ELECTRONICS AND ELECTRICAL ENGINEERING
ISSN 1392-1215 *2006. Nr. 6(70)*
ELEKTRONIKA IR ELEKTROTECHNIKA

MEDICINE TECHNOLOGY
T115
MEDICINOS TECHNOLOGIJA

Cardiac Functional Capacity and QT Prolongation in Patients with CAD in Relation with Exercise-induced BNP Changes

R. Grybauskienė, D. Karčiauskaitė, Z. Bertašienė, G. Urbonavičienė, P. Grybauskas, J. Janėnaitė, I. Milvidaitė
Institute of Cardiology, Kaunas University of Medicine, Lithuania,
e-mail: reggryb@kmu.lt
I. Blužaitė
Division of Cardiology, Department of Internal Medicine, Kantonsspital St.Gallen, Switzerland,
e-mail: ina.bluzaite@kssg.ch

Introduction

Despite significant advances in diagnostic and therapy, patients with various forms of coronary artery disease (CAD) remain at increased risk of cardiac death. On the long list of predictors of mortality are some demographic, functional, hemodynamic, electrophysiological parameters, ventricular function, pharmacological agents and biochemical markers.

Prolonged QT interval corrected for heart rate (QTc) is proposed as a risk factor for development of ventricular arrhythmias and death in patients after myocardial infarction (MI) [1] and in the general population [2]. Recent studies have revealed that new biochemical marker as b-type natriuretic peptide (BNP) can also identify heart failure (HF) patients at increased risk of sudden cardiac death [3, 4].

HF is characterised by reduced tolerance to exercise and cardiac functional capacity. It was shown that combination of plasma BNP levels at rest with peak oxygen uptake (VO_2) and ventilatory response to exercise improves risk stratification of patients with stable HF [5]. What do the changes of BNP during exercise test mean: diagnosis of exercise-induced ischemia or latent heart failure?

The aim of the present study was to determine whether responses of plasma BNP during exercise as cardiac functional capacity test are altered in patients with CAD after MI, or after coronary artery bypass graft (CABG) and reconstructive mitral valve surgery. What relationship is between BNP changes and QT prolongation, could the determination of the dynamics of BNP during exercise test be used in the evaluation of the severity of heart failure.

Study patients and methods

Patients: The study included 57 patients with CAD: - 36 patients 2-3 years post MI (1 group); and 21 patient 3-4 years after CABG and reconstructive mitral valve surgery (2 group). Those patients were invited to perform a physical exercise test, echocardiographic evaluation and biochemical tests. Current medications were not withheld prior to exercise.

Methods*:* Blood for **BNP levels estimation** was collected into an EDTA-coated tubes at the time of evaluation before exercise test (after 20 min of rest) and immediately after peak exercise. Samples were analyzed within 1 hour using Triage BNP assay (Biosite Diagnostics, Inc). Reference level -50 pg/ml. The levels of BNP at rest, after exercise and increment in plasma BNP from rest to peak exercise were divided by the total achieved workload and this ratio was compared between the patients groups.

The bicycle exercise test has been performed according the protocol (beginning from 50W and increasing the load gradually every 2min 25W until submaximal load or load limiting symptoms) and was analysed by means of electrocardiogram (ECG) system "Kaunas-Krūvis". Twelve ECG leads of 10 sec duration were recorded simultaneously every minute until 5 minutes after the end of test. Ventricular repolarization variables – JT, JTc, sum of ST depression in 12 leads (ΣST), JT dispersion (JTd) were computed and analyzed before the load, at the maximum load and at the recovery (first, third and fifth minute after the end of exercise). JT/RR parameter was calculated by dividing JT interval by heart rate (RR). All calculations were made by means of ECG system before analysis excluding by observer all ECG recordings with multiple artifacts. ST-segment level was measured 40 ms after J point in all 12 leads. The ΣST value in all 12 leads was calculated. A mean of JT and QT interval of every series of cardiocycles was computed. JTd – a difference between shortest and longest JT interval in every series was measured only in chest leads, because accuracy of measurement in limb leads was insufficient.

Rest ECG QT interval variables were measured automatically using appropriate computer software. 12 lead rest ECGs were recorded into a computer simultaneously. Noises from electrical network, muscles and breathing waves were eliminated by using low and high frequencies filters, isoelectric line was restored. 12 lead ECG after dividing into 10 s intervals was averaged every 60 s and 10 s. QT and JT intervals were measured from standard (I, II, III, AVR, AVL, AVF) leads and from thoracic (V1-6) leads. Dispersion of QT interval (QTd) and JTd were calculated as follows: from the longest QT or JT intervals the shortest QT or JT intervals were subtracted. The maximal and minimal QT and JT were determinated. The maximal and minimal QT (and JT) was corrected with Bazett's formula as follows: QTc= QT/square root of the RR interval (QTc max, JTc max, QTc min, JTc min). ECGs of high resolution (5 min. duration, 2 kHz, 12 bit, 12-lead) were recorded at rest. Noise was reduced using 21 point triangle moving average filter. Vectorcardiographic X, Y, Z orthogonal Frank leads were synthesized using Dower matrix. Vectorcardiographic 3D T loop was projected onto a vertical plane, and the projection was inscribed into a square. The square was divided into 20x20 subsquares. From the shape of the filled subsquares two parameters of T loop morphology were evaluated: T loop area and T loop index (ratio of T loop area and T loop length) [6]. The third parameter - the angle between the mean QRS and T vectors in frontal plane (αQRS-T) was derived from the lead I and III leads, they were calculated using the formula [7].

