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Brain natriuretic peptide predicts forced vital capacity of the lungs, oxygen pulse and peak oxygen consumption in physiological condition

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ABSTRACT

Brain natriuretic peptide (NT-pro-BNP) is used as marker of cardiac and pulmonary diseases. However, the predictive value of circulating NT-pro-BNP for cardiac and pulmonary performance is unclear in physiological conditions. Standard echocardiography, tissue Doppler and forced spirometry at rest were used to assess cardiac parameters and forced vital capacity (FVC) in two groups of athletes (16 elite male wrestlers (W), 21 water polo player (WP)), as different stress adaptation models, and 20 sedentary subjects (C) matched for age. Cardiopulmonary test on treadmill (CPET), as acute stress model, was used to measure peak oxygen consumption (peak VO2), maximal heart rate (HRmax) and peak oxygen pulse (peak VO2/HR). NT-pro-BNP was measured by immunoassey sandwich technique 10 min before the test – at rest, at the beginning of the test, at maximal effort, at third minute of recovery. FVC was higher in athletes and the highest in W (WP 5.60 ± 0.29 l; W 6.57 ± 1.00 l; C 5.41 ± 0.29 l; $p < 0.01$). Peak VO2 and peak VO2/HR were higher in athletes and the highest in WP. HRmax was not different among groups. In all groups, NT-pro-BNP decreased from rest to the beginning phase, increased in maximal effort and stayed unchanged in recovery. NT-pro-BNP was higher in C than W in all phases; WP had similar values as W and C. On multiple regression analysis, in all three groups together, ΔNT-pro-BNP from rest to the beginning phase independently predicted both peak VO2 and peak VO2/HR ($r = 0.38, 0.35$; $B = 37.40, 0.19$; $p = 0.007$, 0.000, respectively). NT-pro-BNP at rest predicted HRmax ($r = -0.32$, $B = -0.22$, $p = 0.02$). Maximal NT-pro-BNP predicted FVC ($r = -0.22$, $B = -0.07$, $p = 0.02$). These results show noticeable predictive value of NT-pro-BNP for both cardiac and pulmonary performance in physiological conditions suggesting that NT-pro-BNP could be a common regulatory factor coordinating adaptation of heart and lungs to stress condition.

Abbreviations: *A*, left ventricular late diastolic filling velocity; A duration, late diastolic filling duration; *a′*, average annular left ventricular late diastolic filling velocity; BNP, brain natriuretic peptide; BSA, body surface area; BW, body weight; C, controls; CPET, cardiopulmonary exercise test; DBP, diastolic arterial blood pressure; *E*, left ventricular early diastolic filling velocity; *e′*, average annular left ventricular early diastolic filling velocity; EF, left ventricular ejection fraction; FFM, fat free mass; FM, fat mass; FVC, forced vital capacity; HR, heart rate; IVSTd, diastolic septal thickness; LAV, left atrial volume; LV, left ventricle; LVDd, left ventricular end – diastolic diameter; LVVd, left ventricular end – diastolic volume; MAPSE, mitral annular plane systolic exursion; PWTd, diastolic posterior wall thickness; RA, right atrial mid-lateral diameter; RV, right ventricle; RV A, right ventricular late diastolic filling velocity; RV a′, right ventricular lateral late diastolic annular velocity; RVDd, right ventricular end – diastolic diameter; RV E, right ventricular early diastolic filling velocity; RVe′, right ventricular lateral early diastolic annular velocity; RV ET, right ventricular ejection time; RV s′, right ventricular lateral systolic annular velocity; s′, average annular left ventricular systolic velocity; SV, stroke volume; SBP, systolic arterial blood pressure; TAPSE, tricuspid annular plane systolic exursion; TDI, tissue Doppler imaging; VO2 max, maximal oxygen consumption; VCO2 max, maximal carbon-dioxide production; VO2/HR max, maximal oxygen pulse; W, wrestlers; WP, water polo players.

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1. Introduction

Brain natriuretic peptide (BNP, 76 aminoacids) and its sequence NT-pro-BNP (32 aminoacids) is hormone secreted in cardiac chambers as response to wall stress [56]. Known effects of this hormone are predominantly cardiovascular, more precisely diuretic and vasodilatative due to renin-angiotensin-aldosteron inhibition, natriuresis and modulation of vascular tone [54]. Thus, despite of great intraindividual biological variability [63], it is used as marker of systolic and diastolic heart failure [21,27,54], hypertrophic cardiomyopathy [7,23], congenital heart disease [15,43,58], ishaemic heart disease [17,45], and as marker of pulmonary diseases, too [31,57]. However, the role of NT-pro-BNP in regulation of cardiac and pulmonary performance is unclear in physiological conditions. The endocrine system plays a key role in stress situation, also during physical activity which is used as a stress model in laboratory conditions. The intensity of hormonal activity is 10-fold higher during acute physical activity, but hormonal system also plays an important role in chronic adaptation to physical stress [25]. In different stress situations, different cardiac remodeling occurs, clinically manifested by changes in cardiac size, shape and function in response to cardiac injury or increased load [41,44]. Therefore, the secretion of NT-pro-BNP is different at rest and after the exercise and related not only to the ejection fraction value [40], but to the impact of right ventricular function, diastolic left ventricular function, left atrial dimension, and other factors too [40,61]. The aim of this study was to evaluate the secretion of NT-pro-BNP in different stress adaptation models, in this case different athletic population, and to investigate its predictive value for cardiac and pulmonary performance at rest during acute physical stress.

