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The impact of anabolic androgenic steroids abuse and type of training on left ventricular remodeling and function in competitive athletes

Uticaj zloupotrebe androgenih anaboličkih steroida i tipa treninga na remodelovanje i funkciju leve komore kod elitnih sportista

Ivan Ilić*, Vitomir Djordjević†, Ivan Stanković*, Alja Vlahović-Stipac*, Biljana Putniković*, Rade Babić‡, Aleksandar N. Nešković*

***Department of Cardiology, Clinical Hospital Center Zemun, Faculty of Medicine, University of Belgrade, Belgrade, Serbia; †Health Center Dr. Ristić, Belgrade, Serbia; ‡Dedinje Cardiovascular Institute, Belgrade, Serbia**

Abstract

Background/Aim. Long-term intensive training is associated with distinctive cardiac adaptations which are known as athlete's heart. The aim of this study was to determine whether the use of anabolic androgenic steroids (AAS) could affect echocardiographic parameters of left ventricular (LV) morphology and function in elite strength and endurance athletes. **Methods.** A total of 20 elite strength athletes (10 AAS users and 10 non-users) were compared to 12 steroid-free endurance athletes. All the subjects underwent comprehensive standard echocardiography and tissue Doppler imaging. **Results.** After being indexed for body surface area, both left atrium (LA) and LV end-diastolic diameter (LVEDD) were significantly higher in the endurance than strength athletes, regardless of AAS use ($p < 0.05$, for both). A significant correlation was found between LA diameter and LVEDD in the steroid-free endurance athletes, showing that 75% of LA size variability depends on variability of LVEDD ($p < 0.001$). No significant differences in ejection fraction and cardiac output were observed among the groups, although mildly reduced LV ejection fraction was seen only in the AAS users. The AAS-using strength athletes had higher A-peak velocity when compared to steroid-free athletes, regardless of training type ($p < 0.05$ for both). Both AAS-using and AAS-free strength athletes had lower e' peak velocity and higher E/e' ratio than endurance athletes ($p < 0.05$, for all). **Conclusions.** There is no evidence that LV ejection fraction in elite athletes is altered by either type of training or AAS misuse. Long-term endurance training is associated with preferable effects on LV diastolic function compared to strength training, particularly when the latter is combined with AAS abuse.

Key words:
athletes; substance-related disorders; androgens; ventricular remodeling; risk assessment; echocardiography.

Apstrakt

Uvod/Cilj. Dugotrajni intenzivni trening povezan je sa adaptivnim promenama srčanog mišića poznatim kao sportsko srce. Cilj rada bio je da se utvrdi uticaj primene anaboličkih androgenih steroida (AAS) na ehokardiografske parametre morfologije i funkcije leve komore (LV) kod elitnih sportista koji se bave sportovima snage i izdržljivosti. **Metode.** Dvadeset elitnih sportista snage (10 korisnika AAS i 10 onih koji ne koriste AAS) upoređeni su sa 12 sportista izdržljivosti koji ne koriste AAS. Svi ispitanici bili su podvrgnuti standardnom ehokardiografskom pregledu sa tkivnim Dopler-om. **Rezultati.** Nakon indeksiranja prema telesnoj površini, leva pretkomora (LA) i end-dijastolni prečnik leve komore (LVEDD) bili su značajno veći kod sportista izdržljivosti nego kod sportista snage, bez obzira na uzimanje AAS ($p < 0,05$, za oba). Nađena je značajna korelacija između veličine LA i LVEDD kod sportista izdržljivosti koji ne uzimaju AAS, koja pokazuje da 75% varijablnosti veličine LA zavisi od varijabilnosti LVEDD ($p < 0,001$). Nije pokazana značajna razlika u ejekcionoj frakciji (EF) LV (LVEF) i minutnom volumenu između grupa, mada je blago snižena LVEF viđena samo kod sportista koji koriste AAS. Sportisti snage koji koriste AAS imali su veću vrednost pika A-talasa u poređenju sa sportistima koji ne koriste AAS, bez obzira na tip treninga ($p < 0,05$ za oba). Sportisti snage, bez obzira na primenu AAS, imali su niže vrednosti brzine e' talasa i veći E/e' odnos u poređenju sa sportistima izdržljivosti ($p < 0,05$ za sve). **Zaključak.** Nema dokaza da je primena AAS povezana sa promenom LVEF, bez obzira na tip treninga. Dugoročni trening izdržljivosti povezan je sa povoljnim efektima na dijastolnu funkciju LV u poređenju sa treningom snage, pogotovu ako je trening snage povezan sa zloupotrebom AAS.