Echocardiographic investigation was performed in all patients using Hewlett-Packard echocardiograph "Sonos 5500". All estimations were performed according to the criteria of the American Society of Echocardiography. The LV wall motion score index (WMI) was estimated dividing the LV segmental contraction score sum by the number of the segments. Each segment was assigned a score, based on its contractility as assessed visually: normal-1; hypokinesis-2; akinesis-3; dyskinesis-4; aneurysm-5. LV ejection fraction (EF) was obtained from the apical four chamber views and evaluated according to Simpson's method. A LVEF<40% was taken as left ventricular systolic dysfunction (LVSD). LV diastolic dysfunction (LVDD) was evaluated as following: dysfunctional relaxation, when E/A was less than 1 and the deceleration time exceeded more than 240ms; pseudonormal, when E/A was between 1 and 2, the pulmonary venous reserve flow peak a was longer than peak A; restriction, when E/A exceeded 2 and the deceleration time was shorter than 140ms [8]. LV was taken dilated when LVEDD/body surface area was >30mm/m^2. Myocardial performance index was determined according Dagdelen et al [9].

Statistical analysis. Continuous variables are presented as mean± SD. Group comparisons were made by use of Student's tests for independent samples and, if data were not distributed normally, using Mann-Whitney test. Because BNP data was not normally distributed, the BNP values at rest and peak exercise were compared with the Mann-Whitney U-test or natural logarithmic transformation of BNP data was used for statistical analysis. Linear regression analysis was used to determine relationships of BNP changes with exercise test and echocardiographic parameters. The predictors of cardiac functional capacity were assessed by a multivariate linear regression, performed on the covariates found to be statistically significant at univariate linear regression. Receiver operator characteristic (ROC) curve analysis was used to assess the diagnostic value of variable parameters depending on a single cut-off value and was summarized by the area under the curve. Multiple regression analysis with a stepwise procedure was used to model BNP as a function of co-variables. Logistic regression was used in a univariate and a multivariate approaches for evaluating the ability of biochemical markers to identify LV dysfunction, corresponding to QT prolongation and cardiac capacity. Data were analysed using SPSS version 12 (SPSS Inc., Chicago, IL, USA) and STATISTICA 6.0 for Windows. A p value<0.05 was considered significant.

Results

Clinical characteristics. Patients characteristics are presented in Table 1. The majority of patients were males, most were taking ACE inhibitors (82.1%), ß-adrenoblockers (50%), diuretics (64%), anticoagulants (53%) and others.

Table 1. General characteristic of the patients

Data	1 group (n=36)	2 group (n=21)	Total (n=57)
Age (years)	61.5±9.2	66.3±9.6	63.1±9.1
Male (%)	94.44	80.95	89.5
LV EF (%)	38.4±12.6	36.2±13.8	34.8±12.8
LVSD (%)	77.7	81	79.35
LVDD (%)	88.8	61.9*	78.95
LV dilatation (%)	44.4	42.1	43.3
Workload<100W, %	52.8	85.7*	69.2
∑ST >0.1mm (%)	58.3	52.6	55.5
maxQT_c>440ms (%)	38.7	85.7*	62.2
minQT_c>388ms (%)	71.0	95.2*	83.1

1 group- patients after MI vs 2 group- patients after cardiac surgery, *-p<0.05

Response of BNP to exercise and relation with cardiac functional capacity parameters

Significant differences between total workload, exercise duration, $lgBNP_{at\ rest}$, $lgBNP_{exercise}$ were observed. The $BNP_{exercise}$/total workload ratio was higher in 2nd group (p<0.05).

Table 2. Exercise test parameters and BNP changes expressed as mean±SD

Data	1 group (n=36)	2 group (n=21)	p
TW (W)	110.4±24.2	85.5±20.9	0.000
Test duration (s)	6.03±1.72	4.53±1.43	0.002
(W/kg)	1.38±0.37	1.07±0.36	0.005
∑ST (mm)	0.212±0.18	0.203±0.21	0.028
$BNP_{at\ rest}$, (pg/ml)	158.8±256.0	248.5±272.7	NS
$lgBNP_{at\ rest}$	1.9±0.5	2.15±0.5	NS

Continuation of Table 2.

$BNP_{exercise}$ (pg/ml)	188.4±320.8	325.6±366.9	NS
$lgBNP_{exercise}$	1.939±0.53	2.255±0.53	0.037
$\Delta BNP_{exercise}$ (%)	110.9±22.2	125.0±21.7	NS
$BNP_{at\ rest}$ /TW ratio	1.73±3.11	3.91±5.39	NS
$BNP_{exercise}$/TW ratio	2.03±3.90	5.29±7.63	0.04
ΔBNP/TW ratio	0.31±0.92	1.23±2.24	0.037
$BNP_{at\ rest}$ /W ratio	135.1±236.9	313.2±439.8	NS
$BNP_{exercise}$/W ratio	162.9±303.6	427.4±630.9	0.04
ΔBNP/W ratio	30.63±77.7	100.46±189.5	NS

(TW-total workload (W); W-workload/body mass ratio (W/kg) , *-p<0.05)

In all group of patients total workload correlated significantly with $BNP_{at\ rest}$ (pairwise deletion) (r=-0.396; p0.003), resting lgBNP (r=-0.426; p0.01), $BNP_{exercise}$ (r=-0.437; p0.001), ΔBNP (r=-0.504; p0.000). All 3 parameters of BNP (at rest, after exercise and ΔBNP) correlated with ∑ST (r=0.306; p0.023) (Fig. 1), (r=0.289; 90.036) and (r=0.265; p0.051) respectively.

