sin-converting enzyme inhibitor, or an angiotensin receptor blocker. Hypertension. 2007;49(2):276-84.

Heart rate turbulence: a useful parameter in predicting sudden cardiac death

Turbulencia de la frecuencia cardíaca: un parámetro útil en la predicción de muerte súbita cardíaca

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To the Editor:

Prevention of sudden cardiac death (SCD) is one of the most important challenges in modern cardiology. Some variables that increase the risk of SCD have been identified through the years, with more or less validity in clinical practice. In 1999, Schmidt *et al*.[1] published a paper in which they developed a new concept called heart rate turbulence (HRT). This concept describes the physiological heart rate fluctuations that are secondary to ventricular extrasystole (VE). These changes are the initial acceleration of heart rate followed by a deceleration. Although these changes had been identified previously [2], these researchers were able to quantify them for the first time. It is stated that HRT is a measure of the body's autonomic response after disturbances in blood pressure, as a result of the VE. Changes in this parameter have a relevant clinical significance, given its effectiveness in predicting SCD after an acute myocardial infarction (AMI) and other heart diseases.

The main theory explaining the HRT states that this is a form of ventriculophasic sinus arrhythmia, which occurs as a result of nerve reflexes secondary to VE. The initial acceleration results from a transient vagal inactivation and a sympathetic activation in response to an inefficient ventricular contraction. After this process, deceleration occurs, due to the restoration of blood pressure levels as a result of the increase in ventricular filling[1-4].

HRT measurement

Turbulence measurement is performed by the Holter monitor. The two most frequently used measurements for the HRT are turbulence onset (TO) and turbulence slope (TS). The former relates to the acceleration of sinus rhythm after the VE, while the latter allows the measurement of deceleration following the initial acceleration. In healthy subjects, the acceleration of rate after the premature beat is characterized by negative value of TO. The reference value is 0%. Values of this variable < 0% indicate acceleration, while values > 0% indicate deceleration. The presence of positive values indicates abnormality. In the case of the TS, a value of 2.5 ms/RR has been set. A value below this figure is considered abnormal[5].

$$TO = [(RR_1 + RR_2) - (RR\_2 + RR\_1)]*100/(RR\_2 + RR\_1)$$

RR_{-2} y RR_{-1}: Are the two RR intervals preceding the VE.

RR_1 and RR_2: Are the two RR intervals immediately following the compensatory pause of VE.

TS: is defined as the maximum positive slope of regression line assessed in five consecutive RR intervals randomly, within 15 RR intervals after the VE.

Assessment of the HRT in post-AMI patients

As mentioned before, the usefulness of this variable is given by its capacity to predict SCD. A group of researchers characterized HRT in 322 post-MI patients with an ejection fraction <50%, and showed that both the TO as its slope, were useful to identify patients at high risk for cardiac death[6]. Barthel *et al*.[7] published a prospective cohort study of 1 455 patients under 75 years of age with AMI within 4 weeks before the study, and a follow up for 22 months. It was also demonstrated the utility of HRT as a predictor of SCD, confirming previous observations made by other authors[7]. Recently, a one-year-follow-up prospective assessment with 111 post-AMI patients indicated that TO and TS showed greater alteration in patients who did not survive after the occurrence of a heart attack during the study period, compared with those who survived , TO = 0% (0.005; 0.01) vs. -0.01% (-0.013; -0.004), p = 0.004 and TS = 3.34 (2.10; 4.83), vs. 3.82 (4.48; 7.27), p = 0.001; (values in parentheses refer to the 25th and 75th percentiles)[8]. Similar findings were found by Cebula *et al*.[9], who also assessed another category within the HRT that had barely been analyzed previously. This is the case of synchronization of turbulence, a parameter that tells us how fast the sinus rhythm deceleration phase begins. This parameter, like the others, also proved to be effective in the prediction of cardiovascular events in patients with AMI.

Assessment of HRT in patients with heart failure

Patients with heart failure have a worsening of baroreflex sensitivity, with increased activity of the sympathetic nervous system. Therefore, it is common to expect that the HRT is altered in this condition. There is still little data assessing the prognosis of this parameter in patients with this condition. However, two studies have been published which serve as reference on this topic. This is the case of the UK-Heart Trial[10] and MUSIC Study[11]. In the former, abnormal TS values were independent predictors of decompensation, while in the latter the same variable was effective for predicting death in patients with this disorder. Based on these findings, the authors suggested that it might be useful in predicting SCD in these patients. Apparently, this association is present only in cases of ischemic heart failure, because such a link has not been demonstrated in affected individuals without ischemic cause.

HRT in other clinical settings

Abnormal behavior of this parameter has been observed in patients with diabetes mellitus, with or without previous myocardial infarction[12,13]. Furthermore, it appears that disturbances in the turbulence are independent of the existence of diabetic neuropathy, which allows a more effective assessment of these patients. Alterations have also been found in patients with mitral valve prolapse[14] and stenosis[15], in the latter, the TO was associated with an increased severity of symptoms. Other studies have found a deterioration of the parameter in hyperthyroid subjects compared with control subjects[16], and in those subjects who had sleep apnea syndrome[17]. As it is known, both are closely linked to the development of heart disease, thus, its usefulness in predicting the occurrence of alterations in this organ can be very useful for the prognosis of these individuals.