2. Materials and methods

2.1. Patients

Patients for this study were 57 male subjects matched for age (21 elite water-polo players (WP), 16 elite wrestlers (W) and 20 sedentary subjects (C)). Athletes have trained intensively for more than 10 years and all have been successfully competitive at the international level for the past five years. Most of water polo players were the members of the national team and all of wrestlers won medals at the international level. Both groups of athletes performed combined strength and endurance training protocols. Wrestlers were in a period of preparations for the international competition at the time when they were examined. They had 9 h of wrestling a week, 4 h of power training in the gym in order to improve the explosive strength, and 4 h of high intensity running a week (4 km per training, at heart rate 85–100% of maximal). Water polo players were also in a period of preparations for the competition. They trained 12 h a week in the pool, with at least 2 km of swimming per each training, and three additional hours a week in the gym where they performed both power and endurance exercises. Control subjects were not engaged in sporting activities other than at recreational level (lesser then 2 h a week for the last 10 years). Detailed personal and family history of illness was obtained from all participants, and after that they underwent physical examination, blood tests and ECG recording. Except some of them had limb injuries in their personal history, they declared any diseases and risk factors (hypertrophic cardiomyopathy, hypertension, arrhythmias, diabetes, renal diseases, cardiac and other infections, smoking, anabolic steroids usage, etc.), which were the exclusion criteria because of the influence on myocardial function and total functional capacity of the body. There was no chest pain and loss of conscious ever. Physical examination and blood tests showed that all of them were healthy and normotensive. ECG was physiological. There was no family history of hypertrophic cardiomyopathy and sudden cardiac death. The participants underwent the study after giving an informed consent. Local Ethical Committee approved the study.

2.2. Anthropometry

Body weight, fat mass (FM) and fat free mass (FFM) were obtained by bioelectrical impedance analysis using Tanita weight (phase sensitive multi-frequency analyzer Data Input GmbH 2000, using software Nutri 3). Body surface area (BSA) was calculated according to the Du Bois and Du Bois formula [14].

2.3. Echocardiography

Two-dimensional, M-mod, pulsed Doppler and tissue Doppler echocardiography was performed on a Sequoia 512 ultrasound device with a 2.5 MHz transducer. Echocardiograms were obtained by two experienced readers according to criteria of the American Society of Echocardiography [1,28,37,46] and met standard criteria of the technical quality. Three to five consecutive beats during quiet respiration were used for calculation of the Doppler variables in apical four-chamber views with standard transducer positions. Measurements included peak early left and right ventricular filling – E and RV E, peak late ventricular filling – A and RV A, A duration and RV A duration. M-mod echocardiography was performed to assess left and right cavity dimensions and wall thickness. Right ventricular internal end – diastolic diameter (RVDd) was measured along the parasternal long axis view, at outflow tract level according to the protocol of Foale and Nihoyannopoulos [16]. Right atrial mid-lateral (RA) diameter was measured along the four chamber view at ventricular end – systole. M-mod echocardiography was used for systolic evaluation by determination of mitral and tricuspid lateral annular plane systolic excursions (MAPSE, TAPSE). Left ventricular end – diastolic volume (LVVd) was derived from LV internal dimensions by Teicholz's formula. Left ventricular mass was calculated from Penn – cube formula: LVM (g) = 1.04 [(LVDd + IVSd + PWTd)^3 − LVDd] − 13.6, where IVSd and PWTd represent end – diastolic interventricular septal and posterior wall thickness, and LVDd left ventricular end – diastolic diameter [13]. Left ventricular stroke volume (SV) was calculated as difference of left ventricular end – diastolic and end – systolic volume. Tissue Doppler imaging (TDI) was recorded in apical four chamber view during end – expiration at sweep speed of 50 mm/s. Doppler signal angle was less than 25%. Sample volume was positioned at 1 cm within the septal and lateral insertion sites of the mitral leaflets and tricuspid leaflets. Digitally stored loops of tissue Doppler imaging were used for off line calculations of myocardial velocities. Average value of the left ventricular lateral and septal early (e') and late (a') diastolic annular velocities were used to evaluate left ventricular filling, and the right ventricular lateral early (RV e′) and late (RV a′) diastolic annular velocities were measured to evaluate right ventricular filling [35–37]. Average value of the left ventricular septal and lateral annular peak systolic velocity (s'), lateral annular right ventricular peak systolic velocity (RV s′) and right ventricular ejection time (RV ET–RV s′ duration) were measured as systolic parameters. As in athletes the TDI parameters are not independent of loading conditions [9] they were interpreted in the context of ventricular size and function, and adjusted for heart rate, BSA, FFM and FM [42].

2.3.1. Reproducibility of TDI measurements

Reproducibility of measuring annular velocities was determined in 10 randomly chosen subjects. Inter- and intra-observer variability was examined using Bland–Altman analysis. The 95% confidence