

THE RELATIONSHIP BETWEEN HEART RATE TURBULENCE URIC ACID AND BRAIN NATRIURETIC PEPTIDE CONCENTRATIONS IN PATIENTS WITH CONGESTIVE HEART FAILURE.

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Abstract: Uric acid (UA) and brain natriuretic peptide (BNP) concentrations reflect the severity of systolic dysfunction in patients (pts) with congestive heart failure (CHF). Elevated serum level of UA and BNP is associated with higher cardiovascular mortality. Determination of heart rate turbulence (HRT) is a new noninvasive method used to identify patients with high risk of cardiac death.

Aim: to assess the relationship between HRT and BNP and UA concentrations in pts with CHF.

Material and methods: UA and BNP concentrations were measured in 64 pts with clinical and echocardiographic symptoms of CHF (24 women and 40 men, mean age 61 ± 12 years) in NYHA class I – IV with sinus rhythm. Pts with atrial fibrillation were previously excluded from the study. HRT was analyzed from 24-hour Holter ECG recordings (Pathfinder 700) and characterized by two parameters: turbulence onset (TO) and turbulence slope (TS).

Results: There was no relationship between TO and UA and also between TO and BNP level. Negative correlation between the TS and UA concentration ($r = -0,32$; $p = 0,02$) and between TS and BNP ($r = -0,3$; $p = 0,04$).

Conclusions: Blunted HRT, characterized by turbulence slope, is associated with high levels of uric acid and BNP in CHF patients. Significance of these correlations remains to be detected. The combined assessment of HRT, BNP and UA may be useful as a potential prognostic marker in CHF patients.

Introduction:

It is known that congestive heart failure (CHF) is associated with derangements of the autonomic nervous system, which is worsening with disease progression. Measurement of heart rate turbulence (HRT), which describes oscillation in sinus cycle length following a ventricular premature beat (VPB), may be used as noninvasive method to study cardiac autonomic function and baroreflex sensitivity. Several studies have shown that HRT impairment reflects cardiac autonomic dysfunction, in particular, impaired baroreflex sensitivity, and has been proved to be a powerful risk predictor for cardiovascular mortality in patients surviving from an acute myocardial infarction. Furthermore a few studies have demonstrated that an impairment of HRT may have independent prognostic factor also in congestive heart failure patients. Both baroreflex sensitivity and HRT have been shown to be markedly reduced in CHF and significantly associated with the degree of ventricular dysfunction and with further progression of the disease. Also concentrations

of uric acid (UA) and brain natriuretic peptide (BNP) reflect the severity of systolic dysfunction in patients with congestive heart failure. BNP is secreted by the ventricular myocytes in response to volume expansion and pressure overload and it is known as a sensitive marker of CHF.

Aim: to assess the relationship between HRT - UA and BNP serum concentrations in patients with congestive heart failure.

Material and methods:

Sixty four patients (24 women and 40 men, mean age 61 ± 12 years) with a clinical and echocardiographic symptoms of CHF were studied. Other criteria necessary for enrollment to the study were: (1) sinus rhythm in ECG, (2) absence of acute or chronic inflammatory diseases (e.g. pneumonia). Six of the 64 patients were in New York Heart Association (NYHA) functional class I, 32 were in class II, 17 were in class III and 8 were in class IV.

Clinical characteristics of these patients are listed in table 1.

Table 1 Patients characteristics

Age (years) mean \pm SD	61 \pm 12
Age >60	32 (51%)
Hypertension	40 (63%)
Diabetes	16 (25%)
Coronary Artery Disease	38 (60%)
Myocardial Infarction	23 (37%)
Dilated Cardiomyopathy	15 (24%)
LBBB	12 (19%)
RBBB	6 (10%)
Mean EF \pm SD	38 \pm 16%

24 - hour Holter ECG recording with HRT evaluation and blood measurement of BNP (RIA) and UA (enzymatic method) level were performed in each patient.

HRT was assessed using 2 standard parameters: the turbulence onset (TO), which is a measure of the early sinus acceleration after a VPB; and the turbulence slope (TS), which is a measure of the late sinus deceleration after a VPB. TO was expressed by a percentage and was calculated with the following formula: $[(RR1+RR2)-(RR-2 +RR-1)] / (RR-2 +RR-1) \times 100$ where RR1 and RR2 are the first and the second sinus RR intervals after the VPB, and RR-1 and RR-2 are the first and the second sinus RR intervals preceding the VPB. The turbulence slope was obtained as the maximal positive slope among all slopes of a series of regression lines obtained from all sequences (n=16) of 5 consecutive RR intervals included between the first and the 20th RR interval following the compensatory post - VPB pause. TS was expressed as ms/RR.