The analysis of HRT has been included within the useful methods for the prevention of SCD in the Guidelines for the Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death (ACC/AHA/ESC 2006)[18]. Although there have been important developments in this field, there are factors to be taken into account in the interpretation of this predictor. For example, the possible influence of certain factors or variables (decreased ejection fraction, old age, tachycardia) on the reading of the various parameters that form the HRT analysis, and whether these influences are statistically significant to alter the analysis. It is also important to note that the way of obtaining HRT is through Holter monitoring, an instrument that is not always available and requires highly skilled personnel. Despite these difficulties, this predictor has proved to be an effective tool in the

assessment and prognosis of patients with multiple disorders, so it is a factor which should be more widely disseminated among cardiologists.

REFERENCES

1. Schmidt G, Malik M, Barthel P, Schneider R, Ulm K, Rolnitzky L, *et al*. Heart-rate turbulence after ventricular premature beats as a predictor of mortality after acute myocardial infarction. Lancet. 1999; 353(9162):1390-96.
2. Lombardi F, Gnecchi Ruscone T, Malliani A. Premature ventricular contractions and reflex sympathetic activation in cats. Cardiovasc Res. 1989;23(3): 205-212.
3. Davies LC, Francis DP, Ponikowski P, Piepoli MF, Coats AJ. Relation of heart rate and blood pressure turbulence following premature ventricular complexes to baroreflex sensitivity in chronic congestive heart failure. Am J Cardiol. 2001;87(6):737-42.
4. Bauer A, Malik M, Schmidt G, Barthel P, Bonnemeier H, Cygankiewicz I, *et al*. Heart rate turbulence: standards of measurement, physiological interpretation,and clinical use international society for Holter and non invasive electrophysiology consensus. J Am Coll Cardiol. 2008;52(17):1353-65.
5. Francis J, Watanabe MA, Schmidt G. Heart rate turbulence: A new predictor for risk of sudden cardiac death. Ann Noninvasive Electrocardiol. 2005;10(1): 102-9.
6. Exner DV, Kavanagh KM, Slawnych MP, Mitchell LB, Ramadan D, Aggarwal SG, *et al*. Noninvasive risk assessment early after amyocardial infarction: The REFINE Study. J Am Coll Cardiol. 2007;50(24):2275-84.
7. Barthel P, Schneider R, Bauer A, Ulm K, Schmitt C, Schomig A, *et al*. Risk stratification after acute myocardial infarction by heart rate turbulence. Circulation. 2003;108(10):1221-26.
8. Sulimov V, Okisheva E, Tsaregorodtsev D. Noninvasive risk stratification for sudden cardiac death by heart rate turbulence and microvolt T-wave alternans in patients after myocardial infarction. Europace. 2012;14(12):1786-92.
9. Cebula S, Sredniawa B, Kowalczyk J, Musialik-Lydka A, Wozniak A, Sedkowska A, *et al*. The significance of heart rate turbulence in predicting major cardiovascular events in patients after myocardial infarction treated invasively. Ann Noninvasive Electrocardiol. 2012;17(3):230-40.
10. Moore RK, Groves DG, Barlow PE, Fox KA, Shah A, Nolan J, *et al*. Heart rate turbulence and death due to cardiac decompensation in patients with chronic heart failure. Eur J Heart Fail. 2006;8(6):585-90.
11. Cygankiewicz I, Zareba W, Vazquez R, Vallverdu M, Gonzalez-Juanatey JR, Valdés M, *et al*. Heart rate turbulence predicts all-cause mortality and sudden death in congestive heart failure patients. Heart Rhythm. 2008;5(8):1095-1102.
12. Pietrucha A, Wegrzynowska M, Konduracka E, Bobrowiska M, Kubinyi A, Paradowski A, *et al*. Analysis of sinus node dysfunction, diabetes mellitus and surgical heart denervation influence on heart rate turbulence. Folia Cardiol. 2005;12(Suppl C):179.
13. Balcioglu S, Arslan U, Turkoglu S, Ozdemir M, Cengel A. Heart rate variability and heart rate turbulence in patients with type 2 diabetes mellitus with versus without cardiac autonomic neuropathy. Am J Cardiol. 2007;100(5):890-3.
14. Gunduz H, Arinc H, Kayardi M, Akdemir R, Ozyildirim S, Uyan C. Heart rate turbulence and heart rate variability in patients with mitral valve prolapse. Europace. 2006;8(7):515-20.
15. Yalta K, Erdem A, Yilmaz A, Turgut OO, Yilmaz MB, Yontar C, *et al*. Heart rate turbulence: an additional parameter in determining the need for mechanical relief of mitral stenosis? J Heart Valve Dis. 2007; 16(3):255-9.
16. Osman F, Franklyn JA, Daykin J, Chowdhary S, Holder RL, Sheppard MC, *et al*. Heart rate variability and turbulence in hyperthyroidism before, during, and after treatment. Am J Cardiol. 2004;94(4):465-9.
17. Yang A, Schafer H, Manka R, Andrié R, Schwab JO, Lewalter T, *et al*. Influence of obstructive sleep apnea on heart rate turbulence. Basic Res Cardiol. 2005;100(5):439-45.
18. Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, *et al*. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Europace. 2006;8(9):746-837.