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N-Terminal proB-type natriuretic peptide (NT-proBNP) concentrations in elite rugby players at rest and after active and passive recovery following strenuous training sessions

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Abstract

Background: The serum biomarker N-terminal proB-type natriuretic peptide (NT-proBNP), a cleaved fragment of the brain natriuretic peptide (BNP) precursor (amino acids 1–76), is accepted as a standard marker for evaluating and monitoring cardiac injury characterized by myocardial wall stress. Strenuous exercise may generate transitory ischemia, myocardial stress and diastolic left ventricular dysfunction, possibly inducing increased concentrations of NT-proBNP. A purported caveat to prolonged strenuous exercise is based on evidence for biochemical and structural signs of heart dysfunction in recreational athletes after continuous exertion.

Methods: We compared NT-proBNP levels in three groups of physically fit subjects: top-level rugby players, professional soccer players and healthy controls. NT-proBNP concentrations were measured at rest and after an intensive training session followed by two different recovery strategies (passive or active).

Results: A comparison of the three samples showed that NT-proBNP concentrations in the rugby players were lower than those in controls at rest and were similar to those in professional soccer players. Elevated post-training NT-proBNP levels were unaffected by the type of recovery. The relatively high NT-proBNP levels after active recovery when psychophysical stress is higher, because of cycling and cold water immersion, suggest that not only endurance exercise, but also strenuous, stressful short exercise can induce an increase in NT-proBNP concentrations.

Conclusions: In this sample of professional athletes, NT-proBNP was low at rest, and the increase after physical exercise was physiological.

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Introduction

The serum biomarker N-terminal proB-type natriuretic peptide (NT-proBNP), the cleaved fragment of the precursor of brain natriuretic peptide (amino acids 1–76), is accepted as a parameter useful for evaluating and monitoring cardiac injury characterized by myocardial wall stress in association with additional instrumental and biochemical parameters. Strenuous exercise may generate transitory ischemia, myocardial stress and diastolic left ventricular dysfunction, often inducing an increase in biomarker concentrations commonly measured to determine heart anomalies (1).

Cardiac damage during marathon running has been described in 60 recreational athletes who participated in the 2004 and 2005 Boston Marathon: 60% of recreational runners showed increased troponin T after the race and NT-proBNP concentration approximately doubled. Left ventricular size and ejection fraction did not change, but reduced left ventricular compliance was echocardiographically demonstrated. Changes in biochemical signs of cardiac damage were greater in subjects who had a low training workload (2). These data suggest that appropriate training is fundamental for reducing and/or averting possible cardiac injury. A caveat to prolonged, strenuous physical exercise is the potential cardiovascular damage it may cause (1). Increased NT-proBNP levels after physical exercise typically described in endurance athletes (3, 4) were not found to differ between endurance male athletes with athlete's heart and healthy untrained control subjects with a normal sized heart (5). Moreover, NT-proBNP concentrations in a group of professional cyclists at rest were lower than those of sedentary controls (6). The actual meaning of elevated NT-proBNP in athletes clearly needs to be defined more accurately.

We compared the changes in NT-proBNP levels in professional athletes at rest vs. non-athletes and during strenuous training sessions followed by two different methods of recovery that could have affected psychophysical stress and biochemical parameters.

Materials and methods

The study was conducted on 30 professional male rugby players of the Italian National Team during a July training camp before the start of the competitive season. Informed

consent was obtained from all participants. The anthropometrical characteristics were body mass index (BMI, 27.5 ± 1.0 kg/m^2) and age (26 ± 2 years) (mean $\pm$ standard deviation). The athletes were examined by the team sports physicians, sports cardiologists and by means of laboratory tests (7).

Blood samples were drawn before and after training on the same day on K_2 EDTA Vacutainer (Becton Dickinson, Rutherford, NJ, USA) tubes and were immediately centrifuged at 2000 rpm ($1500 \times g$), the obtained plasma and sera were stored at –20°C until analysis. The samples were drawn at 08:00 h (at rest) and at 17:00 h (after training session).

The analyses were performed in a single batch 2 weeks after the collection. The same assay was used for all the samples. The circulating volume was monitored by means of hemoglobin and hematocrit values measured on a Coulter 750 (Coulter, Hialeah, FL, USA).

NT-proBNP, Na^+, K^+ and Mg^{2+} were measured using a Vitros system (Johnson & Johnson, Raritan, NJ, USA); the instrument precision (coefficient of variance) was $<5\%$.

The field session started with speed agility warm-ups followed by step work with ballistic stretching (15 min), on field practice (90 min) with play starts, general movement sequences (up to 8 sequences), and then intense accelerations. Taken together, it was a mixed fuel energy session, with cardio-dominance and lactacid peaks, divided into phases of 10-min workouts and 3-min rest periods between two consecutive phases during which the players had contacts and various play situations. The sample was then divided into three groups of 10 athletes, each randomly assigned to passive recovery (rest) or active recovery (cycling at 180 W) for 10 min followed by cold water immersion (5°C) of the legs for 10 min or cold water immersion of the legs for 10 min followed by active recovery. Athletes whose NT-proBNP values at rest were not immediately available were distributed randomly into one of the three groups.

A second sample of professional athletes were 44 soccer players from the second ($n=36$) and third ($n=12$) divisions of the Italian National Championship league (mean age 23 ± 4 years, BMI 22 ± 0.8 kg/m^2). Blood samples were drawn at rest in July before the start of the training and competitive season.

The control group ($n=12$) was composed of technical and medical staff members of the rugby team, eight of which were former athletes (mean age 38 ± 5 years), who were physically fit, exercised moderately at least 1 h daily and followed a diet and lifestyle similar to those of the athletes.

