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ORIGINAL ARTICLE
SPORT CARDIOLOGY

Cardiac biomarkers alterations in rapid weight loss and high-intensity training in judo athletes: a crossover pilot study

Aleksandra MILOVANČEV [1, 2], Aleksandra ILIĆ [1, 2], Tatjana MILJKOVIĆ [1, 2], Milovan PETROVIĆ [1, 2], Anastazija STOJŠIĆ MILOSAVLJEVIĆ [1, 2], Roberto ROKLICER [3, 4], Tatjana TRIVIC [4], Marko MANOJLOVIC [4], Carlo ROSSI [5] *, Antonino BIANCO [5], Patrik DRID [4]

[1]Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia; [2]Institute of Cardiovascular Diseases of Vojvodina, Sremska Kamenica, Serbia; [3]Faculty of Education, Free University of Bozen-Bolzano, Bressanone, Bolzano, Italy; [4]Faculty of Sport and Physical Education, University of Novi Sad, Novi Sad, Serbia; [5]Unit of Sport and Exercise Sciences Research, University of Palermo, Palermo, Italy

*Corresponding: Carlo Rossi, Unit of Sport and Exercise Sciences Research, University of Palermo, Palermo, Italy. E-mail: carlo.rossi@unipa.it

ABSTRACT

BACKGROUND: Studies evaluating alterations in cardiac biomarkers in rapid sport-associated weight loss (RWL) and high-intensity sport-specific training (HISST) are lacking. This pilot study aimed to examine the effects of RWL and HISST on heart rate, blood pressure, cardiac biomarkers, and left ventricular systolic function. Nine elite male judokas participated in the presented survey.

METHODS: The athletes underwent a baseline assessment and two testing protocols, the first phase with RWL where they had to lose 5% of their body weight simultaneously with HISST, and the second phase after 7 days, in which only HISST was performed. Participants underwent electrocardiogram, biomarker, and transthoracic echocardiogram evaluation after each phase.

RESULTS: In the first phase (RWL and HISST) athletes, heart rate increased significantly, 58.11 (7.78) *versus* 79 (9.25), P=0.001; as well as cardiac biomarkers: lactate dehydrogenase isoenzyme 175.33 (31.22) *vs*. 238.56 (56), P=0.003; aspartate aminotransferase 16.56 (4.61) *vs*. 29 (9.96), P=0.027; creatine kinase isoenzyme-MB 13 (11.5;24) *vs*. 29.11 (10.05), P=0.004; and high sensitivity cardiac troponin 10 (0) *vs*. 14.49 (6.4), P=0.045. In the second phase, only HISST was associated with a significant increase in the alanine aminotransferase isoenzyme, 37.78 (11.22) *vs*. 26 (8.03), P=0.024, together with creatine kinase 472 (185;654) *vs*. 166.88 (56.57), P=0.01, compared to the initial measurement.

CONCLUSIONS: RWL combined with HISST produced significant alterations in cardiac biomarkers without impairment of left ventricular systolic function.

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KEY WORDS: Troponin; Exercise; Athletes; Heart; Martial arts.

Physical activity is increasingly important in preventing and treating numerous nonco mmunicable chronic diseases.[1] Health promotion and evading adverse events should be the most crucial aim of exercise and sports practice for all ages and levels of athletes.[2] Specific biomarkers research has recently gained importance as they are sensitive, highly specific, and useful in everyday clinical practice. Damaged tissue and cells release biomarkers into the bloodstream specific to certain types of damage, and their increased levels may indicate the presence of certain conditions or diseases. Cardiovascular biomarkers represent cornerstones of accurate diagnosis of various cardiovascular and other diseases. Moreover, any cardiac biomarker could be increased postexercise.[3] Biochemical markers of myocardial injury are AST, LDI, MBI, myoglobin, and cardiac troponin.[4] In 2000,[5] guidelines for

defining myocardial infarction pointed out hsTn as highly sensitive and specific for myocardial injury. Heart-specific troponins are primarily expressed in the heart and are part of the myocardial cells' contractile machinery. Cardiac troponin I value has not been reported to occur following injury to non-cardiac tissues.[6] To assess myocardial injury during and after vigorous exercise studies evaluating levels of cardiac troponin were performed. These studies almost exclusively included endurance sports. In a meta-analysis,[3] with 45 studies included, 83% of individuals had increased high-sensitivity cardiac troponin (hsTn) after prolonged and strenuous exercise. Troponin elevation was observed even in short races performed at higher exercise intensities.[7] The pathophysiological mechanism still needs to be better understood. An unanswered question is whether these increases in biomarkers implicate myocardial injury and how repeated alterations affect short and long-term outcomes. In combat sports, athletes are categorized to match their opponents in body size, strength, and agility.[8] Nevertheless, a lot of athletes drastically lose body mass. to obtain an advantage over opponents that are weaker, lighter, and smaller.[9, 10] A reduction of 2-10% of body weight in 1-7 days is considered rapid weight loss (RWL).[11] In most combat sports, forceful and dangerous treatments for rapid weight reduction are highly co mmon, even though rapid weight loss (RWL) has been shown to have detrimental consequences on health status.[12] Although this method is highly prevalent in combat sports such as wrestling,[9] judo,[13] jujitsu,[14] sambo,[15] and others,[16] there is a knowledge gap regarding cardiac biomarkers assessment during RWL. It is essential to address research regarding the response of cardiac biomarkers in power sports. By analyzing the changes in these biomarkers, we could assess the cardiovascular stress induced by power sports-specific training or rapid weight loss and explore potential connections with biomarker alterations and/or adverse cardiovascular events. We hypothesize that RWL with high-intensity sport-specific training (HISST) will be associated with increased cardiac injury biomarkers levels. This pilot study aimed to examine the effects of HISST alone or in combination with RWL on heart rate, blood pressure, cardiac biomarkers, and left ventricular systolic function in judokas.

