Impaired Post Exercise Heart Rate Recovery in Anabolic Steroid Users

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Key words
- heart rate recovery
- functional capacity
- anabolic steroids abuse

Abstract

Previous study showed that muscle sympathetic nerve activity (MSNA) was augmented in anabolic steroids users (AASU). In the present study, we tested the hypothesis that the heart rate (HR) responses after maximal exercise testing would be reduced in AASU. 10 male AASU and 10 AAS nonusers (AASNU) were studied. Cardiopulmonary exercise was performed to assess the functional capacity and heart rate recovery. MSNA was recorded directly from the peroneal nerve by microneurography technique. Peak oxygen consumption (VO_2) was lower in AASU compared to AASNU (43.66±2.24 vs. 52.70±1.68 ml/kg/min, $P=0.005$). HR recovery (HRR) at first and second minute was lower in AASU than AASNU (21±2 vs. 27±2 bpm, $P=0.02$ and 37±4 vs. 45±2 bpm, $P=0.05$, respectively). MSNA was higher in AASU than AASNU (29±3 vs. 20±1 bursts/min, $P=0.01$). Further analysis showed a correlation between HRR and MSNA ($r=-0.64$, $P=0.02$), HRR at first minute and peak VO_2 ($r=0.70$, $P=0.01$) and HRR at second minute and peak VO_2 ($r=0.62$, $P=0.02$). The exacerbated sympathetic outflow associated with a lower parasympathetic activation after maximal exercise, which impairs heart rate recovery, strengthens the idea of autonomic imbalance in AASU.

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Introduction

The use of anabolic androgenic steroids (AAS) has increased considerably among strength athletes because of its effects on protein synthesis and consequent increase in skeletal muscle mass [6]. The problem is that AAS have been associated with heart hypertrophy and hemodynamic and neurovascular alterations [8,12,24]. Studies in isolated human myocytes suggest that AAS bind to androgen receptors causing cardiac hypertrophy [14]. There is also evidence that cardiac hypertrophy with interstitial fibrosis as a consequence of AAS administration is mediated by renin angiotensin system. Previous study demonstrated that losartan treatment prevented left ventricular hypertrophy in rats with AAS administration [22]. Study in humans provides evidence that AAS self-administration increases muscle sympathetic nerve activity (MSNA) [3], which seems to have hemodynamic implications. Systolic and diastolic blood pressure levels are higher in AAS users than in AAS non users [3]. In addition, muscle blood flow is reduced in individuals under AAS self-administration. The effects of AAS can be even more dramatic. Mortality rate is higher in AAS users than in AAS nonusers [1]. Although the cause of the death in these individuals is unclear, the postmortem studies suggest cardiac causes in many cases [18,19]. Case reports link sudden death to acute myocardium syndrome, myocardium infarction and ventricular arrhythmias in AAS abusers [15,27], which are consistent with cardiac anatomical and autonomic alterations.

Heart rate reduction after an exercise bout has been associated with autonomic function, especially cardiac vagal recovery [5]. Moreover, heart rate recovery (HRR) is a useful tool for stratification of risk factor and an independent predictor of mortality [2,5]. In a recent study, we found that resting heart rate and MSNA were higher in AAS users, which favors the idea of cardiac autonomic imbalance in individuals under AAS self-administration [3]. In the present study, we investigated the HRR after maximal exercise test and cardiopulmonary capacity in individuals under self-anabolic steroids administration. Our hypothesis was that HRR would be reduced in AAS users. In addition, we hypothesized that

there was an inverse association between HR recovery and sympathetic nerve activity in AAS users.

Methods

Study population

10 male AAS users (AASU) and 10 age-matched male AAS non-users (AASNU) were invited to participate in the study from the hospital cardiology exercise ambulatory. All individuals had been involved in strength training for at least 2 years. The AASU were self-administering AAS for at least 4 weeks before the study. The most used anabolic steroids were stanozolol, testosterone propionate, nandrolone decanoate, testosterone cypionate between 4–12 weeks. In addition, they had been using AAS for at least 2 years, 2–4 cycles per year. The AASU were not taking other doping substances than AAS. The use of AAS was confirmed by urine test (chromatography-mass spectrometry). The study protocol was approved by the local Human Subject Protection Committee and written consent was given by each individual. Furthermore it was performed in accordance with the ethical standards of the IJSM [11].