Ključne reči:
sportisti; zloupotreba supstanci; androgeni; srce, remodelovanje; rizik, procena; ehokardiografija.

Correspondence to: Ivan Ilić, Department of Cardiology, Clinical Hospital Center Zemun, Vukova 9, 11 080 Belgrade, Serbia. Phone: +381 11 377 27 60, +381 64 137 44 55; Fax: +381 11 316 88 78. Email: ivan1ilic@yahoo.com

Introduction

Long-term intensive training is associated with distinctive cardiac adaptations which are known as athlete's heart [1]. Although a certain relationship between the type of training (endurance *versus* strength exercise) and cardiac remodeling has been documented, the nature and magnitude of training-induced changes are still the subject of debate.

Anabolic androgenic steroids (AAS) have been abused by both professional and recreational athletes to increase muscle mass and improve performance [2]. The use of AAS is particularly prevalent among powerlifters and bodybuilders – as many as 55% of elite powerlifters admitted using these agents [3, 4]. In contrast to numerous documented toxic and hormonal effects of AAS, their impact on left ventricular (LV) structure and function was not been yet completely understood. In animal model, AAS have been shown to induce cardiac renin-angiotensin system, increase cardiac collagen content and impair the beneficial effects of training [5]. In competitive athletes, self-administration of AAS has been linked to serious cardiac adverse events, including sudden cardiac death [6, 7], although reports on their impact on cardiac morphology and function varied [8].

We hypothesized that there would be the differences in echocardiographic parameters of LV morphology and function between strength and endurance athletes and that the magnitude of these differences would be affected by AAS abuse. To test this hypothesis, we compared elite strength athletes using or not using AAS to steroid-free endurance athletes.

Methods

A total of 22 elite male athletes, aged 22–40 years, were recruited from the national power-lifting, bodybuilding, wrestling and running clubs. All the subjects gave written informed consent and were divided into three groups.

The group I consisted of 10 strength athletes (6 powerlifters and 4 bodybuilders) who reported both past and current self-administration of AAS. All the subjects used the combination of oral and injectable substances (methandienone, stanozolol, nandrolone decanoate and testosterone) for at least 3 years, in cycles lasting between 7 and 14 weeks. The group II consisted of 10 strength athletes (4 bodybuilders and 6 wrestlers) who denied taking AAS. They were all negative on several doping tests during and out of competition. The group III consisted of 12 endurance athletes (long-distance runners) who did not use AAS. They were also negative on doping tests performed during professional career. None of the subjects in either group had a history of cardiovascular or any other organic system disorder and were not taking any medications.

Anthropometric measurements

Body mass and height were measured using a balance beam scale and a height gauge, respectively. Lean body mass was calculated according to the formula provided by Hallynck et al. [9], whereas body surface area was calculated using the Mosteller formula [10].

Electrocardiography and blood pressure measurement

Twelve-channel electrocardiography (ECG) recording was done prior to blood pressure measurement and echocardiographic examination.

Blood pressure measurements were done in sitting position, using a cuff adjusted to upper arm circumference. The mean value of two measurements on both arms, 10 min apart, was recorded.

Echocardiographic examination

All examinations were done in supine left decubitus position using a Hewlett–Packard Sonos 2500 machine (Andover, MA, USA), with a 2.5 MHz transducer. Echocardiograms consisted of two-dimensional, M-mode, Doppler flow measurements and tissue Doppler imaging (TDI) from standard parasternal and apical positions. All measurements were made by a single experienced observer (VD) who was blinded to the subjects' data.