The level of statistical significance was set at 0.05. Analysis of variance (ANOVA) was used to evaluate data obtained during the training session. Normal distribution was evaluated with the D'Agostino-Pearson test. Statistical analysis was carried out using MedCalc software (Mariakerke, Belgium).

Results

The median NT-proBNP level was 29.1 pg/mL (range 15.1–70.1 pg/mL) in the rugby players, 32.4 pg/mL (range 11.3–91.8 pg/mL) in the soccer players ($p>0.05$) and 51.9 pg/mL (range 30.1–77.3 pg/mL) in controls ($p<0.001$). The distribution of the values was not normal.

The NT-proBNP values in the rugby players before and after the training session followed by passive and active recovery are presented in Table 1. The training session significantly increased NT-proBNP concentrations across all three groups, regardless of recovery method. The median value after training was 57.1 pg/mL (range 27.2–143.8 pg/mL) and 61.7 pg/mL (range 29.2–176.4 pg/mL) after recovery. Changes in Na^+, K^+ and Mg^{2+} concentrations after training and recovery were not significant, as well as hemoglobin and hematocrit values: the athletes were euvolemic during the observation period.

Discussion

Biochemical markers are routinely used for diagnosing and monitoring heart diseases when necrosis or damage or wall stress is present. NT-proBNP is usually measured to evaluate wall stress and heart failure. Biochemical cardiac markers can show increased concentrations after physical exercise, especially after strenuous exertion (2, 4, 8). Increases in NT-proBNP could be interpreted as transitory heart damage linked to possible harmful consequences for professional or recreational athletes and to exercise intensity and duration (1). The implications for elevated concentrations are controversial. A study on recreational marathon runners showed marked changes between the pre-race median of 106 pg/mL and the post-race median of 182 pg/mL (2). Notably, the concentrations in these marathon runners were higher at rest than the values observed in healthy subjects recruited from the general population (9) and in other marathon runners (mean of 44 pg/mL before the race) (8). One explanation for the elevated pre-race median value is that the recreational athletes probably performed physical exercise before blood drawing, because the accurate instrumental examinations excluded heart diseases. By contrast, we observed low NT-proBNP levels in professional athletes at rest. Rugby is a prevalently aerobic sport characterized by strenuous effort during competitions and training. In our sample, the NT-proBNP concentrations were lower than those observed in physically active non-athletes. Our data are in line with the results from a study on 20 endurance athletes (10 triathletes, 5 cyclists, 5 marathon runners), where a median of 24.7 pg/mL in the athletes vs. 28.9 pg/mL in controls was found (5).

Table 1 Median (and 95% confidence interval) NT-proBNP levels (pg/mL) in rugby players before and after training and recovery.

Type of recovery	Before training	After training	After recovery	p-Value, F-ratio
Passive (rest)	27.1 (17.8–41.3)	47.7 (28.7–71.8)	48.8 (30.6–75.0)	<0.01, 5.1
Cold water immersion followed by active recovery	30.2 (14.1–46.8)	57.4 (28.8–95.2)	64.3 (26.8–85.1)	<0.001, 10.9
Active recovery followed by cold water immersion	38.6 (18.6–75.9)	78.1 (35.3–150.0)	88.6 (33.7–144.0)	<0.05, 5.1

Lippi et al. (6) also found lower mean levels of NT-proBNP in 50 professional cyclists compared with 35 sedentary subjects (23.6 pg/mL vs. 36.3 pg/mL).

In professional athletes NT-proBNP values at rest are low, within the physiological reference interval, and even lower than those observed in non-athletes. The elevation of NT-proBNP levels should be >95th percentile of the general population. A concentration of 125 pg/mL is usually considered as a threshold for pathological values. Thus, most elevated levels during physical exercise could be considered into the variability of the reference range.

Athlete's heart is not characterized by biochemical signs of wall stress. In fact, the absence of a correlation between left ventricular mass and BNP concentration at rest has been reported (5). As strenuous physical exercise induces an increase in NT-proBNP concentrations in professional athletes, it could be argued that appropriately trained athletes have a lower production of the peptide at rest and that the exercise-induced increase is insufficient to reach abnormal limits. In our sample, we found that different training recovery programs did not substantially affect post-training NT-proBNP concentrations. The relatively high levels of NT-proBNP after active recovery, when psychophysical stress is higher because of cycling and cold water immersion, suggest that not only endurance exercise, but also strenuous, stressful and short exercise can induce an increase in NT-proBNP. It should be noted that NT-proBNP has large within-day biological variability in heart failure patients (10): modifications of their concentration could also be induced by circadian changes, although the increase due to heavy effort can easily overcome the biological variability.

Changes in NT-proBNP after passive or active recovery differed from those of creatine kinase released from skeletal muscle (11), but are similar to those reported by Scharhag et al. (3) in mountain bikers and marathon runners after 1 and 3 h of exercise, respectively. Increased NT-proBNP is also linked to the different lifespan of the molecule in comparison with intact BNP, which does not increase after endurance sports performances (12).

A distinction needs to be made between physiological increases in NT-proBNP during and after exercise and abnormal increases due to heart damage. Our data support the hypothesis that rather than signalling heart injury, the growth-regulating properties of BNP in exercise regulate myocardial adaptation in healthy athletes (3) and are physiologically induced by the release of systemic inflammatory cytokines (13). In efforts to solve this dilemma, the athlete could be an efficient and reliable model for studying NT-proBNP changes during exercise-induced myocardial stress.

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