Materials and methods

Study design and participants characteristics

This crossover study prospectively included 9 male elite judokas participating in national and international contests. The research included three phases, baseline assessment and two test protocols, where each participant following all phases suffered a transthoracic 2D echocardiography, medical examination, electrocardiogram (ECG), and testing of a blood sample. Exclusion criteria were as follow: a previous history of diabetes mellitus, hypertension, diseases of the heart, liver, kidney, psychiatric, malignant, and infectious disorders, electrolyte imbalance, and taking any drugs that can influence ECG intervals. All subjects included in the study have already been practicing RWL techniques during the last two years. They filled out the questionnaire about years in training, the number of hours/weekly spent on training, comorbidities, cardiovascular risk factors, and family history of cardiovascular diseases. The experiment, after the baseline assessment, was performed in two phases. The first phase aimed to examine the acute effects of RWL (5% body mass reduction) in combination with HISST on heart rate, blood pressure, cardiac biomarkers, and left ventricular systolic function, The second phase aimed to determine the influence of HISST without body mass reduction on the same variables.

Baseline assessments

Anthropometric measurements, including body weight (BW) and body height (BH) were performed with athletes wearing underwear, using calibrated beam-type balance to the nearest 0.1 kg (bioelectrical impedance Omron weight scale BF511 [Omron, Kyoto, Japan]) and a Harpenden anthropometer to the nearest 0.1 cm, respectively. Body Mass Index (BMI) was calculated (BMI=BW/BH^2 [kg/m^2]) as well as body surface area (BSA) with the following formula (Equation 1):

$$\mathrm{BSA}\ \left(\mathrm{m}^2\right) = \frac{\sqrt{\mathrm{BH(cm)} \times \mathrm{BW(kg)}}}{3600} \quad (1)$$

Electrocardiography

Each participant completed a standard 12-lead surface ECG record while at rest, with a gain of 10 mm/mV and a 25 mm/s paper speed. Each ECG was interpreted by one cardiologist trained to interpret athletes' ECGs. Peculiarities/abnormalities discovered were classified based on Refined criteria.[17]

Echocardiography

With the use of a Vivid E9 (GE Healthcare, Milwaukee, WI, USA) machine outfitted with an M5S-D, 1.5-4.6 MHz transducer and simultaneous ECG monitoring, all individuals underwent two-dimensional transthoracic

echocardiography (ECHO). For the investigation, respondents were told to assume a decubital left lateral posture. Three cardiac cycles of uncompressed data were saved in cine-loop format for each acquisition, and one investigator – who was blind to the subjects' clinical details – evaluated the data offline without blinding himself. Every measurement and computation was carried out using the previously mentioned techniques according to standardized procedures by the American Society for Echocardiography and the European Association of Cardiovascular Imaging.[18] The parasternal thickness of the aortic root, ascending aorta, posterolateral wall, interventricular septum, and diastolic diameter of the ventricle (left ventricle [LV]; LVEDd and LVEDs) were measured using the parasternal long-axis view (2D). Using apical 4-chamber and 2-chamber images at ventricular end-systole, the Simpson method was used to quantify the volumes of the left atrium (LA), which were then normalized for BSA as the LAVs index (LAVsI). The biplane method of disks with EF computed was used to measure the end-diastolic (EDV) and end-systolic (ESV) volumes of the left ventricle. The left ventricular mass (LVM) was determined automatically by software using the area-length method based on measurements taken from a parasternal cross-sectional view. In the apical 4-chamber view, this image delineated the diastolic and systolic mitral-to-apical distance, as well as the epicardial and endocardial surface in the mid-ventricular systolic and diastolic phases, LVM is equal to 1.05 [5/6A2 (L+t) - (5/6A2L)], where A1 and A2 are the epicardial and endocardial areas, respectively, at the end of diastole, L is the end ventricular length, *t* is the average wall thickness (cm), and 1.05 is the muscle's specific gravity (g/mL). The indexed value (LVMi) was calculated by dividing the LVM by the BSA. Left ventricular morphology is categorized into four morphological types based on relative wall thickness (RWT) and left ventricular mass index (LVMI): Normal geometry is typified by LVMI ≤95 g/m^2 and RWT≤42 mm; concentric remodeling is characterized by LVMI≤95 g/m^2 and RWT>42 mm; concentrated hypertrophy is described by LVMI>95 g/m^2 and RWT>42 mm; and eccentric hypertrophy is characterized by LVMI>95 g/m^2 and RWT≤42 mm. Transmittal pulsed-wave (PW) Doppler was obtained at the tips of the mitral leaflets in the apical 4-chamber view. Early peak wave (E) and atrial late (A) diastolic filling velocities, as well as the E/A ratio, were also recorded. The septal and lateral sites of the mitral annulus were imaged using tissue Doppler, from which measurements for the peak early (e') velocities were acquired and averaged. Using the E velocity and averaged e' velocities determined by the mitral annulus's lateral and septal placements, the E/e' ratio was computed. Global left ventricular strain (LVGS) was calculated for each patient utilizing the EchoPAC Clinical Workstation Software (GE Healthcare, Milwaukee, WI, USA) during postprocessing. Every image was captured between 60 and 80 frames per second. Three heart cycles in a row were noted. Three distinct apical views of the heart – the three-chamber view (3CH), the four-chamber view (4CH), and the two-chamber view (2CH) – were used to record cardiac cycles. As can be seen in the apical 3-chamber picture, aortic and mitral valve closure was utilized as the suggested end-diastole and end-systole. The "point-and-click" technique manually marked the endocardial border. A region of interest (ROI) was created by the system automatically by generating the epicardial edge. The software automatically created segments after the ROI was set. Every segment had its quality score automatically determined, and it was either categorized as acceptable or undesirable. Each segment that was first deemed undesirable could have its edge manually corrected. The segments that exhibited insufficient image quality were not included in the analysis. All six left ventricular walls had their LVGS computed, and the software program automatically divided the walls into eighteen pieces to create one model of the bull's eye.