Exercise strength training

Exercise strength training consisted of 3–4 sets of 8–12 repetitions, about 2–4 exercise muscle group, between 80–90% of a maximal repetition (1MR), 5 days/week, 60 min exercise sessions. All the subjects had been training for at least 2 years and were requested not to practice aerobic exercise in order to not influence the measures.

Cardiopulmonary exercise measurements

The maximal cardiopulmonary test was carried out on a treadmill (Quinton Q65, model 645, Quinton Instruments Co, Washington, USA) using a ramp protocol with workload increment every min with energetic demand of about 1 metabolic equivalent (MET) per minute or 3.5 mL/Kg.min of oxygen uptake. Exercise test was conducted between 8 and 14 min. After 2 min of baseline measurements, speed (miles/h) and/or slope were progressively increased. The completion of the test occurred when, despite verbal encouragement, the subject could no longer maintain the exercise. The following criteria was used to define maximal effort: 1) Peak heart rate greater than 95% age-predicted and 2) maximal respiratory exchange ratio > 1.10 [4].

The subjects were instructed to refrain from eating 2 h before the test, and to abstain from caffeine and physical activity at least 24 h leading up to the test. All patients were studied at a controlled-temperature (20°–22°). Oxygen consumption (VO_2) and carbon dioxide output were analyzed by means of breath-by-breath and expressed as 30-s averages using an indirect calorimetry system (Vmax, Mod. 29 S serie YL012278C – Sensor Medics Corporation, California, USA). Before each test, the gas analyzers were calibrated using gases of known concentration, while the flow meter was calibrated using a 3-L syringe. The ventilator parameters during graded exercise were collected after complete adaptation of the mouthpiece and nose clip. Heart rate was continuously recorded at rest and during the graded exercise testing using a 12-lead digital electrocardiogram (EKG) and software ERGO PC 13, MICROMED Biotechnology Ltda., Brasília – DF – Brazil. The peak oxygen consumption (VO_2 peak) was considered the maximum attained VO_2 at the end of the exercise period.

The ventilatory anaerobic threshold (VAT) was determined at the break-point between the increase in the carbon dioxide output and VO_2 or at the point at which the ventilatory equivalent for oxygen and end tidal oxygen partial pressure curves reached their respective minimum values and began to rise without a concomitant rise in ventilatory equivalent for carbon dioxide [28,29]. Individual data were examined independently by 2 investigators experienced in determining VAT. The respiratory compensation point (RCP) was determined at the point where the ventilatory equivalent of carbon dioxide (VE/VCO_2) reached its lowest level before starting to increase and where the end tidal carbon dioxide pressure ($PetCO_2$) reached its maximum value before decreasing [4].

Heart rate recovery evaluation

Heart rate recovery was calculated by the difference between maximal heart rate obtained at the peak of exercise and heart rate at first and second minutes of recovery [5]. During the recovery period, the treadmill was maintained at 2.0 mph/0.0% for 2 min.

Muscle sympathetic nerve activity evaluation

Muscle sympathetic nerve activity (MSNA) was recorded directly from the peroneal nerve using the microneurography technique. Multiunit postganglionic muscle sympathetic nerve recordings were made using a tungsten microelectrode (tip diameter: 5–15 µm). The signals were amplified by a factor of 50 000–100 000 and band passed filtered (700–2 000 Hz). For recordings and analysis, nerve activity was rectified and integrated (time constant: 0.1 s) to obtain a mean voltage display of sympathetic nerve activity that was recorded on paper. All of the recordings of MSNA met previously established and described criteria. MSNA was quantified as burst frequency (bursts per minute). The reproducibility of MSNA measured at different time intervals in the same individual expressed as bursts/min is r = 0.88 [9].

Experimental protocol

All studies were performed in a quiet, temperature controlled (21 °C) room in the morning at approximately the same time of day. They were instructed to restrain from exercise 48 h before the experimental protocol. After EKG leads were placed on the chest a tungsten microelectrode was attached to the peroneal nerve on the right leg. After that, the subject rested quietly for 15 min. MSNA were then recorded for 6 min.

Statistical analysis

Data are presented as mean ± SE. Possible differences between groups in physical characteristics, MSNA, HRR and VO_2 at VAT, RCP and peak were analyzed by means of an unpaired Student's t-test. Pearson correlation coefficient was used to test the correlation between MSNA with HRR and MSNA with peak VO_2. Significant differences were assumed to be at $P \leq 0.05$.

Results

Baseline data

Physical characteristics and neural measures are shown in **Table 1**. There were no significant differences between AASNU and AASU in age, weight, height and resting heart rate. MSNA was higher in AASU compared to AASNU.