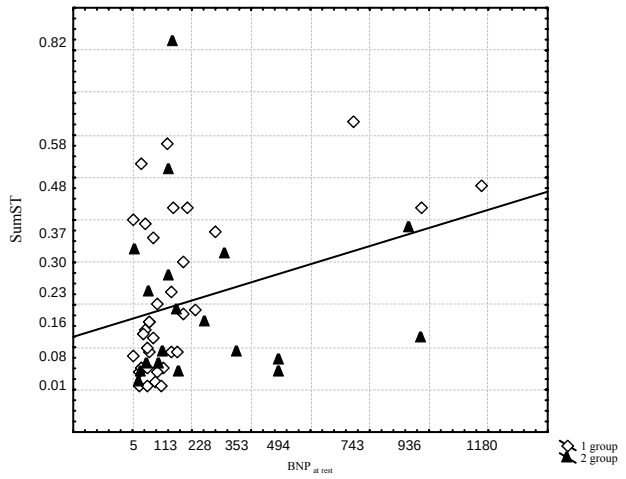


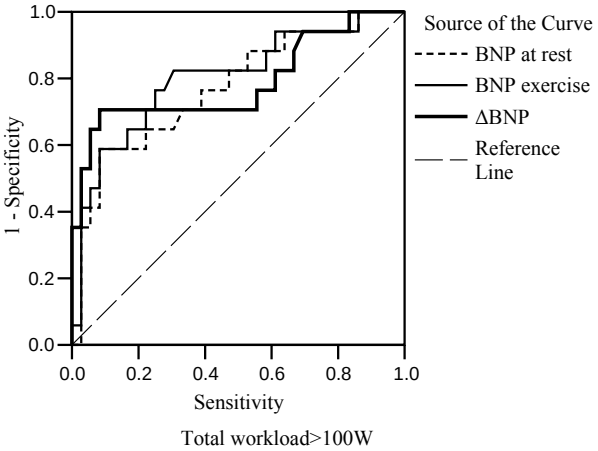
Fig. 1. The regression of all group patients $BNP_{at\ rest}$ and ∑ST after exercise. 1 group- patients after MI, 2 group- patients after cardiac surgery ($BNP_{at\ rest}$ / ∑ST: r = 0.306, p = 0.0231; y = 0.1672 + 0.0002*x)

The relation of $BNP_{at\ rest}$, $BNP_{exercise}$ and ΔBNP with ∑ST in 1 group of patients was stronger than in all group (Table 3). Only $BNP_{at\ rest}$ was significant to prediction the changes of ΣST>0.1mm after exercise by ROC curve analysis (area 0.660; 95%CI (0.511-0.809); p 0.049). There was less significant correlation between BNP and workload in 2nd group, only ΔBNP correlated with total workload (r=-0.5026; p0.034).

Table 3. Correlation between BNP levels and some parameters of exercise test, p<0.05

1 group	Total workload,W	∑ST	Duration of test
$BNP_{at\ rest}$	-0.357	0.518	-0.405
$lgBNP_{at\ rest}$	-0.345	0.425	-0.351
$BNP_{exercise}$	-0.385	0.535	-0.431
$lgBNP_{exercise}$	-0.445	0.434	-0.384
ΔBNP	-0.468	0.509	-0.468

Inverse correlation was determined between duration of exercise test and transformed BNP: $BNP_{at\ rest}$ /total workload ratio (r=-0.557; p0.013) and $BNP_{exercise}$ / workload ratio (r=- 0.591;p0.008). We compared predictions of the ability to achieve total workload >100W by BNP variables according ROC curve analysis (Fig.2). There was significant difference of power between $BNP_{at\ rest}$ and $BNP_{exercise}$ for prediction of functional capacity (p0.036). When $BNP_{at\ rest}$ >135 pg/ml vs <135 pg/ml, the odds ratio for achieved workload <100W was 4.25(1.05-17.2), p0.034.



Variables	AUC	p	Criterion	Sens. %	Spec. %
$BNP_{at\ rest}$	0.770	0.002	≤170 pg/ml	92.1	58.8
$BNP_{exercise}$	0.801	0.000	≤125 pg/ml	69.4	82.4
ΔBNP%	0.698	0.001	≤111 %	63.9	76.5
ΔBNP	0.783	0.001	≤26 pg/ml	91.7	70.6

Fig. 2. Prediction of ability to achieve total workload ≥100W by BNP variables according ROC curve analysis. AUC- area under the curve

We calculated how many units of total workload correspond to each 10% increment of BNP (WB-index) in groups with different total workload in patients after MI, cardiac surgery and total. We found very similar WB-index values between 1st and 2nd group depending of total workload ranges as shown in figure 3. According Kruskal-Wallis test H-statistics in over all group there was significant difference in the level of this derivative depending on the different functional capacity from 25 to 150W (H=40.62; p<0.0001). The same difference obtained regarding the post MI patients (H=19.96; p<0.0001), but less - after cardiac surgery (H=9.99; p<0.02). The average of WB- index was higher in 1st group vs 2nd group (3.07±11.4 and 0.57±1.8); p<0.0014) independently from the functional capacity.

WB-index was higher in patients with workload ≥100W vs <100W (H=19.98;p0.0001), but no difference was observed when $BNP_{at\ rest}$ >135 pg/ml vs $BNP_{at\ rest}$ <135 pg/ml. There was a significant difference in WB-index when patient's $BNP_{at\ rest}$ >135pg/ml and was selected according maxQTc>440 ms (H=9.75;p0.007), but none in cases when $BNP_{at\ rest}$ <135pg/ml .