Test protocol

In phase one, 5% of the competitors' body weight had to be shed with HISST. In this phase, they had to lose weight within 3 days. On the final day of the RWL period, the training (testing) was completed, and then the measurements were taken. In the second phase, no quick weight reduction technique was included, and the identical HISST protocol was followed seven days later. The instruction lasted for ninety minutes in total. The respondents were told to follow the protocol with the same sparring partner during both testing times and were aware of the testing procedure. Four series of a maximum number of throws with a work-rest ratio constituted the HISST (10min:3:30min), specifically the active part was composed of throws and sprints (15s) interspersed with low-intensity running (45 s). Each set was 10 minutes long with a 3-minute break in the middle. During the test, participants performed shoulder throws (Ipon-Seoi-Nage).

HISST-Warm-up

Five minutes of foam rolling as a warm-up was followed by five minutes of dynamic stretching for the participants. The judokas warmed up for a total of twenty-five minutes,

consisting of seven minutes of standard and sport-specific warm-ups, followed by eight minutes of gymnastic and acrobatic elements.

HISST-main part

The central piece of the training included 45 seconds of low-intensity aerobic running alternated with a rigorous throwing technique (15s). In the beginning, the individual started with a 45-second, low-intensity circular run. The respondent was told to position himself nine meters away from his sparring partner five seconds before the test's throwing phase. At the sound signal, they were to sprint as quickly as they could to their sparring partner and execute the throwing method. They had to go back to the 9-meter starting spot as soon as possible following the throw. During these 15 seconds, participants had to run and execute at least 4 shoulder tosses (Ipon-Seoi-Nage). Following the completion of the throwing portion, the respondent began another round of low-intensity running. A 3-minute break was applied after the participant finished the 10-minute session. The given protocol was tested four times, taking a total of forty minutes.

HISST-cool down

The cool-down phase was used after the test protocol. This section involved low-intensity circular running for 12 minutes.

RWL procedure

First day

Following the morning baseline evaluation, the respondents carried out the following workout and diet schedules. For lunch, the individuals consumed one can of tuna. In addition, a lot of liquids were drunk during the remainder of the day, including water and grape and lemon juice. The participants engaged in low-intensity exercise, such as strolling, as active rest before the evening training session. Following this, they attended the scheduled judo training session. The responders had one green apple for dinner.

Second day

Many drinks high in caffeine were ingested on the second day. A cup of green tea was the first thing to drink in the morning. The second drink before the morning workout was a glass of grape, lemon, and ginger juice. Low-intensity aerobic running for 45 minutes was a part of the morning training program. The responders' lunch consisted of lettuce, half a plate of rice, and a slice of salmon. The participants rested during the day and did not consume any additional fluids until the nighttime training session. The evening training session involved low-intensity running in a plastic suit (to cause profuse perspiration) for 45 minutes, broken up by gymnastic and acrobatic movements. The responders used the sauna for three sessions of five minutes in a heated setting following the training, interspersed by a two to five-minute rest (dwelling outside the sauna).

Third day

The HISST, which was previously described, was conducted in the AM on the last day. Before and/or during the test methodology, no drinks were ingested (before the last measurement). Weighing and medical evaluations (ECG, blood sample, and ECHO) were performed following the training. The replies were permitted to start eating and rehydrating when the exams were finished.

