortality in chronic heart failure. *Circulation* 1998;98:1510-1516.

4. **Kleiger RE, Miller JP, Bigger JT, Moss AJ.** Decreased heart rate variability and its association with increased mortality after accute myocardial infarction. *Am J Cardiol* 1987;59:256-62.

5. **Kleiger RE, Bosner MS, Rottman JN, Stein PK.** Time-domain measurements of heart rate variability. *J Ambul Monit* 1993;6(1):1-18.

6. **Algra A, Tijssen JGP, Poelandt JRTC, Pool J, Lubsen J.** Heart rate variability from 24-hour electrocardiography and the 2-year risk for sudden death. *Circulation* 1993;88:180-5.

7. **Ewing DJ, Neilson JMM, Travis P. (1984).** New method for assessing cardiac parasympathetic activity using 24 hour electrocardiograms. *Br Heart J* 1984;52:396-402.

8. **Goldsmith RL, Bigger JT Jr, Steinman RC, et al.** Comparison of 24-hour parasympathetic activity

in endurante-trained and untrained young men. *J AM Coll Cardiol* 1992;20:552.8.

9. **Chakko S, Mulingtapang RF, Huikuri HV, *et al.*** Alterations in heart rate varanility and its circadian rhythm in hypertensive patientes with left ventricular hypertrophy free of coronay artery disease. *Am heart J* 1993;126:1364-72.

10. **Tsuji H, Larson MG, Venditti FJ Jr, *et al.*** Impact of reduced heart rate variability on risk for cardiac events. The Framingham heart study. *Circulation* 1996;94:2850-5.

11. **Zuanetti G, Neilson JMM, Latini R, *et al.*** Prognostic significance of heart rate variability in post-myocardial infarction patients in the fibrinolytic era-The GISSI-2 results. *Circulation* 2006;94:432-6.

12. **Szabo BM, van Veldhuisen DJ. van der Veer N, *et al.*** Prognostic value of heart rate variability in chronic congestive heart failure secondary to idiopathic or ischemic dilaed cardiomyopathy. *Am J Cardiol* 1997;79:978-980.

13. **Singh JP, Larson MG, Tsuji H, *et al.*** Reduced heart rate variability and new-onset hypertion: insights into pathogenesis of hypertension. The Framingham heart study. *Hypertension* 1998;32:293-297.

14. **De la Cruz B, López C, Naranjo J.** Analysis of heart rate variability at rest and during aerobic exercise. A study in healthy people and cardiac patients. *Br J Sports Med* 2008;42:715-20.

15. **Rodas G, Pedret Carballido C, Ramos J, Capdevila L.** Variabilidad de la Frecuencia Cardiaca: concepto, medidas y relación con aspectos clínicos (I). *Arch. Med. Dep.* 2008;123:41-7.

16. **Rodas G, Pedret Carballido C, Ramos J, Capdevila L.** Variabilidad de la Frecuencia Cardiaca: concepto, medidas y relación con aspectos clínicos (II). *Arch. Med. Dep.* 2008;124:119-27.

17. **Mietus JE, Peng C-K, Henry I, Goldsmith RL, Goldberger Al**. The pNNx files: re-examining a widely used heart rate variability measure. *Heart* 2002;88:378-380.