Exercise measures

Peak heart rate was >95% and respiratory exchange ratio (RER) >1.10, which showed the effectiveness of the maximal cardiopulmonary exercise test in all individuals involved in the study. VO_2 at VAT, RCP and peak of exercise were significantly lower in AASU than AASNU individuals (**Table 2**). HR at RCP was lower in AASU group when compared to AASNU group, but no significant differences between groups were found at peak of exercise. HR reduction both at first minute (ΔHR = 21 ± 2 vs. 27 ± 2 beats, P = 0.02) and second minute (ΔHR = 37 ± 4 vs. 45 ± 2 beats, P = 0.05) of recovery period was significantly lower in AASU than in AASNU (**Fig. 1**). There was a significant difference in oxygen pulse at VAT in AASU compared to AASNU (15.2 ± 0.7 vs. 19.4 ± 1.6 mL/beat, P = 0.03). There were no significant differences in oxygen pulse at RCP and peak between groups (RCP: 19.5 ± 1.0 vs. 22.1 ± 1.6 and Peak: 20.6 ± 0.9 vs. 22.6 ± 1.5 mL/beat). Further analysis showed an inverse correlation between HRR and MSNA (r = −0.64, P = 0.02; **Fig. 2**) and a direct correlation between HRR at first minute and peak VO_2 (r = 0.70, p = 0.01; **Fig. 3**) and HRR at second minute and peak VO_2 (r = 0.62, P = 0.02; **Fig. 4**).

Discussion

The main findings of this study are that strength-trained athletes with self-administration of AAS have impaired HRR during post-exercise period and reduced functional capacity when compared to age-paired strength-trained athletes with no self-administration of AAS.

Heart rate reduction after an acute bout of exercise has been used as an important tool to assess cardiac parasympathetic recovery [5]. Moreover, impaired heart rate recovery has been associated with cardiovascular disease [16]. For example, patients with myocardium infarction and heart failure show a delay in heart rate reduction during post-exercise period [10]. Our study extends the knowledge that chronic AAS cause significant attenuation in heart rate recovery in young strength-trained athletes associated with AAS misuse. Thus, it is reasonable to suggest that young individuals with self-administration of AAS may be under increased risk for cardiovascular events. Some investigators have reported that decreased heart

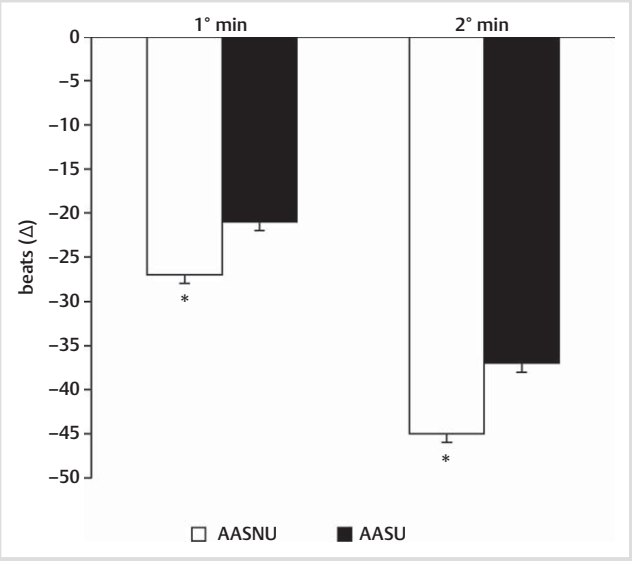

Fig. 1 Delta heart rate recovery at first and second minute during the post-exercise period of maximal cardiopulmonary exercise test in strength-trained young athletes with and without anabolic steroids self-administration. *p < 0.05 vs. AASU.

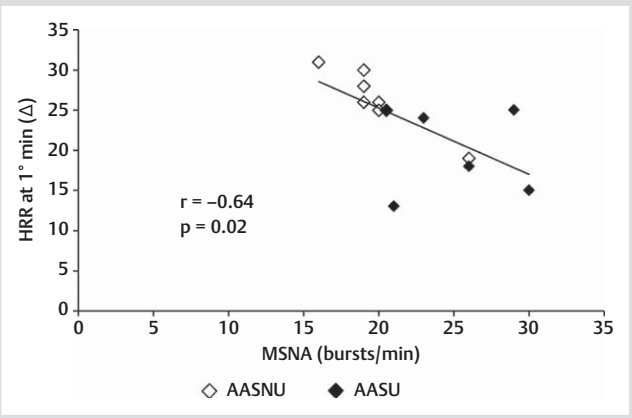

Fig. 2 Association between MSNA and heart rate recovery during the post-exercise period of maximal cardiopulmonary exercise test in strength-trained young athletes with and without anabolic steroids self-administration (n = 13).