Laboratory

Blood samples were taken 7 days before the planned simulation of RWL, 2-4 hours after phase one (RWL combined with HISST), and 2-4 hours after phase two, only HISST. Biochemical parameters were determined routinely using standard methods. Alere NT-pro-BNP and the High Sensitive STAT Troponin I test from Abbott Laboratories, Abbott Park, IL, USA, were the assays used. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDI), creatine kinase (CKI), and creatine kinase-MB isoenzyme (MBI) were determined using co mmercially available standard assays (Sysmex America Inc., Lincolnshire, IL, USA).

Statistical analysis

The analysis included descriptive statistics. For continuous data, continuous variables are shown as means and standard deviations or medians with interquartile ranges of the 25^{th} and 75^{th} percentile. Using the Kolmogorov-Smirnov Test, the normal distribution was examined. Absolute numbers and percentages are used to express categorical variables. Differences between categorical variables were tested by χ^2 test as appropriate. For the within-group comparison, ANOVA for repeated measures with Bonferroni *post hoc* correction was applied. P values less than 0.05 were deemed statistically significant. The statistical package for social sciences, SPSS Version 20.0 (IBM Corp. 20, Armonk, NY, USA), was used for all computations and interpretations.

TABLE I.—*Basic athletes' characteristics.*

Parameters	Mean (SD), median (Q1;Q3), N. (%)
Age (years)	23 (18.5; 23)
Height (cm)	174.43 (3.78)
Weight (kg)	73.37 (4.42)
BMI (kg/m²)	24.11 (0.96)
BSA (m²)	1.88 (0.07)
BP systolic (mmHg)	127.14 (14.68)
BP diastolic (mmHg)	66.42 (8.02)
Heart rate (bpm)	58.11 (7.78)
Family history of CVD	2 (22.22%)
Personal previous medical history	2 (22.22%)
Years in training	12.37 (7.09)
Hours spent on training/weekly (h)	12.56 (1.81)

Values are expressed as N. (%).
BMI: Body Mass Index; BSA: body surface area; BP: blood pressure; bpm: beat per minute; CVD: cardiovascular diseases; Q1: 25 percentile; Q3: 75 percentile.

Results

The basic athletes' characteristics are presented in Table I. The median age was 23 (18.5; 23) years, mean years spent in training were 12.37 (7.09). Two judokas (22.2%) had a previous personal medical history (one had dyslipidemia, and the other had bronchial asthma), and two athletes also (22.2%) reported a positive family history of cardiovascular diseases. Mean systolic arterial blood pressure and mean diastolic blood pressure were 127.14 (14.68) and 66.42 (8.02), respectively (Figure 1). Electrocardiogram showed type one peculiarities in all athletes; 5 (55.56%) had incomplete right bundle branch block, three (33.3%) had ST-segment early repolarization, and one had ectopic premature atrial complex. The echocardiographic parameters of judokas are available in Table II. One athlete exhibited mildly increased interventricular septum and posterolateral wall thickness. The left ventricle showed signs of concentric remodeling in 7 (77.78%) athletes. All judokas had normal systolic and diastolic functions.

RWL and HISST

Baseline heart rate was significantly increased after RWL and HISST, 58.11 (7.78) *vs*. 79 (9.25), respectively, P=0.001 (Figure 2), as well as LDI 175.33 (31.22) *vs*. 238.56 (56), P=0.003; AST 16.56 (4.61) *vs*. 29 (9.96), P=0.027; MBI 13 (11.5;24) *vs*. 29.11 (10.05), P=0.004; and hsTn 10 (0) *vs*. 14.49 (6.4), P=0.045 (Figure 3). RWL and HISST induced increased levels above the reference range relative to the baseline measurements of LDI in 66.7% *vs*. 0% judokas, P=0.004; AST in 33.3% *vs*. 0%, P=0.065: MBI in 66.6% *vs*. 22.2%, P=0.065; and hsTn 55.5% *vs*. 0%, P=0.011.

HISST

After HISST, ALT significantly increased compared to baseline, 37.78 (11.22) *vs*. 26 (8.03), P=0.024, along with CKI 472 (185; 654) *vs*. 166.88 (56.57), P=0.01 (figure 4). Only one athlete (11.1%) had increased ALT above the reference range following HISST, while CKI was increased above the reference range in 3 (33.3%) athletes in baseline, compared to all (100%), P<0.01. In addition, it was observed that AST was above the reference range in 44.4% of judokas after HISST compared to 0% in baseline, P=0.027; MBI in 33.3% *vs*. 22.2%, P=0.609; and troponin in 44.4% *vs*. 0%, P=0.027. After a two-year follow-up, no significant adverse events were observed in all 9 athletes.

