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Changes in BNP and cardiac troponin I after high-intensity interval and endurance exercise in heart failure patients and healthy controls

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To the Editor:

Exercise training represents a cornerstone of contemporary cardiac rehabilitation. Recently, high-intensity interval training (HIT) has been popularized for heart failure (HF) patients (1) and may serve as a superior mode of exercise compared to traditional endurance exercise training. However, there is controversy regarding the safety (2) and the direct effects of HIT on the heart. Previous studies have demonstrated that an acute bout of exercise leads to an increase in cardiac troponin (cTn), a biomarker for cardiac injury, and B-type natriuretic peptide (BNP), a marker for cardiomyocyte stress (3,4). Exercise-induced elevation in these biomarkers is related to exercise intensity and duration (4,5), and may occur to a larger extend in patients with cardiovascular risk factors (6). To date, no previous study: 1. compared changes in cTn and BNP between endurance exercise and HIT, and 2. explored differences in exercise-induced changes in cTn and BNP between HF patients and controls.

We included 13 pharmacologically and clinically stable HF patients NYHA-class I-III (67±7 yrs; male:female 12:1) with impaired left ventricular ejection fraction (35±8%) and 14 healthy controls (60±6 yrs; male:female 11:3, Table 1). The study procedures conformed to the Declaration of Helsinki and were approved by the local ethics committee. All subjects provided written informed consent. A maximal incremental cycling test was performed on a cycle ergometer (Lode Excalibur v1.52/Ergoline, Ergoselect 200k) to determine peak oxygen uptake (VO_{2peak}). As expected, we found that VO_{2peak} was markedly lower in HF patients than in healthy controls (18.7±4.3 *versus* 37.2±10.8 mLO_2/kg/min, $P<0.001$). On visit 2 and 3, subjects performed an isocaloric endurance exercise bout (30-minutes at 65%VO_{2peak}) and HIT (10*1-minute at 90%VO_{2peak}, alternated by 2.5-minutes at 40%VO_{2peak}) in randomized order. Both exercise bouts included comparable warm-up (10-minutes at 40%VO_{2peak}) and cool-down (5-minutes at 30%VO_{2peak}). Exercise intensity was verified using a heart rate monitor (Polar Electro Oy, RS800, Kempele, Finland). To assess cTnI- and BNP-levels, venous blood samples were obtained at baseline (BASE), post-exercise (POST) and 2-hours post-exercise (2H-POST), and analyzed using high-sensitive cTnI-assays (ADVIA Centaur, Siemens, detection limit: 6 ng/L, upper reference limit: 40 ng/L) and BNP-assays (ADVIA Centaur, Siemens, detection limit: 2 pg/mL, upper reference limit: 100 pg/mL). Changes in cTnI- and BNP-levels after exercise

(ΔcTnI, ΔBNP) were analyzed using 3-way Linear Mixed Model analysis, including 'time' (ΔBASE-POST, ΔBASE-2H-POST), 'group' (HF, controls), and 'exercise-mode' (HIT, endurance). cTnI data of the HIT session of one HF patient were classified as statistical outliers (value>2*SD) and hence excluded from analysis.

We found that baseline cTnI- and BNP-levels were higher in HF patients compared to controls (cTnI: 39±133 *versus* 4±10 ng/L, BNP: 80±86 *versus* 8±7 pg/mL, both P<0.001), a characteristic observation when examining HF patients and their healthy peers. Interestingly, exercise-induced ΔcTnI was comparable between both exercise bouts, but also did not differ between groups (Figure 1A). Exercise-induced ΔBNP was significantly larger in HF patients compared to controls. Nonetheless, we found no differences in ΔBNP-levels between both exercise-modes (Figure 1B).

This pilot work indicates that exercise-induced changes in cTnI and BNP were similar between endurance exercise (performed according to current cardiac rehabilitation guidelines (7)) and a single bout of HIT. Although a higher exercise-intensity is associated with a larger cTn-release (4,5), HIT did not induce a larger release in cTnI compared to endurance exercise. We speculate that, despite being performed at high-intensity, the short duration of high-intensity bouts prevents excessive cardiac load (8) and, therefore, does not induce significant biomarker release. Although our observations do not provide information on safety, our data demonstrates that HIT does not cause larger release of biomarkers related to cardiac injury compared to endurance exercise.

Previous work suggested that cardiovascular risk and/or disease is associated with a larger cTnI-release after exercise (6). In contrast, we found similar changes in cTnI in both groups, whilst HF patients show larger BNP increases than controls. Since BNP is related to cardiomyocyte stress, this finding suggests a higher cardiac load during exercise in HF patients compared to controls. Future studies with hemodynamic monitoring are recommended to confirm these observations. Combined, these data suggest that, despite larger myocardial stress in HF patients, endurance exercise nor HIT lead to excessive release of cardiac biomarkers indicative of acute cardiac damage.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology (9).

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Table 1. Baseline characteristics of HF patients and healthy controls.