M-mode measurements were performed for the assessment of LV diastolic and systolic diameters, according to the most recent guidelines [11] and presented both as raw data and adjusted for body surface area (BSA) when appropriate. Measurements obtained with this method served for calculation of LV mass, using the Devereux et al. formula [12]. Relative wall thickness (RWT) was calculated when the sum of interventricular septal wall (IVS) thickness and posterior wall (PW) thickness was divided by LV end-diastolic diameter (LVEDD).

For the assessment of systolic function LV volumes were measured by tracing the endocardial border in apical four- and two-chamber view. The ejection fraction was estimated using the Simpson's biplanar method [11]. Cardiac output was determined by calculating the product of stroke volume and heart rate that was obtained from the final loop of each study.

Pulsed-Doppler LV inflow recordings were made in the apical four-chamber view, with the sample volume placed at the tips level of the mitral valve. Early (E) and atrial (A) peak velocities, E-wave deceleration time and isovolumetric relaxation time were measured. TDI recordings were performed in apical four-chamber view, with the pulse-wave Doppler sample volume placed at the septal and lateral side of mitral annulus. Longitudinal tissue Doppler velocities of a systolic wave (S) and 2 diastolic waves – early (e') and atrial (a') – were reported as the mean of 3 consecutive cardiac cycles. Most recent guidelines on the chamber quantification and the assessment of LV diastolic function were used to define a reference range for all echocardiographic parameters [11, 13].

Statistical analysis

Data are expressed as mean ± standard deviation. Comparison between the groups was performed using the analysis of variance or a Kruskal–Wallis test, with Bonferroni correction for multiple comparisons. The relations between selected measures were calculated by the linear regression analysis and correlation analysis using the Pearson or Spearman's method. A p-value of < 0.05 was considered significant.

Results

The athletes from the 3 groups were comparable for age, body mass, BSA, lean body mass and duration of training (Table1).

After being indexed for BSA, both left atrium (LA) dimension and LVEDD were higher in the endurance than AAS-using strength athletes. Further, a significant correlation between LA diameter and LVEDD was found, but only in the endurance athletes, in whom more than 75% of LA

Table 1

Mean clinical characteristics of the study participants

Characteristics	Athletes type		
	AAS-using strength athletes (n = 10), $\bar{x} \pm SD$	AAS-free strength athletes (n = 10), $\bar{x} \pm SD$	AAS-free endurance athletes (n = 12), $\bar{x} \pm SD$
Age (yrs)	27 ± 6	29 ± 6	27 ± 4
Height (cm)	181 ± 5	179 ± 4	190 ± 11*†
Body mass (kg)	100 ± 19	85 ± 18	87 ± 18
Body surface area (m^2)	2.2 ± 0.2	2.1 ± 0.2	2.1 ± 0.3
Lean body mass (kg)	69 ± 8	64 ± 8	69 ± 12
Heart rate (beats/min)	77 ± 16	68 ± 15	56 ± 8*
PR interval (ms)	150 ± 22	161 ± 25	174 ± 19*
Systolic BP (mmHg)	133 ± 23	128 ± 15	118 ± 12
Diastolic BP (mmHg)	88 ± 14	80 ± 11	71 ± 8*
Duration of training (yrs)	10.1 ± 3.0	13.4 ± 4.2	13.6 ± 2.8
Intensity of training (hrs/week)	11.6 ± 3.0	10.1 ± 3.4	20.8 ± 15.7†

AAS – anabolic androgenic steroids; BP – blood pressure;
***significantly different from AAS-using strength athletes ($p < 0.05$);**
†significantly different from AAS-free strength athletes ($p < 0.05$).

Resting heart rate and diastolic blood pressure were significantly lower in the endurance than the AAS-using strength athletes, with no significant difference between ASS-free athletes.

Standard echocardiographic parameters

The standard echocardiographic parameters are shown in Table 2. No significant differences in wall thickness were found among the 3 groups.

size variability ($R^2 = 0.761$) depended on variability of LVEDD (Figure 1A). It was also shown for this group that each increase of 1 mm in LVEDD was associated with approximately 0.7 mm increase in LA diameter (95% confidence interval (CI) 0.44 to 1.01, $p < 0.001$). A trend towards a significant correlation between LVEDD and LA diameter was noted in the AAS-free strength athletes (Figure 1B), while such correlation was not observed in the AAS-using strength athletes (Figure 1C).