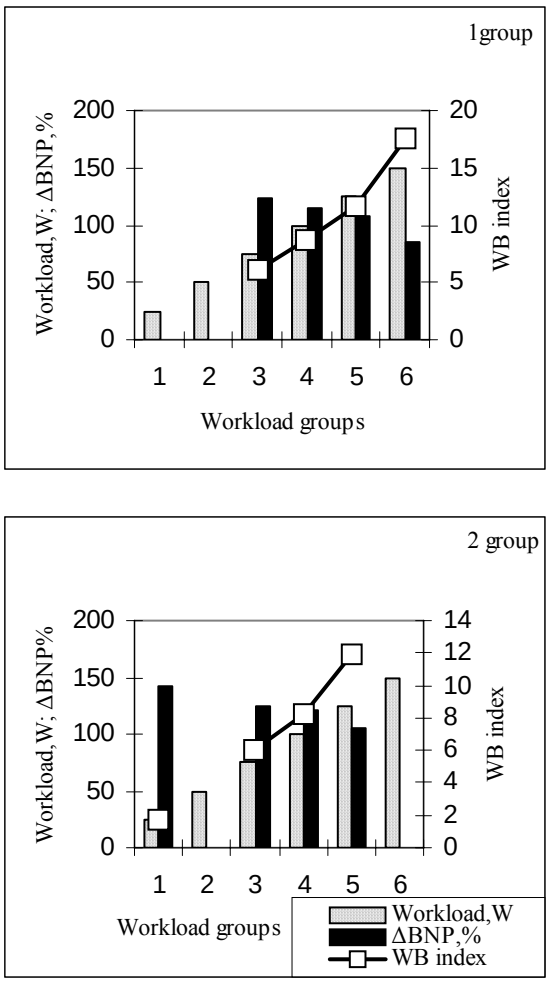


Fig. 3. The workload ranges, ΔBNP% and capacity units counts, which correspond to each 10% increment of BNP (workload ,W / ΔBNP10%) depending on the level of workload in both investigated groups

Thus it is true to say, that BNP augmentation level during exercise was directly related to patient's low cardiac functional capacity.

Response of BNP to exercise and relation with echocardiographic parameters

Echocardiographic parameters are presented in Table 4.

Table 4. Echocardiographic parameters in both investigated groups

Data	1st group (n=36)	2nd group (n=21)
Left ventricular EF (%)	38.38±12.56	36.19±13.83
LVEDD (mm)	52.77±9.15	52.57±8.18
Septal thickness (mm)	10.66±2.59	12.24±1.44*
LV mass index (g/m^2)	111.19±28.49	115.79±22.87
Relative LV wall thickness	0.423±0.10	0.434±0.129
LV wall motion index	1.878±0.481	1.913±0.559
Pulmonary artery acceleration time (s)	0.121±0.023	0.107±0.02*
E/A	0.847±0.472	1.62±1.52*
Posterior LV wall thickness (mm)	10.91±1.18	9.62±3.07*

*-p<0.05

The most significant relations between BNP and echocardiographic parameters were determined in patients after MI: $BNP_{at\ rest}$ correlated with age (r=0.3805; p0.013), LVEF (r=-0.383; p0.012), LV systolic volume (r=0.353; p0.022), E (r=0.507;p0.01) and LV myocardial mass (0.34; p0.028). Even stronger correlation between the echocardiographic parameters (LVEDD, LV systolic volume, relative LV wall thickness, E/A, posterior LV wall thickness) and transformed data of BNP as BNP/body mass at rest, after exercise and ΔBNP was determined.

There were significant differences between all investigated BNP variables depending on LV dilatation (Table 5).

Table 5. BNP (and its derivative) levels at rest and after exercise

Data	LV dilatation	Withouth dilatation	p
$BNP_{at\ rest}$, (pg/ml)	386.9±381.3	141.1±197.3	0.015
lg $BNP_{at\ rest}$	2.36±0.47	1.93±0.43	0.006
$BNP_{exercise}$(pg/ml)	556.7±492.1	161.4±230.3	0.003
ΔBNP (pg/ml)	124.6±133.0	20.3±36.7	0.001
lg $BNP_{exercise}$	2.55±0.46	1.98±0.44	0.001

We analyzed also other BNP derivative parameters such as BNP/ body mass ratio, BNP/ workload (W/kg) ratio and BNP/total workload (W) ratio).They were significantly higher in subgroup of patient with dilatation vs without it (data not shown).

Changes of BNP in relation with ventricular repolarisation variables

There were significant differences in most of investigated ventricular repolarisation parameters. $JTd_{at\ rest}$ was significantly higher in the 1st group, but there was no difference in QTd between groups (Table 6).

Table 6. Repolarisation parameters in both investigated groups: post MI and after cardiac surgery at exercise and at rest ECG

Data	1st group (n=36)	2nd group (n=21)	p
Stress ECG:			
ΣST	0.212±0.18	0.203±0.21	0.028
$JT/RR_{at\ rest}$	0.344±0.04	0.367±0.03	0.04
JT/RR_{max}	0.425±0.04	0.406±0.04	NS
$JTd_{at\ rest}$	42.77±20.92	23.58±17.27	0.001
JTd_{max}	26.11±15.51	17.89±13.32	NS
Rest ECG:			
QTd	37.00±11.06	35.52±20.66	NS
Max QTc	440.0±23.24	462.7±23.49	0.001
Min QTc	401.3±21.24	423.8±33.02	0.004
Max JTc	341.7±24.71	349.0±26.82	NS
Min JTc	306.7±21.40	317.8±33.10	NS
αQRS-T	59.43±60.17	124.53±57.27	0.001
T loop area	224.7±60.84	176.9±62.79	0.0098
T index	1.267±0.827	0.667±0.796	0.01

The significant relationship between repolarisation parameters and BNP before and during exercise test in the groups of patients is shown in Table 7.