Discussion

To our knowledge, this is the first study assessing highly specific cardiac biomarkers during RWL and HISST utilizing supplementary cardiovascular imaging. The study reported significantly increased heart rate and altered cardiac biomarkers after RWL and HISST, while left ventric-

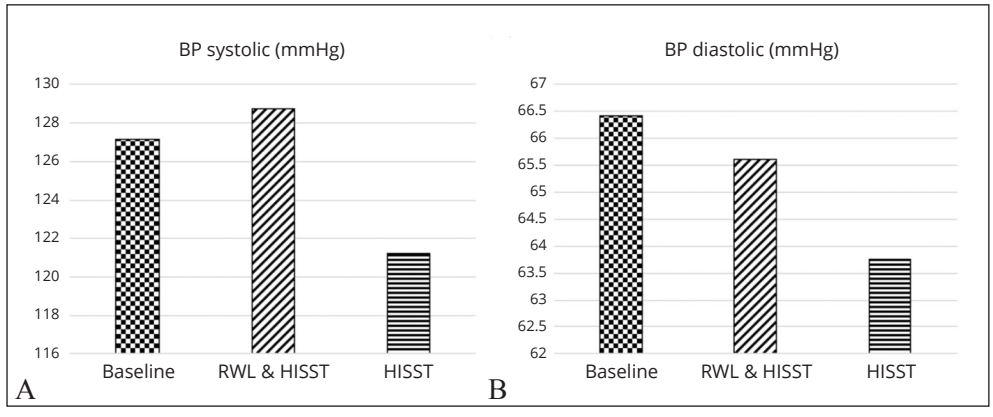

Figure 1.—Systolic (A) and diastolic (B) blood pressure during the 3 phases of the study.
BP: blood pressure; RWL: rapid weight loss; HISST: high-intensity sport-specific training.

TABLE II.—*Echocardiographic characteristics of the examined population.*

Parameters	Mean (SD), Median (Q1, Q3)
LVEDd (mm)	46.67 (1.87)
LVEDd/BSA (mm/m²)	24.83 (1.25)
LVEDs (mm)	28.22 (1.64)
LVEDs/BSA (mm/m²)	15.01 (0.89)
IVS (mm)	10 (9.5;10)
PLW (mm)	10 (9.5;10)
RWT (mm)	0.42 (0.33)
LVM (g)	151.26 (18.69)
LVM/BSA (g/m²)	80.39 (9.34)
EDV (mL)	116 (90.5;117.5)
EDVI (mL/m²)	57.55 (7.77)
ESV (mL)	33.44 (5.41)
ESVI (mL/m²)	17.79 (2.92)
SV (mL)	84 (59;87.50)
SVI (mL/m²)	39.75 (8.09)
EF (%)	64 (60;65)
FS (%)	39.45 (4.02)
LAVs (mL)	52.43 (11.10)
LAVsI (mL/m²)	27.97 (5.82)
Aortic root (mm)	24.4 (2.60)
Ascending aorta (mm)	27.5 (1.69)
E – wave (m/s)	0.94 (0.10)
A (m/s)	0.53 (0.09)
E/A ratio	1.80 (0.32)
e' sep (cm/s)	0.12 (0.02)
E/e'sep ratio	7.71 (1.23)
e' lat (cm/s)	0.13 (0.03)
E/e' lat ratio	7.89 (2.46)
e'average (cm/s)	0.12 (0.01)
E/e' average	7.70 (1.22)

Statistical significance was set at P<0.05.
A: late atrial contraction; E: early wave; E/A ratio: peak early wave to atrial late wave ratio; e'average: average peak early velocity; E/e' average: early wave to average peak early velocity; E/e' sep: early wave to septal peak early velocity; E/e' lat ratio: early wave to lateral peak early velocity; e' lat: lateral peak early velocity; e' sep: septal peak early velocity; E/e' lat ratio: early wave to lateral peak early velocity; LV: left ventricular; EDV: LV end-diastolic volume; EDVI: LV end-diastolic volume/body surface area; EF: ejection fraction % ESV: LV end-systolic volume; ESVI: LV End-systolic volume/ body surface area; FS: fraction of shortening %; IVS: interventricular septum; LAVs: left atrium volume at end-systole; LAVsI: left atrium volume index; LV: Left ventricle; LVM: left ventricle mass; LVMI: left ventricle mass index; LVEDd: LV end-diastolic diameter; LVEDd/BSA: LV end-diastolic diameter and body surface area ratio; LVEDs: LV end-systolic diameter; LVEDs/BSA: LV end-systolic diameter and body surface area ratio; P: statistical significance; PLW: posterolateral wall; RWT: relative wall thickness; SD: standard deviation; SV: Stroke volume; SVI: stroke volume/body surface area; Q1: 25 percentile; Q3: 75 percentile.

ular systolic function remained unchanged. Athletes, after only HISST, experienced biomarker alterations that could mainly be attributed to muscle damage. The use of RWL among athletes competing in weight classes has been considered a problem for years. Still, the extent of the problem and the health and performance consequences have yet to be thoroughly examined, especially studies dealing specifically with the cardiovascular system are lacking. Numerous harmful aspects of physical, physiological, and mental consequences of RWL have been documented.[13] Even cases of death have been reported, with myocardial infarction being the cause in some instances and hyperthermia and dehydration in others.[19] Nevertheless, the prevalence of RWL ranges from 40-90%[20] in combat sports. Biomarkers are early clues for unrevealing alterations that can predict myocardial injury, and studies assessing biomarkers during certain procedures like RWL are highly needed.