Table 2

M-mode and two-dimensional echocardiographic measurements in the study participants

Parameter	Athletes type		
	AAS-using strength athletes (n = 10), $\bar{x} \pm SD$	AAS-free strength athletes (n = 10), $\bar{x} \pm SD$	AAS-free endurance athletes (n = 12), $\bar{x} \pm SD$
LVEDD (mm)	49.9 ± 4.8	52.2 ± 3.2	57.0 ± 3.9*†
LVEDD per unit BSA (mm/m^2)	22.5 ± 3.0	25.7 ± 2.3	27.0 ± 3.3*
LA (mm)	34.2 ± 5.2	34.9 ± 1.9	39.3 ± 4.56*
LA per unit BSA (mm/m^2)	15.3 ± 2.3	17.2 ± 1.9	18.6 ± 2.7*
LV mass (g)	194 ± 44	180 ± 43	239 ± 58*†
LV mass per unit BSA (g/m^2)	87 ± 16	88 ± 21	114 ± 33*
IVS thickness (mm)	10.7 ± 2.2	9.7 ± 1.2	10.7 ± 1.7
PW thickness (mm)	10.3 ± 2.1	8.9 ± 1.3	9.7 ± 1.4
Relative wall thickness	0.41 ± 0.12	0.35 ± 0.04	0.36 ± 0.06

AAS – anabolic androgenic steroids; BSA – body surface area; IVS – interventricular septum; LA – left atrium; LV – left ventricle; LVEDD – left ventricular end-diastolic diameter; PW – posterior wall; *significantly different from AAS-using strength athletes ($p < 0.05$); †significantly different from AAS-free strength athletes ($p < 0.05$).

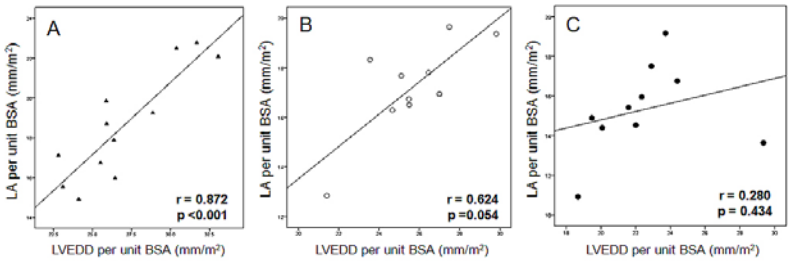

Fig. 1 – Correlation between the left ventricular end-diastolic diameter (LVEDD) and left atrial size (LA), both indexed for body surface area (BSA).

Left ventricular systolic function

No significant differences in ejection fraction, cardiac output and cardiac index were observed among the groups (Table 3). However, 3 of the 10 AAS users had LV ejection fraction below 55%, while all AAS-free athletes had normal LV ejection fraction (≥ 55%). Peak systolic velocity (S) at septal level was significantly higher in the endurance than AAS-free strength athletes.

and higher E/e' ratio than the endurance athletes, when measurements were done at lateral wall level (Table 3). Peak e' velocities at lateral wall level were within reference range in all endurance athletes, while in 30% of AAS-using strength athletes laid outside the normal range.

The 95% confidence itervals (CI) for the peak lateral e' velocity in the endurance steroid-free and steroid-using strength afthletes, compared to the reference range for different age groups are shown in Figure 2.