Table 7. The significant correlations between BNP at rest, during exercise and ΔBNP with repolarisation parameters determined from ECG at rest (p<0.05)

	BNP	lgBNP	BNP	lgBNP	ΔBNP
	At rest		During exercise		
1 gr. (n=36)					
maxQTc	0.519	0.465	0.586	0.556	0.537
MinQTc	0.412	0.330	0.475	0.413	0.476
αQRS-T	0.542	0.434	0.581	0.46	0.427
2 gr. (n=21)					
maxQTc	0.502	0.454	0.451	0.477	0.459
MinQTc	0.619	0.556	0.622	0.586	0.559

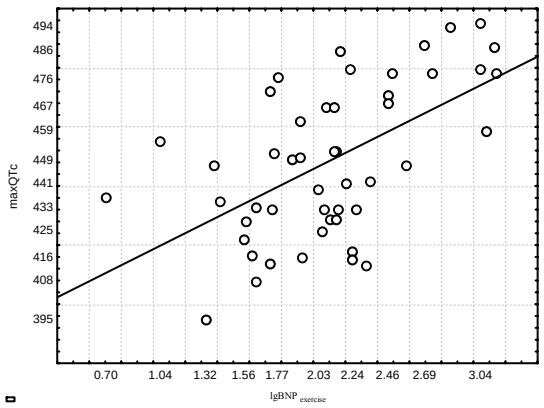


Fig. 4.The relationship between the lgBNP after exercise test and maxQTc in whole group of patients (lgBNP$_{exercise}$:maxQTc: r^2 = 0.317; r = 0.563, p = 0.00003; y = 391.44 + 27.15*x)

The maxQTc and minQTc were related with total workload (r=-0.415; p0.003) and (r=-0.355; p0.012) respectively. The relationship between QTc and BNP variables was stronger when the data of patients only with maxQTc>440ms were analyzed. The relation between maxQTc and BNP$_{at\ rest}$, depending of BNP$_{at\ rest}$ quartiles is shown on figure 5.

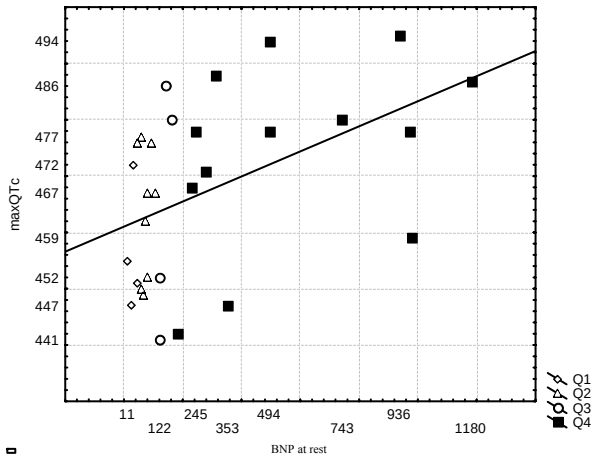
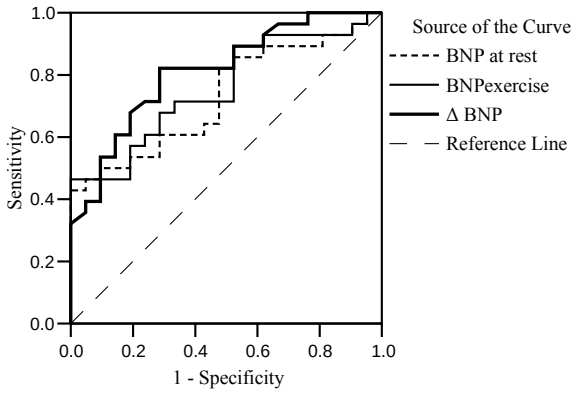


Fig. 5. Regression between maxQTc and BNP$_{at\ rest}$, marked by BNP $_{at\ rest}$ quartiles (BNP$_{at\ rest}$:maxQTc: r^2 = 0.219; r = 0.477, p = 0.0092; y = 461.04 + 0.022*x)

According multiple regression results, the BNP$_{at\ rest}$ was independent predictor to develop maxQTc>440ms (F=18.06; p0.000), and to achieve low total workload (F=8.348; p<0.006) as well.

The compared ability to predict the maxQTc>440 ms by BNP variables is shown on the figure 6.

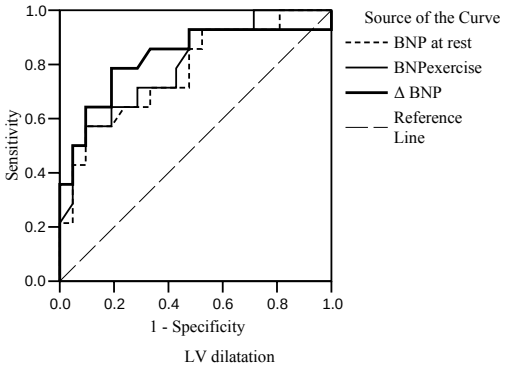


Variables	AUC	p	Criterion	Sens. %	Spec. %
BNP$_{at\ rest}$	0.731	0.006	>213 pg/ml	40.0	100.0
BNP$_{exercise}$	0.757	0.002	>210pg/ml	46.4	100.0
ΔBNP%	0.812	0.000	>108.5%	71.4	61.9

Fig. 6. Compared ability for predicting QTc prolongation by BNP$_{at\ rest}$,, BNP$_{exercise}$, ΔBNP according ROC curves analysis

BNP$_{at\ rest}$, BNP$_{exercise}$ and ΔBNP in 1group correlated with the αQRS-T (r=0.437; p0.004) (r=0.428; p0.000) (r=0.378; p0.014). The αQRS-T correlated with echocardiographic parameters LVEDD (r=0.336; p0.03) and myocardial mass index (r=0.421; p0.005).