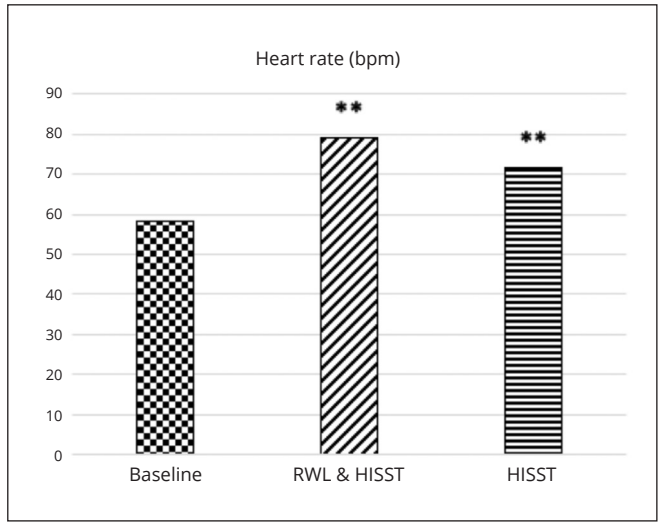

Figure 2.—Heart rate in the 3 different phases.
RWL: rapid weight loss; HISST: high-intensity sport-specific training.
**P<0.01.

Blood pressure and heart rate

In our study, neither RWL and HISST nor HISST alone significantly affected blood pressure. Nascimento-Carvalho *et al*.[21] also observed no differences in blood pressure after RWL, while increased heart rate was attributed to greater sympathetic modulation. Likewise, we observed significantly increased HR after RWL and HISST. Considering there were no significant differences in HR following only HISST, it is plausible that dehydration during RWL played a role in the notable increased HR strain. Higher HR responses were recorded after dehydration and the judo fitness test.[22] The findings of Montain and Coyle[23] indicated a close relationship between the level of graded dehydration (1-4%) and a corresponding rise in HR and a decrease in stroke volume. While systematic review reported that regardless of the percentage of weight loss athletes exhibit increased HR.[24] Gonzalez-Alonso[25] *et al*. also reported that dehydration and hyperthermia markedly impair cardiovascular function (decreased stroke volume and blood pressure as well as increased heart rate). Large weight fluctuations in a short time during RWL are mainly

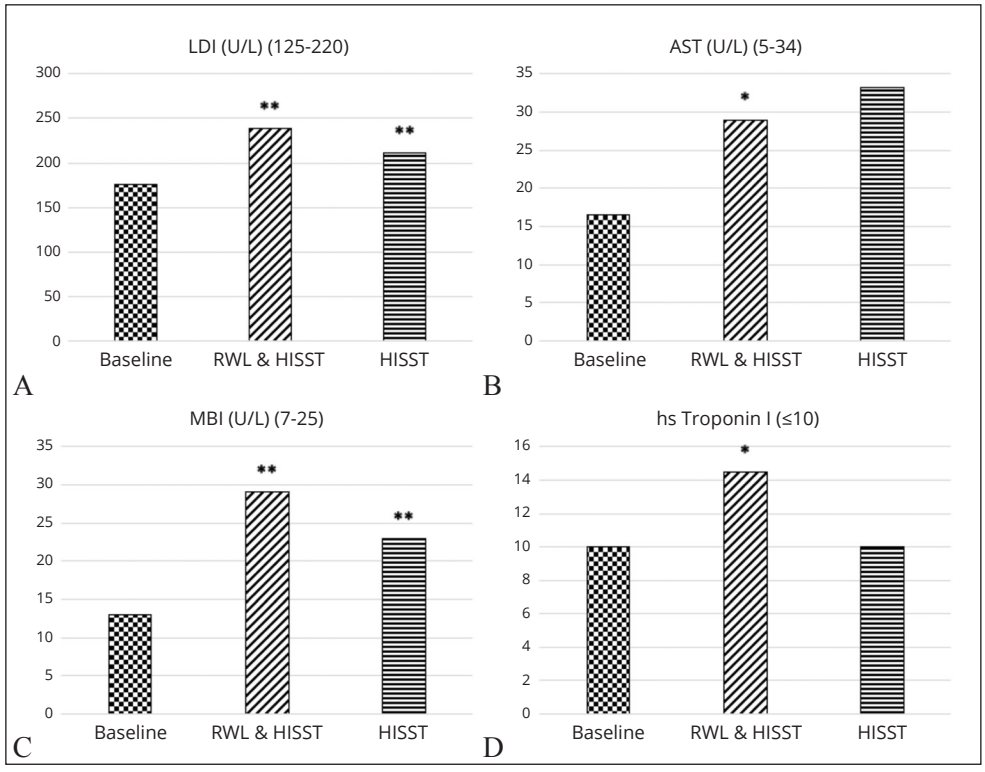

Figure 3.—Trend of biomarkers carried out during the three phases: lactate dehydrogenase isoenzyme (A), aspartate aminotransferase (B), creatine kinase-MB isoenzyme (C) and cardiac troponin (hs troponin I) (D).
LDI: lactate dehydrogenase isoenzyme; RWL: rapid weight loss; HISST: high-intensity sport-specific training; MBI: creatine kinase-MB isoenzyme; hs Troponin I: cardiac troponin.
*P<0.05; **P<0.01.