Results:

The evolution of TS was negatively correlated with UA and BNP levels with respective correlation coefficient of - 0,32 (p=0,02) (Fig. 1) and - 0,3 (p= 0,04) (Fig. 2) .

In contrast the change of TO was not related to UA and BNP concentration.

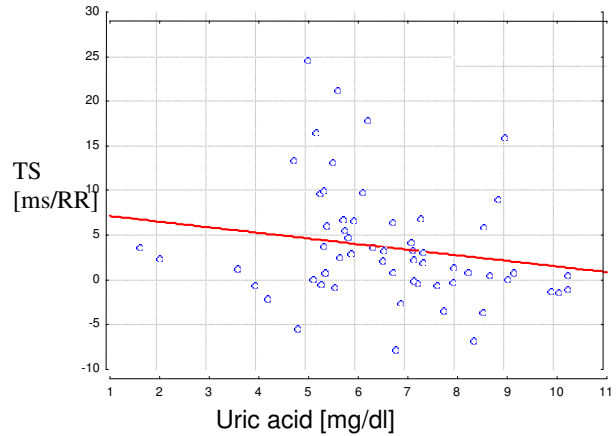


Fig. 1 Relationship between TS and serum UA concentration.

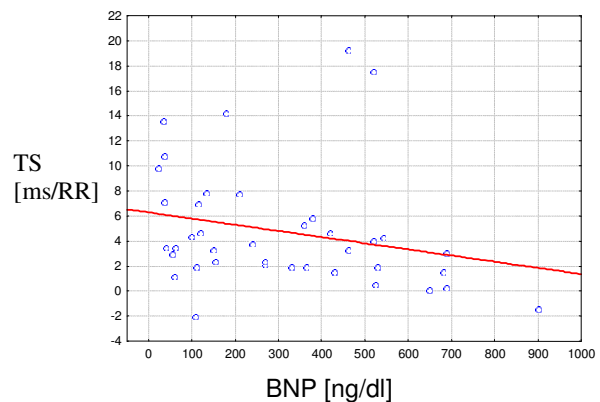


Fig. 2 Relationship between TS and BNP concentration

Conclusions:

Blunted HRT, characterized by TS, is associated with high levels of UA and BNP in CHF patients. Significance of this correlations remains to be detected. Intriguing possibility is that, the combined assessment of HRT, UA and BNP may be more effective in identifying patients with a worse prognosis.

References:

1. Lian – yu Lin, Juey – Jen Hwang et al.: Restoration of heart rate turbulence by tritrated beta-blocker therapy in patients with advanced congestive heart failure. J Cardiovasc Electrophysiol– July 2004, 15; 752
2. Leslie A. Saxon, M.D.: Improvement in heart rate turbulence as a measure of response to beta-blocker therapy for

- heart failure. J Cardiovasc Electrophysiol - July 2004, 15; 757-758.
3. Ceri Davies et al.: 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: 737-742
 4. Voss A., Baier V et al.: Postextrasystolic regulation patterns of blood pressure and heart rate in patients with idiopathic dilated cardiomyopathy. J Physiol 2002 538.1; 271-278
 5. Wichterle D., Melenovsky V., Malik M.: et al.: Mechanisms involved in heart rate turbulence. Card Electrophysiol Rev 2002 Sep;6 (3): 262-266
 6. Schmidt G.: Heart rate turbulence after ventricular premature beats as a predictor of mortality after acute myocardial infarction. The lancet April 1999 Vol. 353 No. 9162 1390-1396
 7. Ghuran A., Reid F.: Heart rate turbulence – based predictors of fatal and nonfatal cardiac arrest (the autonomic tone and reflexes after myocardial infarction substudy) Am Journal of Cardiol Vol 89, January 15, 2002, 184 - 190
 8. Bauer A., Schmidt G.: Heart rate turbulence. J Electrocardiology 2003, 36 Supplement
 9. Sestito A., Valsecchi S. et al.: Differences in heart rate turbulence between patients with coronary artery disease and patients with ventricular arrhythmias but structurally normal hearts. Am J Cardiol May 1, 2004; 93: 1114 - 1118
 10. Bogdan M., Sielski S., Grzešk G.: Brain natriuretic peptide in congestive hart failure. Forum Kardiol 2004, 9 1; 1-7