The trend of BNP changes (ΔBNP >0) during exercise by ROC curve analysis was significant powerful predictor for develop the maxQTc>447 ms (area under the curve 0.849; 95%CI:0.718-0.935, sensitivity 58.5%, specificity 100%; p0.001).



Variables	AUC	p	Criterion	Sens. %	Spec. %
BNP$_{at\ rest}$	0.774	0.007	>182 pg/ml	50.0	90.5
BNP$_{exercise}$	0.799	0.003	>222pg/ml	57.1	90.5
ΔBNP%	0.825	0.001	>110.7%	92.9	61.9

Fig 7. Compared ability of BNP variables to predict of LV dilatation according ROC curve analysis. The best ability to predict the LV dilatation from BNP parameters respond ΔBNP

Similarly, $BNP_{at\ rest}$>213 pg/ml was obtained as able to predict the maxQTc>440ms (area under the curve 0.7(95%CI:0.561-0.822, sensitivity 40.0%; specificity 100%) in whole group of patients, but in selected patients with LV dilatation this capacity was higher (area under the curve 0.833(95%CI:0.556-0.968; sensitivity 77.8%; specificity 100%).

According multiple regression analysis $BNP_{at\ rest}$ was indepent variable to develop QTc prolongation (maxQTc>440ms) (maxQTc=430.56+0.05 $BNP_{at\ rest}$; beta=0.515, t=4.249; p0.000).

Discussion

The results of our study demonstrate that in patients with CAD QTc interval prolongation is associated with degree of BNP level, both - BNP and QTc - known as independent predictors of all-cause, cardiac and pump-failure death [4]. The main findings of our study show that in patients with limited cardiac functional capacity due to HF, prolonged max QTc links with $BNP_{at\ rest}$ >213pg/ml (p0.006).The increase of BNP (ΔBNP) at maximal exercise was higher in patients with LV dilatation and with higher $BNP_{at\ rest,}$ and this was more expressive in post MI patients vs after cardiac surgery. Total workload of patients with LV dilatation also was different in both groups.

Increase in BNP with exercise correlated with LV filling pressures during exercise in patients with HF in the study of Friedl et al [10]. Relationship between natriuretic peptides and hemodynamics has been demonstrated in patients with heart failure after MI at rest and after exercise [11]. BNP elevation during exercise showed that filling pressure may be an important stimulus for BNP secretion. The greater increment in BNP with exercise was estimated in patients with dilated cardiomyopathy compared to patients with mitral stenosis despite the increase in pulmonary capillary wedge pressure being greater in the latter group, indicating that LV diastolic pressure is more important than left atrial pressure in determining BNP augmentation with exercise [12]. According Mottram et al (2004) the relationship of increased BNP to exercise might be a marker of elevated filling pressures in diastolic HF[13].

Our findings are similar with findings of Kato et al, and demonstrate, that the absolute increment and, more importantly, the increase in BNP corrected for the increase in workload is higher in LV dysfunction and progressively higher in patients with heart failure [14]. McNairy showed an increase in BNP with bicycle ergometry in normal subjects, but progressively greater increases in patients with class I to II HF and class 3 to 4 HF. These findings are consistent with BNP augmentation as an adaptive response to exercise in systolic heart failure [15].

Berger et al have demonstrated that elevated plasma BNP is an independent predictor of sudden cardiac death (SCD) in patients with heart failure and a LVEF<35% (19% of SCD in patients with BNP>130pg/ml vs 1% of SCD in patients with BNP level<130 pg/ml)[4]. The neuro-hormonal activation is a hallmark of cardiac remodeling after MI, developed into HF, with disturbed counterbalance vasoconstrictor/sodium retentive system over the vasodilator/natriuretic system. The main trigger of elevated natriuretic peptides is increased myocardial wall stretch as an indicator of elevated intracardiac pressure [16] also the increased activity of renine angiotensine aldosterone system [17]. Elevated BNP levels are not only associated with LV dysfunction, but they are also present in case of LV hypertrophy, atrial fibrillation, and valve disease.The plasma BNP continue to increase along with progression of LV dysfunction. But in contrast, Mottram et al showed that augmentation of BNP with exercise in hypertensive patients with suspected diastolic HF is associated with better exercise capacity, LV systolic and diastolic function, and left atrial function. Peak exercise BNP correlated with peak transmitral E velocity and peak heart rate [13].

Myocardial stretch caused by increased intracardiac pressure has been shown related to slow conduction, enhance refractoriness, and trigger afterdepolarizations and ventricular ectopic beats [18]. ECG parameters of ventricular repolarisation – JT and QT dispersion, JTc, QTc, JT/RR reflect disturbances of repolarisation. Data about the role of duration of QTc and JTc interval, QT and JT dispersion as predictors of cardiac death are controversial. We think that analysis of ventricular repolarisation parameters in patients with HF should be complex with biochemical markers. Our study results confirm data of Vrtovec et al, that such simple parameters as QTc interval and plasma BNP levels can accurately identify subgroups of patients with HF who are at increased risk of overall mortality, SCD and death due to pump failure [19].

Experimental and clinical evidence suggests that brief episodes of ischemia or hypoxia, insufficient to cause alterations in end-diastolic pressure or irreversible tissue injury, can evoke a rapid release of BNP from cardiac tissue too. A functional role for the rapid release of BNP in response to brief periods of myocardial ischemia is not known. The recognition in recent years that several neurohormonal mediators are released from myocardium during brief periods of ischemia underpins the current mechanistic model of ischemic preconditioning. There were observed that postischemic release of endogenous BNP increased in a graded fashion with ischemia severity. Moreover, the increase of tissue BNP after 2-and 5-min ischemia likely reflects cleavage of the stored propeptide in response to ischemia; after a 20-min ischemic stimulus, tissue levels of BNP were reduced as a consequence of massive release of the peptide.The immediate stimulus to BNP release could be either ischemia *per se* or local tissue deformation as a result of ischemia [20]. Our study results supplemented experimental and clinical suggestions that simple assay of BNP correlates with markers of cardiac efficiency obtained during exercise in the patients with HF, in whom ischaemia and left ventricular dysfunction coexists as factors limiting exercise tolerance and possibly changing repolarisation parameters.