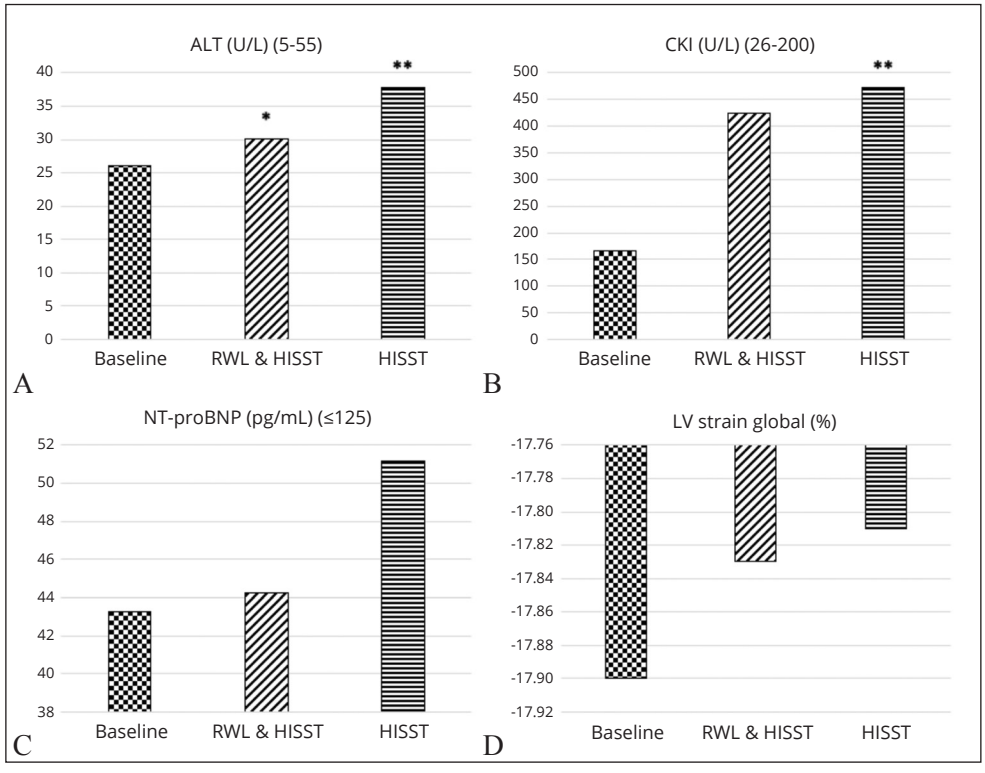

Figure 4.—Trend during the 3 phases of the biomarkers: alanine aminotransferase isoenzyme (A), creatine kinase (B), NT-proB-type natriuretic peptide (C), global LV strain (D).
ALT: alanine aminotransferase isoenzyme; CKI: creatine kinase; NT-proBNP: NT-proB-type natriuretic peptide; LV: left ventricular.

due to dehydration, which can lead to decreased aerobic and anaerobic performance. Altered aerobic capacity can put an additional strain on shifted cardiac autonomic recovery.[26] The American College of Sports Medicine issued guidelines for safe weight loss to avoid adverse outcomes due to the effect of RWL, as it leads to a decrease in plasma volume, an increase in HR, alterations in hemodynamics, and a decreased ability to maintain work at a constant rate.[27]

HISST

In our study, the mean levels of CKI and ALT were significantly increased after HISST compared to baseline. A significant number of athletes experienced an acute rise in AST, and hsTn concentrations exceeded the upper reference limit. Roklicer *et al*.[28] showed that CK, myoglobin, and aldolase markers of skeletal muscle damage were significantly increased during RWL. George *et al*.[29] conducted a unique study in which short-duration, high-intensity cycling bouts (30 s) do not elicit a statistically or clinically significant increase in circulating hsTn. Previous studies reported data on cardiac troponin alterations in endurance athletes,[30] but data on short exercise training on troponin release are rather scarce. CK is a myosin-heavy chain fragment related to muscle damage. It is known that intense exercise leads to muscle tissue injury causing CK to be released into the bloodstream.[31] Marked increases in CK activity are often associated with an increase in higher muscular activity.[32] ALT-raised levels may be traced to muscular infla mmation or muscular trauma.[33] The normal repair process in these cases engenders infla mmation and raises transaminase levels.