Table 1 Physical characteristics and neural measures in anabolic androgenic steroids users and anabolic androgenic steroids nonusers.

	AASU	AASNU	p
N	10	10	
age, years	34 ± 3	29 ± 2	0.21
weight, kg	87.9 ± 2.2	82.2 ± 4.4	0.26
height, cm	176 ± 0.02	177 ± 0.03	0.84
heart rate (bpm)	68 ± 2	66 ± 3	0.61
MSNA, bursts/min	29 ± 3	20 ± 1	0.01

Values are mean ± SE. MSNA, muscle sympathetic nerve activity; AASU, anabolic androgenic steroids; AASNU, anabolic androgenic steroids nonusers

Table 2 Cardiorespiratory variables at VAT, RCP and peak of exercise in anabolic androgenic steroids users (AASU) and anabolic androgenic steroids nonusers (AASNU).

	VAT		RCP		Peak	
	AASNU	AASU	AASNU	AASU	AASNU	AASU
HR (bpm)	136 ± 6	122 ± 5	179 ± 2	163 ± 5*	188 ± 3	180 ± 3
O_2 pulse (mL/beat)	19.4 ± 1.6	15.2 ± 0.7*	22.1 ± 1.6	19.5 ± 1.0	22.6 ± 1.5	20.6 ± 0.9
RER	0.86 ± 0.02	0.92 ± 0.02	1.10 ± 0.02	1.10 ± 0.03	1.24 ± 0.04	1.24 ± 0.03
VO_2 (mL/kg/min)	32.50 ± 3.0	21.50 ± 1.70*	47.90 ± 1.60	36.20 ± 2.10*	52.70 ± 1.68	43.66 ± 2.24*
VO_2 (%)	61 ± 5	49 ± 2*	91 ± 2	83 ± 2*		
work load (watts)					326 ± 13	312 ± 19

Values are means ± SE. VAT, ventilatory anaerobic threshold; RCP, respiratory compensation point; HR, heart rate; RER, respiratory exchange ratio; VO_2, oxygen consumption; O_2 pulse, oxygen pulse. *vs. AASNU (*P* < 0.05)

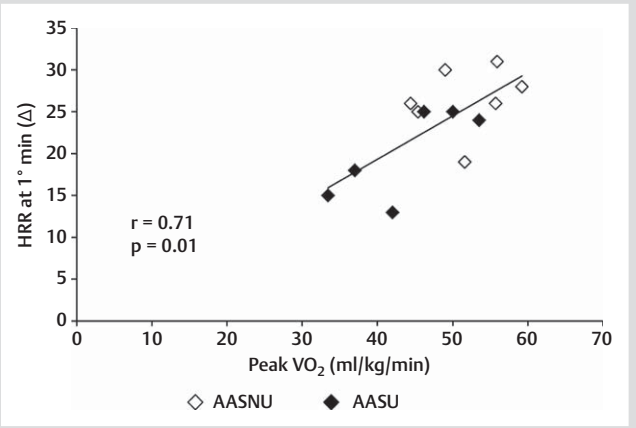

Fig. 3 Association between peak VO_2 and heart rate recovery at first minute during the post-exercise period of maximal cardiopulmonary exercise test in strength-trained young athletes with and without anabolic steroids self-administration (n = 13).

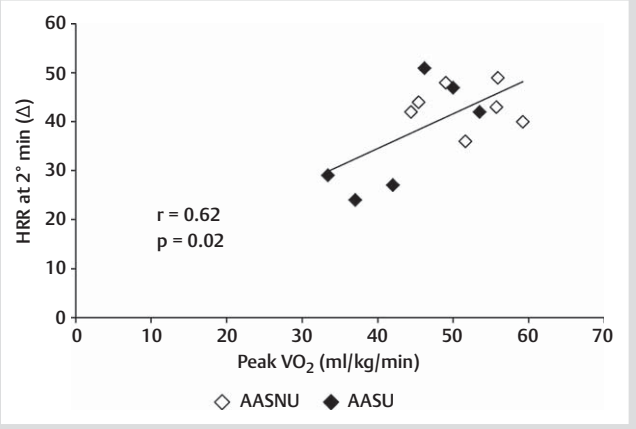

Fig. 4 Association between peak VO_2 and heart rate recovery at second minute during the post-exercise period of maximal cardiopulmonary exercise test in strength-trained young athletes with and without anabolic steroids self-administration (n = 13).

rate recovery is an independent predictor of death for all causes in the general population [5]. Although the reduction in heart rate in our study did not reach the critical levels of 12 beats at first minute [5] and 22 beats at second minute [26] after cessation of exercise, it is significantly decreased compared to age-paired strength-trained athletes without self-administration of AAS.