Conclusions

1. Augmented BNP concentration after exercise test was associated with severity of disease, expressed by LV echocardiographic parameters, particularly LV dilatation.

2. Myocardial repolarization parameters, determined from rest ECG and during the exercise test was significantly associated with BNP concentration at rest and augmentation after exercise test.

3. There was inverse association between cardiac functional capacity and increment of BNP after exercise test.

References

1. **Peters R. W., Byington R. P., Barker A. et al**. Prognostic value of prolonged ventricular repolarization following myocardial infarction: the BHAT experience: the BHAT Study group // J Clin Epidemiol 1990. – 43. – P. 167–172
2. **Montanez A., Ruskin J. N., Hebert P. R,, Lamas G. A., Hennekens C. H.** Prolonged QTc interval and risks of total and cardiovascular mortality and sudden death in the general population: a review and qualitative overview of the prospective cohort studies // Arch Intern Med 2004. – 164. – P. 943-8.
3. **Maisel A.** B-type natriuretic peptide levels: diagnostic and prognostic in congestive heart failure. What's next? // Circulation 2002. – 105. – P. 2328–2331.
4. **Berger R., Huelsman M., Strecker K. et al**. B-type natriuretic peptide predicts sudden death in patients with chronic heart failure // Circulation 2002. – 105. – P. 2392–2397.
5. **De Groote P., Dagorn J., Soudan B., Lamblin N., McFadden E., Bauters C.** B-type natriuretic peptide and peak exercise oxygen consumption provide independent information for risk stratification in patients with stable congestive failure // J Am Coll Cardiol 2004. – 43. – P. 1584–1589.
6. **Tamošiūnaitė M., KučinskasD., Urbonavičienė G., Blužaitė I.** Vectorcardiographic analysis: investigation of T loop morphology for risk stratification after myocardial infarction // Electronics and Electrical Engineering. – Kaunas: Technologija, 2002. – No. 2(37). – P. 23–25.
7. **Matiukas A., Kaminskienė S., Rūtienė S., Jaruševičius G., Gargasas L.** Vektorkardiografijos reikšmė nustatant širdies vainikinių arterijų susiaurėjimus // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2003. – No. 48(6). – P. 74–77.
8. **Nishimura R. A., Tajik A. J.** Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography in the clinician's rosetta stone JACC 1997; 30:8–18.
9. **Dagdelen S., Eren N., Karabulut H., Caglar N.** Importance of the index of myocardial performance in evaluation of left ventricular function // Echocardiography 2002. – 19(4). – P.273–278.
10. **Friedl W., Mair J., Thomas S. et al.** Relationship between natriuretic peptides and hemodynamics in patients with heart failure at rest and after ergometric exercise // Clin Chim Acta 1999. – 281. – P. 121–6.
11. **Marimoto A., Nishikimi T., Takaki H. et al.** Effect of exercise on plasma adrenomedullin and natriuretic peptide levels in myocardial infarction // Clin Exp Pharmacol Physiol 1997. – 24. – P. 315–320.
12. **Matsumoto A., Hirata Y., Mamamura S. et al**. Effects of exercise on plasma level of brain natriuretic peptide in congestive heart failure with and without left ventricular dysfunction // Am Heart J 1995 . – 129. – P. 139–145.
13. **Mottram Ph., Haluska B. A., Marwick Th. H.** Response of B-type natriuretic peptide to exercise in hypertensive patients with suspected diastolic heart failure:Correlation with cardiac function, hemodynamics, and workload // Am Heart J 2004. – 148(2). – P. 365–370.
14. **Kato M., Kinugawa T., Ogino K. et al**. Augmented response in plasma brain natriuretic peptide to dynamic exercise in patients with left ventricular dysfunction and congestive heart failure // J Intern Med 2000. – 248. – P. 309–315.
15. **McNairy M., Gordetto N., Clopton P. et al**.Stability of B-type natriuretic peptide levels during exercise in patients with congestive heart failure: implications for outpatient monitoring with B-type natriuretic peptide // Am Heart J 2002. – 143. – P. 406–411.
16. **Chen H. H., Burnett J. C.** The natriuretic peptides in heart failure: diagnostic and therapeutic potentials // Proc Assoc Am Physicians 1999. - 111. – P. 406–416.
17. **Emdin M., Passino C., Prontera C. et al**. Cardiac natriuretic hormones, neurohormones, thyroid hormones and cytokines in normal subjects and patients with heart failure // Clin Chem Lab Med 2004. – 42. – P. 627–636.
18. **Wang Z., Taylor L. K., Denney W. D. et al**. Initiation of ventricular extrasystoles by myocardial stretch in chronically dilated and failing canine left ventricle // Circulation 1994. – 90. – P. 2022–2031.
19. **Vrtovec B., Delgado R., Zewail A., Thomas C., Richartz B., Radovancevic B.** Prolonged QTc interval and high B-type natriuretic peptide levels together predict mortality in patients with advanced heart failure // Circulation 2003. 107. – P. 1764–1769.
20. **Savio P. D'Souza, Yellon Derek M., Martin Claus, Schulz Rainer, Heusch Gerd, Onody Annamaria, Ferdinandy Peter, Baxter Gary F.** B-type natriuretic peptide limits infarct size in rat isolated hearts via KATP channel opening // Am J Physiol Heart Circ Physiol. 284: H1592–H1600, 2003.