Table 3

Echocardiographic data on the left ventricular systolic and diastolic function

Parameter	Athletes type		
	AAS-using strength athletes (n = 10), $\bar{x}$ ± SD	AAS-free strength athletes (n = 10), $\bar{x}$ ± SD	AAS-free endurance athletes (n = 12), $\bar{x}$ ± SD
Ejection fraction (%)	57 ± 5	59 ± 4	59 ± 4
Stroke volume (mL)	107 ± 24	112 ± 15	129 ± 17*
Cardiac output (L/min)	8.1 ± 1.7	7.6 ± 1.7	7.2 ± 1.3
Cardiac index (L/min/m^2)	3.6 ± 0.9	3.4 ± 0.7	3.4 ± 0.4
Transmitral Doppler			
peak E velocity (cm/s)	84 ± 9	72 ± 15	74 ± 12
peak A velocity (cm/s)	52 ± 10$^{\Delta\square}$	40 ± 10	39 ± 12
peak E/A ratio	1.7 ± 0.4	1.9 ± 0.7	2.1 ± 0.5
e wave DT (ms)	218.1 ± 36.3	233.4 ± 35.1	244.3 ± 32.2
IVRT (ms)	80 ± 8	78 ± 9	78 ± 6
TDI – septal mitral annulus			
s peak (cm/s)	8.3 ± 1.3	7.9 ± 0.64	9.3 ± 1.3†
e' peak (cm/s)	12.1 ± 2.6	12.4 ± 2.7	13.4 ± 2.4
a' peak (cm/s)	8.8 ± 1.4	8.6 ± 2.0	8.4 ± 1.9
E/a' ratio	9.8 ± 1.9	8.9 ± 2.8	9.2 ± 2.5
E/e' ratio	7.2 ± 1.4	6.0 ± 1.8	5.7 ± 0.9*
TDI – lateral mitral annulus			
s peak (cm/s)	10.8 ± 2.0	9.9 ± 1.9	10.6 ± 3.5
e' peak (cm/s)	14.8 ± 2.6	16.4 ± 2.2	19.2 ± 2.6*†
a' peak (cm/s)	8.7 ± 1.8	9.0 ± 1.8	8.4 ± 2.6
E/a' ratio	10.0 ± 2.2	8.8 ± 3.6	9.4 ± 3.1
E/e' ratio	5.2 ± 0.7	5.0 ± 1.0	3.9 ± 0.8*†

AAS – anabolic androgenic steroids; DT – deceleration time; *significantly different from the AAS-using strength athletes ($p < 0.05$); †significantly different from the AAS-free strength athletes ($p < 0.05$); $^{\Delta}$significantly different from the AAS-free endurance athletes ($p < 0.05$); $^{\square}$significantly different from the AAS-free strength athletes ($p < 0.05$).

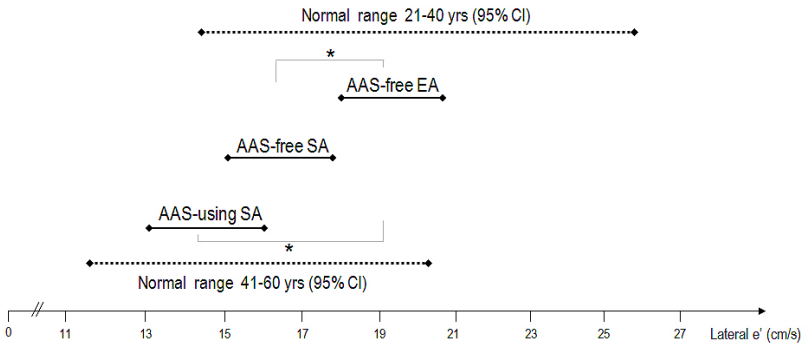

Fig. 2 – The 95% confidence intervals (CI) for the peak lateral e' velocity in the endurance, steroid-free and steroid-using strength athletes, compared to the reference range for different age groups. Normal values (given as 95% CI) are adopted from the most recent guidelines 13. AAS – anabolic androgenic steroids; EA – endurance athletes; SA – strength athletes; *denotes p < 0.05.

Transmitral Doppler velocities and tissue Doppler Imaging data

The AAS-using strength athletes had higher peak A-wave velocity when compared to both endurance and AAS-free strength athletes (Table 3). Regardless of AAS misuse, the strength athletes had significantly lower e' peak velocity

Discussion

Our data indicate that both type of training and AAS abuse may affect LV diastolic function. Although paradoxically associated with increased LA size, it appears that a long-term AAS-free endurance training may have preferable effects on LV filling and relaxation parameters, compared to

strength training, particularly in the presence of AAS abuse. No significant differences between the elite strength and endurance athletes were found for systolic function indices, although mildly reduced LV ejection fraction was seen only in AAS users.