The mechanisms involved in the impaired HRR are not within the scope of our study. However, there are some potential candidates to explain this response in young strength-trained athletes with AAS self-administration. Since heart rate descent during post-exercise period has been associated with parasympathetic control, it is legitimate to attribute the delay in HRR to an impaired cardiac vagal control [5]. Alternatively, the augmented sympathetic activity may counteract the vagal function control. The present study supports this notion. MSNA is significantly increased in the AAS users. Moreover, we found an inverse correlation between HRR and MSNA, which is suggestive of cardiac autonomic imbalance with prevalence of sympathetic outflow. In a previous study, in an animal model, chronic administration of supraphysiological doses of nandrolone decanoate reduced heart rate variability of both time-domain and frequency-domain. In addition, the ratio between low frequency and high frequency, which is related to sympathetic index, tended to be higher in the anabolic group [20]. There is evidence that anabolic androgen steroids act on specific androgen receptors in the central cardiovascular regulatory region stimulating the sympathetic activity [21]. The chronic hypothalamic stimulation can lead to autonomic cardiovascular instability [7] and hypertension. Increased blood pressure levels have been reported in AAS users. These hemodynamic alterations are, in fact, due to changes in sympathetic control, since an increase in blood pressure and electrocardiographic alterations are prevented by C2 spinal section and stellate ganglionectomy, but not by vagotomy [25]. It is possible that the increase in sympathetic nerve activity and in consequence the elevation in blood pressure in AASU is due to arterial baroreflex impairment. A previous study has linked augmented sympathetic outflow and high blood pressure to reduced baroreflex sensitivity in hypertensive patients [13]. This is an interesting topic for future investigations.

Surprisingly, there were no differences in heart rate response during exercise between AASU and AASNU. A previous study demonstrated that the tachycardia during progressive exercise is mediated by vagal withdrawal and sympathetic activation [17]. These findings favor the idea that both vagal and sympathetic cardiac controls during exercise are preserved in strength-trained young athletes with AAS use. Likewise, no alteration in peak oxygen pulse was found in the present study, which suggests that systolic cardiac function is preserved in AASU.

Another interesting finding in the present study was the reduced VO_2 throughout cardiopulmonary exercise test in AASU compared to AASNU. There is no definitive explanation for this finding, but it raises the possibility that the lower peak VO_2 may be associated with reduced muscle blood flow in AASU [3]. It is known that aerobic exercise can enhance the VO_2 consumption but to eliminate this influence both groups did not practice aerobic training. In fact, in a recent study we reported that forearm vascular conductance was significantly lower in individuals with self-administration of AAS compared to individuals with no AAS [3]. Reduction in muscle blood flow during exercise may restrain energy supply to the working muscle and consequently decrease the functional capacity. Previous studies demonstrated that high doses of nandrolone may reverse the beneficial effect caused by physiological doses of testosterone on vascular level via endothelial release of nitric oxide and inhibition of vascular smooth muscle [23,30].

In conclusion, AAS delays HRR during post-exercise period, increases MSNA and decreases peak VO_2 in young strength-trained AASU. The exacerbated sympathetic outflow associated with a lower parasympathetic activation after maximal exercise, showed by impaired heart rate recovery, strengthens the idea of autonomic imbalance in AASU. These findings strongly suggest that AAS increases cardiovascular risk in young individuals.

Limitations

We recognize some limitations in our study. The variation in AAS may limit our interpretation and extrapolation to other subgroups. We were dealing with young individuals. Thus, the impact of AAS in HRR in older individuals is unknown. The same idea can be used for gender. There is no guarantee that the effects of AAS on HRR and functional capacity in women are similar to those found in men. The difference in number of indi-

viduals in our correlation (HRR vs. MSNA) is due to difficulty in the microneurography technique where sometimes the nerve signal is not appropriate and it is impossible to do this technique during cardiopulmonary exercise testing.

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