Submitted 2006 03 27

R. Grybauskienė, D. Karčiauskaitė, Z. Bertašienė, G. Urbonavičienė, P. Grybauskas, J. Janėnaitė, I. Milvidaitė, I. Blužaitė. Cardiac Functional Capacity and QT Prolongation in Patients with CAD in Relation with Exercise-induced BNP Changes // Electronics and Electrical Engineering. – Kaunas: Technologija, 2006. – No. 6 (70). – P. 33–40.

The aim of this study was to determine whether responses of plasma BNP during exercise as cardiac functional capacity test are altered in 57 patients with CAD: 36 patients after 2-3 years post MI and 21 patients – 3–4 years after CABG and mitral valve reconstruction surgery, what relation is between BNP exercise changes and QT prolongation, could the dynamics of BNP during exercise test be used in the evaluation of the heart failure. The BNP analysis was performed with Triage (Biosite Diagnostics). The bicycle exercise test has been performed according the protocol and was analyzed by means of ECG system "Kaunas-Krūvis". QT interval duration was determined from standard 12-lead ECG and corrected by using the Bazett formula. Prolonged QTc was defined as a QTc interval>440ms. Augmented BNP concentration after exercise test was associated with severity of disease, expressed by LV echocardiographic parameters, particularly LV dilatation. Myocardial repolarisation parameters, determined from rest ECG and during the exercise test were significantly associated with BNP concentration at rest and augmentation after exercise test. There was inverse association between cardiac functional capacity and increment of BNP after exercise test. Ill. 7 ,bibl. 20 (in English; summaries in English, Russian and Lithuanian).

Р. Грибаускене, Д. Карчиаускайте, З. Берташене, Г. Урбонавичене, П. Грибаускас, Й. Йаненайте, И. Милвидайте, И. Блужайте. Связь между функциональной способностью сердца, удлинением интервала QT и сдвигами концентрации БНП во время физической нагрузки // Электроника и электротехника. – Каунас: Технология, 2006. – № 6(70). – С. 33–40.

Целью исследования было определение изменений плазменного БНП во время теста физической нагрузки, характеризующего функциональную способность сердца, у 57 больных ишемической болезнью сердца: 36 больных, 2–3 года тому назад перенесших инфаркт миокарда, 21 больного, 3–4 года назад перенесшего операцию реваскуляризации миокарда и реконструкции митрального клапана. Определяли связь между изменениями концентрации БНП во время теста физической нагрузки и удлинением интервала QT, а также возможность оценки прогрессирования СН по динамике БНП во время физической нагрузки. БНП определяли прибором Triage (Biosite Diagnostics). Тест физической нагрузки на велоэргометре проводили по стандартному протоколу, а анализ результатов – специализированной ЭКГ системой «Каунас-Крувис». Продолжительность интервала QT вычисляли из стандартной ЭКГ и коррегировали по формуле Базетта. Удлиненным интервал QTc считали, если интервал QTc был больше 440 мс. Увеличенная концентрация БНП после физической нагрузки указывала на тяжесть заболевания, подтвержденная эхокардиографескими данными левого желудочка, особенно его дилятации. Показатели реполяризации миокарда, установленные по ЭКГ покоя и во время теста физической нагрузки, были достоверно взаимосвязаны с концентрацией БНП в покое и увеличением после нагрузки. Найдена отрицательная связь между функциональным состоянием сердца и сдвигами БНП во время теста физической нагрузки. Ил. 7, библ. 20 (на английском языке; рефераты на английском, русском и литовском яз.).

R. Grybauskienė, D. Karčiauskaitė, Z. Bertašienė, G. Urbonavičienė, P. Grybauskas, J. Janėnaitė, I. Milvidaitė, I. Blužaitė. Sergančiųjų IŠL širdies funkcinio pajėgumo ir QT trukmės pailgėjimo ryšys su BNP pokyčiais fizinio krūvio metu // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2006. – Nr. 6(70). – P 33–40.

Darbo tikslas – nustatyti B-tipo natriuretinio peptido(BNP) pokyčius kraujyje širdies funkcinį pajėgumą nusakančio fizinio krūvio metu. Tirti 57 ligoniai: 36 ligoniai po MI praėjus 2–3 m. (1 gr.) ir 21 ligonis po vainikinių kraujagyslių šuntavimo ir mitralinio vožtuvo operacijos praėjus 3–4 m. (2 gr.). Tirtas tų pokyčių ryšys su QT intervalo pailgėjimu, galimybe vertinti širdies nepakankamumo progresavimą pagal BNP pokyčių raišką. BNP tyrimus atlikome Triage (Biosite Diagnostics) aparatu. Širdies funkcinio pajėgumo veloergometrijos testą atlikome pagal protokolą ir analizavome EKG sistema „Kaunas-Krūvis“. QT intervalo trukmę nustatėme iš standartinės 12 derivacijų EKG ir koregavome pagal Bazett’o formulę. Pailgėjusiu laikėme QTc intervalą >440 ms. Fizinio krūvio metu didėjanti BNP koncentracija buvo susijusi su ligos sunkumu, kairiojo skilvelio echokardiografijos duomenimis, ypač su KS dilatacija. Miokardo repoliarizacijos rodmenys, nustatyti iš ramybės EKG ir po fizinio krūvio, buvo reikšmingai susiję su BNP koncentracija prieš fizinį krvį ir jos pokyčiais fizinio krūvio metu. Nustatytas atvirkščias ryšys tarp širdies funkcinio pajėgumo ir BNP didėjimo fizinio krūvio metu. Il. 7, bibl. 20 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).