Parameters of LV diastolic function

Reflecting the LA-LV pressure gradient during late diastole, mitral A-wave velocity is affected by LV compliance and LA contractile function [13]. In line with this, a significantly higher peak A-velocity in AAS abusers, regardless the type of training, might indicate a relationship between AAS misuse and decreased LV compliance.

On the other hand, peak e' velocity, a parameter of LV relaxation, did not significantly differ between strength athletes with respect to AAS abuse. However, abnormally low values of this parameter were observed only in the AAS abusers – in 30% of AAS-using strength athletes (aged 27–31 years), e' velocities values were as low as they were measured in individuals aged between 41–60 years (Figure 2).

Although all the AAS-free athletes had normal e' velocity and E/e' ratio values, significant differences related to the type of training were observed. The peak e' velocity was higher and E/e' ratio lower in the endurance than the strength athletes, suggesting that strength training may not produce equally favorable effects on diastolic function as endurance exercise.

Mechanisms responsible for the possible alterations of LV diastolic function with AAS abuse are poorly understood. The transient increase in blood pressure, also observed among the AAS users in this study, may negatively alter LV diastolic function, but it is usually mild and its clinical significance remains most likely modest [14].

On the other hand, since no increase in LV wall thickness was found, AAS-mediated changes in myocardial intrinsic properties might be responsible for the differences in LV diastolic function.

Hence, *in vitro* and histological studies have shown that an increase in myocardial collagen content might occur as a repair mechanism against AAS-induced myocardial damage [15], and also that chronic administration of 17a-methyltestosterone, frequently used anabolic steroid, may reduce LV compliance [16].

Data from previous (small-scale) studies are widely inconsistent, showing either negative [17–20] or no effect [21–23] of AAS on LV diastolic function. The inconsistency could be explained by methodological differences (pulsed-wave *vs* tissue Doppler imaging) and by the lack of power to detect true affects of AAS.

Relationship between LA remodeling and LV diastolic function

In non-athletic population, dilatation of LA reflects the cumulative effects of LV filling pressures and is an independent predictor of death, heart failure, atrial fibrillation and stroke [24]. Our data support the belief that LA enlargement in athletes should be regarded as a physiological adaptation to exercise conditioning [25], particularly in endurance athletes. We demonstrated that the variability of LA size was predominantly influenced by LV dimension, but only in the absence of AAS misuse. The correlation between the LVEDD and LA dimension was statistically significant in AAS-free endurance athletes and borderline significant in the group of AAS-free strength athletes. A lack of correlation between LA size and LVEDD in AAS-using strength athletes may therefore be reflective of detrimental effects of AAS on LV diastolic function, regardless of training type. In line with this, the endurance athletes had the largest LA dimension but the lowest E/e' ratio, suggesting that LA enlargement should not be considered pathological in these athletes. Conversely, when LA enlargement occurs in strength athletes, particularly in the presence of AAS abuse, it should not be entirely ascribed to a long-term strength training, as it could also reflect the disturbances of LV diastolic function.

Left ventricular remodeling, type of training and AAS abuse

LV end-diastolic dimensions and LV mass, after being indexed for BSA, were higher in the endurance than in the AAS-using athletes, with no differences between the strength athletes with respect to AAS abuse. Our data are consistent with previous echocardiographic and magnetic resonance imaging studies showing that long-term endurance training has the strongest impact on LV cavity size, mass and thickness while strength training does not necessarily induce wall thickening [18, 26, 27].

A significant increase in LV mass related to AAS administration was observed in some studies [20], but not confirmed by others [21–23].

Left verticular systolic function

Even though we did not observe a significant difference in LVEF among the 3 groups, a mild reduction of LVEF was detected only in the AAS users. Results from recent studies suggest that systolic dysfunction associated with AAS abuse might be subclinical and advanced echo techniques are needed for its detection [28, 29]. It has been shown that chronic misuse of AAS is associated with reduced peak systolic strain, and strongly correlated with mean dosage and duration of AAS use [28]. However, it has been recently reported that, on top of reduced peak strain values, long-term AAS use might even be associated with a clinically relevant reduction in LV ejection fraction [29].