RWL and HISST

In our study, RWL with HISST resulted in significant LDI, AST, MBI, and hsTn alterations. There is only one study that assessed biomarkers of myocardial injury in RWL, Farzidate *et al*.[34] reported that RWL of 2% and 4% significantly increased levels of MBI and Troponin. However, within 24 hours after weight loss, the levels of biomarkers returned to the level of resting. In a study by Ozkan *et al*., dehydration in elite wrestlers resulted in increased AST, LDI, and CK levels.[35] Biomarkers of cardiac injury have excessively been studied in endurance athletes. Initial evidence supported the concept of exercise-induced cardiac injury based on CK-MB. Authors report that increases in CK-MB reflect muscular rather than myocardial injury.[36, 37] It was subsequently shown that CK-MB concentrations lack sensitivity and specificity in heart tissue, particularly in athletes. Exercise-induced myocardial injuries have been generally examined using Troponin. Several meta-analyses showed that endurance exercise is associated with increased levels of cardiac troponin.[38-40] Most of these studies showed significant cardiac troponin increases after exercise. Park *et al*.[41] showed that high levels of physical exercise raised hsTn, CK-MB, and myoglobin. The interpretation of a rise in hsTn remains unclear, even though CK-MB and myoglobin levels are associated with injury to the skeletal muscle. The large observational study of Fortescue *et al*.[38] reported that almost 68% of 482 runners in the Boston Marathon showed cTnT or cTnI increases. These observations were confirmed in the meta-analyses of 26 studies by Shave *et al*.[42] and 16 studies by Regwan *et al*.[39] demonstrated rates of 47% and 51% of increased levels of troponins due to endurance exercise, respectively. Troponin elevation has also been addressed in numerous studies that included endurance athletes, such as endurance running, prolonged marching, high-intensity treadmill running, high-intensity cycling, and clinical exercise tests.[30] Some theories of possible pathophysiology of exercise-related increased hsTn have been suggested, but a consensus has yet to exist. Strengthening exercise has the potential to enhance cardiomyocyte membrane permeability and trigger the release of troponin. This reversible membrane leakage might be due to the production of reactive oxygen species or alterations in calcium, pH, glucose/fat metabolism or co mmunication between integrins, increased mechanical stress on the cardiomyocytes, overload with free radicals, increased body temperature, or prolonged acidosis. Some other suggested mechanisms are infla mmation, vasculitis, the release of troponin degradation products in "blebs," increased cardiovascular stress, dehydration, impaired renal clearance, and expression of cardiac troponin in skeletal muscle. RWL shares a majority of these features, which can cause increased hsTn in our judokas group. Both heavy and light exercise may cause elevated troponin.[40] These findings were considered physiological for a long time, as these elevations often occur in athletes and are not related to cardiac symptoms.[40] Conversely, a meta-analysis of 65.019 participants showed that elevated basal Tn demonstrates strong correlations with a higher risk of cardiovascular and all-cause death in the general population at follow-up.[43] Troponin use is gaining significance as a predictive tool for risk assessment, and future studies with longer follow-ups are needed to evaluate risk, especially in the athlete population. We found no evidence of left ventricular systolic dysfunction after HISST or RWL.

Other studies also documented no functional impairment assessed by echocardiography related to troponin elevation in athletes.[44, 45] In a meta-analysis of 45[4] and 18 studies,[46] acute LV dysfunction was not observed poststrenuous endurance sport exercise.[3, 47] There were no significant changes in NT-proBNP levels in our study. Football and rugby players show increases in NT-proBNP posteffort, as demonstrated by Banfi *et al*., but they view these increases as physiological.[48]

Limitations of the study

During the interpretation of our study, it is important to take a few limitations into the report. First off, because this was an observational, no-randomized study, both known and unknown variables may have had an impact on the results. Second, the cohort is rather small, the study may not have enough statistical strength to detect smaller, yet potentially meaningful, differences or associations and the consistency of the results. Still in this small cohort, significant differences between measured parameters could help us drive the preliminary conclusions for further investigation. Having more troponin values would provide additional insight into troponin dynamics and potentially enhance the understanding of the relationship between troponin levels and rapid weight loss or HISST. Having more frequent measurements would allow for a better understanding of the temporal pattern of troponin release and clearance. This information can help identify peak troponin levels, the duration of elevation, and the rate of decline, which can be clinically relevant for management decisions. While obtaining more troponin values would provide valuable insights, it's important to balance the frequency and timing of measurements with practical considerations such as cost, patient burden, and clinical feasibility. Nonetheless, including more troponin values in future studies can enhance the understanding of troponin dynamics and help refine the interpretation of results.

Conclusions

Rapid weight loss followed by high-intensity sport-specific training resulted in significant cardiac biomarker alterations without functional impairment of left ventricular systolic function. In athletes involved with RWL, we can expect significant increases in LDI, AST, MBI, and hsTn. High-intensity sport-specific training caused changes in biomarkers mainly attributed to muscular damage. Athletes involved in this pilot study did not experience adverse events in two-year follow-up.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions

Aleksandra Milovančev, Roberto Roklicer, Tatjana Trivic and Patrik Drid have given substantial contributions to the study conception; Aleksandra Ilić, Tatjana Miljković, Milovan Petrović and Anastazija Stojšić Milosavljević contributed to the data collection, analysis and interpretation; Aleksandra Milovančev and Patrik Drid contributed to the study supervision; Aleksandra Milovančev, Aleksandra Ilić, Tatjana Miljković, Milovan Petrović, Anastazija Stojšić Milosavljević, Roberto Roklicer and Carlo Rossi contributed to the manuscript draft, all authors revised it critically. All authors read and approved the final version of the manuscript.

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