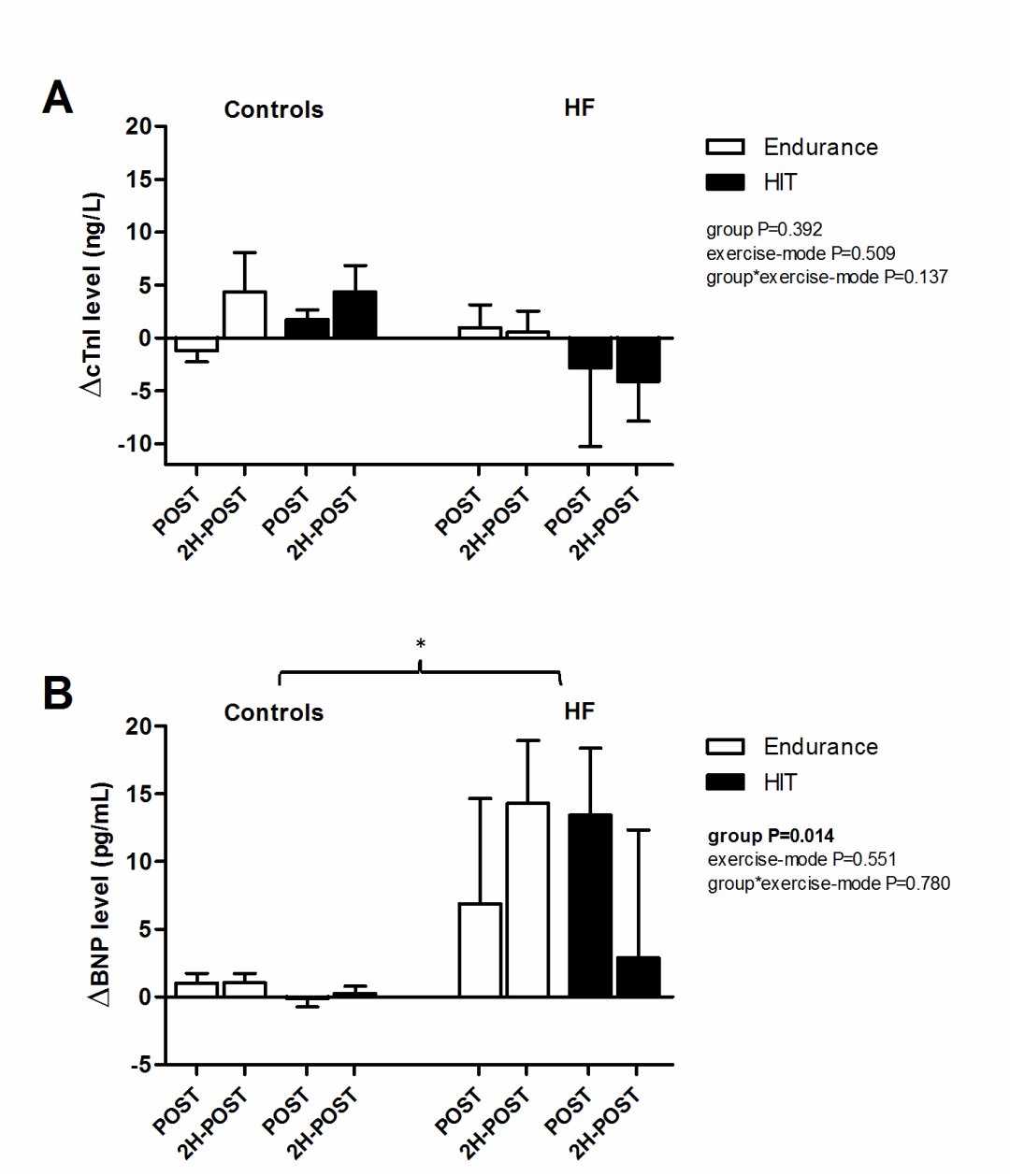
Parameter	Heart failure	Controls	P-value
Age (yrs)	67±7	60±6	0.014
Sex (male:female)	12:1	11:3	0.315
BMI (kg/m^2)	28.5±6.5	24.7±4.6	0.088
LVEF	35±8	N.A.	N.A.
Etiology (ischemic:non-ischemic)	7:6	N.A.	N.A.
NYHA class (I:II:III)	1:10:2	N.A.	N.A.
Systolic blood pressure (mmHg)	130±17	130±14	0.988
Diastolic blood pressure (mmHg)	79±9	85±10	0.168
Resting heart rate (/min)	59±8	60±10	0.792
Peak heart rate (/min)	129±16	165±17	<0.001
Peak oxygen uptake ($mlO_2/kg/min$)	18.7±4.3	37.2±10.8	<0.001
cTnI level (ng/L) [1]	39±133	4±10	<0.001
BNP level (pg/mL)[1]	80±86	8±7	<0.001

Data is presented as mean ± SD. P-value refers to an unpaired Student's *t*-test for continuous variables and the Chi-Square test for sex. [1]P-value refers to a Mann-Whitney U test. BMI; body mass index. LVEF; left ventricular ejection fraction. N.A.; not available. cTnI; cardiac troponin I. BNP; brain natriuretic peptide.

Figure 1

Changes in cTnI (A) and BNP levels (B) immediately after (POST) and two hours after (2H-POST) exercise compared to baseline. HIT; high-intensity interval training. Error bars represent SE. *group-effect $P<0.05$.

Figure 1


A
Controls
HF
ΔcTnI level (ng/L)
20
15
10
5
0
-5
-10
POST
2H-POST
POST
2H-POST
POST
2H-POST
POST
2H-POST
Endurance
HIT
group P=0.392
exercise-mode P=0.509
group*exercise-mode P=0.137
B
*
Controls
HF
ΔBNP level (pg/mL)
20
15
10
5
0
-5
POST
2H-POST
POST
2H-POST
POST
2H-POST
POST
2H-POST
Endurance
HIT
group P=0.014
exercise-mode P=0.551
group*exercise-mode P=0.780