Study limitations

Our study has some important limitations. First, like most previous studies, we did not perform plasma or urine assessment for drug levels and the history of AAS use was self-reported by the athletes included in the study. Although the results should be interpreted cautiously, we believe that the observed differences in athletes' clinical characteristic support the accuracy of athletes' statements regarding AAS use.

Both resting heart rate and diastolic blood pressure, which increase had been previously linked to AAS abuse [30], were highest in the AAS-using athletes, with no difference

between the AAS-denying endurance and strength athletes. The elevation of blood pressure is usually transient, returning to basal levels several weeks or months after drug discontinuation [31] which might explain why the AAS users had not been diagnosed of having hypertension during regular physical examinations.

Second, since AAS abuse is a very sensitive matter in professional sports, particularly among elite athletes, we recruited a small number of subjects. However, this limitation is more likely to produce type II errors (false-negative results) than type I errors (false-positive results) due to a reduced statistical power. On the other hand, type II errors might explain why several nonsignificant trends were observed – there were striking differences in mean values among the 3 groups for several clinical and echocardiographic variables, but with large variance. Therefore, further studies with adequate power are required.

Conclusion

There is no evidence that LV ejection fraction in elite athletes is altered by either type of training or AAS misuse. Long-term endurance training is associated with preferable effects on LV diastolic function compared to strength training, particularly when the latter is combined with AAS abuse.

R E F E R E N C E S

1. *Fagard R.* Athlete's heart. Heart 2003; 89(12): 1455−61.
2. *Kutscher EC, Lund BC, Perry PJ.* Anabolic steroids: a review for the clinician. Sports Med 2002; 32(5): 285−96.
3. *Yesalis CE, Herrick RT, Buckley WE, Friedl KE, Brannon D, Wright JE.* Self-reported use of anabolic-androgenic steroids by elite power lifters. Phys Sportmed 1988; 16(12): 91−100.
4. *Tricker R, O'Neill MR, Cook D.* The incidence of anabolic steroid use among competitive bodybuilders. J Drug Educ 1989; 19(4): 313−25.
5. *Rocha FL, Carmo EC, Roque FR, Hashimoto NY, Rossoni LV, Frimm C,* et al. Anabolic steroids induce cardiac renin-angiotensin system and impair the beneficial effects of aerobic training in rats. Am J Physiol Heart Circ Physiol 2007; 293(6): 3575−83.
6. *Ahlgrim C, Guglin M.* Anabolics and cardiomyopathy in a bodybuilder: case report and literature review. J Card Fail 2009; 15(6): 496−500.
7. *Hausmann R, Hammer S, Betz P.* Performance enhancing drugs (doping agents) and sudden death: a case report and review of the literature. Int J Legal Med 1998; 111(5): 261−4.
8. *Krieg A, Scharhag J, Kindermann W, Urhausen A.* Cardiac tissue Doppler imaging in sports medicine. Sports Med 2007; 37(1): 15−30.
9. *Hallynck TH, Soep HH, Thomis JA, Boelaert J, Daneels R, Dettli L.* Should clearance be normalised to body surface or to lean body mass. Br J Clin Pharmacol 1981; 11(5): 523−6.
10. *Mosteller RD.* Simplified calculation of body-surface area. N Engl J Med 1987; 317(17): 1098.
11. *Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA,* et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardio. J Am Soc Echocardiogr 2005; 18(12): 1440−63.
12. *Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I,* et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986; 57(6): 450−8.
13. *Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA,* et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009; 22(2): 107−33.
14. *Vanberg P, Atar D.* Androgenic anabolic steroid abuse and the cardiovascular system. Handb Exp Pharmacol 2010; 195: 411−57.
15. *Payne JR, Kotwinski PJ, Montgomery HE.* Cardiac effects of anabolic steroids. Heart 2004; 90(5): 473−5.
16. *LeGros T, McConnell D, Murry T, Vettal ME, Racey-Burns LA, Shepherd RE,* et al. The effects of 17.alpha.-methyltestosterone on myocardial function in vitro. Med Sci Sports Exerc 2000; 32(5): 897−903.
17. *d'Andrea A , Caso P, Salerno G, Scarafile R, De CG, Mita C,* et al. Left ventricular early myocardial dysfunction after chronic misuse of anabolic androgenic steroids: a Doppler myocardial and strain imaging analysis. Br J Sports Med 2007; 41(3): 149−55.
18. *Nottin S, Nguyen L, Terbah M, Obert P.* Cardiovascular effects of androgenic anabolic steroids in male bodybuilders determined by tissue Doppler imaging. Am J Cardiol 2006; 97(6): 912−5.
19. *Krieg A, Scharhag J, Albers T, Kindermann W, Urhausen A.* Cardiac tissue Doppler in steroid users. Int J Sports Med 2007; 28(8): 638−43.
20. *de Piccoli B, Giada F, Benettin A, Sartori F, Piccolo E.* Anabolic steroid use in body builders: an echocardiographic study of left ventricle morphology and function. Int J Sports Med 1991; 12(4): 408−12.
21. *Yeater R, Reed C, Ullrich I, Morise A, Borsch M.* Resistance trained athletes using or not using anabolic steroids compared to runners: effects on cardiorespiratory variables, body composition, and plasma lipids. Br J Sports Med 1996; 30(1): 11−4.
22. *Thompson PD, Sadaniantz A, Cullinane EM, Bodziony KS, Catlin DH, Torek-Both G,* et al. Left ventricular function is not impaired in weight-lifters who use anabolic steroids. J Am Coll Cardiol 1992; 19(2): 278−82.
23. *Palatini P, Giada F, Garavelli G, Sinisi F, Mario L, Michieletto M,* et al. Cardiovascular effects of anabolic steroids in weight-trained subjects. J Clin Pharmacol 1996; 36(12): 1132−40.
24. *Abhayaratna WP, Seward JB, Appleton CP, Douglas PS, Oh JK, Tajik JA,* et al. Left atrial size: physiologic determinants and clinical applications. J Am Coll Cardiol 2006; 47(12): 2357−63.
25. *Pelliccia A, Maron BJ, Di PF, Biffi A, Quattrini FM, Pisicchio C,* et al. Prevalence and clinical significance of left atrial remodeling in competitive athletes. J Am Coll Cardiol 2005; 46(4): 690−6.
26. *Pelliccia A, Spataro A, Caselli G, Maron BJ.* Absence of left ventricular wall thickening in athletes engaged in intense power training. Am J Cardiol 1993; 72(14): 1048−54.
27. *Gyimes Z, Pavlik G, Simor T.* Morphological and functional differences in cardiac parameters between power and endurance athletes: a magnetic resonance imaging study. Acta Physiol Hung 2004; 91(1): 49−57.

28. *D'Andrea A, Caso P, Salerno G, Scarafile R, de Corato G, Mita C*, et al. Left ventricular early myocardial dysfunction after chronic misuse of anabolic androgenic steroids: a Doppler myocardial and strain imaging analysis. Br J Sports Med 2007; 41: 149−55.
29. *Baggish AL, Weiner RB, Kanayama G, Hudson JI, Picard MH, Hutter AM,* et al. Long-term anabolic-androgenic steroid use is associated with left ventricular dysfunction. Circ Heart Fail 2010; 3(4): 472−6.
30. *Grace F, Sculthorpe N, Baker J, Davies B.* Blood pressure and rate pressure product response in males using high-dose anabolic androgenic steroids (AAS). J Sci Med Sport 2003; 6(3): 307−12. *Urhausen A, Albers T, Kindermann W*. Are the cardiac effects of anabolic steroid abuse in strength athletes reversible. Heart 2004; 90(5): 496−501.
31. *Urhausen A, Albers T, Kindermann W*. Are the cardiac effects of anabolic steroid abuse in strength athletes reversible. Heart 2004; 90(5): 496−501.

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